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Total Diet Studies

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Foreword by Michael R. Taylor
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Foreword

A safe food supply is a fundamental and global human need. Yet, even with advancements in science, medicine, and technology, we live in an age where foodborne risks to health are increasingly evident. An unsafe or nutritionally inadequate food supply also has trade, economic, and political dimensions that have made food safety a major concern of governments, the food industry and consumers around the world. That focus and concern is, in fact, a positive development, because together we can move toward solutions to problems. Of course, to reduce foodborne risks, we must understand them.

Total Diet Studies (TDSs) are an essential tool that is used to monitor chemicals, such as pesticides, contaminants and nutrients present in food, to estimate dietary exposures, and to characterize associated risk to public health. Conducting a TDS provides a "snapshot" of the composition and nutritional quality of the typical diets for various population subgroups and if conducted regularly, the series of TDSs can provide information on trends over time. They can also be used to help identify possible risk management and risk communication options and to prioritize and target resources.

The U.S. Food and Drug Administration (USFDA) launched the first national TDS in 1961. Today many countries around the globe are conducting these studies, due in large part to the encouragement and support of the World Health Organization (WHO). This book has been prepared by those international TDS practitioners and experts to help countries, especially developing countries, plan, conduct, and organize these studies. The wide range of topics will also be of interest to those who might use the results of a TDS, such as risk managers in the food safety, health, and agriculture sectors. In addition, scientists, researchers, and other interested parties in academia, the food industry and consumer and environmental organizations will benefit by knowing how these complex studies are conducted.

This book on total diet studies is a major contribution to the base of knowledge about exposure assessments of chemicals in food and to the global goal of protecting the health of consumers.

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Preface

Total diet study practitioners and experts from around the world have prepared this book with the aim to promote awareness and implementation of total diet studies in all countries. Total diet studies are the most cost-effective means of assessing the safety and nutritional quality of their diets. This is particularly important in developing countries where other means of assuring the safety of the food supply are beyond their means.

In Part I the reader will gain an appreciation of what total diet studies are, why they are so fundamentally important and how to go about planning, designing, and undertaking a total diet study.

Part II shares the experiences of different countries that are in the process of undertaking their first total diet study through to those countries that have completed numerous total diet studies. For all countries, total diet studies play a pivotal role in their national food monitoring and surveillance programs.

Part III deals with special topics relevant to total diet studies, such as how to influence key stakeholders' support such as politicians, government agencies, and others the role of GEMS/Food in total diet studies to access free international consumption data via GEMS/Food Consumption Cluster Diets.

This important TDS book will be a key reference for those considering to conduct a total diet study. Not only does it explain fundamentals, but also updates recent developments in the field of TDSs. Its goal is to promote reliable and comparable TDSs through harmonized approaches and exchange of international best practices and expertise.

The editors would like to thank the many authors who have given freely of their time and shared their expertise and experience in making this book possible. Finally, the editors would like to thank their wives and families for their support during the book's long gestation period.

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Abbreviations

AAS	Atomic Absorption Spectrophotometry
AAS-FIAS	Atomic Absorption Spectrophotometry with a Flow Injection Analysis System
ADI	Acceptable Daily Intake
AE	Adult Equivalent
AESAN	Spanish Food Safety and Nutrition Agency
AFSSA	Agence Française de Sécurité Sanitaire des Aliments
AI	Adequate Intake
ALARA	As Low As Reasonably Achievable
ANZFA	Australia New Zealand Food Authority
AOAC	Association of Official Analytical Chemists
ARfD	Acute Reference Dose
ATDS	Australian Total Diet Study
BBN	Beta-Binomial-Normal
BMDL	Benchmark Dose Lower Confidence Limit
BMELV	Federal Ministry of Food, Agriculture, and Consumer Protection
BPA	Bisphenol A
BVL	Federal Office of Consumer Protection and Food Safety
bw	Body Weight
CAC	Codex Alimentarius Commission
CCB	Continuing Calibration Blanks
CCCF	Codex Committees on Contaminants in Food
CCFA	Codex Committees on Food Additives
CCPR	Codex Committees on Pesticide Residues
CCRVDF	Codex Committees on Residues of Veterinary Drugs in Food
CCV	Continuing Calibration Verification
CFS	Centre for Food Safety
CFSAN	Center for Food Safety and Applied Nutrition
CPAs	Chlorophenoxy Acid Herbicides and Pentachlorophenol

CRM	Certified Reference Material
CSL	Central Science Laboratory
CU	Consumers Union
CV	Coefficient of Variation
CVUA	State Institute for Chemical and Veterinary Analysis
DAFF	Department of Agriculture, Fisheries and Forestry
DALYs	Disability-Adjusted Life Years
DEEM	Dietary Exposure and Evaluation Model
DHA	Docosahexaenoic Acid
DIAMOND	Dietary Modelling of Nutritional Data
DILs	Derived Intervention Levels
DISHES	Diet Interview Software for Health Examination Studies
DLCs	Dioxin-Like Compounds
dl-PCBs	Dioxin-Like Polychlorinated Biphenyls
DTC	Dithiocarbamate
EAR	Estimated Average Requirement
EBDC	Ethylenebisdithiocarbamate
EFG	European Food Grouping
EFS	Expenditure and Food Survey
EFSA	European Food Safety Authority
EPA	Eicosapentaenoic Acid
ESI	Electrospray Ionization
ESR	Environmental Science and Research Limited
ETU	Ethylenethiourea
EU	European Union
FAO	Food and Agriculture Organization of the United Nations
FAPAS	Food Analysis Proficiency Assessment Scheme
FBDG	Food-Based Dietary Guidelines
FBS	Food Balance Sheets
FCID	Food Commodity Ingredient Database
FCS	Food Consumption Survey
FDA	Food and Drug Administration (United States)
FEHD	Food and Environmental Hygiene Department
FFQ	Food Frequency Questionnaire
FHDD	Family Health and Development Division
FRL	Food Research Laboratory
FRSC	Food Regulation Standing Committee
FSA	Food Standards Agency
FSANZ	Food Standards Australia and New Zealand
FSQD	Food Safety and Quality Division
GC	Gas Chromatography
GC-ECD	Gas Chromatography with Electron Capture Detection

GC-ELCD	Gas Chromatography with Electrolytic Conductivity Detection
GC-FPD	Gas Chromatography with Flame Photometric Detection
GC-MS	Gas Chromatography with Mass Spectrometry
GC-MS/MS	Gas Chromatography with Mass Spectrometry/Mass Spectrometry
GC-MS SIM	Gas Chromatography with Mass Spectroscopic Detection in the Selective Ion Monitoring Mode
GC-PFPD	Gas Chromatography with Pulsed Flame Photometric Detection
GEMS	Global Environment Monitoring System
GEMS/Food	GEMS Food Contamination Monitoring and Assessment Programme
GFAAS	Graphite Furnace Atomic Absorption Spectrometry
GL	Government Laboratory
GLP	Good Laboratory Practices
HBGV	Health-Based Guidance Values
HBS	Household Budget Surveys
HCB	Hexachlorobenzene
HCH	Hexachlorocyclohexane
HGAAS	Hydride Generation Atomic Absorption Spectrometry
HPLC	High Performance Liquid Chromatography
HPLC-EC	High Performance Liquid Chromatography with an Amperometric Electrochemical Detection
HRGC-HRMS	High-Resolution Gas Chromatography with High-Resolution Mass Spectrometry
HRMS	High Resolution Mass Spectrometry
HRV	Health Reference Value
IAS	Institute of Applied Sciences
IC	Individual Composites
ICB	Initial Calibration Blank
ICP-AES	Inductively Coupled Plasma Atomic Emission Spectrometry
ICPMS	Inductively Coupled Plasma Mass Spectrometry
ICPOES	Inductively Coupled Plasma Optical Emission Spectrometry
ICV	Initial Calibration Verification
id	Interior Diameter
IEDI	International Estimate Daily Intake
ILSI	International Life Sciences Institute
IP	Identification Point
IPCS	International Programme on Chemical Safety
ISC	Implementation Sub-committee
JECFA	Joint Expert Committee on Food Additives
JICA	Japan International Cooperation Agency
JMPR	Joint Meetings on Pesticide Residues
KEKP	Kids Eats Kids Play
KFDA	Korean Food and Drug Administration

KM	Kaplan-Meier
KTDS	Korean Total Diet Study
LC-MS	Liquid Chromatography with Mass Spectrometry
LC-MS/MS	Liquid Chromatography with Mass Spectrometry/Mass Spectrometry
LCS	Laboratory Control Sample
LNN	Logistic-Normal-Normal
LOD	Limit of Detection
LOEL	Lowest-Observed-Effect Level
LOQ	Limit of Quantification
LOR	Limit of Reporting
MAFF	Ministry of Agriculture, Forestry, and Fisheries
MB	Market Basket
MBS	Market Basket Study
MCRA	Monte Carlo Risk Assessment
MDA	Minimum Detected Activity
MDC	Minimum Detectable Activity Concentration
MHLW	Ministry of Health, Labor, and Welfare
MINADER	Ministère de l'Agriculture et du Développement Rural
ML	Maximum Level
MLE	Maximum Likelihood Estimation
MOA	Ministry of Agriculture
MOE	Margin of Exposure
MOH	Ministry of Health
MoRT	Ministry of Research and Technology
MPI	Ministry of Primary Industries
MRI	Max Rubner Institute
MRL	Maximum Residue Limit
MRM	Multiple Residue Method
MSDs	Mass Selective Detectors
MSMS	Tandem Mass Spectrometers
MSPD	Matrix Solid-Phase Dispersion
MTDS	Malaysian Total Diet Study
MU	Measurement Uncertainty
MUFA	Mono-unsaturated Fatty Acids
NA	Not Analyzed
NADFC	National Agency for Drug and Food Control
ND	Not Detected
NDNS	National Dietary and Nutrition Survey
NFA	National Food Agency
NHANES	National Health and Nutrition Examination Survey
NHMRC	National Health and Medical Research Council
NIHS	National Institute of Health Sciences
NIPH	National Institute for Public Health

NIST	National Institute of Standards and Technology
NNMB	National Nutrition Monitoring Bureau
NNS	National Nutrition Survey
NOAEL	No-Observed-Adverse-Effect Level
NOEL	No-Observed-Effect Level
NQ	Not Quantified
NRC	National Research Council
NVS II	National Nutrition Survey II
NZFCD	New Zealand Food Composition Database
NZFSA	New Zealand Food Safety Authority
NZTDS	New Zealand Total Diet Study
OH-P&ICs	Organohalogen Pesticide and Industrial Chemicals
OPAL	Operating Program for Analytical Laboratories
OP-P&ICs	Organophosphorus Pesticide and Industrial Chemicals
ORO	Office of Regional Operations
OS	Organosulfur
P&IC	Pesticide and Industrial Chemicals
PAD	Population Adjusted Reference Dose
PAHs	Polycyclic Aromatic Hydrocarbons
PAM	Pesticide Analytical Manual
PBDEs	Polybrominated Diphenyl Ethers
PCB	Polychlorinated Biphenyl
PCDDs	Polychlorinated Dibenzodioxins
PCDD/DFs	Polychlorinated Dibenzo-p-Dioxins and Dibenzofurans
PCDF	Polychlorinated Dibenzofuran
PCN	Polychlorinated Naphthalenes
PEG	Polyethyleneglycol
PFOA	Perfluorooctanoic Acid
PFOS	Perfluorooctane Sulphonate
pg	Picogram
PHS	Public Health Service
PM	Procedures Manual
POP	Persistent Organic Pollutant
ppb	Part Per Billion
PSA	Primary/Secondary Amines
PTMI	Provisional Tolerable Monthly Intake
PTWI	Provisional Tolerable Weekly Intake
PUFA	Polyunsaturated Fatty Acid
QA	Quality Assurance
QA/QC	Quality Assurance and Quality Control
QC	Quality Control
QFFQ	Quantitative Food Frequency Questionnaire
QuEChERS	Quick Easy Cheap Efficient Rugged and Safe

RAC	Raw Agricultural Commodity
RDA	Recommended Daily Allowance
RDI	Recommended Dietary Intake
RfD	Reference Dose
RPD	Relative Percent Difference
RSD	Relative Standard Deviation
RTE	Ready-to-Eat
SCOOP	Scientific Cooperation (European Commission)
SFA	Saturated Fatty Acids
SIM	Selected Ion Monitoring
SOP	Standard Operating Procedure
SO	Sampling Officer
SPE	Solid Phase Extraction
Sr-90	Strontium-90
TDI	Tolerable Daily Intake
TDS	Total Diet Study
TEQs	Toxic Equivalents
tr	Trace Amount
TWI	Tolerable Weekly Intake
UAR	Unidentified Analytical Response
UL	Upper Level of Intake
UNEP	United Nations Environment Programme
UNICEF	United Nations Children's Fund
US	United States
USDA	United States Department of Agriculture
USEPA	United States Environmental Protection Agency
USP	University of the South Pacific
UV-VIS	Ultraviolet-Visible Spectrophotometry
WEAC	Winchester Engineering and Analytical Center
WHO	World Health Organization
WHO TEFs	WHO Toxic Equivalence Factors
WHO-TEQ	WHO-Toxic Equivalent
WTO	World Trade Organization

Part I
Total Diet Study Methodology

Chapter 1
Total Diet Studies—What They Are and Why They Are Important

Gerald G. Moy

Introduction

Chemicals are the building blocks of our bodies and make possible all activities associated with human life. These chemicals are obtained from the food and water that we consume everyday throughout our lives. On the other hand, human exposure to toxic chemicals in food and nutritional imbalances are known to be responsible for a range of human health problems and are implicated in many others. These problems include various cancers, kidney and liver dysfunction, hormonal imbalance, immune system suppression, musculoskeletal diseases, birth defects, premature births, impeded nervous and sensory system development, reproductive disorders, mental health problems, cardiovascular diseases, genitourinary diseases, old-age dementia, and learning disabilities. These conditions are prevalent in all countries, and, to some extent, most can be attributed to past and current exposure to chemicals in the foods we eat. Consequently, the protection of our diets from these hazards must be considered one of the most important public health functions for any country and total diet studies are the most cost-effective tools for assessing dietary exposure to a range of potentially hazardous chemicals as well as certain nutrients.

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What Are Total Diet Studies?

A total diet study consists of purchasing foods which are representative of the diet at the retail level, processing them as for consumption (often combining the foods into food composites), homogenizing them, and analyzing them for toxic chemicals and certain nutrients. Exposures through drinking water and water used in cooking are typically included in the total diet study assessment. Dietary exposures are calculated by combining the concentrations of the chemicals in the food samples with the average amounts of the corresponding food ingested by each population age/sex group or, in more sophisticated form, by using food consumption data of individuals representative of various population subgroups.

What Information Do Total Diet Studies Provide?

The primary purpose of total diet studies is to measure the average amount of each chemical ingested by different age/sex groups living in a country. The dietary exposures of the chemicals can be compared with national or international health-based reference values to assess whether or not a specific chemical poses an unacceptable risk to health. Thus, total diet studies provide a direct measure of the safety of the diet. The World Health Organization (WHO), the lead United Nations agency for public health, recommends total diet studies as the most cost-effective method for assuring that people are not exposed to unsafe levels of chemicals through food.

When conducted over several years, total diet studies provide critical information about the trends of toxic chemicals and other chemicals, such as food additives, in the diet and offer guidance about the need for targeted monitoring or possible intervention programs. They can also identify increasing or decreasing dietary intake of micronutrients that may be naturally present or due to fortification of food or animal feed.

Total diet study information often provides direct evidence on the contribution of different food items or food groups to the dietary exposure of chemicals. This information can be used to establish priorities and assure that limited government resources are used for the greatest health benefit. For example, numerous total diet studies had shown that the overwhelming contributor to the dietary intake of methylmercury is fish. As a result, risk management resources for methylmercury have been largely directed toward addressing consumption of those fish with the highest concentrations.

In addition, total diet studies, by their design, provide background concentrations of the chemicals in the foods analyzed. This baseline information is critical for quickly identifying contaminated foods when food safety emergencies arise. For example, during the Belgium dioxin incident, the availability of background concentrations of polychlorinated dioxins, -dibenzofurans, and -biphenyls in Canadian

foods facilitated the rapid assessment that foods imported into Canada from Belgium did not contain high levels of these chemicals. Also, the availability of baseline information enables rapid identification of food that significantly exceeds normal mean values. With this information, potentially hazardous contamination can be identified early and mitigated before becoming a major health or trade issue. If total diet study samples are stored, they can be used for retrospective studies if a new chemical hazard is identified, as in the case of acrylamide.

How Do Total Diet Studies Differ from Other Surveillance Programs?

Total diet studies differ from other chemical surveillance programs in several ways, namely:

(a) In most surveillance studies, a limited number of different foods are generally analyzed, so that statistically robust sampling of each food can be undertaken. In a total diet study, the focus is on exposure to chemicals from across the whole diet, so that a wide range of different foods are analyzed. With limited resources usually the norm, this often means fewer samples per food type than for surveillance surveys, but the coverage of foods is much more complete.

(b) In most surveillance studies, individual foods are usually analyzed separately. In the total diet study, individual food items from different sources (brands, regions, seasons) may be combined into composite food samples, or if resources are limited, individual food items are combined into food group composites. For example, apples, pears, and quinces are often combined into a pome fruit composite.

(c) Surveillance for trade purposes is conducted to assess whether individual commodities meet regulatory limits i.e. for pesticides, national or Codex Maximum Residue Limits. In these instances, analytical methodologies are developed to monitor these much higher regulatory concentrations. In contrast, a total diet study is conducted to measure background concentrations of these chemicals in food samples, and consequently, the sensitivities of analytical methodologies are much lower.

(d) In a total diet study, foods are analyzed after being prepared as usual for consumption. Thus, they might contain some chemicals, such as acrylamide, which are formed during food processing. On the other hand, they might not contain certain chemicals originally present in the raw foods e.g. those which are destroyed during heating or removed during washing and peeling. Thus, the chemicals in the foods analyzed in a total diet study are more closely representative of what is actually ingested by the consumer rather than what is produced e.g. raw agricultural commodities.

(e) Unlike most surveillance samples, total diet samples are usually analyzed for many different chemicals to save sampling costs. This has the additional benefit of

facilitating risk-benefit analysis for different chemicals, such as polychlorinated biphenyls, mercury, and omega-3-fatty acids in fish.

(f) Because the total diet studies are complex in nature, a high degree of expertise and organization is needed. In addition, more expensive measurement instruments, such as high-resolution mass spectrometers, are often required to measure the low levels of contaminants and nutrients that occur in food.

Why Are Total Diet Studies Important?

In most countries, food safety legislation has placed the primary responsibility for ensuring the safety of food on commercial food enterprises that produce, process, distribute or prepare food for the consumer. With varying degrees of success, governments have established regulatory and other limits for contaminants in various foods. The Codex Alimentarius Commission also had provided guidance in this regard [1]. However, most of these limits are based on Good Agricultural Practices and/or Good Manufacturing Practices and not on risk assessments themselves. Because safe or tolerable levels for chemicals, such as the Acceptable Daily Intake and the Provisional Tolerable Weekly Intake, are specified in terms of total intake from all ingested sources, contributions to exposure from many individual foods need to be taken into account to assess the aggregate risk from chemicals in food and water. The overall assessment of the safety of the food supply is one of the essential responsibilities of governments. This was recognized in the Beijing Declaration on Food Safety [2], which urged all countries to "Establish food and total diet monitoring programs with linkages to human and food-animal disease surveillance systems to obtain rapid and reliable information on prevalence and emergence of foodborne diseases and hazards in the food supply." A survey carried out in 2011 by the European Food Safety Authority in cooperation with WHO and the Food and Agriculture Organization of the United Nations (FAO) revealed that 33 countries have already conducted total diet studies [3].

In many developing countries where neither the government nor the food industry conduct testing of foods for chemical contaminants, it is all the more imperative that government authorities have a cost-effective means for ensuring that levels of chemical contaminants in the total diet do not pose a risk to the health of their populations. Because toxic chemicals in food cannot generally be detected by the senses or be removed by normal processing, consumers are not in a position to protect themselves from these types of hazards. For this reason, many consumer groups have strongly supported measures by governments to protect the population against potentially toxic chemicals in food. As a consequence, governments in most developed countries have monitoring programs for chemicals in food and conduct total diet studies. On the other hand, except for a few high-value foods for export, few developing countries have monitoring programs for chemicals in food and even fewer conduct total diet studies.

It should also be noted that in addition to contaminants, most total diet studies include selected nutrients. Although assessing the long-term exposure to potentially toxic chemicals in food as consumed is the purpose of total diet studies, the inclusion of intake assessments for certain nutrients, especially micronutrients, is extremely cost-effective, as the same samples can be used. Total diet studies have also been applied to certain food additives as well as to processing contaminants, such as acrylamide and chloropropanols.

While unsafe levels of chemicals in food may cause serious health problems, they also pose threats to trade and the environment. Food production, processing, and preparation are among the most important economic activities for almost all countries and any disruption caused by toxic chemicals in food can have a major impact on the country and on consumer confidence in the safety of the food supply chain. It is estimated that the global economic and trade burden from these contaminants in food totals many billions of dollars annually [4]. For developing countries, the foreign exchange earned from food exports is often essential for their economic development. Food exports may also be threatened by unjustified health and safety requirements, which can serve as non-tariff trade barriers. Total diet studies can also provide a scientific assessment of the risk posed by exposure to toxic chemicals as evidence of the acceptability (or not) of proposed national or Codex food standards.

In addition, total diet study results can be indicators of environmental contamination by chemicals and can be used to assess the effectiveness of specific risk management measures. For example, persistent organic pollutants, the so-called POPs, have been shown to cause adverse effects on wildlife and their endocrine disruption potential has been suggested to cause human diseases, such as cancer and behavioral disorders [5]. Given that POPs are highly fat soluble, they concentrate in the food chain. As a result, human exposure to POPs is almost wholly through food. As the upper atmospheric transport of such chemicals is well documented, the contamination of food is often remote from the source of the pollution. Therefore, it is becoming increasingly important to assess the exposure of humans to background concentrations of these as well as the other environmental pollutants that may end up in our diets.

The WHO's Global Environment Monitoring System/Food Contamination Monitoring and Assessment Programme (GEMS/Food) has encouraged all countries, and in particular developing countries, to undertake total diet studies as a matter of public health importance, while recognizing the significance of total diet studies to standards development and trade as well as environmental risk management. The overall cost of conducting a basic total diet study is much less than any other exposure assessment method available. A major part of the cost of a total diet study is the expense of analyzing samples at low limits of detection. Total diet studies can be conducted for less cost by rationalizing either the size of the food list or the range of chemicals to be analyzed. Total diet studies can also be run over a number of years to spread out the costs. In addition, for certain chemicals, the necessary analyses may be performed in other laboratories on a contract basis. If the total diet study then indicates that exposure to a chemical is well within its safe limits, there may be no need to establish expensive analytical capabilities for the

chemical. In this regard, total diet studies are useful priority-setting tools that enable risk managers and society to focus limited resources on those chemicals that pose the greatest risks to public health.

Another expense associated with conducting a total diet study (or any other exposure method for that matter) is the need to have reliable food consumption data. In this regard, countries might elect to use one of the GEMS/Food Consumption Cluster Diets [6] (See Chap. 43 – GEMS/Food Consumption Cluster Diets). However, more detailed individual food consumption data will allow specific exposure estimates for different age/sex groups as well as population groups of special interest, such as vegetarians or ethnic groups. Many countries use the 24-hour recall method that is supplemented by a food frequency questionnaire. The cost of such a food consumption survey will vary considerably depending on the local cost of labor. However, the cost can be averaged over a number of years as dietary patterns usually change slowly. The cost of such a survey may also be shared with other stakeholders with an interest in such data, including the agriculture sector and the food industry.

It should be borne in mind that the cost of a total diet study is more than balanced by the health and economic benefits that can accrue. In one developed country, a study of the economic impact on Parkinson's disease, hypothyroidism, diabetes, and nervous system and IQ effects suggested that the current negative impact of previous and current human exposure to toxic chemicals, including nutritional imbalances, likely exceeds US$800 for every man, woman, and child each year [7]. These enormous costs to countries' economies can be reduced by lowering exposure of the population to toxic chemicals and by optimizing their nutritional balance. On the other hand, the negative economic impact can be expected to continue or increase if relevant research and monitoring activities are not implemented.

While total diet studies are health-oriented and population-based, such studies can often reveal point sources of contamination, which can be corrected before actual health or trade problems occur. However, even when the health risks are assessed to be minimal, impact on trade can be severe. For example, contamination of a single batch of animal feed with oil contaminated with polychlorinated biphenyls and dioxins in Belgium resulted in economic losses exceeding US$2 billion with the majority of these losses borne by industry and individual farmers.

In regard to trade, the World Trade Organization (WTO) under its Agreement on the Application of Sanitary and Phytosanitary Measures requires that health and safety decisions be based on sound scientific risk assessments. For example, in the Czech Republic, results of a total diet study were successfully used to defend safety measures taken to halt the importation of chicken contaminated by arsenic, even though the exporting country complained to the WTO and sought damages from economic losses. In addition to hazard characterization, a risk assessment of a chemical in food requires an assessment of human exposure. For this purpose, total diet studies are considered to be one of the best means of estimating human dietary exposure and such studies are frequently included in safety evaluations performed by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) [8] as well as by national and regional expert bodies.

Where to Start?

Government policy- and decision-makers need to be aware of the importance of total diet studies for assuring the safety of the food supply. In this regard, realistic risk assessments simply cannot be performed without an assessment of exposure. As a first step, national expertise in total diet studies needs to be developed through training and participation in international networks, such as WHO GEMS/Food. At the same time, the food safety and applied nutrition communities in countries need to mobilize support for total diet studies. This includes stakeholders in government, academia, and industry as well as consumer groups. WHO has recognized total diet studies as the most cost-effective means for governments to protect public health from chemicals in the food supply. For the food industry, total diet studies provide a scientific basis for the development of standards and for the orderly development of the food industry. Consumers and their advocacy groups should recognize that total diet studies are essential public health measures that serve to safeguard the food supply from potentially hazardous chemicals and to ensure adequate levels of nutrients in the diet.

In order to promote the availability of competent people with the technical and logistical skills to conduct total diet studies, WHO GEMS/Food in cooperation with national food safety agencies periodically holds training courses at the regional and international levels. These training courses have been facilitated by WHO Collaborating Centers for Food Contamination Monitoring and particularly the one located at the Institute for Environmental Science and Research in Christchurch. However, practical experience can also be gained by placement of personnel in institutions already conducting total diet studies. Governments, particularly in developing countries, need to support the development of human and infrastructure capacities to undertake total diet studies in their countries. Once a country has completed its first total diet study, experience has shown that support for future studies is almost always assured. This is due particularly to the ability of non-technical persons to understand the concept and results of total diet studies and their significance to human health. Finally, because it is based on a transparent scientific method that is internationally accepted, total diet studies are increasingly recognized as the key to providing essential assurance that people's diets are safe and nutritionally adequate.

General information on food contamination monitoring, including total diet studies, is available in a number of WHO publications [9, 10]. In addition, the European Food Safety Authority in cooperation with WHO and FAO has developed a harmonized protocol for European Union countries that may be useful to consult [11].

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Chapter 2
The Origin of Total Diet Studies

Katie Egan

Introduction

The concept of total diet studies emerged in the late 1950s in the United States of America in response to two types of environmental contaminants that had made their way into the food chain, namely, radionuclides from fallout from nuclear weapons testing and residues of chemical pesticides from agricultural applications.

Nuclear weapons testing, which began in the mid-1940s and reached a peak in the early 1960s, led to worldwide concern about environmental contamination from radioactive fallout. Two radioisotopes – cesium-137 (Cs-137) and strontium-90 (Sr-90) – were considered the most dangerous to health and the environment in terms of their long-term effects. Both are released in large quantities during a nuclear explosion and are highly radioactive. Since both are biologically similar to essential dietary elements (Sr-90 is similar to calcium, as Cs-137 is to potassium), they also have the potential to be absorbed by living organisms and passed up the food chain. Sr-90 was of particular concern because of its long half-life, its ability to be absorbed by and stored in bones, and its potential to lead to various bone disorders and diseases. Milk was considered to be the major dietary source of Sr-90 since it was consumed by a large portion of the population and in relatively large quantities by children [1–8].

At about the same time that radionuclide fallout was gaining attention, there was also concern about the wide use of pesticides and the associated residues that remained in food. Organochlorine pesticides such as DDT, hexachlorobenzene, dieldrin, aldrin, and chlordane were the first group of synthetic insecticides that came into widespread use after World War II. Use of these chemicals increased during the 1950s, peaked around 1975, and was largely phased out by 1990 at least in

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developed countries. Organochlorine compounds are highly stable and they persist in the environment, especially in the soil. They are fat-soluble and can accumulate in humans, animals, and plants, with the concentrations increasing in animals higher up the food chain, i.e. biomagnified. Widespread public opposition to DDT began with the publication of Rachel Carson's book *Silent Spring* in 1962. Carson demonstrated that DDT not only had detrimental effects on the environment but it was exponentially concentrated as it moved to higher levels in the food chain. The potential for pesticides to biomagnify and their long-term toxicity became widely recognized, and pest resistance became increasingly evident [9]. Another group of chemicals – organophosphorus pesticides – had a wide array of chemical structures, properties, and agricultural uses. Organophosphorus pesticides are mostly biodegradable and do not concentrate in the food chain; however, they act on the central nervous system of insects and animals, and in high doses are severely toxic [10–12].

Concerns about the long-term health effects of both radionuclides and pesticides and their potential to enter the food supply led to efforts to monitor the food supply and to estimate the dietary exposure to these contaminants, so any potential risks could be effectively assessed, managed, and communicated.

Early Monitoring Activities

The Atomic Energy Commission (AEC), an agency of the United States (US) government, was established after World War II to foster and control the peacetime development of atomic science and technology. The AEC was responsible for nuclear regulation in the US, and part of its mission was to study the effects of radioactive fallout and to measure their concentrations in air, soil, water and foods [1, 3]. In 1975, responsibilities of the AEC were transferred to the Nuclear Regulatory Commission (NRC).

Although the AEC had primary responsibility for monitoring radioactive fallout at that time, the US Public Health Service (PHS) also studied fallout in air and in foods, particularly in milk. In 1957, the PHS began studying Sr-90 levels in milk about once a month in five geographic regions of the US. The next year, the study was expanded to include ten regions [1]. As late as 1958, many scientists were convinced that milk was the chief carrier of Sr-90 and thus milk had been the main food targeted for sampling. At about that time, the AEC and similar agencies in the United Kingdom, Germany, and Japan began limited testing of the Sr-90 content of other foods, but it was clear that the problem of radionuclide contamination of food was complex and that more monitoring was necessary [6].

The First Studies of the Total Diet

Consumers Union (CU), an independent nonprofit organization in the USA, also recognized the seriousness of the problem. CU was founded in 1936 with a mission to test consumer products, inform the public, and protect consumers. In 1960, CU

helped to create the global consumers group Consumers International. Food safety is among the many issues that CU has advocated since its formation [13].

CU had followed the issue of contamination from radioactive fallout and in the summer of 1958 it conducted a study of radionuclide levels in nationally representative samples of milk. This was a more comprehensive study than had been done previously by government agencies in the US. As they designed this testing program, CU consulted with groups that had experience with monitoring radionuclide levels in foods: the AEC, the US Department of Agriculture (USDA), the PHS, and Columbia University's Lamont Geological Observatory. In CU's monitoring study, milk samples were collected from 48 cities in the US and two Canadian cities close to the US border. At each location, milk samples were collected weekly over the period of 1 month. A second series of milk samples were collected and analyzed for radionuclide levels the following summer (1959); sampling was undertaken in 27 cities, 21 of which had been included in the previous study [1–4].

Up to that time, milk had been the focus of most monitoring programs since it was assumed to be the primary source of Sr-90 in the diet, but no one had measured Sr-90 levels in other major components of a typical diet. By 1959, CU had established a new unit – the Public Service Projects Department – that among other things initiated a study to estimate the total exposure to Sr-90 from a typical diet of children 10–15 years of age. CU enlisted the help of home economics departments in colleges and universities in 24 cities across the US and in one city in Canada. Menus representing a typical diet for a teenager for a 14-day period were developed. In November 1959, home economists from each of the collaborating colleges and universities launched what is believed to be the first total diet study (TDS). They purchased the foods that comprised the typical 14-day menu, and then prepared the foods and beverages, as they would be consumed: inedible portions of foods were removed, foods consumed raw were washed, and other foods were cooked using standard recipes. After the foods were prepared, the specified portions from each meal were combined to form a single analytical composite. In addition to total diet composites, CU analyzed separately milk samples taken from the same bottles as those used to make up the total diet composites in order to determine specifically how much of the Sr-90 in the diet came from milk. Results of this total diet study showed for the first time that other foods contributed significantly to the total dietary exposure to Sr-90, with milk contributing only about half of exposure in the average diet [4, 5].

CU conducted a second TDS in 1961, using the same approach as in the previous study. Samples were collected again in 25 cities, 23 of which had been included in the previous study. This time they included diets for several economic status and age levels besides the middle-income teenage diet tested in 1959, and each TDS composite was analyzed for Sr-90 as well as seven other radionuclides.

At about the same time, both the AEC and the PHS were researching total diet methods [5]. The AEC was doing a small-scale diet sampling method in which Sr-90 levels in the total diet were calculated from average Sr-90 levels in groups of specific foods. A grant from the AEC helped to fund the 1961 CU TDS, in part to provide a crosscheck of the two total diet methods. The PHS was investigating the technical feasibility of setting up a monthly total diet monitoring system.

Results of CU's second TDS showed that total exposure to Sr-90 had decreased since the 1959 study but that it was still present in foods across the country. Both studies also showed that levels of Sr-90 contamination varied from place to place and from one period of time to another. CU suggested that more comprehensive testing was needed and proposed that a systematic and extensive total diet monitoring program should be initiated, preferably by the Federal government.

In 1959, the main responsibility for monitoring fallout in the US was passed from the AEC to the PHS and the Food and Drug Administration (FDA) [3]. Data on Sr-90 levels in foods collected by FDA throughout the country confirmed that levels varied widely across different regions as well as among different foods. FDA recognized that estimating total dietary exposure to Sr-90 from data on individual foods would require not only large numbers of samples in a wide range of foods, but also detailed information on food consumption. It concluded that the composite approach used by CU offered a method of approximating the total dietary exposure to Sr-90 provided that representative diets could be described and that a sufficient number of samples could be collected in each city. Although this approach would not enable them to identify the contributions of individual foods to total dietary exposure, the composite approach provided an efficient and cost-effective way to provide a broad picture of regional and temporal trends in total dietary exposure [6].

FDA chose the diet of teenage boys as the basis for its first study. The rationale was the same one used by CU, namely that this population group consumes the largest quantity of foods and would, therefore, be expected to have the highest dietary intake of Sr-90 or other food constituents of interest. The USDA conducted periodic nationwide surveys of household food consumption; results of a recent study had shown that consumption patterns across the country were fairly uniform, so that a single model diet could be used to simulate a nationally representative diet. USDA had also devised several nutritionally adequate dietary plans for specific age-sex groups based on household economic status. The 14-day Food Plan at Moderate Cost for boys 16–19 years of age provided the types and quantities of foods sampled in FDA's first TDS.

FDA's first TDS was initiated in May 1961 and consisted of four market baskets conducted quarterly in the metropolitan area of Washington, District of Columbia. The shopping list for each market basket included 82 food and beverage items. For each market basket, samples of the 82 items were purchased at four different retail stores. All samples were sent to an institutional kitchen in Baltimore, Maryland, where the foods were prepared "as consumed" by professional dietitians. Edible portions of the foods were combined in quantities specified in the 14-day diets to form single quarterly composites, which were analyzed in the FDA laboratories in Baltimore and Washington.

A second year of FDA's study began in May 1962 and geographic coverage was expanded to include four additional cities: San Francisco, California; St. Louis, Missouri; Minneapolis, Minnesota; and Atlanta, Georgia. During this series of quarterly market baskets, samples were collected at two retail markets in each city for each market basket. As in the first year of the study, a single analytical composite of

all 82 foods was formed for each quarterly market basket per city. In addition, an extra market basket was collected each quarter in Washington and the samples were grouped by food type to create 11 commodity composites. Each commodity composite was analyzed separately to provide more information about specific dietary sources of Sr-90.

Throughout the 1960s, FDA's TDS continued to evolve. Between 18 and 44 market baskets were conducted each year. Foods were prepared in institutional kitchens in the cities where samples were collected and samples were analyzed in the regional FDA laboratories. Beginning in 1965, FDA replaced the single-quarterly market basket composite approach used in the earlier studies with TDS food samples now subdivided into 12 different food group composites e.g. meats, grains, etc.

As originally planned, FDA's TDS was to focus on Sr-90 and Cs-37 in the diet, but it recognized that these widely representative samples could be useful for analyzing other food components such as pesticide residues and nutrients. In the early studies, the samples were analyzed for levels of Sr-90 and Cs-137 as well as residues of organochlorine and organophosphorus pesticides. Throughout the 1960s and early 1970s, additional pesticide residues and toxic elements were analyzed in the TDS, and FDA's Division of Nutrition used the TDS as an opportunity to obtain information on the nutrient content of foods as typically prepared in the home [6].

Total Diet Studies Go Global

Under the auspices of the Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO), the Joint FAO/WHO Meeting on Pesticide Residues (JMPR) has met regularly and published meeting reports since 1963. JMPR is an international expert scientific group responsible for reviewing data on the safety and use of pesticides. In the report of its 1967 meeting, JMPR briefly described the concept of a total diet study. The report also emphasized that such studies of pesticide residues at the consumer level are valuable in determining how estimated dietary exposures compared with Acceptable Daily Intakes (ADIs). Several countries took note of the recommendation and initiated their own TDSs [14].

In the United Kingdom, monitoring of pesticide residues had been carried out for some time and was initially focused mainly on selected foods. In 1965, the British Scientific Sub-Committee of the Advisory Committee on Pesticides and Other Toxic Chemicals recommended that a comprehensive total diet study should be undertaken. The purpose of such a study was to be twofold: to study the concentration levels of pesticides in the average national diet and to identify other dietary sources of pesticide residues aside from the foods targeted in their previous monitoring studies. It was agreed that samples should be analyzed for residues of organochlorine and organophosphorus pesticides. Further, it was suggested that the TDS samples could be analyzed for mercury, lead and various nutrients [15–17].

In Canada, levels of pesticide residues in foods had been monitored during the 1960s but only in foods as purchased – not in foods as consumed. In response to the recommendation by JMPR, the Canadian Food and Drug Directorate decided to conduct its first TDS in 1969. Samples from the first two market baskets were analyzed for organochlorine pesticide residues; organophosphorus pesticide residues were analyzed in the third and fourth market baskets [18, 19].

In Australia, the National Residue Survey was established in 1961 to monitor pesticide residues in produce. In 1969, the National Health and Medical Research Council (NHMRC) recommended that a market basket survey be carried out to examine the levels of pesticide residues and contaminants in the average Australian diet. The first survey – then called the Australian Market Basket Study – was conducted in 1970. Subsequent surveys were conducted about every 2 years: sampling and analysis of foods usually takes place in the first year, and compiling results and planning for the next survey occurs in the second year [11, 12].

New Zealand also followed the recommendation of JMPR and conducted its first total diet study from April 1974 through January 1975. The study, which focused on measuring pesticide residues and trace elements in foods, was carried out by the Department of Health (now the Ministry of Health) and what is now the Institute for Environmental Science and Research.

In 1977, Japan initiated its first TDS through the collaboration of the National Institute of Hygienic Sciences and a number of the Prefectural Institutes of Public Health. Samples of foods were analyzed for pesticide residues and polychlorinated biphenyls (PCBs) [20].

In April 1986, the Chernobyl Nuclear Power Plant in Ukraine experienced a massive explosion that dispersed large amounts of radioactive particulate and gaseous debris containing Cs-137 and Sr-90. Radioactive particles were carried by wind across international borders. In response to this disaster, the Swedish National Food Administration put into action a plan to monitor levels of radioactive cesium in foods. A major part of this monitoring involved collection of market baskets from eight major towns in various parts of the country. Market baskets were collected on seven different occasions between June 1986 and December 1987 [21].

Other countries have also been involved in TDSs for some years: Netherlands [22], Denmark [23], China [24, 25], Spain (Basque country) [26, 27] and the Czech Republic [28, 29]. More recently, many more countries have initiated TDSs of their own: France in 2000, Korea in 2000, Egypt in 2001, Ireland in 2002, Fiji in 2004, Taiwan, China in 2003, Cameroon and Malaysia in 2006, Indonesia in 2007, and Hong Kong in 2009.

This chapter has touched on just the beginnings of total diet studies around the world. The remainder of the book shares the expertise of those who organized and conducted the training during the international and regional TDS workshops, as well as the experiences of the many countries that have conducted total diet studies over the past 50 years.

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Chapter 3
Risk Analysis Paradigm and Total Diet Studies

Philippe J.-P. Verger

Introduction

The risk analysis framework was introduced in the field of food safety in 1983 by the report of the US National Research Council entitled *Risk Assessment in the Federal Government: Managing the Process* and commonly known as the "Red Book" [1]. The risk analysis process is composed of three interrelated elements which are risk assessment, risk management, and risk communication. Risk assessment is a science-based evaluation aiming to estimate potential magnitude and seriousness of adverse health effects posed by harmful chemicals found in food and to inform a range of possible decisions for ensuring consumer safety. Risk management is the process of weighing policy alternatives in the light of the results of risk assessment and selecting and implementing appropriate control options, including monitoring/surveillance activities. Together with public health concerns, risk managers also need to take into account other aspects, such as the social, economic, and political impact of any regulatory or voluntary measures, before deciding on a risk reduction option. These aspects are dealing in particular with the cost-effectiveness of regulatory or voluntary measures. Risk communication is defined as an interactive exchange of information and opinions throughout the entire risk analysis process concerning risk. It should involve risk assessors and risk managers, but also consumers, the food industry, and a wide range of other actual or potential stakeholders.

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Role of International Organizations

The rapid expansion and globalization of trade has resulted in the transboundary movement of food, which may contribute to increased incidences of foodborne diseases. In addition, the development of new or alternative food production technologies and practices underlines the importance of an adequate system to identify and assess emerging risks in the food production chain and to manage such risks. Therefore, in 1963, the World Health Organization (WHO) in collaboration with the Food and Agriculture Organization of the United Nations (FAO) established the Codex Alimentarius Commission, which develops recommended international standards for foods. However, the adoption of such standards was voluntary and most countries did not strictly adhere to Codex standards. In 1995, the World Trade Organization (WTO) gave another dimension to Codex standards and their underlying risk assessments with the coming into force of its Agreement on the Application of Sanitary and Phytosanitary (SPS) Measures [2]. The objective of this WTO agreement is to avoid the use of unproven sanitary arguments and technical barriers by a WTO Member State to restrain imports of food from other countries. In this agreement it is in particular mentioned that:

> Members ensure that their SPS measures are based on an assessment, as appropriate to the circumstances, of the risks to human, animal, or plant life or health, taking into account risk assessment techniques developed by the relevant international organizations.

As this is part of a binding agreement, risk assessment now plays a fundamental role in the setting of food safety standards applicable to food in both international and domestic trade. The standards, guidelines, and other recommendations of the Codex are considered by the WTO to reflect international consensus regarding the requirements for protecting human health from foodborne risks. At the same time, organizations, like FAO, WHO, the Codex Alimentarius Commission and the European Union have been active in the design of risk analysis procedures for foods. These include FAO/WHO expert consultations on risk assessment in 1995 [3], risk management in 1997 [4], and risk communication in 1998 [5], Codex Definitions for Risk Analysis Terms Related to Food Safety [6], Working Principles for Risk Analysis for Application in the Framework of the Codex Alimentarius in 2003 [7], and an EU Scientific Steering Committee Report on the Harmonization of Risk Assessment Procedures in 2000 [8].

Components of Risk Analysis

Despite numerous reviews and adaptations, the successive steps of the food risk analysis paradigm described in the "*Red Book*" have remained quite stable since their first elaboration. Presently, the general framework for the risk analysis tends to be represented as cyclic (See Fig. 3.1). The figure includes red arrows pointing to those functions that may benefit directly or indirectly from total diet studies.
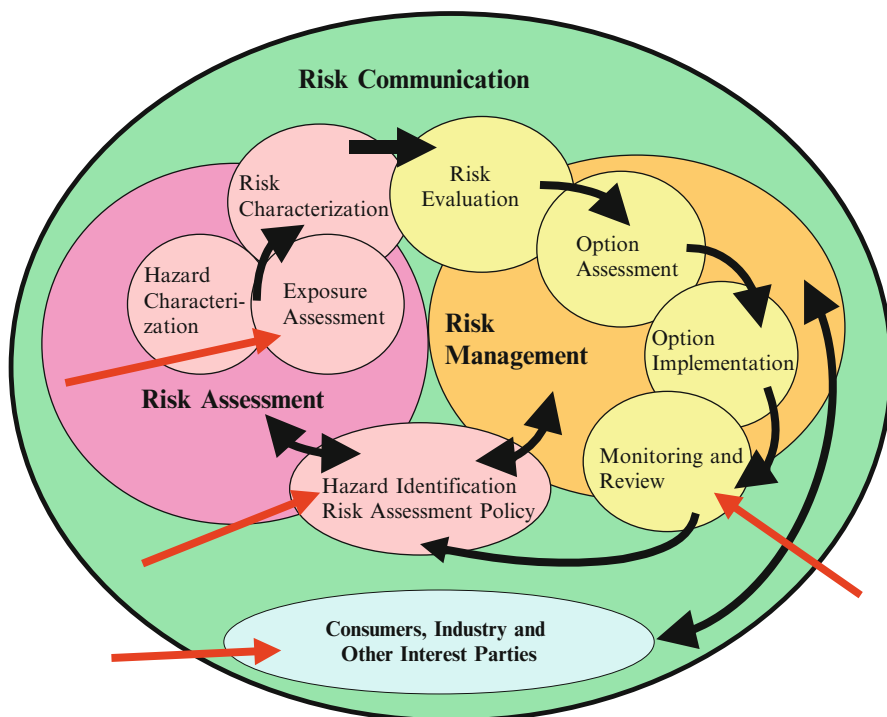
Fig. 3.1 Dynamics of the risk analysis paradigm (*Red* arrows indicate functions that may use results of total diet studies)

Note that the idea behind this representation is to suggest an iterative process in which risk assessment and management are subject to review and reconsideration as new information and conditions arise. For example, if a risk assessment of a chemical contaminant indicated a potential health risk, a risk management option, such as a regulatory or voluntary measure, might be implemented to reduce exposure of the population to the chemical. A monitoring program, such as a total diet study, would then be used to assess the effectiveness of the intervention and provide the basis for possibly revising the risk assessment or changing the risk management approach.

Risk Assessment

The risk assessment process, i.e. the scientific part of the risk analysis, is itself composed of four successive steps, namely the hazard identification, the hazard characterization, the exposure assessment, and the risk characterization. Risk assessment

describes what research findings do and do not tell us about threats to human health from hazards in food. Within these four steps, the hazard identification is a shared responsibility between the risk assessor and the risk manager. It forms the basis for making the basic decision to conduct a full risk assessment of the potential hazard. In many instances, total diet studies have contributed to the hazard identification step since the cost-effective monitoring of many chemicals simultaneously is an important characteristic of total diet studies. If little is known about the chemical, then hazard identification is the process by which specific chemicals are causally linked to the production of particular health effects. The process involves gathering and evaluating toxicity data obtained from animal and human studies to determine the types of health effects, such as neurotoxicity, birth defects, reproductive abnormalities, developmental effects, immunotoxicity, toxicity to the liver, kidneys, or lung, or cancer.

The next step in risk assessment is the hazard characterization, sometimes referred to as dose–response assessment, which aims to determine for each chemical or biological agent under consideration, the threshold below which the risk is considered to be negligible. This concept of threshold of risk is the basis for safety assessments, which were developed since 1956 within the Joint FAO/WHO Expert Committee on Food Additives (JECFA). For noncarcinogenic chemicals intentionally added to food, such as food additives, pesticide residues, and veterinary drug residues, this threshold risk assessment approach led to the establishment of the Acceptable Daily Intake (ADI), which is by definition the amount of a considered chemical which can be ingested every day over a whole human lifetime without appreciable health risks. To estimate the threshold for noncarcinogens, toxicology studies generally try to identify two dose levels: one just at the threshold at which effects are seen (i.e. the Lowest-Observed-Effect Level, or LOEL), and the one presumably just below the threshold at which no effects are seen (i.e. No-Observed-Effect Level, or NOEL). NOELs are derived from toxicology studies involving small homogeneous groups of animals. To allow for differences in the animal to human extrapolation and to consider variability in human responses, uncertainty factors (also sometimes referred to as safety factors) are used, and may range from 1 to 10,000 [9]. The most common safety factor is 100, which is rationalized as 10-fold uncertainty for test species variation multiplied by 10-fold uncertainty for human variation. The US Environmental Protection Agency has replaced the term ADI with an analogous term, toxicity reference dose (RfD), thereby removing the concept of "acceptability", which may carry the connotation of a nonscientific value judgment. An alternative to the NOEL approach is the concept of benchmark dose, which provides a consistent basis for calculating the RfD. It considers the dose/response model, and uses all available experimental data, in contrast to the NOEL approach, which ignores the shape of the dose–response curve [10]. In contrast, the hazard characterization of a substance that is both carcinogenic and genotoxic, assumes that no threshold level of exposure exists or adequate data are not available to establish such a threshold. In such cases, risk is estimated based on the toxic potency of the chemical, which is

often extrapolated from feeding studies in animals and when available, from human epidemiology studies.

Exposure assessment is the next and most crucial step in the process of assessing risk [11]. One may know of a hazard from environmental or occupation health data and have its toxicity well characterized, but without assessing human exposure, one has no means of assessing the risk. Total diet studies are key exposure assessment tools, and therefore, crucial in assessing the risk of chemicals from the diet. Once the potential to cause harm of a certain substance is understood, risk managers need to know the potential population vulnerable to it and the number of persons that may be affected. To be able to provide this, a quantitative evaluation of the likely exposure of substances via food is essential. This information collected in the context of exposure assessment is by definition location specific: information is needed on concentration of the hazard in food and how much of the relevant food is consumed in the typical diet. Dietary exposures are likely to differ across world regions and sometimes even within countries. Total diet studies measure concentrations of chemicals in foods 'as normally consumed', so therefore provide the best means of assessing the exposure and hence the potential risk to the consumer. Total diet studies are again one of the most cost-effective means for obtaining the specific information on dietary exposures of chemicals to complete the risk assessment process. Once the population's mean or median exposure to a certain chemical hazard is estimated, the identification of individual foods or food groups that contribute significantly to this estimated exposure is useful to generate distribution curves that help risk managers in formulating control options. The identification of such high concentrations of contaminants can, for instance, result in risk managers proposing maximum levels of the chemical in the relevant food or food group. Therefore, in addition to specific surveillance and monitoring plans based on individual samples, TDS can also be used to estimate the average contamination for a specifically polluted area and to estimate the long-term exposure of local populations.

Risk assessment ends with risk characterization. This involves hazard characterization and exposure assessment being integrated to come to a final estimation of the likelihood of the occurrence and severity of an adverse health effect. For a hazard for which a threshold of negligible concern was established, risk characterization aims to compare dietary exposure with this health based guidance value. A dietary exposure below this threshold allows one to conclude the absence of a safety concern. When an ADI cannot be established, such as for inadvertent contaminants in food, risk characterization is often specified as a Provisional Tolerable Intake, which can be expressed on a daily, weekly and even monthly basis. In the case of substances that are both carcinogenic and genotoxic or when data are not sufficient to allow a safe threshold to be established, the hazard characterization aims to quantify the risk in order to identify an appropriate level of protection. In such cases, the Margin of Exposure (i.e. the margin between the dose leading to adverse effects and the actual exposure for human populations) is estimated.

Risk Management

Risk management should be functionally separated from risk assessment in order to ensure the scientific integrity of the risk assessment process and to reduce any conflict of interest between risk assessment and risk management. However, it is recognized that interactions between risk managers and risk assessors are essential in practice. Risk management should follow a structured approach starting with the framing and the elaboration of the terms of reference for the risk assessment, which is elaborated as soon as the hazard is identified. Once the risk is characterized, risk managers should conduct a risk evaluation to integrate the health risk with other considerations including a cost-benefit analysis. Secondly, the various management options should be assessed and a decision should be taken to reduce the risk. Note that a decision may be made to request further data and advice from risk assessors, which reflects the iterative process. Finally, if a decision is taken, it should be implemented, together with criteria for assessing the success of the intervention. Decisions on appropriate levels of protection should be determined primarily by human health considerations even when consideration of other factors (e.g. economic costs, health benefits, technical feasibility, and societal preferences) may be relevant in some risk management contexts. However, all decisions should not be arbitrary and should be made transparently.

Finally, risk managers need to establish means for the monitoring and review of intervention, either directly or indirectly. Compliance of the food industry with a maximum limit might be used as a basis for monitoring. However, actual reduction in exposure of the population to the hazard is the best measure of success. Again, total diet studies can provide this overall assurance in terms of concentrations and exposures to a chemical in our diet, and associated trends.

Risk Communication

Risk communication is an integral part of the risk assessment and management process. It is more than the dissemination of information and consists in reciprocal communication among all interested parties. Risk communication may originate from official sources at international, national, or local levels. It may also be from other sources such as industry, trade, consumers, and other interested parties. One fundamental activity of risk communication is to provide meaningful, relevant, and accurate information, in clear and understandable terms targeted to a specific audience. In this respect, results from total diet studies are an excellent means of communicating to the non-scientific audience.

Total diet studies may lead to more widely understood and accepted risk management decisions. Total diet studies may also facilitate a higher degree of consensus and support by all interested parties for the risk management option(s) being proposed. It is essential to separate "facts" from "values" in considering risk management options. As a practical matter, it is useful to report the facts that are

known at the time as well as what uncertainties are involved in the risk management decisions being proposed or implemented. The risk communicator bears the responsibility to explain what is known as fact and where the limits of this knowledge begins and ends. Value judgments are involved in the concept of appropriate levels of protection. Consequently, risk communicators should be able to justify the policy chosen regarding the protection of public health and total diet studies are a key component of effective risk communication involving chemicals in the food supply.

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Chapter 4
Overview of Dietary Exposure

Barbara J. Petersen

Dietary exposure assessment is the estimation of dietary intake of components in food of public health interest. Most often, the terms "dietary exposure" and "dietary intake" are used interchangeably depending on existing practices, regulatory frameworks, and other considerations. However, in the context of risk assessment, the term "dietary exposure" is preferred, as this has been defined within the context of the risk analysis paradigm (see Chap. 3 – Risk Analysis Paradigm and Total Diet Studies).

Dietary exposure assessments are used for a wide variety of purposes, most importantly, the formulation and evaluation of risk management decisions and setting priorities for future studies. Typically, a total diet study (TDS) is used to assess dietary exposure to chemical substances in foods as close as possible to forms that are actually consumed. When conducted on a periodic basis, a TDS can also be used to monitor trends in dietary exposure to substances and assess the effectiveness of risk management strategies, as well as anticipate public health problems before they appear in the population.

General Principles

The general principles of dietary exposure assessment are the same regardless of the intended application. However, the specific methods will vary for different applications. The objective of the dietary exposure assessment must be clearly identified before the appropriate data and algorithms can be chosen. The World Health Organization (WHO) and the Food and Agriculture Organization of the United Nations (FAO) have prepared an overview of the various dietary exposure

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assessments, including recommended methodologies and approaches to interpreting the results for international, regional, national, and local applications [1]. This chapter briefly describes some of the different applications but focuses on TDS-related principles and methods.

Dietary exposure assessments combine food consumption data with data on the concentration of chemicals in food. Typically, the available data on food consumption patterns is collected independently and used in conjunction with analytical results generated as part of the TDS.

The general equation for dietary exposure is as follows:

$$Dietary\ Exposure = \Sigma\left(Food\ Consumption \times Food\ Chemical\ Concentration\right)$$

Although mathematically straightforward, applying this formula to estimate exposure is complicated because of the diversity of most food supplies and variations in eating habits. Estimating a single individual's dietary practices is complex because each person consumes multiple foods on the same day and different multiple foods on other days. Dietary patterns for weekdays are usually different for weekends and holidays. Consumption practices also vary with the seasons. Our foods come from different sources and are prepared in different ways. Capturing information about foods consumed outside the home presents another challenge in being able to quantitatively define a person's diet. Estimating exposure for the entire population requires combining food consumption data for many individuals on many days.

Fortunately, with today's computing capabilities, it is possible to use the complex dietary patterns of many people to estimate exposure for consumers. Computer modeling can also be used to conduct simulations, which consider the impact of different assumptions and different policy options on the resulting exposure estimate.

Dietary exposure analysis is often used to assist in designing a TDS. Preliminary data can be used to identify the chemicals of interest and the foods and forms of those foods likely to contribute the most to exposure. The resulting data are then used to address science, policy and regulatory issues. TDS data are particularly valuable because they focus on chemicals in the total diet rather than individual foods and because the levels are measured in foods as consumed. A TDS is designed to assess chronic dietary exposure to food chemicals ingested by the population living in a country and, if possible, population subgroups [1].

While the initial focus of most TDSs have been on assessing dietary exposure to radionuclides, pesticide residues, contaminants, and nutrients, TDSs have also been used for estimating dietary exposure to food additives. TDSs differ from other chemical surveillance or monitoring programs because they aim to assess dietary exposure to multiple food chemicals across the total diet in one study and involve actual analysis of foods and food composites for those chemicals in foods as consumed. Usually, TDSs do not include direct measurements of the amounts of the foods consumed, but use the population's food consumption data from other sources,

including national surveys or typical diets based on models. TDSs can estimate typical or high consumer exposures if the available food consumption data allow such refinements. Also, if there is a need for more realistic estimates of exposure, it is possible to use more refined methods when the underlying food consumption data are available for individuals within the population or if the analytical data are more precise. For example, if sufficient data are available, it is possible to estimate the upper percentiles of exposure. Even where adequate data are not available, it is possible to approximate high consumer exposures by using model diets or other statistical techniques. Sometimes standard factors can be used in combination with the mean consumption values and with the TDS food chemical data to estimate high-consumer dietary exposures [2]. Similarly, it is possible to use TDS data to estimate dietary exposure for specific population subgroups (e.g. women or young children) by combining the TDS results with appropriate food consumption data for the population of interest. It is even possible to estimate the distribution of exposure by combining food consumption data from individuals with the distribution of food chemical data available in a TDS. It is also possible to use the distribution of consumption data with one fixed value for the concentration of the chemical in the foods of interest. This latter approach is used by several countries, such as Australia, France, the United States, and the United Kingdom.

Interpreting Results of Dietary Exposure Assessments

Dietary exposure estimates are best interpreted by comparison to a toxicological endpoint or nutritional reference value for the food chemical of concern. Typically, a mean dietary exposure will be compared with a chronic (long-term) toxicological reference value, such as the ADI, PTWI, or Benchmark Dose.

The specific approach that is most appropriate for use in estimating dietary exposure within a TDS depends on several considerations, including (1) the type of substance being evaluated (food additive, pesticide, veterinary drug, contaminant, or nutrient) and whether the concern of the potential for exposure is too much, too little or both, as in the case of some nutrients, (2) the duration of exposure required to produce the effect, (3) the potential for different exposures in different subgroups or individuals within a subgroup, and (4) the type of estimate needed (point estimate versus probabilistic characterization of the distribution of exposures) [1]. Since multiple food chemicals are analyzed in each food sample, it is also possible to estimate exposure to more than one chemical at a time, e.g. the cumulative exposure to a class of pesticides, such as organophosphates.

Exposure assessments should cover the general population, as well as other important cohorts that could have exposures that are significantly different from those of the general population, such as, toddlers, children, pregnant women, ethnic groups, occupational groups, vegetarians, and the elderly.

Food Consumption Data

There are four broad categories of food consumption data: (1) food balance sheets, (2) household or community inventories, (3) household food use data, and (4) surveys of individual food consumption patterns. These are briefly discussed as follows.

Food Balance Sheets

Food balance sheets (FBS) based on food supply and market disappearance data, are prepared by most countries for internal purposes, such as agricultural planning and food marketing. Each year, the FAO requests this information from its member countries in a standard format, compiles the data and makes it available to various users [3]. FBS provide data on macroindicators of food availability, such as total production plus imports minus exports and diversion to animal feed and nonfood uses, rather than actual food consumption at the consumer level. The data are collected for the entire country and per capita estimates are calculated by dividing by the number of individuals in the country. FBS describe a country's food supply during a specific year and consequently, averaging FBS data over 5 years serves to reduce data variabilities, especially those caused by climatic variations between years. Daily mean per capita availability of a food or commodity is calculated by dividing total availability of the food by the total population of the country and then by 365 days. The data are typically provided for raw and semi-processed agricultural commodities. These surveys provide an estimate of the mean amounts of various foods available for the consumption of the country's population. The data can be useful designing a TDS and in priority setting.

There are some limitations in the use of FBSs to estimate exposures. Waste at the household and individual levels are not considered. Therefore, exposure estimates based on food supply data are higher than estimates based on actual food consumption survey data. Also, consumers of specific foods cannot be distinguished from nonconsumers, which makes it difficult to estimate the high percentile exposure among individuals. Also, FBSs usually only provide data for raw commodities and a few semi-processed foods, like flour and oils, and therefore there is little information processed foods or multicomponent foods.

Another source of food consumption data is the WHO GEMS/Food Consumption Cluster Diets, which incorporate national FBS data into regional/cultural consumption patterns [4]. These diets are currently used for international exposure estimates for contaminants and pesticide residues and are discussed in detail in Chap. 43 – GEMS/Food Consumption Cluster Diets.

Household Inventories

Household surveys generally can be categorized as (1) household or community inventories or (2) household food use. These tools are used to estimate what foods are available in the household including estimates of the foods that entered the household and the foods that were used up by the household. Ideally they also identify whether household members, guests, and/or tenants consumed the foods and what amount of food should be excluded that was wasted or fed to animals. Inventories vary in the level of detail that is collected. For example, sometimes, but not always, there is information about forms of the food (i.e. canned, frozen, or fresh), source (i.e. grown, purchased, or provided through a food program), cost, or preparation. Quantities of foods may be inventoried as purchased, as grown, with inedible parts included or removed, as cooked, or as raw. Such data are available from many countries including Germany, the United Kingdom, Hungary, Poland, Greece, Belgium, Ireland, Luxembourg, Norway, and Spain [5–7].

Household Food Use Data

Food use studies are usually conducted at the household or family level. Survey methods used include food accounts, inventories, records, and list recalls [8]. These methods account for foods used in the home during the survey period. Different methods are used to collect the information. Typically, a representative of the household will complete an inventory of foods on hand and then add foods as they are brought into the home. Sometimes this is accomplished using receipts for foods purchased. Although household food use data have been used for a variety of purposes, including exposure assessment, limitations associated with data from these surveys should be noted. Usually the data do not capture the preparation methods and food waste is not estimated. The household members who did and did not consume a particular food cannot be distinguished, and variations in intake from day to day cannot be determined. Exposures by subpopulations based on age, gender, health status, and other variables for individuals can only be estimated based on standard proportions or equivalents for age/gender categories. China [9] and Japan also use these methods.

Individual Consumption Studies

Individual consumption studies provide data on food consumption by specific individuals. Methods for assessing food consumption of individuals may be retrospective (e.g. 24-h or other short-term recalls, food frequency questionnaires, and diet histories), prospective (e.g. food diaries, food records, or duplicate portions),

or a combination thereof. The most commonly used studies are those that use a combination of the recall or record methods and the food frequency method. For example, national dietary surveys have been conducted in Australia for the entire population as well as for school children and other subgroups [10]. The U.S. National Health and Nutrition Examination Survey (NHANES) collects retrospective, prospective, and food frequency data from its respondents on a continuing basis [11]. Another technique that has some limited use has been to collect receipts from respondents for food consumption away from home [12].

Food recall studies are also used to collect information on foods consumed in the past. The unit of observation is the individual who is asked to recall what foods and beverages he or she consumed and to estimate the amount consumed. Food frequency questionnaire surveys typically allow qualitative estimates of exposure for a limited number of foods. A checklist is used to determine the frequency of consumption of the foods of interest. This is useful in estimating the number of consumers who rarely or never consume a particular food item as well as to determine how often a food is typically consumed. However, it is difficult for consumers to provide this information for many foods and the accuracy of their responses is limited by their ability to recall consumption patterns over longer periods of time [13].

Food Chemical Concentration Data

Concentration data from a TDS differ from data obtained from other chemical surveillance or monitoring programs because concentrations of chemicals are measured in foods after they have been prepared as for normal consumption. The selection of the sampling, analysis, and reporting procedures to use to generate data within the TDS framework is critical [1]. A TDS also incorporates the impact of cooking, which in general reduces the levels of chemicals of toxicological concern, but in some cases, can produce new toxic chemicals, as in the cases of ethylene thiourea, acrylamide, and nitrosamine. Analytical methods used in a TDS should be capable of measuring concentrations of chemicals in foods at appropriate levels, which are usually an order of magnitude lower than methods used for monitoring compliance with legal limits.

Overview of Methods Used to Estimate Consumer Exposure

Acute Dietary Exposure Assessments

Acute exposure assessments are important for substances that have toxicological properties that cause effects due to short-term exposures. Acute dietary exposure assessments are designed to estimate exposure as a result of consuming a single

commodity unit, single meal or single day's intake matched with a high residue concentration. Methods have been developed and are described in some detail in JMPR and WHO documents [14]. Typically, these assessments do not rely on TDS data because TDS data are usually highly composited. Usually acute exposures are estimated for consumers with the highest potential consumption of a food item, such as the upper 97.5th percentile consumer.

Chronic Dietary Exposure Assessments

Chronic exposure assessments are important for substances that have toxicological properties that cause effects as a result of long-term exposures. Chronic exposure assessments may incorporate deterministic (point values) or distributional models. The latter is also known as a probabilistic model. Deterministic models pick a single value for each parameter. For example, the mean dietary exposure may be calculated by applying a deterministic model using average food consumption levels and the average concentrations in the relevant food products. In the case of a non-staple food (i.e. a food not typically consumed every day by each consumer), some individuals never eat a particular food and others may eat it only occasionally. Thus, high-percentile estimates based on the whole population "dilute" the quantities of food eaten and consequently underestimate the exposure of high percentile consumers. When estimates are intended to protect a high percentile of the population, a high percentile of consumption can be included in place of the mean consumption. This approach over estimates exposure for most consumers. In order to characterize the range of exposures across the population, a distributional model can be employed [15]. The distributional model will incorporate data about the distribution of food consumption (including which foods are consumed on the same day), as well as for the distribution of chemical levels. Estimates for specific population subgroups (e.g. women or young children) can also be determined if food consumption data are available for those subgroups.

Tiered Approaches

Generally, it is most efficient to use a stepwise approach to assess dietary exposure beginning with very conservative "worst case" assumptions and methods and refining those as the situation demands [1]. The conservatism of an exposure estimate is determined by the data and assumptions that are applied. Exposure estimates can range from initial screening methods that use very few data and generally include very conservative assumptions to refined exposure assessments that include extensive underlying data and probabilistic statistical modeling in order to realistically calculate the actual exposure estimates.

Screening Levels

Screening methods, which require less data and less staff time, can be used to identify chemicals or exposure scenarios that do not present any concern. In these cases it is appropriate to use conservative, "worst case" assumptions, which greatly overestimate exposure. For chemicals that pass such a screen, no refined exposure assessment is needed. Generally, in order to effectively screen chemical substances and establish risk assessment priorities, the screening procedure should not use such unrealistic assumptions as to render the model irrelevant to consumer practices. Screening models typically estimate a single value (e.g. a mean, median, or maximum) to represent the residue (i.e. concentration of the chemical) in the food and one number to represent consumption of the food by that population. Average exposures can be estimated by combining data on average consumption of a food and average concentration levels of the substance. It is also possible to estimate maximum exposures by assuming all food contains the maximum permissible levels and that extremely high amounts are consumed. In estimating average exposure using point estimates, the arithmetic mean is most commonly used; however, if the distribution of the parameter of interest is known to be log normal (as is typical of food consumption data), use of the geometric mean or median (or 50th percentile) for consumption is more appropriate [16].

Progressive Levels

Further steps to allow the refinement of the dietary exposure assessment should be designed in such a way that potential high dietary exposures to a specific chemical are not underestimated, but at the same time, so that they are more representative of potential exposures. For example, an average consumer's exposure is calculated as the product of the average consumption of the foods of interest (as measured in a national food consumption survey) and the average concentrations of the chemical substances of interest in those foods (as measured in the national TDS). The resulting exposure estimate can be further modified by additional adjustment factors, as appropriate, to better simulate consumer practices. A point estimate of a high consumer's exposure (such as for the upper 90th or even the 97.5th percentile consumer) can also be calculated, provided the appropriate data are available.

For nutrients such as iodine, erring on the side of caution means that potential high dietary exposures assessment (possible toxicity) must therefore not be underestimated, but also low dietary exposures (possible nutritional inadequacy) must therefore not be overestimated.

Characterizing Uncertainty and Variability

It is important to describe the uncertainty and variability in an exposure assessment.

Uncertainty describes the assessor's level of knowledge about the relationship between the available data and the real values. Therefore, uncertainty can be

decreased as the quantity or quality of the information improves. In contrast, variability is an inherent characteristic of any population and their food intake. Its characterization can be improved by better information, but it cannot be decreased or eliminated. Examples of the range of methods that are currently in use have been described elsewhere (see Chap. 18 – Addressing Uncertainty and Variability in Total Diet Studies).

Deterministic Versus Distributional Exposure Estimates

Deterministic models rely on single values for each parameter. The quantity and underlying quality of the data along with appropriate selection of assumptions for the intended application affects the reliability and usefulness of the results. While deterministic models are particularly useful for assessing mean exposures (or other measures of central tendency), they can also be used to estimate other measures, such as high percentiles of exposure.

The structure of a distributional model is usually similar to that of the corresponding deterministic models in that it will be based on the same basic equations. However, as noted above, distributional models rely on the full range of data for the model parameter. For example, distributional models will incorporate all of the analytical results rather than a single value. Some distributional assessments are in fact combinations of deterministic and distributional data, e.g. the assessments uses a distribution of consumption while using a single value for the concentration.

Conclusion

The most appropriate data, algorithms, and models for conducting an exposure assessment will depend upon the purpose of the assessment and the availability of data. Generally, it is best to conduct preliminary screening analyses to conserve resources and to guide the design of more refined analyses. A TDS provides data that are particularly useful for conducting assessments for chemicals found in multiple foods over long periods of time. Acute exposures are best analyzed using other methods. TDSs can combine food consumption data collected using a variety of different methods with the analytical results to estimate exposure for the entire population as well as for subgroups of the population. High-quality TDS exposure estimates based on levels of the chemical in foods as consumed provide the best estimates of the populations' long-term exposure from the entire diet.

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Chapter 5
Scope, Planning and Practicalities of a Total Diet Study

Richard W. Vannoort

Introduction

The World Health Organization (WHO) recommends that all countries undertake a total diet study (TDS) as the most cost-effective means of assessing dietary exposures to chemicals and their associated health risks to public health. While a simple TDS could conceivably be undertaken for as little as US$50,000, this would likely involve significant compromises in the range of foods included, chemicals considered or other aspects. A basic TDS can, however, serve to illustrate the importance and value of a TDS to key stakeholders. As a result, more resources may be made available for future studies. Accordingly, TDSs evolve over time and become increasingly flexible and comprehensive. Planning and design of a TDS are challenging yet crucial to maximizing benefits while minimizing costs. They are also important to avoid potential pitfalls that may compromise the results of the study.

In this regard, a clear idea of the relevant risk questions being asked and how they can be adequately addressed is essential in shaping and directing the TDS design. Examples of such questions include:

- Is the focus across all foods or chemicals, or a more restricted subset (i.e. mercury in fish)?
- Is the possible risk limited to just one age-gender cohort (i.e. infants), or relevant to the whole population?
- Is the possible concern in just one city or region, or the whole country, or is it useful to pilot the TDS in one region first?
- Do we know what data are available to help inform planning, and what time, expertise and financial resources are available?

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Whether it is a country's first TDS or not, it is important to understand and clearly define its objectives, management structure and key components.

Objectives of a Total Diet Study

The key objective of a TDS is to assess the actual dietary exposure of a population (or population cohorts) to chemicals, such as pesticide residues, veterinary drug residues, contaminants, nutrients, food additives, mycotoxins, radionuclides, and processing contaminants. Foods are analyzed after being prepared as for normal consumption. The exposure assessment provided by a TDS is essential for evaluating any potential health risks to the different age/gender cohorts, so that health risks can then be effectively managed and communicated.

A TDS priority may be to also identify which food groups or individual foods and/or geographic regions/seasons are the key contributors to dietary exposure, or a particular health concern, such as iodine deficiency or lead toxicity.

TDSs provide critical baseline information on actual levels in foods and dietary exposures. This data can also be useful if subsequent contamination episodes occur, to help identify which foods or exposures may be exceeding usual background levels.

For countries that retain their TDS samples, re-analysis of samples for a newly discovered hazard, such as acrylamide, can provide a historical record of where and when the contamination first occurred as well as estimates of past exposure to the hazard.

An advantage of conducting consecutive TDSs is that they can reveal trends of food chemical concentrations and dietary exposures over time and thereby assess the need for, and effectiveness of, risk management interventions, including risk communication activities.

In addition, a TDS can provide robust and concrete scientific data about the chemical safety and quality of the food supply to key stakeholders, such as consumers, government agencies, food producers, food importers and exporters, manufacturers, retailers, academia, researchers and politicians.

TDS data can be used to help establish, inform, prioritize and appropriately resource risk management activities, such as developing food safety regulations, standards or policies, identifying appropriate follow up investigations, research, surveillance or monitoring program needed, and justifying associated capability and capacity building. TDS outputs also help direct risk communication, such as advice to industry or consumers, or public health protection and nutrition promotion programs. TDSs also provide useful data to international risk assessment and regulatory bodies such as the Codex Alimentarius Commission, the Joint Food and Agriculture Organization of the United Nations (FAO)/WHO Meetings on Pesticide Residues (JMPR), the Joint FAO/WHO Expert Committee on Food Additives (JECFA) and the WHO GEMS/Food network of laboratories involved in TDSs and other exposure assessment activities.

It is, therefore, most important to ensure that the objectives of a TDS are well defined, clear and unambiguous, and that they are both realistic and achievable in the timeframe with the resources and expertise available.

Management of a Total Diet Study

While the TDS can be managed by a committee approach, it may prove most beneficial to have a designated TDS project leader, who has the authority to make the definitive decisions. Ideally this leader should have a solid understanding of the issues involved in a TDS. If not, they should call on others who have specific areas of expertise, with defined roles and accountabilities within the TDS management team. This may include TDS stakeholders, funders, samplers, key staff from the sample preparation facility, analytical laboratories, or other experts. With such a diverse range of responsibilities, it will be important to define the relevant and appropriate lines of communication for all staff on the TDS team (see Chap. 8 – Preparing a Procedures Manual for a Total Diet Study). With the possibility of a potential health or trade issue being identified in the course of the TDS, it is important that an appropriate 'red alert' protocol be defined and agreed by all parties. The protocol should identify who would take specific actions and in which order. All members of the TDS management team play different and important roles. Teamwork is important, as the success or failure of a TDS depends on all team members doing their jobs effectively at the required times. They are each like links in a chain, which ultimately are only as strong as the weakest link.

Once all the components of the TDS are agreed upon, then milestones with due dates and performance parameters are established for monitoring the progress of the TDS by the TDS project leader and management team.

Components of a Total Diet Study

Planning Meetings

A well-established maxim is that it is better to 'look before you leap'. To that end, no matter how hard one tries, poor planning often leads to poor results. A successful TDS, therefore, needs adequate planning, and it is recommended that a series of meetings be undertaken, prior to commencing a TDS to enable effective planning, and during its implementation to monitor progress. At the conclusion of the TDS, additional meetings should be held to review its successes and any difficulties that may need to be redressed and documented for future TDSs.

Useful background documents include *Guidelines for the study of dietary intakes on chemical contaminants* [1] and others found on the WHO GEMS/Food

website [2], including reports of previous WHO TDS workshops. Previous national surveillance or monitoring data can also help guide TDS planning in regards to foods, chemicals and regions to be targeted. Similarly other countries' TDS reports can usefully illustrate planning and design considerations (see Part II).

Indicative Budget

Budgetary constraints are often a determining factor in a TDS. While US$125,000 may be a realistic budget for a TDS in a developed country, this will vary among countries. An initial TDS could perhaps be effectively undertaken for as little as US$50,000, although this would require a major compromise on the breadth, depth or quality of what may be achieved. A bigger budget will, understandably enable much more to be achieved. The TDS design always needs to fit the indicative TDS budget, and this usually means reassessing and prioritizing TDS components in the context of the TDS objectives, timeframes, and available capabilities and resources. Some countries like New Zealand have a long and successful history of TDSs (Chap. 35 – New Zealand's Experience in Total Diet Studies), and their importance as a part of a risk-based food surveillance and monitoring program is well established. For this reason, New Zealand invests significant funding in the New Zealand Total Diet Study (NZTDS), but these costs have also been spread over a 4-year cycle to make them more manageable and acceptable. For example, year 1 is for preliminary planning; year 2 finalizes planning, procedures, and starts sampling, sample preparation, and analyses; year 3 completes sampling, sample preparation and analyses, determines exposure estimates, and starts report preparation; and year 4 completes the report and undertakes risk communication with the media and key stakeholders.

Scope of the TDS Food List

The food list in a TDS needs to be representative of those foods most commonly consumed by the respective population cohorts in the country. Besides age groups and gender, particular ethnic groups may also be included as a cohort. The food list will include both nationally distributed foods (including imported foods) and regional foods. The TDS food list may also include some foods relevant to defined population cohorts (e.g. infant foods), as well as foods that may be consumed in relatively small amounts but have the potential to make a significant contribution to the dietary exposure because of their high chemical content (e.g. heavy metals in shellfish and offal). Drinking water is also included in the TDS food list of most countries. A general target for foods in the TDS food list would be to aggregate to >80 % of the total food consumption for the respective cohorts being considered. The objectives of a TDS will also help focus the scope of the food list, i.e. if the

target chemicals for dietary exposure assessment are only in certain foods. The development of a TDS food list is explained in more detail in Chap. 6 – Preparing a Food List for a Total Diet Study.

Which Chemical Analyses to Use?

The highly sensitive analyses of food samples in a TDS require specialized expertise, consumables like ultrapure solvents, and sophisticated equipment, which can be expensive. With a defined budget, it is unlikely that all of the analyses desired can be undertaken, so that prioritization may be necessary. WHO GEMS/Food has developed three TDS priority lists for analysis, namely core, intermediate and comprehensive [3]. Priorities may also include other chemicals that are of public concern or emerging international issues. The capability, cost and capacity of analytical laboratories to do the work may also be important considerations. This is discussed further in Chap. 7 – Selecting Chemicals for a Total Diet Study.

Which Organic Chemical Analyses?

Organic analyses in a TDS may include pesticide residues by multi-residue screening techniques involving, *inter alia,* gas chromatography-mass spectrometry/mass spectrometry (GC-MS/MS) or liquid chromatography-mass spectrometry/mass spectrometry (LC-MS/MS). Such screening methods enable up to 300 pesticides to be analyzed in one screen, and are thus very cost-effective at approximately US$150 per sample. Depending on equipment and expertise, these multi-residue techniques may or may not be able to also include N-methyl carbamates, benzimidazoles, and acid herbicides in the one screen. Some specific analytes may require separate dedicated screens, such as for dithiocarbamates (DTCs), ethylenethiourea (ETU), aflatoxins, volatile organic compounds (VOCs) like benzene and toluene, and polycyclic aromatic hydrocarbons (PAHs), with each separate screen accruing additional costs. Some other toxic chemicals may require much more sensitive and specialized sample preparation and analytical equipment, such as dioxins and polychlorinated biphenyls (PCBs), and these can cost up to US$1,500 per sample. More recently, acrylamide and even additives, such as benzoates or sorbates, have been included in some TDSs [4]. These types of methods are explained further in Chap. 10 – Analyzing Food Samples—Organic Chemicals.

Which Inorganic Analyses?

A wide range of inorganic analytes can be investigated. Traditional priority in a TDS has been given to toxic contaminant heavy metals such as cadmium, lead, and mercury, with arsenic also included. Some countries have also chosen to measure

key nutrient elements in their TDS food samples, to take advantage of these foods being already sampled and prepared. Nutrient elements may include, *inter alia,* iodine, selenium, iron, sodium, calcium, copper, fluoride, magnesium, manganese, phosphorus, potassium, and zinc. While technically considered inorganic elements, radionuclides are also often included in TDSs, but their analysis requires specialized instrumentation. Further details about analyzing inorganic chemicals in a TDS are given in Chap. 11 – Analyzing Food Samples—Inorganic Chemicals, and in Chap. 12 – Analyzing Food Samples—Radionuclides.

Analytical Considerations

A TDS needs to measure concentrations of chemicals in foods prepared for normal consumption, and these concentrations are often just at or below background levels. As such, it is essential that the limits of detection (LOD) in a TDS must be low enough to provide meaningful results for subsequent exposure estimates. Generally LODs for enforcement monitoring purposes only need to be about 0.5 mg/kg, to be confident of robust quantitation if the regulatory limit is 1 mg/kg. However, for valid TDS exposure estimates, LODs often need to be two-three orders of magnitude below 0.5 mg/kg, at 0.005–0.0005 mg/kg, and sometimes even lower. It is critical, therefore, that analytical laboratories can achieve the necessary LODs for TDS and have excellent quality assurance and quality control (QA/QC) systems in place, to deliver accurate, precise and reliable analytical results. The importance of QA/QC cannot be overemphasized enough in a TDS, and is detailed further in Chap. 13 – Quality Control and Assurance Issues Relating to Sampling and Analysis in a Total Diet Study. QA/QC considerations would include adequate and demonstrable limits of detection, blanks, duplicates/blind duplicates, certified reference materials (CRMs) if available in the desired analyte/matrix combination, spike recovery, documentation and Standard Operating Procedures (SOPs), and laboratory accreditation.

Different organizations may not have the necessary high quality analytical equipment or methods in-house that are capable of reaching the low limits of detection needed in the wide range of TDS food matrices. Another issue is the capacity to cope adequately with the large number of samples involved, so it may be more cost-effective to subcontract commercial analytical laboratories to conduct certain analyses (see Chap. 14 – Commercial Analytical Laboratories—Tendering, Selecting, Contracting and Managing Performance).

Analytical Plan: Food Group Composite or Individual Foods Approach

The analytical plan is essential for formalizing and prioritizing which foods will be analyzed in a TDS and for which respective analytes. It also defines if analyses will be

based on a *food group* or an *individual foods* approach. These TDS concepts are more fully explained, along with their advantages and disadvantages in Chap. 9 – Food Sampling and Preparation in a Total Diet Study. The *food group* approach, which combines different foods from the same food group, is more suitable for those practitioners with limited resources, such as those undertaking their first TDS, as it reduces the number of analyses and therefore the cost.

The *individual foods* approach analyzes all foods in the TDS food list separately. This can be undertaken in a phased approach, depending on the available resources and objectives. The analytical plan may have different brands or regions in a season combined and analyzed just as seasonal composites (SC) for that individual food. This may occur where resources are still somewhat limited or there is little benefit envisaged relative to the additional cost of analyzing each brand or region separately. However, if resources permit and the additional information is useful, then the analytical plan for the individual foods may also require analyses of the separate brands or regions for each season and for each of the individual foods.

These differing approaches are usefully illustrated by experiences in the NZTDS. In the two earliest NZTDSs, the *food group* approach was used. As it developed, the NZTDSs changed design to the *individual foods* approach, which became more comprehensive over time. In the 3rd NZTDS, all brands/regions and seasons were composited for each individual food, resulting in 105 samples for analyses, one for each food in the list. In the 4th (1990/1991) and 5th (1997/1998) NZTDSs, the *individual foods* approach was extended so that more individual composites (IC) of brands or regions per season were undertaken for each individual food. Selected foods in the analytical plan for the 1997/1998 NZTDS are given in Table 5.1 as an example. Criteria used to decide if the foods were to be analyzed as individual composites of brand or region per season, or seasonal composites were:

- High contribution to exposure according to WHO GEMS/Food
- High contribution to exposure compared to previous NZTDS
- High concentration in previous NZTDS
- LODs of chemical in respective food matrices
- Available budget (recognizing differential costs for agricultural compounds and elements)
- Increase in individual analyses from previous NZTDS

Dithiocarbamate (DTC) fungicides are only approved for use on fresh fruit and vegetables, so these foods were analyzed as individual composites. As it was considered highly unlikely for residues of these chemicals to be present in grains, dairy or meat products, they were consequently not analyzed for DTCs. Multi-residue pesticide analyses were undertaken on individual composites of those foods (i.e. bread, butter, luncheon sausage, lettuce, apples), which were more significant contributors to exposure or more likely to have residues based on previous NZTDS, WHO GEMS/Food or national residue monitoring programs. On the other hand, potatoes or bananas (which are peeled and/or cooked before analyses), only had seasonal composites analyzed. Mercury was prioritized for individual analyses in fish and seafood, but not analyzed in most foods as it was below detection limits, but was

Table 5.1 Extracts from the analytical plan for 1997/1998 NZTDS

Food number	Food	Type	Number of brands or regions collected per season	Total number of analytical samples	Multi-residue pesticides	DTC	Elements	Iodine	Mercury
1	Bran cereal	N	5	2 or 10	IC	NA	SC	SC	NA
7	Chocolate biscuits	N	5	2 or 10	IC	NA	SC	IC	NA
12	Rice, white	N	5	2 or 10	SC	NA	SC	SC	NA
15	Wheatmeal bread	R	4	8	IC	NA	IC	IC	NA
18	Butter	R	4	2 or 8	IC	NA	SC	NA	NA
23	Milk, whole	R	4	2 or 8	SC	NA	SC	NA	NA
29	Beef, minced	R	4	2 or 8	SC	NA	SC	IC	SC
32	Egg, boiled	R	4	2 or 8	SC	NA	SC	IC	SC
33	Fish, Terakihi	R	4	2 or 8	SC	NA	IC	IC	IC
36	Luncheon sausage	R	4	2 or 8	IC	NA	SC	IC	SC
50	Lettuce	R	4	8	IC	IC	IC	NA	NA
54	Potatoes, peeled	R	4	2 or 8	SC	IC	IC	NA	NA
59	Tomato	R	4	2 or 8	SC	IC	SC	NA	NA
67	Apples	R	4	8	IC	IC	IC	NA	NA
68	Bananas	N	1	2 or 4	SC	IC	SC	NA	NA
95	Pizza	R	4	2	SC	NA	SC	SC	NA
100	Carbonated cola	N	5	2	SC	NA	SC	NA	NA
105	Water	R	4	2 or 8	SC	NA	IC	NA	NA

R regional food, *N* national food, *DTC* dithiocarbamate fungicides, *Elements* = arsenic, cadmium, lead, tin, selenium, *IC* individual composite samples analyzed, *SC* seasonal composite samples analyzed, *NA* food not analyzed for this analyte

analyzed in eggs because fish meal is fed to chickens in New Zealand. Iodine intake is low in New Zealand so priorities for individual composite analyses were given to key contributors, like bread and fish, while many were not analyzed as they were expected to be below the LOD. Dairy products are a major contributor to iodine intake in New Zealand, but were not analyzed in the 1997/1998 NZTDS because an extensive independent study was being undertaken specifically for iodine. Although not included until the 6th (2003/2004) NZTDS, the leading brands of infant foods were analyzed separately, given that brand loyalty is often associated with these types of foods.

Sampling

Sampling is undertaken on the foods contained in the TDS food list. The TDS sampling plan explains whether the respective foods are considered to be *National* or *Regional* foods, and if so, how many regions and cities per region to sample. It would define who would sample and when to sample. Sampling plans should include purchasing instructions and shopping lists. It will explain what to sample (in terms of brands), how much to sample, where to sample (i.e. what types of food outlets), how to handle and transport them and what documentation is required. Further details of sampling in a TDS are given in Chap. 9 – Food Sampling and Preparation in a Total Diet Study.

Sample Preparation

The defining characteristic of a TDS, which differentiates it from other food commodity surveys, is that foods are analyzed after being prepared as for normal consumption, so in a TDS, food preparation is very important. Cooking and other food preparation steps may reduce the levels of certain chemicals (e.g. pesticide residues), while actually generating other hazardous chemicals (e.g. acrylamide and furan). Sample preparation may be undertaken by an outsourced contract kitchen facility, or by facilities associated with the analytical laboratory. Undertaking all the sample preparation at one site overcomes potential problems associated with variable preparation methods and doing it at the analytical laboratory eliminates the need to transport and simplifies the storage of prepared samples before analysis. While individual dietary foods or prepared dishes may have a number of different preparation methods in a country, it is generally simplest to use the most common method. To ensure consistency of sample preparation for the same foods between the different sampling seasons and between different TDSs, it is essential that SOPs be documented for sample preparation, ideally in a procedures manual (see Chap. 8 – Preparing a Procedures Manual for a Total Diet Study). The SOPs for sample preparation would define which foods are being prepared, how to prepare them, the associated

equipment, terminology (e.g. mixing, chopping, blending, etc.) and how to minimize the risk of contaminating the samples during sample preparation, such as the use of specific sample containers. It may also identify special considerations for certain foods and analyses. Further details of key aspects of sample preparation in a TDS are given in Chap. 9 – Food Sampling and Preparation in a Total Diet Study.

System Pre-test/Pilot Test

TDSs can be quite large and logistically complex surveys, with major resources committed and no firm idea of their success until the final dietary exposures are estimated. As another key management step, it is strongly advised that once all the sampling and sample preparation SOPs are in place and the laboratory has confirmed its ability to analyze down to the required LODs, a very small scale TDS pre-test or pilot project be undertaken. This would generally involve sampling three to four different foods, such as grain, meat, dairy and fruit or vegetable. In New Zealand this involved bread, beef, milk, and tomatoes. Samples should be obtained in all sampling sites and are intended to validate the following: sampling, documentation, transport, receipt, sample preparation, and organic and inorganic analyses. As there are only a few samples, analytical results should be available within a relatively short timeframe, i.e. a few weeks to a month. Once the results are available, they can be assessed to ensure adequate LODs are being achieved, QA/QC data are satisfactory, and no apparent contamination of the samples has occurred. A review meeting can be held to refine any procedures, including sampling and sample preparation, which may be necessary.

Data Evaluation

When TDS analytical results are received, a number of screening checks should be made to ensure the results are realistic and explicable. For example, in New Zealand, cadmium levels in milk would be expected to be less than 0.0001 mg/kg, whereas the levels in tomatoes would be approximately 0.001 mg/kg, breads approximately 0.010 mg/kg, potato crisps about 0.070 mg/kg, and dredge oysters much higher ranging from 0.6 to 5.3 mg/kg of cadmium. It is also advantageous to see if the results are consistent with previous TDS results (national or international) for the same foods, recognizing there will be some variability both analytically and in regards to natural content (see Chap. 18 – Addressing Uncertainty and Variability in Total Diet Studies). However, analytical results should not be orders of magnitude different from expectations. If so, further investigation is warranted. If the results are not consistent with other samples of the same food in the TDS, an investigation would need to include analytical results for blanks in the run, spiked sample recoveries, accuracy of certified reference materials, laboratory control samples, and duplicate analyses. QA/QC aspects are considered in detail in Chap. 13 – Quality Control and Assurance Issues Relating to Sampling and Analysis in a Total Diet Study.

Statistical analyses can also be undertaken on the TDS data generated, including minimum, mean, maximum, median, standard deviation, confidence interval, and coefficient of variation (CV). If sample numbers are sufficient, statistical differences between regions, brands, seasons or cultivars can be assessed. This, however, is not a principal objective of a TDS. It may best be undertaken in subsequent follow-up surveys. TDS data may well direct which foods/regions/brands to target more fully in a separate study. Such a study would have much more statistically robust sample numbers on only a few foods.

Reanalyses

By their very nature, TDS analyses push analytical methods and associated LODs down as low as possible to measure background concentrations needed for meaningful exposure estimates. TDSs undertake very low level analyses of a wide and complex variety of prepared food matrices (e.g. a chocolate biscuit is more complex to analyze than raw wheat, and a sausage is more complex than raw beef). Inevitably, some analytical data or accompanying QA/QC data may prove questionable or unsatisfactory, so reanalyses may be needed. If the problem is an analytical or QA/QC issue, then the laboratory should rectify it at their expense. It is also important to remember to allocate adequate time in the TDS timeline for such reanalyses to be undertaken.

Consumption Data

Dietary exposures are obtained by combining food concentration data with food consumption data, so both play a critical part in a TDS. If a country does not have consumption data, then a number of options exist. Per capita food availability can be derived from a country's Food Balance Sheets (FBS). This can be supplemented by using the WHO/GEMS/Food Consumption Cluster Diets (Chap. 43 – GEMS/Food Consumption Cluster Diets). Simulated or model diets based on macronutrient (energy, protein, fat, carbohydrate) requirements for different age/gender cohorts in the population can be derived for the foods in the TDS food list. Ideally, data from a national nutrition survey using two or more non-consecutive 24-h recall surveys supplemented with a food frequency questionnaire is preferred. Further details about obtaining consumption data for a TDS are given in Chap. 4 – Overview of Dietary Exposure; Chap. 6 – Preparing a Food List for a Total Diet Study; and Chap. 17 – Dietary Exposure Assessment in a Total Diet Study. Given that dietary consumption is a major factor influencing dietary exposures and that consumption patterns change continuously, such data should be updated regularly if resources permit as it is important for various purposes, including TDSs.

Exposure Estimates: Use a Tiered Approach

The primary objective of a TDS is to estimate dietary exposures for a population or population cohorts within a country. Given expertise and resources are usually limited, this should be undertaken in a tiered approach [5]. Firstly a deterministic approach (sometimes referred to as 'point estimate') is recommended, which combines mean concentration data with mean consumption data. This generates mean dietary exposures for an average consumer. Often an exposure estimate is made for high consumers by combining mean concentration data with high consumption values, usually the 90th, 95th or 97.5th percentiles. If this initial dietary exposure estimate suggests that a significant or potential problem may exist, then this may warrant further investigations, which could include analyzing the food group composites, or even the individual foods in the TDS regional/brand composites, to better assess where the problem originates. It may also involve new targeted follow-up surveys being commissioned to investigate the situation more fully.

More sophisticated exposure estimate approaches may also be undertaken in a TDS, including semi-distributional modeling (whereby mean concentration data may be combined with a distribution of consumption data). Semi-distributional modeling requires much more data and expertise. It does not provide more accurate data, but it does provide potentially useful information about the lower and upper tails of the exposure distributions (low and high percentiles), where there may be inadequate nutrition or toxic exceedances, respectively. Exposure estimates are more fully explained in Chap. 4 – Overview of Dietary Exposure; and in Chap. 17 – Dietary Exposure Assessment in a Total Diet Study. Different options also exist for automating dietary exposure calculations (see Chap. 45 – Automated Programs for Calculating Dietary Exposure).

Risk Characterization

This firstly involves converting the estimated dietary exposures/intake estimates to the correct units, usually (µg or mg/day) for nutrients and (µg or mg)/kg bw/ (day or week or month) for pesticides or contaminants, and then comparing these to the relevant national or international health-based guidance values (HBGV), such as the Acceptable Daily Intake (ADI), Provisional Tolerable Weekly Intake (PTWI), Estimated Average Requirement (EAR), or Upper Level of intake (UL). Risk characterization is an integral part of risk analysis and is explained more fully in Chap. 3 – Risk Analysis Paradigm and Total Diet Studies. It is also very important that all assumptions, limitations and uncertainties associated with the TDS design and methodologies be well documented, so that the estimated exposures can be put into a more balanced context for the risk assessment and to better inform subsequent risk management decision-making.

Analytical Data Reports

Given the TDS can take some years from its initial planning until completion of the final interpretative reports and media releases, consideration may also be given to releasing analytical data reports as they are generated after each sampling period, whether it is quarterly, biannually or annually. The reports could explain *inter alia* the purpose of the TDS, the food list, the sampling, analyses undertaken and associated limits of detection (LOD), and then the full analytical data. This can provide useful and timely feedback to interested stakeholders on progress of the TDS. Any results of public health significance would also be explained. In the subsequent final interpretative report, the analytical data can be consolidated in the appendices by just specifying the minimum, maximum, mean, 95th percentile, LOD and number of samples analyzed.

Interpretative Report and/or Papers

These will consolidate all of the information of the TDS and its key findings. It is advisable that the report contain a separate executive summary, including any recommendations. While the report may be targeted for a more general readership, the report will inevitably contain some technical and scientific descriptions, so will need to contain a glossary of terms and abbreviations. It should explain why a TDS is important, and the methods used – food selection, sampling, preparation, analyses, and consumption data/diets. The results section should explain protocols used, and may be structured on an analyte by analyte, or group by group basis (i.e. heavy metals, pesticides, nutrient elements, etc.). Following a risk analysis format, each section could also explain why the analyte/group is important to study (hazard identification and hazard characterization), a summary of consolidated raw data (prevalence/occurrence), and possibly include a comparison of results to previous TDS or data from other countries. The section would also detail estimated dietary exposures (exposure assessments) and their public health significance (risk characterization). Any observed trends over time can be described if previous TDSs have been conducted. It may be interesting to compare TDS exposures with those of other countries, while also acknowledging that differences in design, LOD and other factors may have an impact on the results.

Peer Review

Any report or papers should be subject to both internal and external peer reviews, and amendments and corrective actions should be made as needed. Time and cost for these reviews needs to be factored into the TDS timeline and budget.

Effective Risk Communication

Risk communication is another key part of risk analysis (see Chap. 19 – Communicating Results in a Total Diet Study). In the context of a TDS, it may also involve appropriate production and distribution of the final interpretative TDS report, use of websites, appropriate media releases and conference presentations. If need be, relevant follow-up activities may also involve advice to producers and importers, more intensive and focused follow-up surveys, consideration of legislative changes, consumer education programs and other risk management interventions.

TDS Management

It is important to recognize that managing a TDS is time consuming and this needs to be factored into the budget. Associated travel and per diem costs may also need to be included.

Standard Operating Procedures (SOPs)

These are essential to not only document the project procedures, but also to standardize approaches and ensure consistency. SOPs should document the TDS management structure as a whole, with key contact details and lines of communication, and most importantly, details of sampling, sample preparation, and analytical methods. It is also important to budget for the time and any costs needed to prepare, review and update the SOPs (see also Chap. 8 – Preparing a Procedures Manual for a Total Diet Study).

Revising the TDS

Once the initial TDS plan has been developed, it is important to consider the plan in light of the TDS objectives, available resources, expertise and deliverables. Securing quotes from key subcontractors (which may include samplers, kitchen facility, and analytical laboratories) may be necessary. It is imperative that the same deliverables are compared from each subcontractor in assessing prices, especially in terms of quality and timeliness. If a bid seems unduly inexpensive, make sure that it is not at the expense of something critical, like LODs, QA/QC or timeliness. This is discussed in Chap. 14 – Commercial Analytical Laboratories—Tendering, Selecting, Contracting and Managing Performance.

TDS Project Timeline

Having developed the TDS plan, it then needs to be broken down into its respective components, considering constraints and interdependence of both resources and time. For example, food samples in Quarter 3 (Q3) cannot be analyzed until Q3 food samples have been prepared, and that cannot occur until foods for Q3 have actually been sampled. It is also a worthwhile management strategy to build in some contingencies into TDS timelines. Inevitably some things may not go completely as planned, so some flexibility should be built into the TDS milestones.

Conclusion

The TDS is a very important exposure assessment tool that is essential for public health risk assessment. It can provide invaluable, concrete data about the safety of a country's food supply, and help target where future resources or risk management activities are needed.

  Those considering a TDS for the first time should not be discouraged by the fact that a TDS can be a challenging and complex undertaking for a country. Rather the focus should be on its multiple positive benefits. This chapter has provided the basic information on the scope, planning and practicalities of a TDS, which are important for conducting a successful TDS.

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Chapter 6
Preparing a Food List for a Total Diet Study

U. Ruth Charrondiere

Introduction

The food list is an important part of a total diet study (TDS), as it contributes significantly to the precision and accuracy of the dietary exposure assessment for the chemicals examined. It is also the pivotal part reflecting many decisions taken in other parts of the TDS, such as objective of the study, data available, sampling, analysis of chemicals in the foods, representativeness of the results and the resources available to conduct the TDS.

Which Foods and How to Describe Them?

For a total diet study, the foods to be analyzed are 'foods as consumed', i.e. the edible part of the foods in the form they are eaten. Examples are cooked foods (e.g. grilled steak without bone; vegetable soup; boiled rice; steamed fish without bones, skin, or head), processed foods (e.g. cornflakes, bread, biscuits) or foods eaten raw but without the inedible part (e.g. banana without peel). Foods also include beverages (e.g. brewed coffee, black tea in liquid form, whole milk, beer, and wine) and drinking water. The latter is often forgotten because drinking water is usually not included in food consumption or supply data.

Accurate food descriptions are essential in order to clearly identify foods which are to be sampled and analyzed for the TDS and to assure that they are the same as

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those that were reported to be consumed by the population. In addition, foods may take different forms and have very different compositions, including contaminants. For example, 'tea' could be 'tea leaves', 'liquid tea', or 'tea powder' – and all would have different levels of contaminants. Therefore, it is important that a precise and clear food description be given for all individually analyzed foods as well as for those foods included as contributors to composite food samples.

When data from household budget surveys (HBS) or food supply/availability data (e.g. FAOSTAT or GEMS/Food Consumption Cluster Diets) are used to construct the a food list, they are reported raw agricultural commodiites (RAC) or 'as purchased', i.e. in the form they are bought (e.g. melon with skin, raw steak with bone, uncooked rice). Foods in such forms need to be transformed by appropriate edible coefficients and yield factors to foods 'as consumed' and the food descriptions of the TDS foods need to be adapted accordingly to avoid misinterpretation of results. The edible coefficient is the percent weight loss when discarding the inedible portion of a food. For example, a sample of 100 g of meat may contain 20 g of bones. Therefore, the edible coefficient would be 0.8. The yield factor indicates the percent weight change in foods or recipes due to cooking. For example, 100 g raw rice becomes 280 g boiled rice and the yield factor is 2.8; or when grilling beef, 30 % of its initial weight is lost and the yield factor is 0.7. More information on food description, nomenclature and food groups is found in the literature, such as Greenfield and Southgate (2003) [1] and Charrondiere et al. (2011) [2].

Before using food consumption survey data for TDS, they often have to be 'cleaned', i.e. implausible outliers need to be eliminated. Data deriving from 24-h-recalls often need to be aggregated, e.g. several brand names of the same food are grouped to avoid the possibility that important foods are not selected because they are split into too many smaller food records.

Construction of a Food List

The TDS food list is constructed in several steps. The first one is to select the most important foods in relation to exposure, the second to add special foods, the next step to consider other factors, and then lastly optimize the size of the TDS food list. The criteria used in the different steps are listed as follows:

Step 1. Identify most important foods in relation to exposure:

- Option 1: Select the foods or recipes consumed in largest amounts, e.g. >10 g/day then remaining foods consumed > 1 g/d [3];
- Option 2: Select the foods 'as consumed', arranged in descending order of consumption, contributing to a high percentage of the total diet by weight (ideally at least 90 % of the food intake) [4]; and
  Check that all key foods in the diet are included.

Step 2. Identify additional foods to be included for specific reasons:

- Add foods consumed by a significant proportion of the population, e.g. > 15 % of consumers;
- Add foods that may be consumed infrequently or in small amounts but are important in terms of potential contribution to dietary exposure, e.g. oysters or liver for heavy metals; or dried or powdered foods; or spices in certain diets; and
- Add foods important only for specific population groups or regions, e.g. infant formula, tofu, hummus

Step 3. Optimizing the food list:

- Organize all foods into foods groups;
- Eliminate foods NOT consumed by the population groups of interest;
- If the food consumption data is not very detailed, e.g. from HBSs, investigate the different forms that the food is consumed. For example, tomatoes – dried, canned or fresh; or chicken - fried, roast, stewed, tandoori;
- Check that all important foods are included potentially contributing to the exposure of the chemicals to be analyzed. For example, if only considering dithiocarbamates, the main priority foods should be fruits and vegetables, not oils or sweets;
- Decide which foods will be sampled as a regional or seasonal food (samples of the same food will be taken in different regions and/or seasons because it is believed that the concentration of the chemical may depend on the region and/or season) or as a national food (the food will be sampled at one site and season as the chemical concentration is supposedly similar throughout the year in the whole country); and
- Consider the available budget to decide which foods can be analyzed individually or as food group composites (i.e. several foods of the same food group are analyzed together), and for which chemicals. This would also consider the total number of foods on the list that will actually need to be purchased, transported, prepared and analyzed.

Ideally, foods included in the TDS should enable exposure assessments to be calculated for all important subgroups of the population, such as age/gender and ethnic groups taking regional or seasonal differences into account. To do so, however, all or most food samples would have to be analyzed separately. However, as this would require a very large budget, the process of constructing a food list will be a compromise between budgetary considerations and quality of exposure data which is in general highest when analyzing mostly individual foods. In other words, the goal is to have the least number of composites of different foods in order to obtain the optimal quality of the exposure assessments.

When conducting multi-national TDS, additional difficulties and decisions are involved and a harmonized methodology needs to be developed to assure data comparability. Concerning the food list, decisions will have to be taken, if foods would be country-specific or all in common or a mixture of common and country-specific foods. However, the same criteria and considerations apply as for a national TDS.

The determination of the final list of foods to be analyzed for a TDS depends therefore mainly on: (1) the objective of the TDS; (2) the availability of food consumption data; and (3) the budget available for the TDS.

Objectives of the TDS

The objective of the TDS determines the foods to be included and whether they will be analyzed separately or as a composite sample. If the objective of the study is to estimate heavy metal exposure, all foods potentially containing heavy metals should be included. If the objective is to estimate exposure to many contaminants, the food selection has to include all foods where they can be present, i.e. the entire food supply. Another example is the population to be covered; if different age and gender groups and/or regions should be covered, more foods should be analyzed individually (not as a composite of several foods) because the consumption of foods may differ significantly among these groups and regions. If the food consumption data permits only an exposure assessment per capita or per adult equivalent at a national level, a higher degree of compositing of different foods is possible.

Availability of Food Consumption Data

For every country, food consumption or supply data (See Chap. 4 – Overview of Dietary Exposure) are essential to build a reliable food list for a TDS. Ideally, every country should investigate the food consumption of its population on a regular basis for policy and planning purposes. However, this may not be done in many countries due to lack of resources. In the absence of such data, these countries should then start by using internationally compiled food supply data for their country such as published by FAOSTAT [5] (See Chap. 4 – Overview of Dietary Exposure) or the GEMS/Food Consumption Cluster Diets [6] (See Chap. 43 – GEMS/Food Consumption Cluster Diets) for their region.

Most countries would likely have some food consumption data, either on the household level or individual data. Household Budget Surveys (HBS) provide food consumption estimates per household of foods purchased or otherwise acquired (See Chap. 4 – Overview of Dietary Exposure). These data can be divided by the number of household members, if available, to obtain food consumption per adult equivalent (i.e. adjusted for age and sex requirements [7]) or per capita. In most cases, food consumption outside the household is not recorded, leading to an underestimation of food consumption. In some cases, only the amount of money spent for food purchase is available, which needs to be transformed into amounts of foods as purchased (through food prices at the time of the survey) and then into foods as consumed through edible coefficient and yield factor (See Fig. 6.1)

Individual food consumption surveys data are derived from food frequency questionnaires (FFQ), 24-h-recalls, food records, or dietary history. They are already expressed in foods as consumed per person per day, which means that no further

Fig. 6.1 Transformation of household budget survey (HBS) food consumption data to food as consumed per person or adult equivalent

TDS food consumption - transformation to be done for HBS

Price of foods

| prices

↓

Foods as purchased in HH

| yield and edible factors

↓

Foods as consumed in HH

| factors per age and sex

↓

Foods as consumed per capita/ adult equivalent
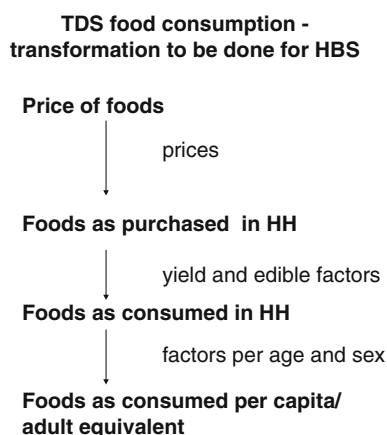
Table 6.1 Food consumption/supply data provided from different sources

	Individual food consumption surveys	Household budget survey	GEMS/food; FAOSTAT
Data quality	High	Intermediate	Low
Availability	Exist in few countries and researchers normally are reluctant to release data, except published summary data	Exist in many countries, e.g. from statistical office	Can be downloaded from the FAO and WHO Internet sites
Resources needed to carry out a survey	High	Medium	Already available on web
Data provided	Edible foods as consumed	Foods as purchased	Raw commodities (food supply data)
Disaggregation	Age, sex, bodyweight, socio-economic status, ethnicity, region, etc.	None	None
Data needed to transform	None	Sometimes prices Edible portion Yield factor Adult equivalent (AE) factors	Edible portion Yield factor
Results	Individual consumption of edible foods as consumed	Consumption of edible foods as consumed per AE	Consumption of edible foods as consumed per capita

transformation is necessary to build the TDS food list. These data, if available from a national survey, are of the best quality and should be used as a first priority. Summary information of the different food consumption/supply data is shown in Table 6.1 and more detailed information on these data and surveys is available [8].

It is appropriate to include foods and recipes in the TDS as most people do not always eat single foods, but eat them in the form of mixed dishes. Recipes can be

prepared at home or bought as such (e.g. hamburgers, restaurant meals). FFQs and 24-h-recalls normally report foods and recipes and the most common dishes could be included in the TDS. However, food supply or HBS data do not include recipes and if these data are used, it is therefore necessary to investigate how the foods to be included in the TDS food list are prepared by the population. This information can be obtained from cook books, focus group discussions, published literature, or other reports. Foods are normally prepared in a number of different ways (e.g. potatoes are boiled with or without skin, fried, mashed, deep fried as fries and chips or are roasted). Each of these may have a different contamination level, as in the case of acrylamide. The TDS investigator has therefore to decide which forms of the different foods will be included in the TDS. The options include: (1) all reported preparation methods, (2) only the single most prevalent one, or (3) the most important ones. Some select only one preparation per food, while others choose the most important ones, especially if the preparation method is known to change the contamination level.

If recipes are analyzed, it will be difficult to determine the food(s) containing the contamination. Therefore, some TDS only analyze foods and no recipes, meaning that they will add the amount of each recipe ingredients to the corresponding foods.

Sometimes, food consumption surveys do not cover the whole year and therefore, seasonal foods might not be reported or in too small amounts. Additional investigations may be necessary in this case and result in an increase in some amounts consumed.

In many countries, certain foods are fortified and some people consume vitamin and mineral supplements. Therefore, care should be taken to include these data, if available, in the study design of TDS, especially if minerals and other nutrients are to be analyzed. If this was not done, the nutrient intake could be grossly underestimated.

Data from HBS and individual consumption surveys allow the construction of a distribution curve, which is useful for more sophisticated exposure assessments. It is often necessary to purchase food consumption data from institutes or statistical departments. In these cases, the TDS convener has to communicate to the data owner which data should be extracted from the database for the population groups of interested and if possible, separated by age, gender, region and for consumers only, e.g. mean and/or median food consumption and to represent high consumers also the high percentiles, preferably 97.5th.

Budget

The bigger the budget allocation for the TDS, the more foods can be analyzed individually and the more foods per region and seasons can be investigated. TDSs usually have limited funds available and therefore have to include greater numbers of composites of different foods and/or lower numbers of chemicals to be analyzed. If the budget is insufficient, the objective of the TDS needs to be adapted accordingly, e.g. more composites of different foods and/or fewer analytes, food samples, regions, brands and/or seasons. The advantages and disadvantages of compositing samples,

and individual food versus food group composites are discussed in Chap. 9 – Food Sampling and Preparation in a Total Diet Study. It is, however, unwise to compromise on the analytical quality because low quality analytical data will jeopardize the whole TDS (See Chap. 13 – Quality Control and Assurance Issues Relating to Sampling and Analysis in a Total Diet Study). The quality of the TDS also depends on the dilution effect i.e. when compositing many foods of different concentration levels the final concentration may be under the limit of detection or quantification and the overall exposure to the chemical could significantly be underestimated.

If a broad exposure assessment to many contaminants is the main purpose of the TDS and only a limited budget is available, it will be necessary to have a greater number of composite samples for the different foods. If regional differences in exposure to one group of hazards (e.g. heavy metals) is the main objective, then more regional food samples need to be collected, but more foods may have to be composited into one sample to keep the number of analyzed foods reasonable.

It takes about 5 years (probably less for a HBS) to plan, implement and analyze a food consumption survey on individuals and significant of resources (budget and technical expertise) are required. It is therefore often better to access existing or purchase available food consumption data than to carry out a food consumption survey, even if not all of the desired data were available.

Compositing of Food Samples

The purpose of compositing foods is to retain their contribution to exposure while saving funds on the cost of analysis because fewer samples need to be analyzed. The disadvantage of compositing is that: (1) it is not possible to know the contamination of each food; (2) the dilution of the contamination of one food in the composited sample; and (3) the amounts of each contributing food in the composite are fixed for the age-gender group being considered and cannot be adapted to different consumption amounts of different population groups or regions. Compositing of foods, as mentioned earlier, is mainly guided by financial considerations. In order to obtain good analytical data for the exposure assessment, the choice of compositing could be guided by the following principles:

1. Highly consumed foods should be analyzed separately.
2. Foods with known or potentially high contamination levels should be analyzed separately for the specific contaminant.
3. Less frequently consumed foods of the same food group can be composited
4. Foods of the same food group with expected low and similar contamination can be composited.
5. Compositing of foods can be done differently for different contaminants as long as all foods are included in a composite or analyzed individually for this contaminant.
6. Compositing of foods from different regions or seasons to one national food is reasonable if the contamination is known, or thought, to be equally distributed.

7. When very limited funds are available, compositing of foods is the only means of obtaining a rough estimation of exposure, e.g. some TDSs have one composite per food group.
8. Many first-time TDS have a higher percentage of compositing because of limited funding. With time and recognition of the usefulness of the results, funding may increase and therefore the percentage of compositing may decrease.

Examples

Composite of a single food:

- 15 apples of different varieties as consumed in the population
- For 'yogurt' a mix of different yogurts: plain yogurt, with flavor, with fruits, of whole milk or skimmed milk according to the consumption pattern in the population
- Biscuits: five main brands

Composite of different foods:

- Fruits infrequently consumed, e.g. in a European country, mix of mangoes, papayas, starfruits, and lychees.
- All fruits consumed.
- Millet and sorghum composite: Mix of 40 % raw white millet + 40 % raw yellow millet + 10 % raw sorghum. The mix is then prepared in two ways: boiled couscous and porridge. Final composite consists of 50 % prepared couscous + 50 % porridge.

Practical Considerations When Constructing a Food List

The following steps could be performed (See also Fig. 6.1):

1. 'Clean' the food consumption data (e.g. disregard implausible outliers).
2. Select for each food the appropriate preparation method (as prepared by the majority of the population).
3. Select and apply appropriate edible coefficients and yield factors (to calculate food consumption for foods as consumed).
4. In a spreadsheet, such as Excel, sort the food consumption data for the entire population in descending order (most consumed foods on top of the list), add cumulative consumption in g/d and in %.
5. In a spreadsheet, such as Excel, sort the food consumption data for consumers only, if these data are available, in descending order (most consumed foods on top of the list), add cumulative consumption in g/d and in %.
6. Select foods for the TDS according to your main criteria (see criteria above).
7. Add foods not selected with the main criteria (see criteria above).
8. Put the foods into food groups.

9. Optimize the food list and decide on compositing of foods within a food group (see criteria above).
10. Decide on chemicals to be analyzed in each composited food sample.
11. Calculate costs for sampling, transportation and analysis of foods and of other costs.
12. Compare costs with available budget.
13. Adjust the number of foods and composited foods as required.

Useful Resources

Examples of food lists are found in the publications of national TDS reports or in the corresponding scientific articles. The following resources provide useful guides to food nomenclature and yield factors and edible coefficients, as well as on the new EFSA/FAO/WHO guidance document on TDS [4] and the accompanying document describing selected TDS studies [3].

Food Nomenclature

LANGUAL – The International Framework for Food Description. Available at http://www.langual.org
INFOODS – Food Nomenclature. Available at http://www.fao.org/infoods/infoods/standards-guidelines/food-nomenclature/en/
Langual Food Description Thesaurus and the Food Product Indexer. Available at http://www.langual.org/langual_food_product_indexer_database_2012.asp

Yield Factors and Edible Coefficients (see http://toolbox.foodcomp.info/ToolBox_RecipeCalculation.asp)

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Chapter 7
Selecting Chemicals for a Total Diet Study

Jiri Ruprich

Introduction

Depending on political, economic, or cultural practices and traditions, societies may have different perceptions regarding the selection of priorities in relation to the protection and promotion of health. In most societies, responsibility for protecting public health from potential hazards in the food supply is delegated to food safety risk managers who are advised on these matters by risk assessors. Chemical hazards, in addition to microbiological and physical hazards, are perceived as prime objectives of such food safety agencies. Presently, the assessment of health risks, including exposure assessment, is considered the primary basis for national and international regulation of food [1]. However, selecting priorities for laboratory analysis may not be a simple scientific matter. Depending on the situation in the country, regional unions of countries or international communities, the decision may be influenced by the following factors:

- Size of the food trade, including imports and exports, and the ability of the food safety agency to effectively regulate it
- Political will and resources to address the problems associated with food safety and security
- Political will and resources to address nutritional deficiencies, poor quality of foods, and harmful dietary choices of individuals and groups in a given population
- Preparedness of key stakeholders to recognize and respond to robust scientific results, even when they are not desirable
- Knowledge of the health problems in the population or groups associated with unusual dietary patterns

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- Adequate technical facilities and capable personnel to enable high-quality laboratory analyses
- Financial support for long-term exposure assessment studies to assess trends in exposure

When ranking chemical hazards, the initial tendency is to focus on the inherent acute and chronic toxicity of substances and their potential to adversely affect public health. But nutritionally important chemicals in the diet also need to be considered because their deficiency or excess can also cause significant health problems. Therefore, a critical analysis of health statistics for a given population should be undertaken as the first step in the selection of chemical hazards. Epidemiological studies [2] linking disease outcomes with particular chemicals can help to narrow objectives and more effectively target available resources when a total diet study (TDS) is planned.

Chemical Agents in Food

Foods are basically composed of complex mixtures of chemical substances, from simple inorganic compounds (e.g. water and salts), to extremely complex organic compounds (e.g. proteins and macromolecules). Most chemicals in food are considered healthy and beneficial and some are considered essential (e.g. micronutrients such as copper, iron, iodine, and selenium), while other chemicals may be intentionally added to foods (e.g. preservatives and colors). Foods may contain chemical residues after being deliberately applied at other points in the food production chain (e.g. pesticides and veterinary drug residues), or chemicals from the environment may also contaminate food at various points, such as mercury, lead, polychlorinated biphenyls (PCBs), and dioxins. Some contaminants occur naturally, such as mycotoxins and certain alkaloids. Chemical contaminants can also be formed in food due to processing (e.g. polyaromatic hydrocarbons (PAHs) and acrylamide), or are transferred from food packaging or food contact materials, such as phthalates and bisphenol A. Finally, there are chemicals that are illegally added to food, such as melamine and certain unapproved additives and colors. The universe of potentially hazardous chemicals is perhaps daunting given that there is very little information about many of the more than 100,000 chemical substances in common use [3]. In reality, however, there are only about 300–500 chemicals that are of main concern for food safety authorities. This is nonetheless a long list, especially for a country just starting to undertake a TDS. Therefore, the development of chemical priorities is an important exercise that should be undertaken by risk managers in close consultation with risk assessors and with the involvement of all key stakeholders.

Differing priorities can be set for monitoring of chemicals in foods with the potential to harm health or affect the nutritional status of the population. Such monitoring usually targets pesticides, industrial contaminants, heavy metals, and mycotoxins. A special program may also be established for monitoring of radionuclides. The globalization of food trade has raised the demand for monitoring of other chemicals which are not usually expected in foods. An example is melamine, which

was used to fraudulently disguise the protein content of food. Other toxic substances are being discovered in foods that were previously not expected to be present, such as acrylamide in cereal products and furans in canned foods. Another focus of food monitoring programs is on chemicals beneficial to human health, such as omega-3 fatty acids. If included, such results can then be used for weighing the risks and benefits of certain diets [4]. Attention has focused also on monitoring of some important nutrients such as sodium, iron, vitamin A, iodine and folic acid. Antinutrients such as trans fatty acids are also becoming noteworthy.

Criteria for Setting Priorities

A TDS is usually tailored to include the analysis of staples and other key foods, which comprise the usual diet of the population or subgroups [5] in the country as a whole, or in defined regions. Chemical analyses are conducted after preparing food ready-to-eat. If the TDS includes a cross section of all major items of the diet (usually representing more than 90–95 % by weight of a typical diet), this will by necessity require analysis of a large number of different food samples. For this reason and the need to have TDS methods capable of measuring down to extremely low limits of detection, the costs of TDS analyses can be significant. If analytical costs need to be reduced, foods can be combined into individual composites and/or different foods aggregated into mixed food group composites (see Chap. 5 – Scope, Planning and Practicalities of a Total Diet Study and Chap. 9 – Food Sampling and Preparation in a Total Diet Study). The disadvantage of such composites is that the ability to trace high results to individual samples of food is lost and more generally, estimates of the variability in the occurrence of chemicals is not possible. These cost considerations need to be factored into the selection of priorities, especially for those contaminants that are expensive to analyze, such as dioxins.

Sampling of food to some extent determines the chemical substances to be quantified within a TDS. For example, aflatoxins require each sample to weigh 20 kg, which is not only expensive, but also a challenge to equipment when this amount needs to be homogenized to a fine powder. The common methods of sampling in a TDS are especially useful for chemicals that are present in measurable concentrations in most foods or certain categories of foods. An example might be the presence of certain heavy metals, such as lead and cadmium, which have measurable concentrations in a wide range of foods. Conversely, if a chemical of interest is found only in a limited number of specific foods, especially minor foods on a weight basis in the total diet, it may prove unreliable to use the routine TDS food sampling scheme. By way of example, when the diet is monitored for methylmercury in a small number of food samples involved in the TDS sampling plan, some countries may inadvertently distort their exposure estimates because they fail to select some specific foods high in methylmercury (e.g. fish/seafood) because their consumption may not be normally distributed in the population and the upper percentiles of high consumers is easily neglected.

A possible technical approach for the systematic selection of priority chemical hazards in a TDS is to use a scoring system. These systems are based on predetermined criteria of selection, such as the character of the toxic effect, expected range of exposure, known data gaps, international recommendations, technical feasibility of analyses, stakeholder interest, and economic factors, where every criterion has its own numeric scale of weighting, such as 1–5 or 1–10. A panel of selected stakeholder representatives then evaluates the potential list of chemical hazards, taking into account the criteria for evaluation and the justification to assign numerical values for each factor. A total summation can then help inform the final decision-making process. Use of this approach to select priorities for chemical hazards is, however, likely to be somewhat varied around the world. In general, selection of priority chemical hazards in a TDS has often been based on two basic criteria:

Chemicals Recognized as Health Risks to the Population

Chemicals selected as priorities under these criteria are those for which the evaluation of toxicological information and exposure data indicate a potential public health risk. The risk assessment may be carried out by another country or international body, e.g. Joint FAO/WHO Expert Committee on Food Additives, Joint FAO/WHO Meetings on Pesticide Residues, or the European Food Safety Authority. If the chemical occurs in specific foods, control measures for those foods are usually established at the national, regional, or international levels, such as guideline or action levels and maximum limits. In most cases, the public has at least a basic understanding of the need to control these chemical hazards. The TDS can verify the effectiveness of risk management measures, provide information on dietary exposure trends, and direct risk communication with stakeholders. Many long-established hazards with well-characterized risks are usually selected according to these criteria, including heavy metals, PCBs, radionuclides, and pesticide residues.

Chemicals Recognized as Highly Toxic, But Exposure Is Uncertain

In this case, chemicals are selectively prioritized because of their toxic profile, but unknown or little known total dietary exposure, including in foods that are may be significant contributors to exposure. Often these chemicals have been classified as genotoxic and carcinogenic, which would suggest low thresholds of safety or tolerance. At times, these chemicals come to wide media attention because of outbreaks of human disease or mortality. Therefore, the criteria to prioritize these chemicals are similar to those used for "hazard identification" in that the risk assessors and risk managers are required to take decisions based on incomplete data and where economic, political, and cultural factors may also play a role. Examples include acrylamide and melamine.

Recommendations for Priority Chemicals

As it is essential for planning, TDS experts meeting in Brisbane in 2002 prepared a list of recommended priorities for total diet studies [6], which included the corresponding foods in which the chemicals were likely to occur. In 2006 at another expert meeting in Beijing, additional chemicals were included on the list [7]. At this time, these priority chemicals reflect the best advice of TDS practitioners around the world and should be given due consideration in developing a priority list for any TDS (see Table 7.1). It should be noted that besides this comprehensive priority list, TDS experts have also produced a core list and an intermediate list for countries with fewer resources or who are just beginning their TDS programs [7].

Table 7.1 Priority chemicals for total diet studies

Group	Contaminant
Pesticides	*Aldrin*
	DDT (total)
	o,p′-DDD
	p,p′-DDD
	o,p′-DDE
	p,p′-DDE
	o,p′-DDT
	p,p′-DDT
	Dieldrin
	Endosulfan (total)
	Endosulfan
	Endosulfan epoxide
	Endrin (total)
	Endrin
	Endrin ketone
	Hexachlorocyclohexane (HCH) (total)
	Alpha-HCH
	Beta-HCH
	Gamma-HCH
	Hexachlorobenzene
	Heptachlor (total)
	Heptachlor
	Heptachlor-epoxide
	Diazinon
	Fenitrothion
	Malathion
	Parathion
	Methyl parathion
	Dithiocarbamates (total) (as CS_2 equiv.)
Heavy metals	*Cadmium*
	Lead
	Methylmercury
	Arsenic (inorganic)

Table 7.1 (continued)

Group	Contaminant
Industrial chemicals	*Polychlorinated biphenyls* (PCBs) (total expressed in WHO TEFs)
	Marker PCBs
	IUPAC No. 28
	IUPAC No. 52
	IUPAC No. 101
	IUPAC No. 138
	IUPAC No. 153
	IUPAC No. 180
	Polychlorinated Dibenzodioxins (PCDDs) (total expressed in WHO TEFs)
	2,3,7,8-TCDD
	1,2,3,7,8-PeCDD
	1,2,3,6,7,8-HxCDD
	1,2,3,4,7,8-HxCDD
	1,2,3,7,8,9-HxCDD
	1,2,3,4,6,7,8-HpCDD
	1,2,3,4,6,7,8,9-OCDD
	Polychlorinated Dibenzofurans (PCDFs) (total expressed in WHO TEFs)
	2,3,7,8-TCDF
	1,2,3,7,8-PeCDF
	2,3,4,7,8-PeCDF
	1,2,3,6,7,8-HxCDF
	1,2,3,4,7,8-HxCDF
	1,2,3,7,8,9-HxCDF
	2,3,4,6,7,8-HxCDF
	1,2,3,4,6,7,8-HpCDF
	1,2,3,4,7,8,9-HpCDF
	1,2,3,4,6,7,8,9-OCDF
	Polychlorinated Biphenyls (PCBs) (total expressed in WHO TEFs)
	Mono-ortho PCBs
	IUPAC No. 105
	IUPAC No. 114
	IUPAC No. 118
	IUPAC No. 123
	IUPAC No. 156
	IUPAC No. 157
	IUPAC No. 167
	IUPAC No. 189
	Non-ortho PCBs
	IUPAC No. 77
	IUPAC No. 81
	IUPAC No. 126
	IUPAC No. 169

(continued)

Table 7.1 (continued)

Group	Contaminant
Mycotoxins	*Aflatoxins* (total)
	Aflatoxin B_1
	Aflatoxin B_2
	Aflatoxin G_1
	Aflatoxin G_2
	Patulin
	Fumonisin B_1
	Ochratoxin A

Conclusions

The selection of priority chemical hazards to be studied by TDS should be based not only on available scientific information concerning risk, but should also reflect the perceptions and concerns of the society. The technical feasibility of doing the analyses (capability and capacity) and ability to include the desired chemical priorities within budgetary constraints may also be key factors. Ultimately, priorities selected through an open and transparent communication process will serve to make the TDS more useful and valuable for all stakeholders.

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Chapter 8
Preparing a Procedures Manual for a Total Diet Study

Janice L. Abbey, Christel Leemhuis, and Carolyn Mooney

What Is a Total Diet Study Procedures Manual?

A total diet study (TDS) procedures manual is a document which specifies the roles of all relevant personnel participating in the study in relation to management, purchasing, preparing and storing of food samples for analysis. It is an important part of quality assurance and quality control (QA/QC) in a TDS and is an adjunct to good laboratory practices (GLP), which is the responsibility of the analytical laboratory. The manual provides detailed direction to sampling officers in collecting, handling and shipping of food samples, the types of foods, the total amounts of each food required and to sample preparers in preparing, storing and transporting of samples prior to analysis. It can help clarify critical aspects of a TDS, and reduce ambiguities and uncertainties in food sampling and preparation, leading to a more uniform and robust approach in the TDS. For example, sample variation among sampling officers within a country can, to a certain extent, be managed by careful adherence to the procedures manual. This is particularly important if food samples are collected from more than one region in a country or over more than one season. Therefore, this manual is designed as a reference tool for sampling officers, sample preparers and laboratory analysts as well as for TDS liaison officers who are responsible for coordinating the TDS sampling at the state/provincial/municipal levels. It is useful for planning and training prior to the TDS and for guidance during the TDS. It can also be used to identify any areas for improvement for the current TDS, as well as for future studies. It is a dynamic document that should be updated

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with any changes in personnel or procedures by an authorized person, usually the TDS project manager. It also ensures that valuable experience with TDSs is not lost and the associated intellectual capital in TDS procedures is secured over time.

When Is a TDS Procedures Manual Prepared?

It is important that the procedures manual and its associated Standard Operating Procedures (SOPs) contained therein are prepared before the TDS commences. Given the complexity of a TDS, preparing the manual in advance of the study will ensure that all aspects in regard to sampling, food preparation and handling have been addressed. In addition, a single consistent document outlining these procedures will enhance consistent performance by the different participants ensuring a robust and quality study.

How to Develop a TDS Procedures Manual and What Does It Include?

For a country undertaking their first TDS, the procedures manual should be drafted based on a TDS procedures manual that had already been developed in another country, preferably a country with experience in conducting TDSs. That manual should then be adapted using the collective knowledge of key members in the TDS management team (see below). It should then be distributed for comment to key end users (liaison officers, sampling officers, sample preparers and analysts) and designated stakeholders to ensure that all key components are correct and clear.

In developing a procedures manual, it is important to have already determined:

- Who will need to participate in the study and what are their roles?
- What are the types and nature of foods that will be sampled (see Chap. 6 – Preparing a Food List for a Total Diet Study)?
- What is the full list of analytes (see Chap. 7 – Selecting Chemicals for a Total Diet Study)?

These are essential elements of the study to be clarified prior to the development of the procedures manual, as it affects the type of information included in the manual, including sampling, preparation and handling requirements for the different food samples.

Total Diet Study Management Team

At the beginning of organizing a TDS project, it is important to form a TDS management team including all key personnel. Led by the TDS project manager,
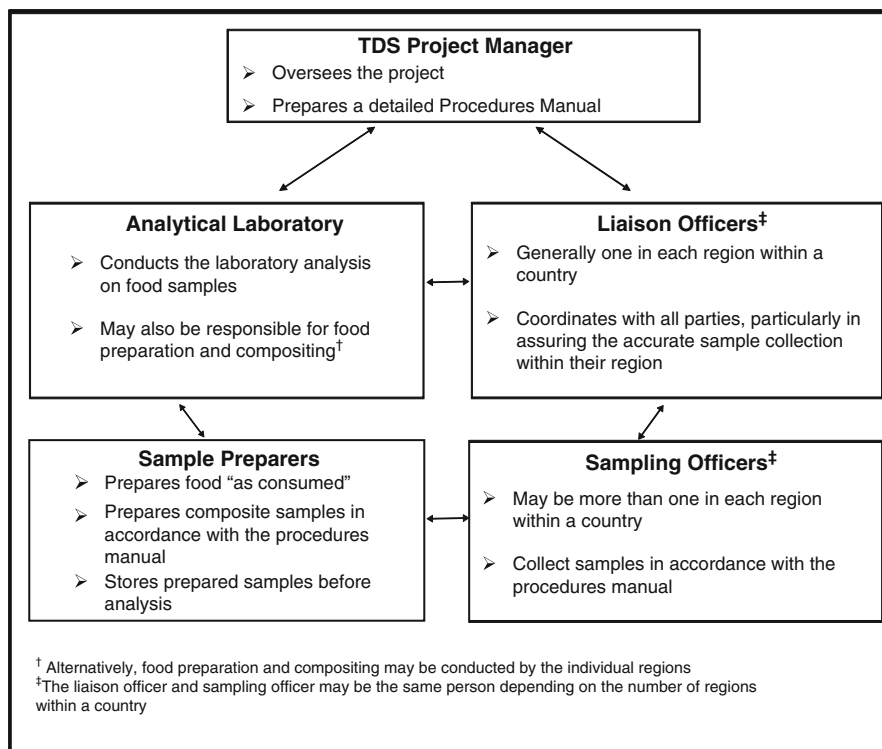
Fig. 8.1 The role of the participants in a TDS

members should include representatives of sampling and liaison officers, sample preparers and the analytical laboratory. Therefore, the first part of the procedures manual should include the identification of all TDS personnel and their contact information. A clear statement defining their roles and the responsibility of each participant should be included and is important to ensure all requirements are met. For example, in Australia, Food Standards Australia New Zealand (FSANZ) manages and coordinates the Australian TDS, however a total of eight distinct regions within Australia (states and territories) participate by purchasing food samples, which are forwarded directly to the analytical laboratory for sample preparation and analyses. Alternatively, food preparation and compositing may be conducted by the individual regions and forwarded to a central laboratory for analysis, or all activities (sampling, preparation and analysis) may be conducted in the regions and results forwarded to a central point for collation, assessment and report writing.

As there are a number of participants involved in the study, it is important that the roles and responsibilities of each participant are clearly communicated in the beginning. The complexity and flow of information between the various participants in a TDS is represented in Fig. 8.1. It is important that lines of communication are unambiguous and well understood.

Sampling

Purchasing Instructions for Food Samples

The procedures manual should contain specific instructions on the samples to be purchased for each region/country. This manual is designed so that all of the manual, or the relevant parts of it, can be taken with the sampling officer at the times of sample collection. Therefore it is imperative that the specific food types (where applicable) and total amounts for all analyses are stipulated. There are a number of factors which influence sample purchasing, such as the:

- Sampling period and purchase dates
- Sampling regions, districts or suburbs
- Retail outlets where samples are collected
- Foods to purchase
- Range of brands/use by dates/batch numbers

For additional information, please refer to Chap. 9 – Food Sampling and Preparation in a Total Diet Study.

Using Samples for Additional Analysis

As the TDS collects a wide variety of foods common to the typical diet, these representative foods can be used in additional exposure survey activities (see Chap. 51 – Polybrominated Diphenyl Ethers in Food in Australia—An Additional Use of the Australian Total Diet Study). This should preferably be decided prior to sampling and additional amounts of each food collected to account for the extra analyses. In this case, the buying instructions may need to specify particular retail outlets, the exact brands/varieties or types of the food that must be purchased, particularly if this additional data is to fill specific data gaps.

Sampling Instructions

Specific sampling instructions outlining the product to be sampled, the number of purchases for each region and the amount to be purchased in grams/milliliters or kilograms/liters should be included in the procedures manual. Additional comments can be included to guide the sampling officer in selecting specific brands or avoiding certain forms of the food. An example for almonds and apples is presented in Box 8.1.

Recording Purchase Information

Accurate documentation of all samples purchased for the study is important to ensure that comparable samples are collected in regions and for duplicate analysis

Box 8.1

Almonds
Three purchases in total from each designated region in each designated sampling period.

Each Purchase: One Packet, 300 g minimum.

Comments: Any brands including House Brands. Do not purchase blanched, flaked or slivered almonds, or almonds in shell. The almonds should be shelled but still have their skin.

Sometimes these are described as 'raw'.

Apples
Three purchases in total from each designated region in each designated sampling period.

Each Purchase: Minimum weight 500 g.

Comments: Include a number of varieties: Pink Lady, Fuji, Jonathans, Gala, Bonza, Red Delicious, Golden Delicious, Granny Smith and any other commonly available variety.

if necessary. While the primary purpose of the TDS is to estimate dietary exposure to contaminants, nutrients, additives, pesticide and veterinary drug residues and assess the risk to public health and safety, results can also inform about potential areas for further investigation in relation to compliance with the relevant regulatory limits. Therefore, detailed information for each food purchase should be recorded. This is facilitated by using an appropriate spreadsheet program. The multiple purchases of each food should be clearly identified in the spreadsheet and labeled (e.g. A, B, C etc.). For each purchase of the same type of food (e.g. A, B and C), the following information must be recorded:

- Variety/brand (e.g. Pink Lady apples, cherry tomatoes)
- Batch/lot number/expiry date (where applicable)
- Country of origin
- Purchase date
- Store/location of purchase

An example of the type of information to be recorded is shown in Table 8.1.

As there may be more than one region involved in the collection of food samples, the procedures manual should provide an appropriate template which can be completed as samples are purchased. This assists in the consistency of sample recording between sampling officers in different regions. Such a template also simplifies the merging of information from different sampling periods. Accurate recording at the time of sample purchase is particularly relevant for foods that are purchased unlabeled such as fruit and vegetables, or meats from a delicatessen.

Table 8.1 An example of the level of detail of total diet study sample information that could be recorded

Food	Purchase ID	Variety/brand	Batch/Lot no./ expiry date (if applicable)	Country of origin	Buying date (d/m/y)	Store name/ suburb
Apples	A	Pink Lady	N/A	Australia	22/8/07	Griffins Foods, Auckland
Apples	B	Royal Gala	N/A	Australia	22/8/07	Green Grocer, Christchurch
Apples	C	Delicious	N/A	Australia	24/8/07	Speight's, Wellington
Peanut butter	A	Mark and Spencers	23 JUL 08	Australia	22/8/07	Marks and Spencers, Auckland
Peanut butter	B	Skippy	178955553	USA	22/8/07	Richard's Market, Christchurch
Peanut butter	C	All Black	KW00009	New Zealand	24/8/07	Kiwi Minimart, Wellington

If resources permit, sampling officers could be provided with laptop computers to record the sampling information, which can then be forwarded electronically to the sample preparation facility. If not, a standard copy of the sampling spreadsheet template should be provided to sampling officers in hard copy and/or in electronic form. Some information will need to be recorded at the time of purchase, such as variety and country of origin of unpackaged foods (e.g. fruit and vegetables). It is important that the sampling spreadsheet is completed fully and accurately by the sampling officer. A hard copy of the completed sampling spreadsheet should be sent with the corresponding food samples.

Another option for recording sample information is to photograph the products. This could be done by either the sampling officer or the sample preparation facility/laboratory. Photographs would be taken in addition to recording information on the sampling spreadsheet and could serve as a more detailed record of the products. For example, in addition to brand name and country of origin which are recorded on the sampling spreadsheet, other information such as manufacturing details, ingredients and nutrition panel information could be captured. If photographs are to be taken, it is suggested that a color digital camera be used for this purpose. Also, more than one photograph may be needed per product to capture all the required information. For fresh products, photographs could be taken by the sampling officer with sample information recorded on a sign which is photographed with the product.

Transportation of Food Samples

Prior to sample collection, suitable sample containers, transportation containers and ice bricks, if required, should be obtained. Consultation with the analytical laboratory as to the most appropriate containers and types of transportation is advised.

For sensitive samples, laboratories may even coordinate the delivery of sample and provide transportation containers and ice bricks to the liaison officers in each region.

Only foods that are purchased in an unpackaged state (e.g. cold meats from a delicatessen) need to be placed in sample containers. All other foods should be sent in unopened original packaging to the sample preparation facility/laboratory to ensure the integrity of the product and avoid any cross-contamination. The liaison officer should organize secure storage for the sample and transportation containers and ensure they remain free of contamination and are not used for any purpose other than the TDS.

Transportation containers should be packed in a manner that ensures the perishable samples are maintained in a chilled or frozen state. Samples are to be placed in the transportation containers with sufficient packing material so that the samples are not damaged. Packing material such as newspaper or polystyrene chips around the samples would assist with this. A list of the purchasing information should accompany the samples upon dispatch to the analytical laboratory.

Sample Preparation

There are a number of aspects to consider regarding sample preparation, some of which are discussed below while others are discussed in Chap. 9 – Food Sampling and Preparation in a Total Diet Study.

Handling Purchases for Food Preparation

Each purchase provided by the sampling officer should arrive at the sample preparation facility in separate packaging. Purchases from each region will be in certain number lots specified by the project manager. Each purchase will represent a primary sample. Unprocessed, raw foods, such as steak and chicken fillets, will be in separate packages clearly labeled with the name of the food and primary sample identification code which will correspond with the detailed information on the spreadsheet completed by the sampling officer. The sample spreadsheet should be checked by the preparation facility for completeness and to ensure that recorded information corresponds to sample labels.

General Food Preparation Instructions

As storage and preparation of food are known to affect the concentration of some chemicals in food, an analysis of foods prepared 'as consumed' will result in more accurate estimations of dietary exposure. As a variety of foods are collected for the TDS, some samples will require preparation to an 'as consumed' state such as peeling (e.g. oranges or bananas) or cooking prior to analysis (e.g. beef and chicken).

In the USA, sample preparation is conducted in a dedicated TDS kitchen using the same utensils and equipment. Simple food preparation may be conducted by sampling or liaison officers in the regions and prepared samples forwarded directly to the laboratory for analysis, or alternatively, can be completed by the laboratory conducting the analyses. Preparation by a single sample preparation facility/laboratory offers the advantage that it can control for variations in preparation among different regions and between sampling periods. However, for some countries, cooking styles or recipes may be quite different in the regions and regional preparation may be preferred. In either case, specific instructions should be detailed in the procedures manual as to general handling of food samples prior to and following preparation, as well as detailed instructions on how each individual food type should be prepared. These instructions should be clear, defining all terms such as frying, boiling and washing. While these preparation procedures seem straight forward, there are small differences in how individuals would carry this task out. For example, in frying a food, should oil be used? Questions such as this should be pre-empted and specific guidance provided in the procedures manual glossary.

Procedures Manual Glossary

A brief glossary defining generic terms used in the procedures manual is important to ensure consistency in sample preparation. Cooking practices involving boiling water, frying, grilling, washing, microwaving and mixing can be widely interpreted by individuals. Therefore specifying what these terms mean will assist in controlling variation in the preparation methods. The glossary of terms should be developed under the supervision of the TDS project manager and should be specific to the country's food preparation practices.

Preparing Food Samples for Analysis

Primary samples (individual purchases) should first be prepared in their 'as consumed' state. For some samples this may require cooking. In preparing foods for TDS analysis, it is imperative that preparation instructions are followed exactly and that any deviation be carefully documented. For example, any juices from fruit are regarded as an integral part of the food being prepared for analysis. However, the proportional amount of juice and seeds (for fruits where seeds are typically eaten) must therefore be included in the sample containers. An example of preparation requirements for some typical foods consumed in Australia is demonstrated in Table 8.2.

Once food is prepared to an 'as consumed' state, it is important that the sample remains homogeneous and does not separate out. This is particularly important for liquid samples. Therefore, all samples should be mixed well to ensure the sample is homogenous prior to transfer to sample containers for storage. For each sample, a sufficient amount of the prepared primary sample should be retained in an amount which would allow for additional analyses if required.

Table 8.2 The preparations required for some foods which are not purchased in an "as consumed" state

Food	Preparation instructions
Apples	Remove core and stem (do not peel)
Bacon	Remove rind and dry fry
Bananas	Remove peel
Beans, green	Top and tail, remove string if necessary and microwave until just cooked
Broccoli	Remove stalk and microwave
Chicken breast	Grill and discard fat in grill tray
Eggs	Hard boil for 5 min in unsalted tap water and remove shell
Lamb chops, loin	Grill. When cooked, cut all the meat away from the bone and trim off excess fat. Discard the bone and fat in the grill tray
Pasta	Boil in tap water according to the instructions on the packaging (do not add salt)
Potatoes	Wash, peel and boil in unsalted tap water

Preparing Composite Samples for Analysis

As multiple samples of the same food types may be collected in one region, it may be necessary to combine a portion of each purchase to produce 'composite samples' (see Chap. 9 – Food Sampling and Preparation in a Total Diet Study). Compositing of individual samples should be done only after preparatory work (e.g. peeling or cooking) on individual purchases is complete and they are in an 'as consumed' state. If composite samples are to be prepared and analyzed, this should be repeated for each primary sample (individual purchase) in the composite sample. The composite sample should be labeled with a unique identifier that will definitively link to the primary sample information recorded by the sampling officer. The contrast of individual versus composite sample preparation and analysis is depicted in Fig. 8.2.

To prepare composite samples, the number of primary samples (individual purchases) to be combined in the composite must be known and is specified in the procedures manual. In determining the number of primary samples used to make a composite sample, it is worth noting that compositing samples eliminates the possibility of determining variations in analyte concentration among the individual samples. The larger the number of primary samples included in one composite, the less likely a sample with a high level will be detected. Therefore the number of individual samples to be combined into one composite must be carefully considered. For example, if nine individual purchases are combined into one composite, each primary sample contributes 1/9th of the final volume and therefore each sample is diluted one in nine (Fig. 8.3a). In contrast, if nine individual purchases are split into three groups of three individual samples and one composite is only made up of three individual purchases, then each primary sample contributes 1/3rd of the final volume and therefore each sample is diluted one in three (Fig. 8.3b).

Composite samples should be prepared by accurately measuring the minimum amount required of each primary sample and combining in a vessel for further mixing or blending. Solids and semi-solids should be weighed (grams/kilograms) and
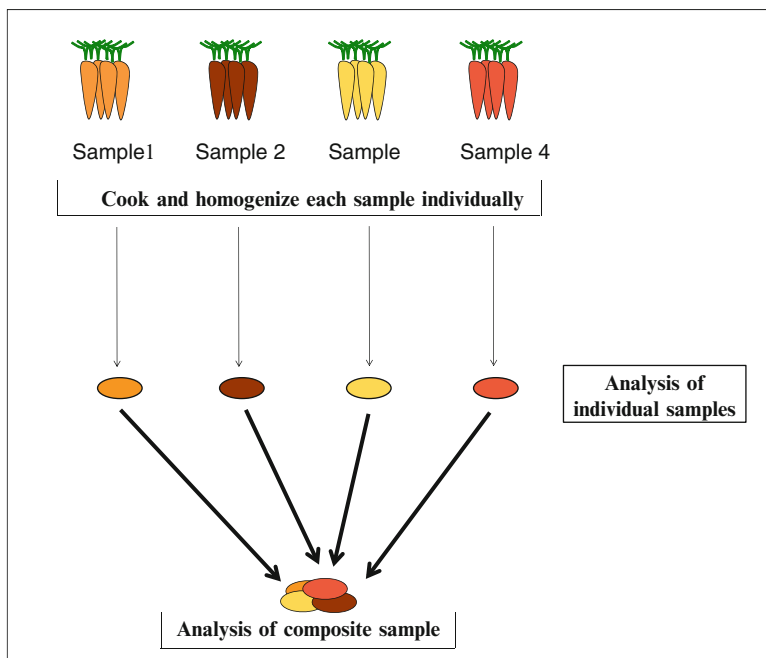
Fig. 8.2 A comparison of the preparation and analysis of individual and composite samples

liquids measured by volume (milliliters/liters). For example, if a composite was made up of three individual samples (primary purchases), the minimum amount of each sample would be one third of the total amount required for the composite sample allowing for some wastage. An example for fruit juice is depicted in Fig. 8.4, where 300 ml of fruit juice is required for triplicate analysis for each analysis. This would require at least 100 ml of each primary sample ('purchase') of fruit juice to prepare the composite sample.

Once all of the primary samples are added together, the composite sample should be homogenized or mixed thoroughly to ensure the sample is homogeneous. Sometimes homogenization maybe needed prior to compositing if the primary sample is not uniform (e.g. a hamburger). If the sample is a liquid, it should not be allowed to separate before compositing. The composite sample should be transferred to a suitable sized labeled storage container, with enough sample to allow for all the analytical tests specified as well as one repeat analysis of each specified test. This may also include a sufficient amount for one inter-lab check test if required. The container should be labeled in a way that the composite sample can be definitively linked to its three constituent primary samples and the analytical results.

Unused composite samples should be stored for a period of time that is agreed upon between the project manager and the analytical laboratory, after completion of the study. This period of time should be documented in the procedures manual, as well as in the contract with the laboratory (see Chap. 14 – Commercial Analytical Laboratories—Tendering, Selecting, Contracting and Managing Performance).
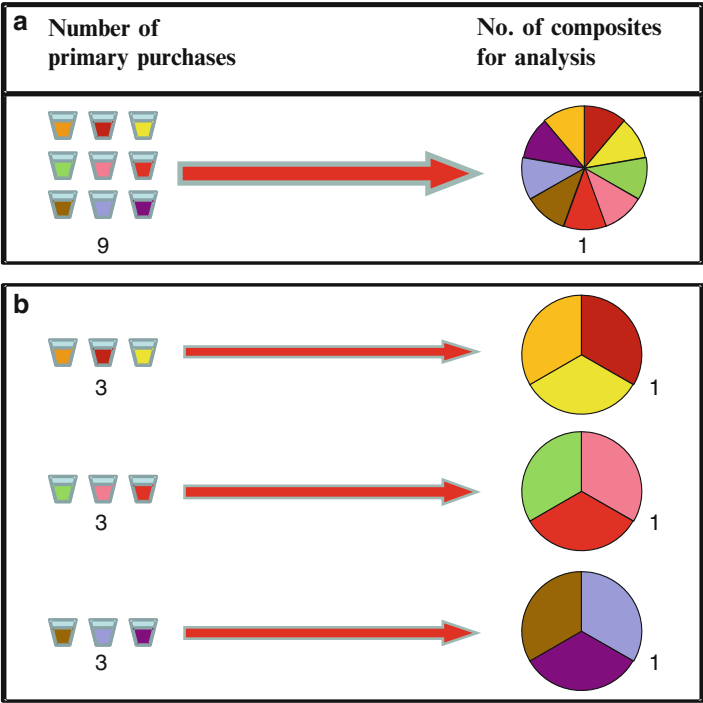
Fig. 8.3 A comparison of the proportion each primary sample contributes to a composite sample

General Instructions for Handling Individual and Composites Samples

General instructions including precautions to take when handling individual and composite samples and any specific washing instructions for reusable equipment should be included in the procedures manual. Issues to consider include:

- Avoiding cross contamination
- Carefully selecting the equipment and utensils used for food preparation
- Gloves
- Washing of equipment used in preparation

Additional information on these aspects are available in Chap. 9 – Food Sampling and Preparation in a Total Diet Study.

Storing Prepared Samples

Prepared samples should be stored in sealed sample containers that are clearly marked with identifying numbers that correlate with the sample recording on the sampling

Individual samples

Purchase 1   **Purchase 2**   **Purchase 3**

FRUIT JUICE A   FRUIT JUICE B   FRUIT JUICE C

100 mls   *100 mls*   *100 mls*

Fruit Juice composite 300mls†

†Volume required for triplicate analysis for each screen/analyte
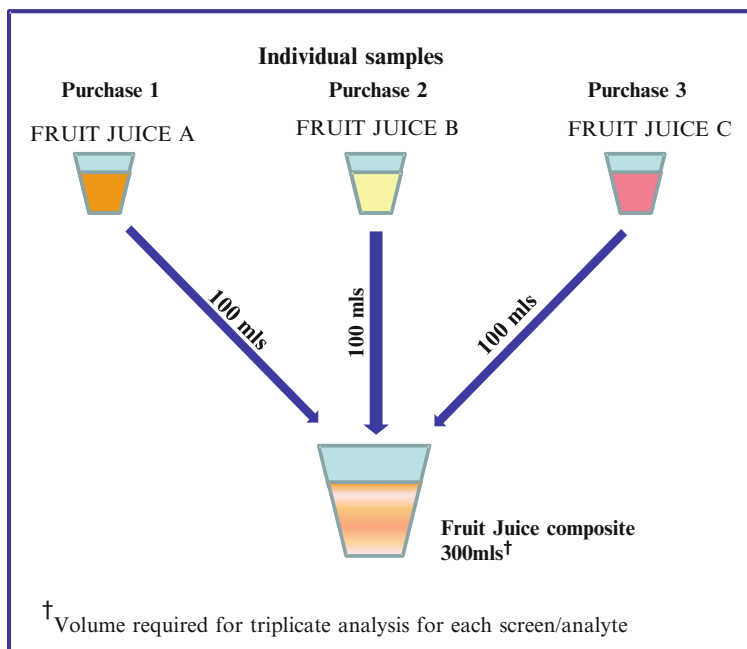
Fig. 8.4 An example of the preparation of a composite sample

spreadsheet. Samples should be stored in a manner that does not compromise the integrity of the sample as it may be required for further analysis. Advice from the analytical laboratory should be sought as to the best storage conditions for the food samples noting that some samples may have temperature or light sensitivities.

Conclusion

Total diet studies typically have a large number of people involved in the study and potentially from a number of regions within a country. Consistency in sampling and preparing foods is essential to reduce variability in the study, and also enable more effective comparisons between studies. Therefore the accuracy and comprehensiveness of the procedures manual is critical as it influences the manner in which food samples are purchased, handled, prepared, and stored before analysis. These decisions can influence the quality and representative nature of the entire total diet study.

Chapter 9
Food Sampling and Preparation in a Total Diet Study

Richard W. Vannoort, Janice L. Abbey, Christel Leemhuis, and Carolyn Mooney

Introduction

A key characteristic of a total diet study (TDS) that differentiates it from food commodity or other exposure assessment surveys is that the foods are analyzed for chemicals of interest after the foods are prepared as normally consumed. By this means, a TDS provides the best estimates of consumer exposures and therefore, potential health risks. To do this effectively, the foods in a TDS first need to be adequately sampled, and then appropriately prepared prior to analysis.

Sampling in a Total Diet Study

In planning the sampling of foods in a TDS, one needs to consider **which** foods to sample, **who** should sample them, and **when**, **where** and **how** they should be sampled. A budget should be set aside for sampling, which includes the cost of the samples, sampling equipment and supplies, and the time of the person doing the sampling. To ensure consistency in TDS food sampling, it is important to have details documented by Standard Operating Procedures (SOPs) and consolidated in a procedures manual (see Chap. 8 – Preparing a Procedures Manual for a Total Diet Study).

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Table 9.1 Number of total diet study foods of selected countries and their population

Countries	Population (million)	Number of TDS foods
New Zealand	4.4	123
Australia	21	92
Czech Republic	10	108
UK	61	119
USA	304	285

Which Foods Should Be Sampled?

The food list for a TDS should identify the most commonly consumed foods in the general population. Some foods may also be included which are relevant only to specific population subgroups (e.g. infants, vegetarians, etc.), or are foods of interest because of their potential contaminant content (e.g. heavy metals in liver and shellfish). Food consumption patterns change over time and among cultural groups, so the food list will need to be revised and regularly updated, ideally before each TDS.

There is no hard and fast rule about how many foods should be in a TDS food list. However, if a country is planning its first TDS, then it is advised to limit the food list to about 50 foods or food groups to simplify logistics. This should also enable resources to be used elsewhere in the TDS.

In New Zealand, which has a population of approximately 4.4 million (4.4 m) people, the 2009 New Zealand Total Diet Study (NZTDS) food list contained 123 foods, of which 112 represent those foods most commonly consumed in New Zealand, the remaining 11 foods covered specific subgroups, such as infant foods, children's snack foods, shellfish and offal [1]. By way of comparison, other countries which have completed multiple TDSs have adopted the following:- the Czech Republic had 108 foods in its TDS food list [2], Australia included 92 foods in its 23rd Australian TDS (ATDS) [3], the UK investigated 119 foods combined into 20 food groups for analyses [4], and the USA had 285 TDS foods [5]. However, the population of a country does not necessarily correlate with the number of food items (Table 9.1).

In organizing a food list for sampling, each food should be identified with a unique 'searchable' identifier, usually an alphanumeric code. It is also useful to identify if foods are '*National*' or '*Regional*', as these have implications for sampling sites. '*National*' foods are defined as being manufactured in one or a few sites but are distributed nationally. This would also include imported foods. 'Regional' foods are defined as those that are produced locally or regionally and may be expected to demonstrate variations in their levels of agricultural chemicals, contaminants and/or nutrients. 'Regional' foods often include meat, milk, breads, fruit, vegetables, and take-aways.

In addition, the TDS food list may also be grouped based on the different food types, i.e. grains, dairy, fruit, etc. Groupings will depend on the TDS design, i.e. whether it be on an *individual food* basis or a *food group* basis.

In the *individual food* approach (as used by New Zealand, Australia and the USA), the food groupings in the TDS food list are less critical, as each individual food in the food group is analyzed. For organizing its NZTDS food list, the individual foods were assigned to 12 food groupings, namely: grains, fruit, vegetables, dairy, chicken/eggs/fish/meat, spreads and sweets, nuts, alcohol, beverages (non-alcoholic), take-aways, infant foods, children snacks, and offal/shellfish [1].

In the *food group* approach (as used by the UK), it is important to separate out food staples, such as bread, potatoes and milk into separate *food groups*. Animal products, such as poultry, eggs, fish, carcase meat, offal, and meat products are also each categorized into separate *food groups*. Other food groupings could include fresh fruit, fruit products, dairy products or infant foods. If resources permit, subgroups of vegetables, such as roots/tubers, leafy greens, stems/flowers and legumes could also be included; or for fruits, the subgroups might be pome, citrus, stone, berries, and fruits with inedible peel.

The advantages and disadvantages of the *individual food* or *food group* approaches are discussed later in this chapter in the Preparation of TDS Analytical Samples section.

Once the TDS food list is finalized, it can be sorted either by food alphabetically, by food group then foods alphabetically within each food group, or by a unique TDS food identification code. Further details on how to develop a food list for a TDS are given elsewhere in this book (see Chap. 6 – Preparing a Food List for a Total Diet Study and Chap. 44 – Food Mapping in a Total Diet Study).

Who Should Sample the TDS Foods?

Regional foods can be obtained by sampling officers (SOs) who are otherwise employed by the government, such as food inspectors or environmental health officers. Sampling can also be done by contracted civilians. In either situation, it is important that SOs are familiar with the sampling instructions in the procedures manual, including which foods to sample, when, where, and how to sample. SOs need to understand the critical role that they play in the success of a TDS. For example, if foods are not sampled at the proper time, then the schedule for preparation and analysis will be disrupted resulting in delays in the TDS. Similarly, if samples of a food are collected days later than others, it makes management of sample receipt, storage and subsequent preparation of multiple samples of the same food in batches much more difficult to manage. SOs should each be given copies of the procedures manual, and given adequate time to review and study it. If possible, SOs should attend an organizational meeting held prior to the commencement of sampling to ask questions and clarify any ambiguities that may exist in the procedures manual. Any changes or amendments to the procedures manual should be documented and revised instructions issued if necessary. This will ensure there is a common understanding of sampling requirements for the TDS. Such a meeting demonstrates the importance of their role in the success of the TDS, and contributes to their ownership of the study and to TDS team building.

When Should TDS Foods Be Sampled?

Sampling of specific foods should occur in relatively short, well-defined time frames, within the context of the whole TDS. The timing is usually decided by the TDS project leader/coordinator, in consultation with key participants on the team, such as the SOs and contacts in the analytical laboratory. Sampling usually occurs at the start of the week, so that food samples can arrive at the sample preparation facility in a timely manner, and ensure food and sample preparation can be completed before the next week's samples arrive. In New Zealand, approximately 1,600 kg of food is sampled over the course of a TDS calendar year. With such a volume of food, NZTDS sampling is divided over four quarters (Q1, Q2, Q3, and Q4). Quarterly sampling also captures potential seasonal variation, which can be important for produce, such as fruits and vegetables. Each quarter is further broken down into 5 or 6 weeks (W1, W2, …) resulting in work periods (Q1W1, Q1W2, …, Q4W6) that enabled the sampling, sample preparation and analytical workflows and volumes to be more manageable and efficient. The beginning of the first NZTDS sampling period and the end of the last define the TDS, so for the 2009 NZTDS, sampling began in January 2009 and ended in December 2009 [1].

There are alternative approaches to sampling which reflect variations in scope and specificity of the study. For example, the 23rd Australian TDS was conducted with two sampling periods, which covered both summer and winter foods [3]. The number of sampling periods and approach to sampling preparation is likely to vary between countries. The best approach for each country should be determined on a case-by-case basis taking into account the available resources for the study and the agro-climatic conditions of the country.

Where Are TDS Foods Sampled?

The aim of sampling in a TDS is that the samples collected be as nationally representative as possible. In New Zealand, sampling occurs at a range of retail outlets, such as supermarkets, as foods from these sources most readily reflect what is generally available and purchased by consumers (see Fig. 9.1). The NZTDS also includes some specialty shops, such as butcheries, bakeries, market garden stalls and delicatessens, for those consumers who buy their foods from these alternative sources.

'National' foods, which by definition are nationally distributed but manufactured at one or only a few sites, need only be sampled in one city, but from a variety of different retail outlets. Samples of the same food product should be from different batches/date marks. It is, therefore, most effective to sample 'National' foods in the same city where the sample preparation facility is located to facilitate organization, minimize transportation and reduce costs.

'Regional' foods are grown or manufactured locally and should be sampled at a number of regional sites. Questions to consider are: how many regions are needed to be representative, how many cities per region, and how many food outlets per

Fig. 9.1 Sampling officer in supermarket using food purchasing instructions

Table 9.2 Some total diet study design details of selected countries

Countries	Number of TDS foods	Number of regions sampled	Number of cities sampled per region
New Zealand	123	4	1
Australia	92	8	1
Czech Republic	108	4	3
UK	119	20	1
USA	285	3 (12 per year)	3 (12 per year)

city? As there is no specific guidance for this, each country must develop their own plan for where to sample based on their own unique characteristics. By way of examples, New Zealand collects samples in one city for 'National' foods and in the main city in each of the four regions (two in the North Island and two in the South Island) for the 'Regional' foods. In the Czech Republic, samples are collected in four regions, three cities per region [2]. In Australia, samples are collected from eight regions [3]; in the UK, samples are collected in 20 regions, one city in each [4]; in the USA, samples are collected in three regions, three cities per region. Note that the USA changes the regions being sampled across the country over the four sample collection cycles per year [5, 6] (Table 9.2).

How to Sample TDS Foods?

The ideal sampling plan is statistically valid for the purpose at hand. For regulatory monitoring, this requires taking about 300 samples per lot of food for a 95 %

probability of picking up 1 % of positive results [7]. Fortunately, these statistics are not applicable for total diet studies since only the mean concentration is needed. While a larger number of samples can better characterize variability, the mean requires many fewer samples to be considered robust. There is always a compromise between the:

- budget available,
- number of foods on the TDS list,
- range of chemicals to be analyzed,
- number of samples to be analyzed,
- time frame available, and
- quality of the results, including the sensitivity of the analytical method

For this reason, the aim of a TDS is to generate meaningful exposure estimates which are fit-for-purpose and the best value for the budget available, with the most representative sampling as possible. Samples should be chosen at random within the designated areas and cover rural, regional and suburban areas. If budgetary constraints are significant, then multiple purchases of the same food, which provide a broader sampling base, can always be combined during sample preparation into composite samples to reduce the number of samples for analyses (see also Chap. 8 – Preparing a Procedures Manual for a Total Diet Study).

How Much Food Should Be Sampled?

Planning effective sampling also involves decisions about what volume, weight, or number of units need to be purchased per food/brand and/or cultivar. Factors that contribute to this determination are:

- What weights are actually needed by the analytical laboratory for each of the respective analyses to be undertaken?
- Are analyses going to be on individual foods, or composites of individual foods across regions or brands, or on food group composites?
- Is excess sample required to allow for replicate analyses, possible loss/errors or trace-back analysis?

In New Zealand, for each sample sent from the sample preparation facility to the analytical laboratories (located in other cities), a reserve back-up sample was retained in case of loss or damage during transit or analytical errors. This effectively means doubling the weight of sample required to account for this. In Australia, reserve back-up samples of prepared individual samples and composite samples are stored by the analytical laboratory for an agreed period (see Chap. 14 – Commercial Analytical Laboratories—Tendering, Selecting, Contracting and Managing Performance).

Samples of foods that have inedible portions will need to be increased to compensate for these losses. For example, oranges and bananas are peeled because only the edible portion is analyzed in a NZ or Australian TDS. These losses are usually about 30 % of the whole fruit by weight. Similarly, apples are cored and watermelons have

the hard rind and seeds removed. The loss in weight by the removal of skins and seeds need to be factored into the amount that should be purchased. It is also useful to factor in that on cooking, meats lose moisture/weight, whereas other foods gain significant moisture/weight (e.g. rice or pasta). If a food may be used as an ingredient in some other mixed dish, then extra food sample would also be needed. In some cases, the amount of a specific TDS food to be sampled may not correspond exactly to what is available (i.e. 1.5 kg may be needed but pack sizes are only 1 kg). In this case, the SO should be instructed to purchase more than what is needed (i.e. 2 kg). If a portion of the prepared sample is to be archived, this also needs to be taken into consideration.

Other Sampling Considerations: By Food Group, by Sample Preparation Required, or by Volumes to Transport

In organizing sampling, it can be advantageous to sample foods by food group as much as practicable (e.g. grains such breads, biscuits, pasta; or fruits such as apples, bananas, oranges), so that foods with similar characteristics can be purchased, prepared and analyzed at the same time.

In developing a sampling plan, consideration should be given to those foods that may also require extra sample preparation. For example, if all the foods sampled in a week required intensive preparation, such as trimming meats, peeling, cooking, mixing and homogenizing, the sample preparation facility may not be able to accommodate all the samples for preparation. Therefore, sampling of foods that need only minimal preparation should be included in the sampling scheduled along with the foods that require more extensive preparation.

The weight and volumes of food that need to be transported can also be an important consideration, especially when shipping is involved. There is a significant difference in volume between transporting cabbages, bread, watermelons in 1 week and peas, apples, kiwifruit the next week. For this reason, it is recommended that the weight and volume of foods to be sampled each week are spread out as evenly as possible.

Importance of Sampling SOPs, Labels, and Unique TDS Food Sample Identification Codes

Standard Operating Procedures (SOPs) are very important for ensuring a uniform approach is undertaken for TDS sampling by the different SOs around the country. The SOPs should specify the sample types ('National' or 'Regional'), sample description, the sampling dates, retail outlets, range of brands/use by dates/batch numbers, the TDS identification codes and purchasing instructions for each of the TDS foods. It is critical that the SOs have a good understanding of the SOPs and that any ambiguities are resolved prior to sampling. It can also be beneficial to provide SOs with pre-prepared, self-adhesive labels with unique TDS sample identification codes to complete and affix to their food sample purchases.

Fig. 9.2 Examples of TDS food sample labels, containing unique sample identification codes

In New Zealand, the unique NZTDS food sample identification code includes the food number (i.e. 001 to 123) for each of the individual foods on the TDS list, the quarter and week being sampled (i.e. Q1W1 to Q4W6), the region or regions where the sample is to be taken (i.e. AK, NP, CH or DN, which are abbreviations for the city names where regional foods are sampled), and the brand that is sampled if it is a 'National' food (i.e. Nat/BR1 to Nat/BR4). In the case of a 'Regional' food, the number of the sample may be added in some cases (i.e. S1–S20). An example of an NZTDS 'National' food sample identification code is 057/Q4W4/Nat/BR1 and an example of an NZTDS 'Regional' food code is 073/Q3W2/CH/S4 (see Fig. 9.2).

In organizing effective sampling, it can also be helpful to the SOs to provide them with shopping lists, so they can check off each purchase. SOs play a critical role, and making their job simpler can only be of benefit. An example of a portion of a 'Regional' food shopping checklist is given in Fig. 9.3.

Specificity of Sampling Instructions

The more specific the instructions can be, the less likely there is to be inconsistencies in sampling, and therefore the less potential impact on results of the TDS. For example, if tomatoes are to be sampled, it is essential to state if they are to be fresh, canned, jarred, whole, diced, pureed, or dried.

Range of Brands/Use by Dates/Batch Numbers

In general, commonly available food varieties and brands should be selected. In most cases the brands to be purchased are not specified and samples should be chosen at random within the designated areas and cover rural and regional areas as well as suburbs within a city. However, where available, information on the most commonly purchased brands can be provided to assist sampling officers. Brands are selected depending on their market share. For example, in Australia, the *"Australian Grocery Industry Marking Guide"* is used.

For purchasing food products for which brands are not specified, a range of locally available brands, including house brands (often referred to as generic brands), should be sampled. If the number of brands available is limited, then a range of date marks or batch numbers within each brand should be included as this also broadens the representativeness of the sampling (see also Box 8.1, Chap.

Regional Food Purchasing Tick Check List (one to be completed by sampling officer (SO) for each sampling period). Each column represents the regional purchases of that food product. Refer to purchasing instructions for more details regarding each purchase

Region (R) _____   Sampling Period (S) _____

Food No	Food	Type R/N	Sampled by	No samples purchased per R per S	Min Weight (grams) per R per S needed	AK*	NP*	CH*	DN*
1	Bread, mixed grain	R	SOs	3	2100				
2	Bread, wheatmeal	R	SOs	3	2100				
3	Bread, white	R	SOs	4	2800				
4	Cake	R	SOs	8	1600				
11	Muffin	R	SOs	20	1600				
18	Butter	R	SOs	2	1000				
20	Cream	R	SOs	2 or 4	1000				
22	Milk 0.5% fat	R	SOs	2	2000				
23	Milk 3.25% fat	R	SOs	2	2000				
24	Milk, flavoured	R	SOs	4	1300				

* Regional sampling occurs in and around four New Zealand cities :
AK = Auckland, NP = Napier, CH = Christchurch, and DN = Dunedin

Fig. 9.3 Example of part of a food purchasing tick list

8 – Preparing a Procedures Manual for a Total Diet Study). Where domestic and imported lines are available for a particular food, e.g. wine, the purchasing officer is at liberty to randomly choose a range of samples, assuming the range covers what is typically bought for the average household. Foods that are boutique or exotic lines should be avoided, although occasional targeting may provide useful additional information if brands are analyzed separately (e.g. an 'organic' sample only among the range of baby foods).

Food Sample Handling and Transportation

In handling pre-packaged food purchases, it is desirable to retain point of sale packaging so relevant additional information from the label can be recorded on receipt of food samples at the sample preparation. This will assist with sample traceability if required later in the study. Samples requiring refrigeration (e.g. meats, milk and cheese) should be stored appropriately in accordance with customary practices in the home and/or in accordance with instructions on the label or packaging. For transportation to the laboratory, samples should be packed with an

appropriate coolant, e.g. ice or dry ice, or frozen blocks in suitable containers (e.g. chilly bins). Other foods, such as breads or biscuits, should be packaged separately in cardboard boxes for transportation. SOs in outlying regions can be provided with pre-prepared courier labels addressed to the sample preparation facility and if possible, pre-paid courier tickets. A protocol should exist whereby the sample preparation facility will confirm the safe receipt of samples to the SOs and project leader. If TDS samples are not confirmed within 24 h or when anticipated to arrive, then a follow-up procedure should be initiated. This is especially important for perishable foods. The safe and expeditious transport of samples to the preparation facility is critical to the integrity of the food samples and ultimately the success of the TDS project.

Budget for Sampling

Budgetary considerations for sampling may need to include the purchase cost of the foods sampled, payment for SOs (where relevant), coolers and ice-bricks/cooler packs/ice/dry ice, sample identification labels, and food transportation costs.

Sample Preparation in a Total Diet Study

A TDS analyzes foods after they have been prepared as normally consumed. Sample preparation is, therefore, a key component of a successful TDS. Such preparation may be carried out in cooking facilities associated with the analytical laboratory, or else in a contracted food kitchen facility. To ensure consistency in TDS food preparation, it is again important to have an associated set of SOPs. All relevant staff should be familiar with these SOPs, otherwise they should be closely supervised. The SOPs for sample preparation should ideally be consolidated in a procedures manual (see Chap. 8 – Preparing a procedures manual for a Total Diet Study).

TDS Food Sample Receipt

It is important that all samples received by the sample preparation facility are properly registered to provide a check on the completeness of the sampling process. It is also important to ensure that the quantity of the sample is sufficient and that the sample has not been compromised in transit and is in an acceptable condition for preparation (see Fig. 9.4). Any damaged, missing or insufficient samples should be notified to the respective SOs with instructions to recollect the sample as soon as possible.

Fig. 9.4 Sample preparation manager checking off TDS food samples after receipt

TDS Food Sample Documentation and Registration

It is important that all relevant sample details are captured for later reference. Sample details may be recorded either using an Excel-like spreadsheet or a database, such as Access (see Fig. 9.5; see also Table 8.1 – Preparing a Procedures Manual for a TDS). Useful information in the database might include: the TDS sample identification code, food type, SO identification code, date purchased, date received at sample preparation facility, brand name or food variety/cultivar, manufacturer, country of origin, batch number, best before/use by date, type of retail outlet (e.g. supermarket, butcher, green grocer, etc.), name of food outlet, weight of unit purchased, number of units purchased, total weight, whether sample is to be prepared as 'Regional' or 'National' composite of the individual foods, or as an individual food composite for each food on a regional or brand (for national foods) basis, estimated percentage of the sampled food that is edible, analytical assays to be undertaken, and dates for the scheduled and actual shipping of the prepared food samples to the respective laboratories for analyses.

With the advent of digital cameras, it is now routine to also take photos of TDS food samples received. Such photos detail additional key information, like label ingredients, which can be useful if subsequent follow up investigations are needed. Photos also allow food sample packaging to be discarded, which saves on storage and simplifies logistics.

TDS Food Sample Pre-sorting and Prioritization

With many different TDS foods coming into the sample preparation facility each week, it is important to pre-sort and prioritize them for more effective and efficient sample preparation. Different regions or brands should be kept separate, if these

Fig. 9.5 TDS sample
information being entered
into computer

are to be analyzed separately for each 'Regional' or 'National' food, respectively. Fresh fruit and vegetables for labile chemicals, like dithiocarbamates (DTCs) should be prioritized for immediate processing. Highly perishable foods, such as meats, seafood, and most dairy products, should be refrigerated and processed within 48 h. If this is not possible, they should be frozen for later processing. However, freezing is less desirable as subsequent thawing of such products can cause problems with matrix breakdown or separation. Other perishables, such as fresh fruit and vegetables, should also be refrigerated until prepared. Foods like breads should be stored in a cool place and prepared within 72 h of receipt. Non- or low perishable foods (frozen foods, dried foods, canned foods, etc.) can be stored as per usual procedures in the home and processed at the first subsequent opportunity. In prioritizing foods, consideration should also be given to foods for which substantial preparation is needed. For example, beef needs to be trimmed, cooked and homogenized, whereas minimal preparation is required for other foods e.g. homogenizing biscuits, mixing milks.

Sample Preparation SOPs

Foods in a TDS are prepared as for consumption. This may involve steps including washing, peeling and cooking (see Figs. 9.6 and 9.7). As with sampling, SOPs for sample preparation are essential in a TDS and should be included in the procedures manual. Not only does it standardize preparation methods to be used, but it documents the approaches taken, which can then be referred to at a later date if needed, or modified in a future TDS. It would be advisable to have a glossary to explain terms such as 'chop' (e.g. coarse), 'blend' (e.g. with a food processor or blender), 'mix' (dry, semi-dry, foods with juice, liquids)', 'homogenize' (what is acceptable), and 'composite' (combine equal or weighed amounts of the same or different brands).

Fig. 9.6 Technician peeling potatoes, prior to boiling

Fig. 9.7 Technical assistant cooking four regions of pumpkin separately

Equipment for TDS Food Sample Preparation

The SOPs would also describe the sample preparation equipment to be used. It is important that care is taken to ensure that there is no cross contamination of any kind between the samples of different regions or brands purchased when preparing composite samples. This means careful cleaning and drying of utensils in between use.

Gloves should be worn whenever the food being prepared could come into contact with hands. Gloves without powdered lubricant are preferred, as the powder can accidentally contaminate TDS food samples. Utensils, such as stainless steel knives,

Fig. 9.8 Pictures of TDS sample containers with labels for respective foods and analyses

wooden, glass or hard plastic chopping boards (smooth and free from cracks), and pyrex, stainless steel or Teflon-coated bowls and pots should be used if possible. Ceramic or enamelware should be avoided as these may contain heavy metals and potentially contaminate samples during food preparation. Prior to food preparation, advice should be sought from the analytical laboratory to ensure that food preparation equipment will not interfere with the specific analysis. This can be done in advance of sampling, to ensure all required equipment is available. The analytical laboratory, or sample preparation facility in consultation with the analytical laboratory, should specify the procedure to be used in the washing of food preparation equipment. The detergent chosen should not interfere with the methods of analysis to be used.

SOPs should also detail the sample containers in terms of materials and size for the respective analyses. Laboratory-grade storage containers suitable for long-term freezing without leaching should be used for TDS food samples. It may also be advisable to explain how to fill them, as those filled completely can expand on freezing and may burst. Samples should be stored in a manner that does not compromise the integrity of the sample. Advice from the analytical laboratory should be sought as to the best storage conditions for the food samples, noting that some samples may have temperature or light sensitivities.

Each TDS food sample container should be adequately labeled and a label also included on the lid, if practical. Pre-prepared self-adhesive labels are helpful but should be of a size consistent with the container. Standard sample containers and associated labels used in the NZTDS for pesticide residue analysis (250 ml) and those for elemental analyses (60 ml) are shown in Fig. 9.8.

For every TDS food sample prepared for analyses, a duplicate sample is also made as a back-up reserve. This is an important precaution in the event that

- The primary sample is lost or damaged in transit to the analytical laboratory.
- The primary sample is used up or lost during analyses.
- The primary sample gives unusual or unsatisfactory analytical results that need confirmation.

Contamination Control

Given the TDS is measuring chemicals at backgrounds levels in the foods as prepared for consumption, it is critical to ensure that sample preparation does not inadvertently contaminate samples prior to analysis. If this has occurred, the subsequent estimated dietary exposure will be incorrectly elevated. Contamination control is a critical analytical quality control point and ways to achieve it will be explained in a later chapter (see Chap. 13 – Quality Control and Assurance Issues Relating to Sampling and Analysis in a Total Diet Study).

Preparation of TDS Analytical Samples: Food Group or Individual Foods Approach?

After the foods have been prepared as normally consumed in the home, two main options exist for preparing the TDS analytical samples, namely the *food group* approach or the *individual foods* approach. Each has its advantages and disadvantages.

Food Group TDS Approach

In this approach, different foods from the same food group are combined to form a new *food group* sample for analysis (e.g. apples and pears to form 'pome fruit group') or more extensively (apples, bananas, oranges, kiwifruit, etc. to form 'fruit group'). There are a number of criteria to consider when using the *food group* approach, such as not to combine foods across different food groups or for which combined food consumption data do not exist, or where the chemical concentration in different foods from the same group may be expected to be widely variable or different. These criteria have been explained in more detail in Chap. 6 – Preparing a Food List for a Total Diet Study.

By combining food samples using a *food group* approach, a much smaller number of composite samples are required to represent the total diet. This can considerably reduce expenses associated with analytical costs.

With a fixed budget, the food group approach also enables more TDS samples to be collected, which can be useful where geographical or ethnic diversity is an issue as it allows separate market baskets reflecting those differences to be analyzed.

One disadvantage of the *food group* approach is the dilution effect of combining a number of different foods into the same sample. For example, if a food has concentrations of the chemical of interest well above detectable levels, its combination with numerous other foods with no detectable concentrations may result in the composite sample being diluted below the Limit Of Detection (LOD).

Another disadvantage is that when an elevated concentration or dietary exposure is identified as resulting from a specific food group sample e.g. grains, it is not

possible to determine which foods in the grains food group sample may be a major contributor to the increase. For this reason, samples of the original foods contributing to the food group composite sample should be retained. These can then facilitate trace-back analysis to the individual food samples that actually contributed to the elevated dietary exposure within that food group.

Another major disadvantage of the *food group* approach is the rigidity in calculating the total diet exposure for different population subgroups. For example, the combination of bread, rice and pasta to produce a 'grains food group' composite must combine amounts of those individual foods in the ratio defined by one population cohort, such as an adult male. Because that ratio of such foods may differ for different cohorts, the food group composite sample based on the selected cohort cannot be readily used to calculate exposure for other population cohorts (e.g. a teenage female, a child or an infant). Because each of those individual foods in the composite will have different concentrations, the mean concentration of the chemical of interest in the composites of each cohort could be different.

Individual Foods TDS Approach

In this approach, each food in the TDS food list is analyzed separately. In New Zealand, this may involve:

- each region or brand for each individual food being analyzed separately each sampling season and
- different regions or brands for an individual food being combined on a seasonal basis for analyses.

In Australia, which also uses the *individual foods* approach, different brands are combined to form multiple composites of the individual foods.

For the *individual foods* approach, the major advantage is that it enables much greater flexibility in calculating dietary exposures for different age/gender cohorts, provided that the respective consumption data are available (see Chap. 4 – Overview of Dietary Exposure and Chap. 17 – Dietary Exposure Assessment in a Total Diet Study). In addition, it reduces the 'dilution effect' which occurs in the *food group* approach discussed above. The disadvantage is the larger number of samples that need to be analyzed to represent the foods commonly consumed by the population (>100–280 individual foods compared to perhaps only 20–50 *food groups*).

Even within the *individual foods* approach, the degree of compositing that may occur needs to be determined. For example, in New Zealand, broad sampling of brands and regions for each individual food is conducted to get as representative a picture of the foods available to the consumer as possible. The multiple purchases on a brand ('National' food) or on a regional basis ('Regional' food) are combined into a composite sample. For example, while five cans of each of the four leading brands of carbonated lemonade may be purchased, each lot of five cans is then combined in equal portions to generate individual composites for each of the four
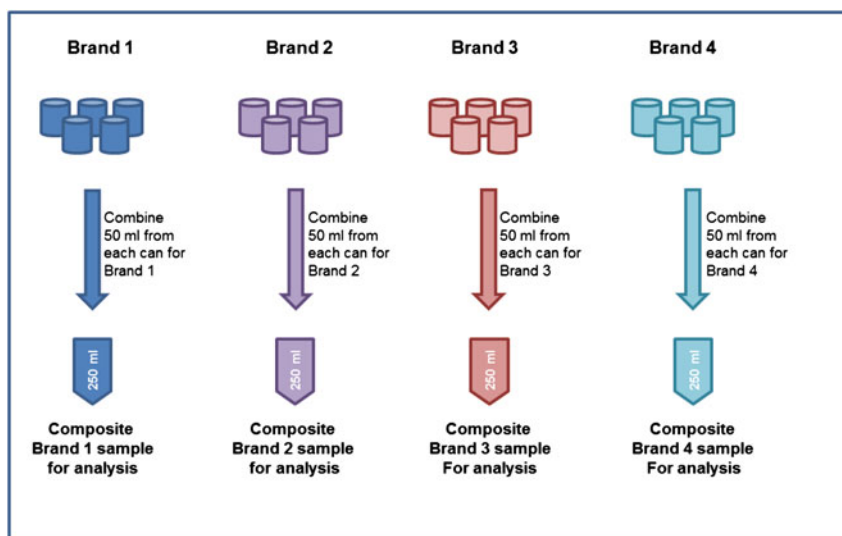
Fig. 9.9 Preparation of individual composites of four different brands of lemonade beverage

different brands of lemonade (see Fig. 9.9). This means only four samples of lemonade for analysis, not 20. If so desired, each of the four separate brands could even be combined to yield just one analytical sample of lemonade for each sampling season. However for breads, which are an important staple food in New Zealand, three different types of breads in the NZTDS list (white, wholemeal, and mixed grain) are sampled from four regions. SOs are instructed to purchase one loaf of each of the four leading brands for each of the three bread types in each of the four regions during each of the two sampling seasons. This could result in 4 leading brands × 3 bread types × 4 regions × 2 seasons = 96 samples of bread for analyses. However, for the 2009 NZTDS, compositing of the different brands for each bread type per region per season reduced the number of samples by a factor of 4, which gave a total of 24 samples for analysis.

Other Food Preparation Factors to Consider: Fat, Bone, Distilled Water, Salt

There are other factors in the preparation which need to be considered. The approach taken will be dependent on the analytes of interest in the study and the influence food preparation may have on the concentration levels detected in the food.

For example, in New Zealand, the fat is trimmed off meat and the meat dry fried. Chicken preparation involves the bone being removed, the fat and skin

Fig. 9.10 Sample preparation manager packing frozen samples for dispatch to pesticide laboratory

being trimmed off before dry frying. Apples are rinsed and cored and oranges/kiwifruit/bananas are peeled. Canned fish has the liquid drained off and discarded. Distilled water is used for cooking the foods and for brewing coffee and tea to ensure additional chemicals are not added to the foods. In contrast, some countries cook plantain bananas before consuming, and even use the peel for making beverages. Others collect water samples from all the key regions in very large quantity and use the sampled water for cooking each regional sample that requires boiling or steaming.

Often when consumers cook specific foods (e.g. pasta), salt is added. In the food preparation in the NZTDS, foods are not cooked or seasoned with added salt (some of which is iodized), as the goal is to ascertain what the sodium and iodine exposures are coming from the foods themselves. Some countries, however, choose to cook TDS foods with salt, and also add salt after they are cooked and homogenized to mimic that added at the table for taste. The preference for salt can be highly variable among consumers, so the different scenarios of salt addition should be modeled separately. Regardless of the decisions made in the preparation of food for analysis, it is important to clearly document the approaches and methodologies that are used to permit the effective interpretation of the results of the TDS.

Labeling, Dispatch and Storage of Prepared TDS Samples

Once food samples have been prepared, all regions/brands should be packed into separate containers if they are to be analyzed on that basis, and the individual or food group composite samples should be labeled for the correct analyses before they are dispatched to the analytical laboratory (see Fig. 9.10). It is useful to track and document the dispatch of prepared samples in a spreadsheet, or database.

When prepared samples have been dispatched to analytical laboratories which are in a different city from the sample preparation facility, the analytical laboratories should be appropriately informed. In turn, the laboratories should provide a confirmation that the samples have been received in an acceptable state.

Reserve samples are usually retained for at least 3 months after the TDS results have been verified and reported. They may also be stored for longer as a resource for subsequent related investigations involving food matrices, such as in Chap. 51 – Polybrominated Diphenyl Ethers in Food in Australia—An Additional Use of the Australian Total Diet Study.

Conclusion

Adequate and appropriate food sampling and preparation are critical components of a successful TDS. They should be carefully planned and precisely undertaken, using well documented SOPs contained in a procedures manual. Without this, the accuracy and precision of the TDS can be compromised.

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Chapter 10
Analyzing Food Samples—Organic Chemicals

Chris A. Sack

Introduction

The challenge for the analysis of organic chemicals in an advanced total diet study (TDS) is that the most extreme and varied food matrices in the diet of the population must be analyzed for a large number of residues at very low levels. In the United States Food and Drug Administration (FDA) TDS program, approximately 280 foods are analyzed for more than 500 organic chemicals at levels as low as 0.1 part per billion (ppb). This feat is accomplished by using several means. Samples are analyzed by multiple analytical methods ranging from single residue methods designed for specific types of matrices to general screening procedures capable of determining hundreds of analytes found in the full spectrum of TDS matrices. A variety of instruments are employed for the determinations, including some the newest and most sophisticated technologies available, and a few that are older and simpler, yet still fit-for-purpose. Critical attention is applied to the correct identification of residues, the most important task in residue analysis. In addition, all analyses are conducted within an exhaustive quality management system. These topics are briefly addressed in this chapter.

The procedures described within are general outlines and do not include all techniques and cautions. The full set of operational instructions can be found within the references listed below and are available from the FDA Kansas City District Laboratory.

Note: Reference to any commercial materials, equipment, or process does not in any way constitute approval, endorsement, or recommendation by the US Food and Drug Administration.

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Analytical Methodologies

Overview

The analysis of pesticide and industrial chemicals (P&IC) in simple matrices is difficult, at best. As analytical screening levels are lowered, the challenge of accurate analyte quantification and identification increases because the analyte responses decrease compared to interferences from instrumental noise and matrix responses. It is significantly more demanding to determine a chemical contaminant in a simple standard solution at 1 ppb than at the percent level because instrumental noise and matrix responses remain constant, but analyte responses diminish as their concentration decreases. At a concentration normally referred to as the Limit of Detection (LOD), the response of the analyte can no longer confidently be distinguished from the interferences and noise. The introduction of complex food matrices complicates the process geometrically.

A P&IC analytical method is essentially a separation process that removes an analyte from the matrix and isolates it for measurement. Methods for the analysis of P&ICs generally consist of three steps: extraction, cleanup and determination. In the extraction step, the chemical residues are dissolved in a solvent, and then physically separated from the solid sample matrix through filtration or centrifugation. The cleanup step selectively removes matrix coextractants that would interfere with the determination. The analyte is detected, characterized, and quantified in the determinative step.

The extent of each step is determined by the scope of targeted analytes for the procedure. For multiple residue methods (MRMs), the analyte scope may range from a few dozen to a thousand P&ICs; and for selected residue methods (SRMs), the scope will generally consist of a single analyte, e.g. perchlorate, or a class of P&ICs, such as the carbamate insecticides.

MRMs provide the most efficient screening proficiency because they cover more residues per analysis than SRMs; however, they present particular challenges. The extraction solvent must be able penetrate complex and varied food matrices to dissolve analytes that have a wide range of polarities and chemical affinities. Acetone and acetonitrile are the two most commonly used solvents for nonfat food matrices because they are mid-polar organic solvents that are able to dissolve most P&ICs; and they are miscible with water, the primary constituent of nonfat foods. Given their universal ability to solvate chemicals and residues, the extraction of foods with acetone or acetonitrile results in extremely complex mixtures of matrix coextractants that can often interfere with the determination of the targeted analytes. Therefore, MRM extracts usually undergo a cleanup step to selectively remove matrix coextractants prior to determination. Cleanup procedures must be applied judiciously, however, because some residues may also be partially or fully removed from the extract with the coextractants. Even with a reasonably applied cleanup, interpretation of instrumental determinations of the residues in these complex matrix extracts can be problematic.

Table 10.1 US Total Diet Study pesticide and industrial chemical analytical methods

SOP[*]	Method	Analytes	US TDS food items
51[7]	Analysis for pesticide and industrial chemical residues in fatty items	~350 P&ICs	125
52[8]	Analysis for pesticide and industrial chemical residues in nonfat items	~450 P&ICs	155
53[9]	Determination of chlorophenoxy acid herbicides and pentachlorophenol	15 CPAs	20
54[10]	Determination of phenylurea herbicides	10 Phenylureas	56
55[11]	Determination of carbamate pesticides	12 Carbamates	117
56[12]	Determination of ethylenethiourea	ETU	94
57[13]	Determination of benzimidazoles	2 Benzimidazoles	101
71[14]	Perchlorate analysis in food items	Perchlorate	280

[*]USFDA TDS Standard Operating Procedure

SRMs, on the other hand, have the opposite advantages and disadvantages. By limiting their scope to a single analyte, or class of analytes, the complexity of the extraction method can be reduced tremendously, but their screening efficiency is drastically reduced. The US TDS procedure for ethylenethiourea (ETU) is an excellent example of a classic SRM. ETU is a suspected carcinogen occurring in foods as a result of the degradation of the ethylenebisdithiocarbamate (EBDC) fungicides used extensively to preserve raw agricultural commodities. ETU is extracted using aqueous methanol, an extremely polar solvent that effectively discriminates against nonpolar coextractants. Once dissolved, the polar coextractants are removed using alumina column chromatography. After cleanup, the extracted ETU is determined using high performance liquid chromatography (HPLC) with amperometric detection at a very low voltage, as ETU is oxidized at a much lower potential than most food matrix coextractants. The procedure is quite specific for ETU. Being an SRM, however, this may be considered an inefficient use of resources unless the analysis of the parent fungicides had indicated a potential problem.

Historically, P&ICs have been analyzed in the US TDS program using a combination of MRMs and SRMs [1–8]. Table 10.1 presents the current list of methods and their analytical scope. These procedures are primarily based upon methods found in the FDA Pesticide Analytical Manual [9] (PAM). FDA pesticide laboratories are currently collaborating in the development of a modified QuEChERS [10–14] method that will be used in the US TDS to consolidate the methods for nonfat TDS items (SOPs 52, 54, 55, 56 and 57 in Table 10.1).

MRM Analysis of Fatty Food Items

In the MRMs for fatty food items (SOP KAN-LAB-PES.51), samples are extracted with lipophylic solvents, such as hexane, petroleum ether (hexanes), ethyl ether, or supercritical fluid carbon dioxide (SOP KAN-LAB-PES.61 [15]); solids are

removed by filtration or centrifugation; dissolved lipids are removed by gel permeation chromatography (GPC) per SOP KAN-LAB-PES.63 [16]; and polar coextractants are removed using Florisil chromatography (SOP KAN-LAB-PES.64 [17]). The extracts are analyzed for about 150 organophosphorus P&ICs (OP-P&ICs) using gas chromatography with a flame photometric detector (GC-FPD) and for approximately 200 organohalogen P&ICs (OH-P&ICs) using gas chromatography with an electrolytic conductivity detector in the halogen mode (GC-ELCD).

MRM Analysis of Nonfatty Food Items

In the MRMs for nonfatty foods (SOP KAN-LAB-PES.52), TDS items are extracted with acetone; solids are removed by filtration or centrifugation; water from the sample is removed by partitioning the acetone/aqueous extract with methylene chloride; the extract is solvent exchanged to acetone and concentrated to approximately 2.8 g sample/ml per SOP KAN-LAB-PES.62 [18]. This extract is analyzed for about 200 OPs on a gas chromatograph with a pulsed flame photometric detector (GC-PFPD) and approximately 120 other P&ICs by gas chromatography with mass spectroscopic detection in the selective ion monitoring mode (GC-MS SIM). Over 150 OH-P&ICs are determined using GC-ELCD after a portion of the acetone extract has been cleaned up using Florisil chromatography to remove polar coextractants.

SRM Analysis for Carbamates

The acetone extract from the nonfatty MRM is also used for the analysis of carbamate pesticides per SOP KAN-LAB-PES.55. The acetone extract is passed thru an aminopropyl solid phase extraction (SPE) column to remove acidic and cationic coextractants before determination by high pressure liquid chromatography with tandem mass spectrometry (LC-MS/MS) using electrospray ionization (ESI) in the multiple reaction monitoring mode.

SRM Analysis for Phenylurea Herbicides

Phenylurea herbicides are analyzed per SOP KAN-LAB-PES.54. TDS items are extracted with methanol/water; solids are removed by filtration or centrifugation; the analytes are partitioned into methylene chloride; polar coextractants are removed by Florisil column chromatography; and the residues are determined by LC-MS/MS.

SRM Analysis for Benzimidazole Fungicides

In the analysis of benzimidazole fungicides (SOP KAN-LAB-PES.57) items are extracted with methanol/water; solids are removed by filtration or centrifugation; the extract is acidified and the fatty acids and nonpolar coextractants are separated by partitioning them into methylene chloride; the extract is basified and the analytes are partitioned into methylene chloride. The residues are determined by LC-MS/ MS.

SRM Analysis for Ethylenethiourea (ETU)

For the analysis of ETU (SOP KAN-LAB-PES.56) the sample is extracted with methanol/water; solids are removed by filtration or centrifugation; the analytes are partitioned into methylene chloride; polar coextractants are removed using alumina chromatography; and ETU determination is by high pressure liquid chromatography with an amperometric electrochemical detector (HPLC-EC) using a mercury and gold amalgamated electrode at a very low potential of 350 mV.

SRM Analysis for Chlorophenoxy Acid Herbicides and Pentachlorophenol

Chlorophenoxy acid herbicides and pentachlorophenol (CPAs) are extracted using acidified methanol to inhibit ionization by the deprotonation of the acid; the CPAs are methylated to volatilize them for determination by GC-MSD; prior to determination the methylated extract is passed though Florisil to remove polar coextractants. This procedure is not posted because it is being replaced by a new method for the analysis of CPAs using an acidified QuEChERS procedure with determination by LC-MS/MS using negative electrospray ionization in the multiple reaction monitoring mode.

SRM Analysis for Perchlorate Ion

The procedure for the analysis of perchlorate ion is provided in SOP KAN-LAB-PES.71. In the method perchlorate ion is extracted with acidified acetonitrile; neutral and lipophylic coextractants are removed by filtering the extract through carbon SPE, and perchlorate is determined using ion chromatography with LC-MS/MS. The use of the $^{18}O_4$ isotope of perchlorate as an internal standard enhances the quality of the analysis because it eliminates extraction volume errors and matrix/analyte interaction biases. Isotope usage for residue work is encouraged due to the aforementioned benefits; however it is impractical for MRMs due to the lack of availability and the cost of isotopes.

Analysis of Nonfat Items by QuEChERS

Since the introduction of the QuEChERS (Quick Easy Cheap Efficient Rugged and Safe) procedure, many residue testing labs around the world have adapted and modified it for inclusion in their surveillance programs. The FDA has recently validated and collaborated the procedure for regulatory analysis of P&IC residues [19]. In the method, residues are extracted with acetonitrile; water is removed by salting out with sodium chloride and magnesium sulfate; dispersive SPE using primary/secondary amines (PSA) is used to remove coextractants from a small portion of the acetonitrile extract and diluted for LC-MS/MS determination of approximately 200 pesticides. The rest of the acetonitrile extract is diluted 1+3 with toluene; dispersive SPE using graphitized carbon black is used to remove matrix coextractants; the extract is concentrated for determination of over 300 P&ICs by GC-MS in the SIM mode.

Determination Procedures and Instrumentation

Instrumental determination of TDS samples is largely driven by their selectivity and sensitivity. As previously stated the challenge for TDS analysis of chemical contaminants is that the lowest level of chemical residues are measured in the most extreme and varied food matrices. For the US TDS program the goal is to analyze and detect residues at levels of 1 ppb; however, the nominal reporting limit of 0.1 ppb is routinely achieved and reported. To achieve this, the instruments must be capable of detecting analytes at the 10–100 picogram (pg) levels while discriminating against matrix responses. Additionally, the thermal stability and volatility of the analytes must be considered. In the US TDS, LC-MS/MS is used in the determination of thermolabile and nonvolatile compounds. For thermally stable and volatile compounds, multiple configurations of gas chromatographs (GCs) with selective detection are used: GC-FPD in the phosphorus mode, GC-ELCD in the halogen mode, and GC-MS in the SIM mode.

Determination by GC Using Selective Heteroatom Detection

Amongst chemical residue programs, GC with various detector configurations is the most commonly used determination procedure for the analysis of P&ICs. Separation of analyte and matrix responses is accomplished by temperature-programmed capillary chromatography on multiple GC systems equipped with different stationary phases. Specific instructions and instrument parameters for GC determinations using element selective detectors are provided in SOP KAN-LAB-PES.59 [20]. For the FPD and ELCD element selective detectors capillary column dimensions are 30 m length×0.53 mm interior diameter (id), and the two most commonly used stationary

phases are 100 % methylpolysiloxane (DB-1) or 50 % phenyl methylpolysiloxane (DB-17). The nonpolar DB-1 stationary phase provides distinctly different chromatographic elution patterns from the mid-polar DB-17 phase. Other stationary phases used to provide additional elution patterns include the cyanopropylphenyl methylpolysiloxane phases with cyanopropylphenyl concentrations of 6 %, 14 %, and 50 %. The 6 % and 14 % phases are mid-polar and the 50 % mixture is considered a polar column. The disadvantage of using the cyanopropylphenyl columns is that they become unstable with prolonged use at temperatures above 200 °C resulting in column bleed.

Temperature programs are designed to elute the full scope of compounds listed in the Pestdata tables in Appendix 1 of PAM I. For example, temperature programs for halogenated P&IC's would chromatograph early eluting compounds, such as dichlobenil, monuron, hexachlorocyclopentadiene, etc., after the solvent front, and late eluters, such as deltamethrin, tralomethrin, fluvalinate, etc., prior to the end of the program. Likewise, for the initial determination of general organophosphates, the temperature program is designed to elute methamidophos, dichlorvos, trichlorfon, etc., after the solvent front and coumaphos, pyrazophos, bensulide, etc., prior to the end of the program. A typical program used in the US TDS for the GC-ELCDs and GC-FPDs is 120–280 °C @ 5 °C/minute, hold 5 min.

OP-P&ICs are determined using GC-FPDs and GC-PFPDs in the phosphorus mode. These detectors are essentially the same with slight variations in their mode of releasing elemental phosphorus from their molecular setting and raising the excitation level of the phosphorus electrons. They are extremely sensitive and selective for residues containing phosphorus. However the PFPD is approximately 5–10 times more sensitive than the FPD. One difficulty with both detectors arises with samples containing high levels of organosulfur (OS) coextractants, such as those found in onions and brassica vegetables, which can overwhelm the detector and obscure OP-P&IC analyte responses. Fortunately, very few products have high levels of OS and/or OP-P&IC coextractants. Some of the more polar OP-P&ICs, e.g. acephate, dimethoate, methamidophos, and omethoate, do not chromatograph well on the relatively nonpolar DB-1 and DB-17 stationary phases, but they perform much more consistently and exhibit greater sensitivity when analyzed by LC-MS/MS; therefore they have been added to the LC-MS/MS screening procedure and will be removed from GC-FPD and GC-PFPD determinations in the future.

OH-P&ICs are determined by GC-ELCD in the halogen mode. Like the GC-FPDs and GC-PFPDs the GC-ELCD responds to high levels of OS coextractants that can overwhelm the detector. It also responds to high levels of hydrocarbon coextractants if it is not maintained properly. GC-ELCDs are temperamental, requiring constant maintenance; however, they are still the most sensitive and selective instruments for the determination of OH-P&ICs.

Recent advances in instrument and computer processing technologies and efficiency indicate that the triple-quadripole GC-MS/MS operated in multiple reaction monitoring mode is approaching the sensitivity needed for the detection of sub ppb chemical residue levels. It is likely the US TDS will replace the use of selective GC detectors, like the GC-FPDs, GC-PFPDS, and the GC-ELCD, with GC-MS/MS in the near future.

Determination by GC-MS in the SIM Mode

Around 2003, GC-MS in the SIM mode was incorporated into the US TDS to detect analytes without halogen and phosphorous heteroatoms. Approximately 135 P&ICs are currently determined using the GC-MS SIM method per SOP KAN-LAB-PES.67 [21]. Analytes are separated on a 30 m length × 0.32 mm id with 5 % phenyl methylpolysiloxane capillary column using a segmented temperature program to optimize resolution of over 130 compounds: 50–130 °C @ 10 °C/minute, 130–230 °C @ 4 °C/minute, 230–290 °C @ 10 °C/minute, hold 7 min. A single quadripole mass spectrometer is programmed to capture the response of 3–4 selected ions characteristic of each analyte. Specificity relies on a combination of selective ion monitoring for brief elution windows, retention time, and agreement of ion ratios.

The SIM method does not generally meet the sensitivity requirements for the US TDS as many analytes cannot be detected below the 100 pg level resulting in LODs of 1–50 ppb. However, the P&ICs targeted by the procedure had not been previously included in the TDS screening regimen. As a result, 26 of the 135 compounds targeted by the procedure have now been reported in the US TDS since its implementation. As with the GC selective detectors, the GC-MS SIM method will likely be replaced by GC-MS/MS because of its increased sensitivity and selectivity.

LC-MS/MS Determination

Until recently, only determination by GC with element selective detection provided the selectivity and sensitivity required for sub ppb level TDS determinations; however, new advances in MS technology have enabled their implementation in the US TDS. In 2009, an LC-MS/MS procedure that replaces the HPLC detection of benzimidazoles, phenylureas, and carbamates was validated and collaborated in the USFDA pesticide laboratories [22], and implemented in the US TDS. The method detects an additional 160 selected P&ICs for a total of over 190 compounds (SOP KAN-LAB-PES.72 [23]). Analytes are separated on a 2.1 mm id x 10 cm long octyldecylsilane column with 3 μm particles. Mobile phase is 0.1 % formic acid/4 mM ammonium formate in water (aqueous) and methanol (organic). The mobile phase composition is programmed from 0 % to 90 % organic modifier in 12 min at a flow of 400 μl/min. Detection is by multiple reaction monitoring of molecular ions: two transition ions are monitored per analyte. A 10–20 μl of a 50 ng/ml standard is used to calibrate the system; Fig. 10.1 is a chromatogram of the standard containing 190 compounds. Samples of 10–20 μl are diluted to 0.5 g/ml before injection. Average LOD for all compounds is about 2–3 ppb, with a range of 0.1–20 ppb.
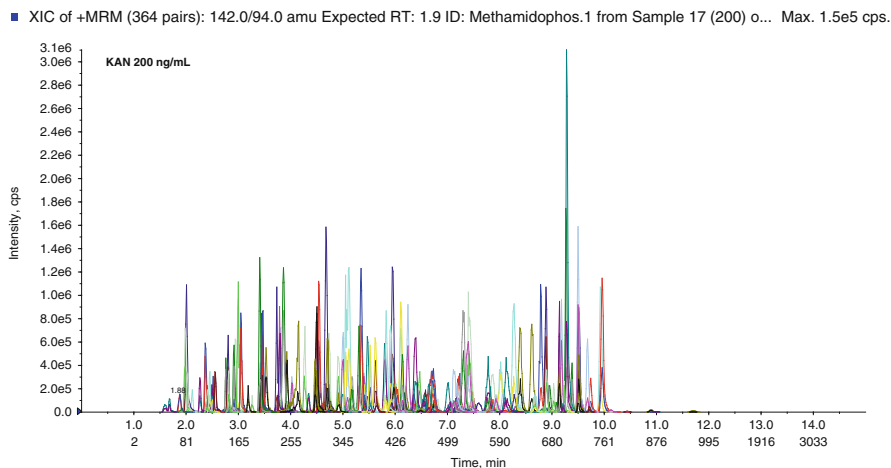
■ XIC of +MRM (364 pairs): 142.0/94.0 amu Expected RT: 1.9 ID: Methamidophos.1 from Sample 17 (200) o... Max. 1.5e5 cps.

Fig. 10.1 LC-MS/MS chromatograph of 190 P&ICs at 200 ng/ml

Identification of Chemical Residues

The most critical aspect of chemical residue analysis is the correct identification of the residue. Analysis of chemical residues at 1 ppb means exactly that, i.e. the analyte is one billion times less concentrated than the sum of the matrix components. The probability of incorrectly identifying a matrix interference response as the analyte of interest increases exponentially as the concentration of the analyte in the matrix decreases. For mass spectral determination this problem is compounded by the fact most chemical contaminants are small (100–500 Da), therefore they have less distinctive unit-resolved masses and ion fragments than larger molecules found in typical food matrices, such as proteins, that have molecular weights of several thousand daltons.

Identification Point System

The strategy for correctly identifying chemical contaminants is to reduce the probability of misidentification to acceptable levels by comparing empirical evidence of the sample to standard responses. To that end an identification point (IP) system was implemented for the analysis of P&IC residues. It was first developed and adopted in the Europe [24] to standardize the process of identifying residues in light of the explosion of available analytical technologies and has been modified and implemented in various forms in the US [25–27]. In the system IPs are assigned to each

Table 10.2 Assignment of identification points

	Criteria	Point assignment
a.	Low resolution MS ion	1 point per ion
b.	Low resolution MS/MS precursor ion	1 point per precursor ion
c.	Low resolution MS/MS product ion (transition)	1.5 points per ion
d.	High resolution MS (HRMS) ion	2.0 points per ion
e.	High resolution MS precursor ion	2.0 points per ion
f.	High resolution MS product ion (transition)	2.5 points per ion
g.	Matching chromatographic retention time (RT)	1 point per alternative systems
h.	Selective detection with matching RT	1 point per detector
i.	Quantitative agreement between alternate column/detectors	1 point per sample
j.	Isomers with matching RT	1 point

analytical technique, rather than adopting specific identification protocols. Identification of residues is accomplished when enough points have been obtained. While a minimum of 4 IPs are usually required, as few as 3 IPs might be sufficient when other nonempirical evidence is available.

The IP system is extremely flexible, allowing for the use of multiple analytical techniques, such as GC-MS, GC-MS/MS, LC-MS, LC-MS/MS, selective detectors, etc., for the identification of a residue. IPs are assigned by comparing the responses of samples to traceable reference standards analyzed concurrently on the same instrument. Spectral libraries and historical reference determinations may be used to investigate the identity of analytical residues, but IPs are only assigned for matching co-determined samples and standards. Typical analytical techniques used for P&IC residues are listed in Table 10.2 with their assigned IP values.

MS ions found in samples that match ions in standards are not automatically assigned IPs; the probability of encountering an MS ion in complex food matrices that matches a standard is too high. This probability is reduced by using the ion selection and ratio criteria listed below.

Ion Selection Criteria

(a) All selected ions must have a minimum signal to noise ratio of 3:1.
(b) Not more than two diagnostic ions may be selected from an isotopic cluster.
(c) If the molecular ion abundance is at least 10 % of the most abundant ion, it should be selected.
(d) Ions must have unique mass differences, e.g. avoid differences of 18 amu due to water loss, SRMs generated due to loss of adducts, such as ammonium ion (17 amu), etc.
(e) For LC-MS only one molecular ion species may be selected. For example, avoid the use of SRMs resulting from the loss of a adduct ion, such as ammonium adducts ($M-NH_4^+$) and the corresponding molecular ion (M^+) due to the loss of 17 amu (NH_3).

Table 10.3 Comparison of tolerance windows and percent of base peaks for GCMS and LCMS

Relative intensity	Tolerance window	
(% of base peak)	GCMS	LCMS
> 40 %	± 10 % absolute units	± 20 % relative units
≤ 40 %	± 25 % relative units	± 25 % relative units

Ion Ratio Criteria

Ion ratios are determined using the most abundant ion. In some cases, such as ultra trace residue levels or ion ratios less that 10 %, additional effort might be necessary to meet the criteria. For example, matrix interferences might be removed using background subtraction or standard addition. Ion ratio criteria are segregated between chromatographic technologies (HPLC vs. GC) and the relative intensities to the base peak response. Table 10.3 compares the tolerance windows for GCMS and LCMS as a percentage of their base peaks.

One point is assigned for each alternative chromatographic system provided the column chemistries are sufficiently different and the retention times of the sample and standard are within ± 0.05 min for GC and ± 5 % for HPLC. Matrices may shift analyte retention times in which case matrix matched standards or standard additions might be necessary. Large concentration differences between sample and standard might also cause a shift in retention times requiring the matching of analyte concentration in the sample and standard. Alternative chromatographic column chemistries are defined separately for GC and HPLC.

Alternative GC columns are based upon differences in their polarity ranging from nonpolar to mid-polar to polar chemistries as defined by their Kovats Retention Indices and McReynold's numbers available thru most column vendors. Examples of column chemistries demonstrating sufficiently different polarities include:

- Nonpolar: 100 % methyl, 95:5 methyl/phenyl
- Mid-Polar: 65:35 methyl/phenyl, 50:50 methyl/phenyl, 14:86 cyanopropylphenyl/methyl
- Polar: 50:50 cyanopropyl/phenyl, polyethyleneglycol (PEG)

Alternative HPLC columns are defined by more complex chemical interactions, including polarity, hydro- and lipophilicities, pi-bond interactions, to name a few. Examples of alternative reverse-phase columns include C8 or C18 versus cyano versus phenyl moieties. Alterative reverse phases using hydrophilic interaction chemistries would require empirical demonstration of chromatographic discrimination between analytes and matrices. Additionally, normal phase chromatography systems may always be used to confirm reverse phase systems.

One IP is assigned when alternative selective detectors are utilized. Alternative selective detectors must respond to different heteroatoms in the analyte. An example of alternative detectors would be a GC with a flame photometric detector (GC-FPD) in the phosphorus mode that responds primarily to phosphorus in

organophosphate residues, and a GC with electron capture detector (GC-EC) that responds primarily to electrophylic heteroatoms, such as halogens and oxygen. If a sample residue response matches the retention time and relative intensity of the same standard on a GC-FPD and a GC-EC, then one IP may be assigned. Only one IP may be assigned for alternative detectors.

An IP may be assigned for quantitative agreement between alternate columns or detectors. For some analytes that are difficult to quantify and for concentrations near the limit of quantification (LOQ) this requirement might be increased based upon the discretion of experienced analysts. A maximum of one IP may be assigned in this manner.

A single IP is assigned for each low resolution MS ion, including selected ion monitoring (SIM) and full scan acquisitions. Higher IP values are assigned based upon their probability of uniqueness to the analyte. For example, 1.5 points are assigned for low resolution product ion (transition) obtained using MS^n acquisition, including selected reaction monitoring and full scan acquisitions, because product ions are generated from specific parent ions that have been isolated and fragmented in the mass spectrometer. The probability of encountering a product ion in the sample that matches a standard product ion within the same chromatographic retention window is significantly reduced. That probability is further reduced when using high resolution mass spectroscopy. Two points are assigned for each high resolution ion as opposed to one point for a low resolution ion; and 2.5 points are assigned for each high resolution product ion compared to 1.5 points for low resolution product ions.

For residues with multiple isomers, one IP is assigned for the detection of isomers with matching retention times and relative responses. For example, one IP is assigned if all four isomers of cyfluthrin are detected. This IP may only be assigned once per analyte.

Some examples of positive identification of analytical residues using the IP system might include:

(i) Three ions from low resolution GC-MS in the SIM mode that meet the ion selection and ratio criteria and the retention time of sample and standard responses are within 0.05 min – 4 points (1 IP for each ion and 1 IP for the RT match). Note that although this meets the point criteria, identification using at least 4 GC-MS ions in the SIM mode is encouraged, but not always possible.

(ii) Two LC-MS/MS MRM product ions that meet the ion selection and ratio criteria and the retention times of the analyte and standard match within 5 % – 4 points (1.5 IP per product ion plus 1 IP for retention time match).

(iii) Analyte response of sample and standard have matching retention times on two different GC detection systems, e.g. GC-FPD and GC-ECD, that use a nonpolar column, and on an additional GC-FPD that uses an alternative GC midpolar column, and agreement of quantification between all three detection systems is within ± 30 % – 4 points (1 IP for each alternative detector plus 1 IP for matching retention times on alternative chromatographic systems plus 1 IP for the agreement of the quantifications).

Nonempirical Tools for Residue Identification

Heretofore, the process for the identification of P&IC residues in complex matrices has been limited to examination of empirical data, i.e. by comparing sample and standard analyte responses. However, judicious use of nonempirical information can augment the identification process. One extremely powerful tool for residue identification in a continuous US TDS is the table of historical findings. For example, an examination of the list of all the residues found in the TDS item "whole wheat bread" reveals that the pesticide malathion has been found in the item for 100 % of the samples analyzed. This is consistent with the fact that malathion is used extensively on grain products in the US. Given the historical information, one could say malathion is "expected to be detected" in whole wheat bread. Historical findings tables provide the analyst with an invaluable head start when investigating complex trace level instrument responses in samples. They are also useful when negating a suspect residue. If the empirical evidence is questionable and the suspected residue is not listed in an item's historical findings, then the probability of the residue being incurred in the item is unlikely. Additional evidence to support a new residue/item combination is required.

Maximum Residue Limits (MRLs), or tolerances, and regulated uses of P&ICs are another sources of nonempirical evidence of the likelihood that a suspected P&IC is legitimate. Some multicomponent TDS items can limit the effectiveness of this tactic because MRLs and prescriptive uses for chemical contaminants are assigned to specific raw agricultural commodities. All of the P&ICs reported with frequencies of 2 or more findings in the historical findings for whole wheat bread have tolerances and prescribed uses for wheat grain with the exception of a few industrial compounds commonly found in processed foods and the ubiquitous (in the US) perchlorate ion.

An additional tool to assist with the identification of residues is characterization of matrix responses, sometimes called "product peaks". Figure 10.2 contains two chromatograms that exhibit typical matrix responses of the brassica products cauliflower and cabbage, where: Fig. 10.2a is a chromatogram of cauliflower from a GC-ELCD; and Fig. 10.2b is a chromatogram of cabbage extract from a GC-PFPD. Sample responses labeled "Cole product peaks" are characteristic for all Cole products analyzed in the US TDS. The product peaks can be characterized by a retention index, which requires some work to establish a retention database. Another simpler practice is to catalog chromatograms of product peaks for easy visual reference.

Of course, the danger of using historical data, MRLs, and product peak characterization is self-evident, i.e. residues might be falsely reported positive or negative based upon nonempirical data. False reporting of a residue (false positive) can be avoided by requiring all residues to comply with the identification point criteria. The converse problem of not reporting a residue (false negative) can only be overcome by a healthy diligence to uncover and report trace level residues.
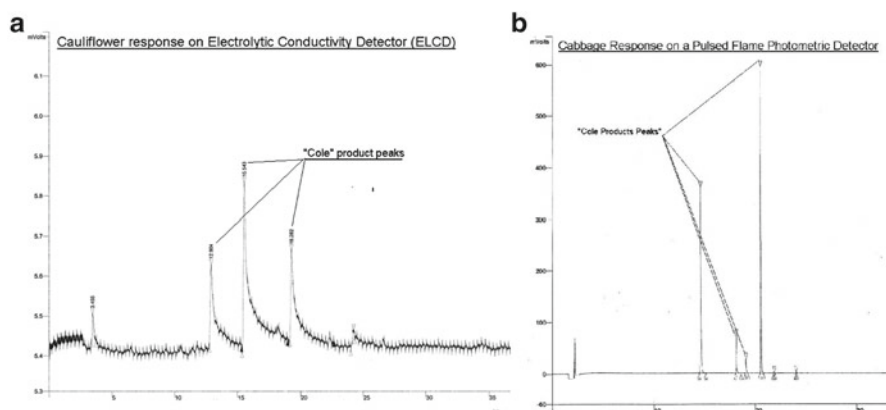
Fig. 10.2 Typical matrix responses. (**a**) cauliflower response on GC-ELCD, and (**b**) cabbage response on GC-PFPD

Contraindicating Data

Contraindicating data is any empirical evidence that a suspected residue is not present in an item. Regardless of how much data is generated to support positive identification of a suspected residue, when data is available that contradicts that identification it must be considered and overcome. For example, if a residue analyzed on a GC-MS generates retention and spectral data that meets the minimum IP criteria of 4 points, but data from a different analysis on a different instrument, e.g. an LC-MS/MS, is negative for the same residue, contradicting the GC-MS data, then the residue cannot be positively identified until the contraindicating data has been investigated and negated. In this example the GC-MS data would need to be carefully reviewed to determine its validity. The investigation might include determining whether the residue is present in blank or control sample analyses on the GC-MS, whether both instruments were calibrated correctly, whether the LC-MS/MS could detect the residue in the matrix, whether the sample integrity is violated because of cross-contamination, etc. In this example, the import of the investigation extends beyond the sample itself, because the capability of both the GC-MS and LC-MS/MS determinations is being questioned, so the investigation must be conclusive to resolve the contraindication. Additional examples of contraindicating data include:

- Unexplained or abnormal analytical behavior
- Abnormal chromatographic peak shape
- Lack of response on expected detector
- Unexplained differences between original and check analysis
- Absence of an expected diagnostic MS ion or the ion ratio is not within criteria

Quality Control

Quality assurance (QA) is a management system that assures data generated by a laboratory is of acceptable quality. Critical to the success of a QA program is the incorporation of quality control (QC) into the routine analytical regimen. QC is the empirical real-time measure of method and instrument performance, including analysis of method blanks and fortified samples and verification of instrument calibration initially and throughout the analytical determination. QC in analysis is also discussed in Chap. 13 – Quality Control and Assurance Issues Relating to Sampling and Analysis in a Total Diet Study. Procedures for the implementation of QC in the US TDS program are provided in KAN-LAB-PES.50 [28] and key aspects expanded briefly below

Method and Batch Quality Controls

Typical method performance QCs used in the pesticide laboratory include the analysis of blanks and fortified samples (spikes) with each batch of samples. Sample batches are defined as a group of samples that are analyzed concurrently using the same reagents and laboratory resources. While batch size could be as high as hundreds of samples, practical and logistical considerations of pesticide analysis generally limit batch sizes to less than 50.

Method, or reagent, blanks are analyzed with each batch to document interferences from laboratory contaminants that are occasionally detected during P&IC analysis. Matrix blanks, or control samples, would be optimal because they allow for the additional determination of matrix interferences; however control samples are very seldom available for P&IC analysis. Detection of actual target analytes in the blank is extremely rare and normally indicative of cross-contamination. More commonly detected are cleaning chemicals used in washing of the labware, equipment lubricants, hand lotions, creams, antimicrobial agents, and cleansers used by maintenance personnel. For example, shortly after the introduction of antimicrobial hand cleansers an Unidentified Analytical Response (UAR) was detected on the GC-ELCDs used for the detection of OH-P&ICs. The levels were too low to analyze by GC-MS until one sample had particularly high response of the UAR. Analysis by GC-MS in the full scan mode identified the UAR as triclosan, a common antimicrobial agent used in hand cleaners. Further investigation found the source of the triclosan was from several bottles of hand soap distributed within the lab by a well-intentioned maintenance worker. The bottles of hand cleanser were removed and the triclosan cross-contamination diminished but was not removed altogether; traces are still detected occasionally, probably from food-handling establishments and consumers.

Method accuracy and precision are demonstrated by the analysis of spikes with each batch of samples. The use of standard reference materials containing certified levels of P&IC residues would be ideal, as in the case of elemental analysis;

Table 10.4 Spike recovery limits for US TDS P&IC methods

Analysis	Analyte	Level (ppm)	Limits[a] Recoveries	RPD
GC determination of P&IC residues in fatty items	Dieldrin	20	50–130	40
	Parathion	20	45–115	40
GC determination of P&IC residues in nonfat items	Dieldrin	20	45–125	35
	Parathion	20	55–140	35
LC-FL determination of benzimidazole fungicides	Benomyl	100	60–110	20
LC-MS/MS determination of carbamate pesticides	Carbaryl	80	60–110	20
LC-EC determination of ethylenethiourea (ETU)	ETU	50	50–115	25
LC-MS/MS determination of phenylurea herbicides	Diuron	50	70–120	20
GC determination of chlorophenoxy acids and pentachlorophenol residues	2,4-D	100	40–120	40

[a]Calculated at the 99 % confidence level

however, they are generally not available for P&IC analysis. Method accuracy is verified by the calculation of the spike recovery. For example, in the US TDS duplicate samples are fortified at 20 ppb of dieldrin and parathion and analyzed for P&ICs using the general pesticide MRMs for the analysis of fatty and nonfat items by GC. A spike with a net residue concentration of 16 ppb parathion, i.e. after subtracting the amount of parathion in the sample, the recovery would be 80 % = 16/80*100 %.

Method precision is verified by statistical analysis of multiple spike recoveries. The best statistical indicator of precision is the Relative Standard Deviation (RSD); however, this statistic requires a minimum of 5 iterations to provide valid calculation of the standard deviation. In some P&IC programs each sample is fortified with a nontargeted analyte(s) that is not anticipated to be found by the screening procedure. Ideally, the spiked analyte does not interfere with the targeted analyte(s) and nearly approximates their performance. The RSD of the recoveries of the spiked compound provides an excellent measure of method precision. Alternatively, analytical precision can be estimated by calculating the Relative Percent Difference (RPD) between duplicate spike recoveries. RPD is determined by comparing the difference of the two spike recoveries with the average spike recovery. Typical spike recoveries of 90 % and 110 % would result in an RPD of 20 % = [110–90]/[(110+90)/2]*100 %.

Specifications for acceptable accuracy and precision are evaluated annually by statistical analysis of spike recoveries and RPDs. Limits are calculated for each spike analyte corresponding to the 99 % confidence level of the average recovery ± 3 SD. Table 10.4 contains the current US TDS spike recovery and RPD limits for each analytical/procedure combination. Spike recoveries outside the limits indicate the analysis may have failed and must be investigated.

Ideally, each matrix would be spiked with all the compounds within the scope of the procedure to assure acceptable accuracy of analytes in all matrices. Good examples of this technique are the analyses of perchlorate and dioxins that use isotopes

as internal standards. Because they are chemically identical to their respective analyte, analysis of isotopes provides the best measure of analyte performance; however, they are very costly, not always available, and require MS determination.

Analysis of every matrix fortified with all target analytes is not practical for a typical P&IC screening analysis, except in cases where the scope of analytes and matrices is extremely limited. One solution is the use of marker compound recoveries to represent the performance of all analytes. Marker compounds are chemicals that are known to be fully recovered by the methods employed. The analytes in Table 10.4 are the marker compounds utilized for their respective methods in the US TDS.

Other P&IC survey compounds may also be included in the fortification of the sample. Recoveries of these compounds are used to establish and maintain the scope of chemicals for the procedure; they are not generally used to assess the quality of an analysis.

Fortification standard solutions are prepared so their concentration result in a fortification level approximately 10 times their LOQ. In some cases, incurred residue levels or the presence of interfering sample coextractants may require the use of higher fortification levels. Fortification levels for the US TDS are also listed in Table 10.4. The dilution solvent used in preparation of the spike solution is chosen to minimally interfere with the extraction chemistry and volume of the procedure. Because spike recoveries are not useful to evaluate or monitor extraction efficiency, the spike sample is typically fortified during the initial sample extraction step, rather than fortifying the sample itself.

Instrument Quality Controls

In addition to the method, instrument performance is also monitored. Routine QC to monitor pesticide instrument performance includes the analysis of an initial calibration verification standard (ICV) and subsequent analysis of continuing calibration verification (CCV) and limit of quantification (LOQ) standards. The ICV is a standard solution prepared separately from the calibration standard solution that contains at least one of the calibration standard analytes. The response of the ICV is monitored to verify the calibration standard has been properly prepared, and the instrument has been calibrated correctly. Once the calibration has been shown to be acceptable, the LOQ standard is analyzed. The LOQ standard is one of the calibration standards diluted 5–10 times lower than the calibration level. In some P&IC analysis programs, the response of the LOQ standard is visually examined to ensure it is greater than the 5 times the noise level of the instrument. In the US TDS because so many residues are determined at the trace level, the LOQ standard is quantified and must be ±50 % of its nominal concentration.

After the ICV and LOQ standards have been analyzed and found acceptable, samples are analyzed. The calibration standard is intermittently analyzed at least once every 10–20 injections to verify the instrument calibration is maintained throughout

Table 10.5 ICV and CCV specifications

Determination	ICV limits		CCV limits	
	Low	High	Low	High
GC-FPD	55	135	70	130
GC-ELCD	50	150	55	145
GC-MSD	55	135	80	120
HPLC-FL (phenylureas)	80	120	80	120
HPLC-FL (carbamates)	80	120	80	120
HPLC-EC (ETU)	80	120	80	120
HPLC-FL (benzimidazoles)	80	120	80	120

an analytical run. As in the case of the marker compound spike recoveries, the specifications for the ICVs and CCVs are determined statistically each year based upon a 99 % confidence level. Table 10.5 lists some of the current ICV and CCV limits for the US FDA TDS program.

Quality Assurance

The FDA laboratories have incorporated all the fourteen management and ten laboratory requirements for the ISO 17025 standard into a total national quality management system. A complete discussion of the laboratory quality assurance program is beyond the scope of this chapter; however some aspects of the QA program as applied to P&IC analyses are highlighted, including control charting of QC data, reference standard preparation, review, and standard operating procedures. Chapter 13 – Quality Control and Assurance Issues Relating to Sampling and Analysis in a Total Diet Study also addresses QA in analyses.

Control Charting QC Data

As discussed earlier, method accuracy and precision are monitored in real time by comparing the batch spike recoveries and RPDs with the annually calculated statistical limits for the method/analyte combination. Method accuracy and precision are also evaluated for outliers and trends over time by control charting marker compound recoveries and RPDs on scatter plots. Figure 10.3 is a control chart of the marker compound parathion recoveries for a 12 month period. Examination of the recoveries reveals no outliers or trends, i.e. the recoveries are evenly scattered around the average recovery of 96 %. The three standard deviation values calculated from the graphed data of 62 % and 135 % are within the annually calculated control limits of 55 % and 140 % percent listed in Table 10.4.
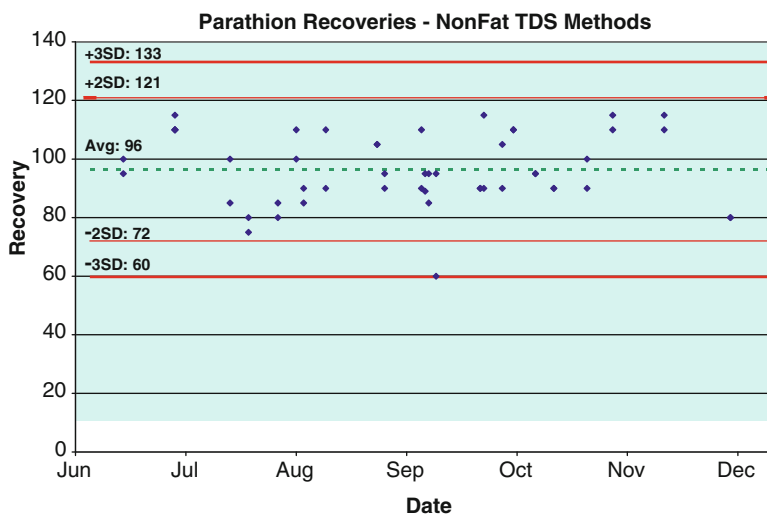
Fig. 10.3 Control chart of marker compound (Parathion) recoveries for nonfat TDS MRMs

Figure 10.4 is a scatter plot of the RPDs of the duplicate batch recoveries plotted in Fig. 10.3 with two and three standard deviation levels calculated from the data. The three standard deviation RPD level of 30 % is slightly better than the annually calculated limit of 35 % listed in Table 10.4 calculated for parathion and nonfat methods. Although no trends are apparent, one RPD of 45 % corresponding to duplicate spike recoveries of 60 % and 95 % is clearly an outlier, both of which are within the current limits of 55–140 % listed in Table 10.4. An investigation of the data uncovered no apparent reason for the disparity of the recoveries, so the data was not rejected.

Standards Preparation and Analysis

P&IC standards are prepared per KAN-LAB-PES.60 [29] and the general guidelines provided in the PAM. Reference standards are traceable to a certifiable source with the exception of a few for which a certifiable source is not available. Reference standard mixes used for routine P&IC analyses are prepared annually. Reference solutions prepared from neat standards are validated prior to use. In most cases the newly prepared standards are compared to the current reference standard mixes; agreement between them must be within 10 %. P&ICs not included in the current reference standard mixes are prepared in duplicate by different analysts, and then compared to assure they are within 10 % agreement.
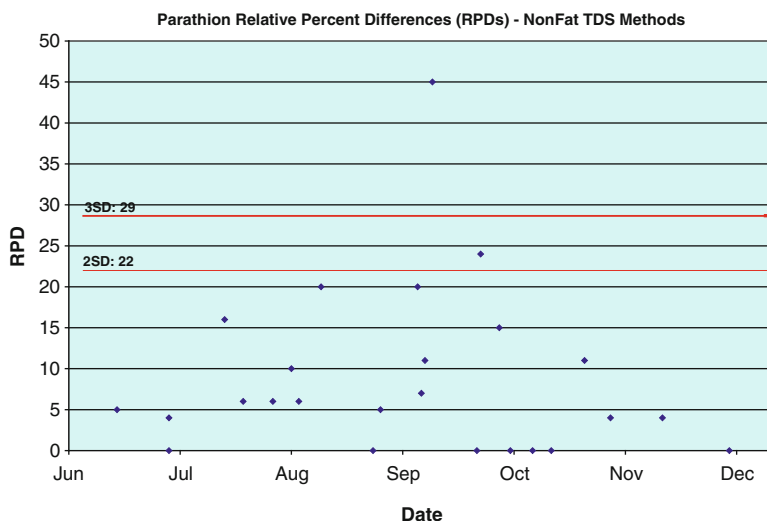
Fig. 10.4 Control chart of relative percent differences of duplicate marker compound (Parathion) recoveries for nonfat TDS methods

The reference standard mixes are designed by pesticide specialists who review historical residue findings, notifications from the US Environmental Protection Agency that establishes the MRLs, and other literature to determine anticipated residue findings in the coming year. This information is used along with known GC elutions and sensitivities to design screening standards composed of compounds with similar modes of detection. For example, several mixtures of organohalogens are prepared for determination by GC-ELCD, thermolabile and water soluble compounds are included in the LC-MS/MS mixtures. Once the screening standards are designed, concentrated mixes are either prepared or purchased from a certified vendor. Final injection standards are diluted from the concentrated mixes.

Review

As noted in the introduction, P&IC analysis is extremely difficult under the best circumstances; hence multiple levels of review are essential for the accurate identification and quantification of chemical residues in complex food matrices. Initially, all analytical work is reviewed by peers to ensure that analytical findings are accurately reported, e.g. identification criteria were met, integration of chromatographic responses are appropriate, instruments were properly operated and calibrated, no transcription errors were made, etc. A secondary review is conducted by a residue specialist to confirm the proper identification of the residue and the scientific plausibility of the finding. A third review is conducted to evaluate the historical and

regulatory significance of the residue and matrix combination. Finally, all P&IC results are recorded in a national database that is reviewed for accuracy.

The US TDS undertakes four regional market baskets (MBs) per year, each MB covering a different region across the US, and three different cities per region (See Chap. 41 – United States Food and Drug Administration's Total Diet Study Program for more details). After the data from each MB has been entered into the national database, several reports are generated to evaluate the data for trends. Spike recovery statistics are calculated to determine if average marker compound recoveries and RPDs are consistent with past MBs. Duplicate incurred residue findings are examined for agreement; and residue frequencies for each compound are compared to previous MBs. All new residue/item combinations are investigated and referenced to current and past US and international MRLs; items with a residue that is not listed in the US MRLs are reanalyzed. After all review is completed, the TDS MB report is prepared summarizing the MB logistics, program changes, residue frequencies, and new/unusual findings.

Standard Operating Procedures

Almost every aspect of the US TDS is addressed in Standard Operating Procedures (SOPs) specifically written for the TDS program; including the pesticide procedures previously mentioned. SOPs are controlled documents from their inception thru their retirement. Management approves and oversees the development of each procedure, ensures they are reviewed and updated annually, and controls user access to them. SOPs for the analysis of P&ICs in the US TDS provide specific instructions and specifications for all methods including an overview to the analysis of pesticides (KAN-LAB-PES.66 [30]), determination of moistures (KAN-LAB-PES.151 [31]), maintenance of instrumentation (KAN-LAB-PES.65 [32]), preparation and maintenance of standards, and quality assurance. The preparation of the TDS samples is addressed in SOPs KAN-LAB-PES.152 [33] and KAN-LAB-PES.161 [34]. The TDS procedures mentioned here are just a small fraction of the many SOPs, protocols, policies, and manuals required to assure quality and good laboratory practices in the laboratory.

Conclusion

The challenge of analyzing ultratrace levels of organic chemicals in an advanced TDS is substantial, but the benefits are invaluable. Residue incidence and levels found in table-ready foods provide overwhelming evidence of the effectiveness of the regulation of pesticide use and application. In regulatory pesticide programs, unprocessed raw agricultural commodities are analyzed for chemical contaminants and the levels found are compared to maximum residue levels to ensure their proper

use and application, however regulatory pesticide analyses do not provide information about the levels of contaminants in the diet of the consumer. The real evidence that the regulatory pesticide program is protecting the consumer from unsafe levels of chemical contaminants is found in the TDS program.

Furthermore, because TDS programs are designed around actual food consumption levels, the residue levels found in the TDS program can be converted to exposures and compared to the Acceptable Daily Intakes (ADIs) and other reference values established by the World Health Organization.

In the US TDS program the exposure levels of the most frequently found pesticides in the highest risk group (infants and toddlers) are more than 200 times below their ADIs. Even for the most extreme case, such as dieldrin, which has an ADI of 0.0001 mg/kg body weight/day that is 10–100 times lower than the typical level, the average exposure levels determined in the US TDS are 50 times below their ADI. These exposure levels provide solid evidence of the effectiveness of the pesticide regulatory program and ultimately the safety of the food supply; the challenge to protect the consumer is achieved.

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Chapter 11
Analyzing Food Samples—Inorganic Chemicals

Sean M. Ryan

Introduction

In 2009, over 300 different varieties and types of foods were being analyzed in the United States Food and Drug Administration (FDA) total diet study (TDS) program for inorganic chemicals/elements. However, not every element is determined in every item. Presently, 16 elements are routinely determined in these foods. Previously, as many as 24 elements were determined, but for various reasons, some of these elements have been dropped from the analytical list.

A total of 5 different analytical techniques are used to determine the 16 elements of interest. Four of these analytical techniques require the sample to be digested and dissolved in an acidic aqueous solution prior to introduction of the sample into the analytical instrument. Three different sample preparation techniques are used for these digestions. The fifth technique, the analysis of mercury, does not require sample digestion.

The procedures described within are general outlines and do not include all techniques and cautions. The full set of operational instructions can be found within the references listed below and are available from the FDA Kansas City Laboratory.

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Sample Preparation Techniques

Ternary Acid Digestion

This digestion scheme provides the avenue for the multiple determinations of elements in total diet items using Inductively Coupled Plasma Atomic Emission Spectrometry (ICP-AES) [1–3] and Hydride Generation Atomic Absorption Spectrometry (HGAAS) [4] techniques.

Arsenic, calcium, copper, iron, magnesium, manganese, phosphorus, potassium, selenium, sodium, and zinc are determined after the samples have been digested in a mixture of nitric, perchloric and sulfuric acids. Other elements including aluminum, antimony, cobalt, chromium, molybdenum, strontium, tin, titanium, and vanadium will be or have been previously determined in solutions prepared by using this technique. Approximately 260 total diet items are analyzed using this technique.

Depending upon the amount of lipids/solids and percent moisture, between 2.00 and 20.0 g of well-homogenized sample are placed within a quartz Kjeldahl flask. A small amount of deionized water may be used to wash down the sample into the flask. This is then followed by an acid mixture (4:1:1 by volume) of nitric, perchloric and sulfuric acids. It is advantageous to cover the Kjeldahl flask with a clean plastic beaker and allow the solution to react over night at room temperature. Following the Standard Operating Procedure [2] (SOP), carefully heat until only a clear solution of sulfuric acid remains. Initially, the more easily oxidized portion is attacked by nitric acid. Once all the nitric acid is consumed and/or boiled off, the temperature rises to the boiling point of perchloric acid. Perchloric acid attacks the more difficult oxidizable materials (such as fats). Eventually, all the perchloric acid is then boiled off, the temperature rises again and a clear solution of boiling concentrated sulfuric acid remains.

As the nitric acid is consumed, some samples may begin to char, which will adversely affect the recoveries of certain elements. Charring may be controlled by careful, small additions of nitric acid. Should it be necessary to add nitric acid at this point, it must be done with extreme caution, as rapid additions will result in violent expulsion of the solution. Once the digestion is complete, with the sample remaining in only sulfuric acid, it may be cooled and carefully diluted to a known volume with deionized water. After the initial dilution to volume, the digest may be volumetrically split for the separate ICP-AES and GFAAS determinations. Follow all appropriate laboratory contamination control procedures [5].

For the ternary acid digestion, each analytical batch consists of one method blank and one matrix spike/matrix spike duplicate sample fortified with the elements of interest, and 17 analytical samples. This gives a total of 20 sample flasks per batch. The first batch should also include the nonfortified analytical sample, preferably prepared in duplicate, which is then repeatedly chosen for the matrix spike/matrix spike duplicate pairs used in the remaining analytical batches.

Ternary Acid Digestion for Iodine

Iodine is determined after the samples have been digested in a mixture of nitric, perchloric, and sulfuric acids [1, 6]. All total diet items are analyzed for iodine. This digestion scheme provides the avenue for the determination of iodine in total diet items using ultraviolet-visible spectrophotometry [5] (UV-VIS) techniques. Iodine, in various forms, is oxidized to iodate (or higher oxides) during the digestion and is then prereduced to iodide by arsenic (III) in acid solution. Iodide catalyzes the reduction of cerium (IV) [yellow] to cerium (III) [colorless] by arsenic (III) in a somewhat involved process, which is enhanced by the presence of chloride. The disappearance of the yellow color of cerium (IV) is monitored at 420 nm.

Depending upon the amount of lipids/solids and percent moisture, between 1.00 and 2.1 g of well-homogenized sample are placed within a dry quartz Kjeldahl flask. A small amount of deionized water may be added to the dry reference material. (Never add any more than 1 ml of water per gram of reference material sample. Do not add any water to any analytical samples). This is then followed by 10 ml of nitric acid, 20 ml of perchloric acid, and 5.5 ml of sulfuric acid. It is advantageous to cover the Kjeldahl flask with a clean plastic beaker and allow the solution to react over night at room temperature.

The samples are heated and refluxed, using a cold finger condenser placed into the neck of the Kjeldahl flask. After the reflux period is complete (minimum of 1 h), the heat is turned off, the solutions allowed to cool, and the condenser is rinsed with deionized water, directing the rinsings into the flask. The condensers are then removed and the heaters are turned up to reinitiate boiling. The solutions are now heated to drive off all nitric and perchloric acids, leaving only sulfuric acid. Completion of the digestion is indicated when a condensation ring begins to rise up the neck of the flask. Iodine is easily lost during digestion sequences, so it is important that all procedures described in the reference [6] are followed meticulously. Proper weighing and handling techniques are critical to the success of the digestion. Also, assure that appropriate contamination control procedures are observed.

For the ternary acid digestion for iodine, each analytical batch consists of 100 total diet food items, six method blanks, at least one National Institute of Standards and Technology (NIST) reference material, five working standard solutions, one to two diluting solutions, one initial calibration verification (ICV) standard and six matrix spike/matrix spike duplicate sample pairs fortified with known quantities of potassium biiodate. This batch should also include the nonfortified analytical sample, preferably prepared in duplicate, which is then repeatedly chosen for use of the matrix spike/matrix spike duplicate pairs used in the remaining analytical batches.

Nitric Acid Solubilization and Direct Ashing Preparation
for Cadmium, Lead and Nickel

This digestion scheme provides the avenue for the determinations of cadmium, lead, and nickel [7] in total diet study items using heated Graphite Furnace Atomic Absorption Spectrometry [8] (GFAAS). Lead, cadmium, and nickel are determined after the samples have been digested with nitric acid, the nitric acid driven off, and the samples then oxidized further, using a stepwise furnace program, ramping up to 470 °C. Lead, in all total diet items, is determined using this technique and cadmium and nickel are determined in about 260 total diet items.

Depending of the type of sample, from 1 to 9 g of sample are weighed into a quartz beaker [9]. Suggested weights for sample types are shown in the referenced SOP [7]. A small amount of nitric acid and 1 ml of 200 mg/ml magnesium nitrate are added and the beaker is covered with a vented lid to prevent contamination. Magnesium nitrate is utilized to provide oxygen for conversion of the elements to low volatility oxides. It is advantageous to allow the sample to sit overnight before heating, to initiate digestion and reduce the chance of violent reaction upon heating. The covered beakers are placed on a hotplate at a low temperature and allowed to digest until vigorous reaction ceases and the samples are completely wetted. Careful observation is important at this point to manipulate temperatures and beakers to avoid spattering.

Once the sample solutions cease to exhibit vigorous reaction, the beakers are cooled and placed in a convection oven, where the temperature is gradually increased through a series of steps to continue the digestion and drive off the acid solution. After the prescribed solubilization steps are accomplished in the convection oven, the beakers are cooled and transferred to a muffle furnace where they are subjected to a programmed heating ramp to perform the dry ashing of the samples. The maximum suggested temperature of the muffling operation is 470 °C. At this temperature, the metallic oxides will not volatilize. The appearance of the ashed samples at this point should be light gray to white, with no remaining carbon. If ashing appears incomplete at this point, further treatment will be required, as described in the SOP. The sample residue remaining in the beakers can now be dissolved, with heating, with a small amount of dilute acid and diluted volumetrically for determination on the GFAAS.

For the nitric acid solubilization/direct ashing digestion, each analytical batch consists of one method blank and one matrix spike/matrix spike duplicate sample fortified with the elements of interest, and 17 analytical samples for a total of 20 sample flasks per batch. The first batch should also include the nonfortified analytical sample, preferably prepared in duplicate, which is then repeatedly chosen for use of the matrix spike/matrix spike duplicate pairs used in the remaining analytical batches.

Sample Analysis Techniques

Inductively Coupled Plasma Atomic Emission Spectrophotometry (ICP-AES)

Calcium, chromium, copper, iron, magnesium, manganese, molybdenum, phosphorus, potassium, sodium, and zinc are determined and reported using an axial view ICP-AES [3]. A radial view ICP-AES may also be used, although the sensitivity will be lower. Arsenic, cadmium, nickel and selenium are also determined using this technique, but generally these elements are not reported using this method.

As described in the ternary acid digestion [2], the sample preparation results in a 10 % sulfuric acid solution. Prepare all calibration standards similarly. Follow instrument manufacturer's recommended conditions and consult the reference [3] for the specific instrumental parameters. The use of an internal standard is preferred. Yttrium, indium, or scandium may be used for internal standards.

Following the initial instrumental calibration of all elements of interest, an initial calibration blank (ICB) is followed by another independently prepared initial calibration verification (ICV) standard. This ICV standard should be prepared independently from the standards used in the calibration curves. Ideally, this ICV standard would be prepared or obtained from sources different than those used for the calibration standards. The ICV is used primarily to verify the accuracy of the standard calibration curve. Quality control criteria should be set for the recovery of analytes determined in the ICV and linearity of the calibration standards. Generally, 100 ± 10 % of the known ICV reference value is acceptable and a correlation coefficient (r) of $>= 0.9975$ of the calibration curves are in order. These two criteria must be met in order to proceed further.

Blocks of ten samples each (including method blanks, reference materials, samples, and matrix spikes) are followed by continuing calibration blanks (CCB) and continuing calibration verification standards (CCV). The CCV can be any standard, preferably with known concentrations near the midpoint of the calibration curve. Criteria must also be set for CCV standard, typically 100 ± 10 or 15 %. The CCV is used primarily to verify that instrumental drift of the calibration curve has not occurred. Criteria for ICBs and CCBs can also be set, if needed. Should any element fail the recovery criteria, the analyses must be stopped and only the results preceding the last acceptable CCV can be reported. The problem must be investigated and remedied before the analyses can be restarted. Criteria should also be set for the recovery of reference material and matrix spikes. Generally, 100 ± 20 or 25 % recoveries are typical. Duplicate analyses results, for results greater than the limit of quantification (LOQ) should be $<= 30$ % Relative Percent Difference (RPD) [10].

Although modified slightly for each analytical technique, each of the other analytical techniques has similar quality control requirements.

Hydride Generation Atomic Absorption Spectrometry (HGAAS) Determination of Selenium and Arsenic

Selenium and arsenic are determined sequentially from a solution aliquot obtained from the ternary acid digestion using a hydride generation atomic absorption technique [4]. A known volume of hydrochloric acid is added to a known volume of the resultant 10 % sulfuric acid sample solution. Selenium (VI) is reduced to selenium (IV) under these conditions. The sample solution is introduced into the instrument sampling loop, and is mixed with a basic solution of sodium borohydride. Selenium in the sample is reduced to gaseous selenium hydride, the gas passed into a gas/liquid separator, and the resultant dried gas introduced into a heated quartz cell, where elemental selenium results. Selenium is then determined by atomic absorption spectrometry.

Once selenium has been successfully determined, a known amount of ascorbic acid/potassium iodide solution is added to the remaining solution. Mix and allow this solution to stand overnight in order to reduce the arsenic (V) to arsenic (III). Calibration standards should be treated identically. Arsenic is then determined similarly to selenium.

Prepare all calibration standards in a matrix of 10 % sulfuric acid and 6 % hydrochloric acid. Follow instrument manufacturer's recommended conditions and consult the reference [4] for the specific instrumental parameters. Quality control procedures, similar to those above in inductively coupled plasma section, should be followed. Consult the reference [4] for the exact quality control requirements.

UV-VIS Spectrophotometry Determination for Iodine

Ce(IV) ions are reduced by As(III) and the reaction is catalyzed by iodide (I⁻) in an acid solution [6, 11, 12]. The reduction of the yellow Ce(IV) to colorless Ce(III) is followed spectrophotometrically at 420 nm. The inverse absorbance is proportional to the concentration of iodide in the samples.

Potassium biiodate, primary standard grade, is used for the preparation of all stock and working iodine calibration standards. Prepare all calibration standards in deionized water and carry all calibration standards through the digestion procedure. Failure to digest calibration standards will result in a poor standard curve. Follow instrument manufacturer's recommended conditions and consult the reference [6, 12] for the specific instrumental parameters. Quality control procedures, similar to those above in inductively coupled plasma section, should be followed. Consult the reference [6] for the exact quality control requirements.

Determination of Lead, Cadmium, and Nickel by GFAAS

Lead, cadmium, and nickel are each determined individually using Graphite Furnace Atomic Absorption Spectroscopy (GFAAS) [8]. As described in the nitric acid

solublization direct ashing digestion [7], the sample preparation results in a 5 % nitric acid solution. Prepare all calibration standards similarly. Follow instrument manufacturer's recommended conditions and consult the reference [3] for the specific instrumental parameters. Each element analyzed will require differing instrument conditions, analytical wavelengths, graphite tubes, and matrix modifiers.

Peak area rather than peak height is the preferred method of measurement. Other species (such as chlorides, sulfates, sulfites etc.) have slightly different atomization temperatures that result in peak broadening, rendering simple peak height measurements questionable. Background correction should always be used, and Zeeman background correction is to be preferred.

All appropriate laboratory contamination control procedures should be followed as lead, nickel, and cadmium are common laboratory contaminants when determined at the exceeding low levels required for total diet analyses. Quality control procedures, similar to those above in inductively coupled plasma section, should be followed. Consult the reference [8] for the exact quality control requirements.

Determination of Total Mercury

Unlike the previous four determinations for elements in the US TDS, analysis for mercury does not require the sample be digested/solubilized [13, 14]. Historically, analysis of total mercury in the total diet program involved a wet block digestion procedure followed by analysis using cold vapor atomic absorption. This older procedure and SOP is still available upon request [15]. This preparation procedure and analysis has now been replaced. An automated direct mercury analyzer, the Teledyne Hydra-C Automated Direct Mercury Analyzer, is now the instrument used for the analysis of mercury in the FDA TDS. The procedure used for mercury analysis is based upon the U.S. Environmental Protection Agency method 7473.

The analytical process [14] involves combusting of the sample in an atmosphere of oxygen at high temperature. The gases formed are passed through a heated catalyst that removes halogens, nitrogen oxides and sulfur oxides. The remaining combustion products including elemental mercury are swept into a gold amalgamation tube. The amalgamation tube captures all the mercury and then the tube is heated to release the mercury. The mercury vapor is then swept into a cold vapor atomic absorption spectrometer and the mercury determined. Quality control procedures, similar to those above in inductively coupled plasma section, should be followed. Consult the reference [13] for the exact quality control requirements.

Inductively Coupled Plasma Mass Spectrophotometry (ICPMS)

One of the goals of the FDA TDS program is to replace many of the previously mentioned preparation techniques and instruments with one sample preparation and one instrumental analysis determination [16]. Sample preparation using microwave

oven technology followed by ICPMS determination of elements will likely meet this goal. All of the previously mentioned preparations and determinations (with the exception of iodine and perhaps mercury) will likely in the future be replaced and samples digested by microwave and determined by ICPMS only. Any additional elements added at a later date can easily be determined by this procedure.

The amount of sample digested will likely be reduced from the amount presently used. This will result in even greater challenges in obtaining a representative homogeneous sample for microwave sample preparation than is experienced today. The focus of investigational work may be shifted from analytical means to sample preparation.

References

1. This procedure should only be attempted by personnel familiar with the hazards associated with hot, boiling, concentrated acids. Proper use of safety equipment is absolutely necessary, particularly in dealing with the safe use of perchloric acid. Violent reactions can sometimes occur during or prior to heating, especially with samples containing alcohols or high amounts of lipids. Follow all safety procedures indicated in all laboratory procedures and references within
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5. KAN-LAB-MET.90: Elemental analysis – contamination control, Laboratory Procedure. Food and Drug Administration, Kansas City District
6. KAN-LAB-MET.95: Determination of iodine in foods, Laboratory Procedure. Food and Drug Administration, Kansas City District
7. KAN-LAB-MET.97: Nitric acid solubilization and direct ashing procedure for lead, cadmium and nickel, Laboratory Procedure. Food and Drug Administration, Kansas City District
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Chapter 12
Analyzing Food Samples—Radionuclides

Pamela Mackill and Cong Wei

Introduction

The United States Food and Drug Administration (US FDA) started its first total diet study (TDS) in 1961 as a program to monitor for radioactive contamination of foods [1]. Since then, it has become a program that determines levels of various contaminants and nutrients in foods, which are purchased throughout the US and prepared as they would be normally consumed. The radiological component of the TDS program provides a basis for realistic evaluations of the dietary exposures of the analyzed radioisotopes by the US population. It also establishes a baseline of analyzed radioisotopes in the US population's dietary intake. If it is designed and planned appropriately, the program can also serve as an effective tool for ensuring the nation's food safety and food defense.

Sample Collections and Analyses

General TDS samples are prepared four times a year and each time the samples are collected from different geographic regions of the US. The radiological component of the TDS involves analyzing radioisotopes in the samples from two of the four sample collections. Currently, the radiological TDS program requires US FDA's Winchester Engineering and Analytical Center (WEAC) to conduct gamma-ray analysis and analysis for strontium 90 (Sr-90), a beta-particle-emitting radioisotope.

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Gamma-Ray Analysis of the TDS Samples

This section briefly describes how gamma-ray analysis has been conducted at WEAC [2]. Basically, the food samples are prepared and then gamma-ray emitting radioisotopes in samples are analyzed using high-purity germanium spectrometers. Given varieties of densities among various food matrices, attenuation of the measured activities due to food density is corrected. The procedure also corrects counting losses due to cascade summing.

Sample Preparation

Samples are obtained and secured according to appropriate sample handling procedures. Samples are also maintained in accordance with labeled instructions for preservation and storage. When no labeling or instruction for storage is indicated, the analyst is expected to take appropriate measures to maintain the quality of the food until the time of compositing. These measures may involve refrigeration and freezing. Typical sample preparation involves thawing the sample if necessary, maintaining the food at refrigerated temperature if necessary, and avoiding delay between compositing and counting to minimize uncertainties due to composite layer separation and settling.

The inedible portion of the sample should be removed from all portions that will be used for analysis. Any utensils used in the sample preparation are to be clean, and cannot be used again for another sample until they have been cleaned per standard procedures. The edible portions of sample are combined according to procedures, usually using a food processor or blender to create a homogenous composite. A standard container holding approximately 400 ml of sample is used for hosting sample and counting.

Sample Analysis

Once a geometry is chosen, the composited sample is homogenized, packed into the chosen geometry container and weighed. The identification and the mass of the sample are recorded. The sample is then placed on a gamma-ray detector for counting for a certain time interval depending upon the program requirement. Gamma-ray spectrometers are configured to accumulate counts from gamma-ray emissions of 50–2,000 keV. The gamma-ray counts collected by the detector produce a spectrum which allows an application software provided by the equipment supplier to identify various spectral lines and to compare and correlate those spectral lines with responsible gamma-ray emitting radioisotopes using a selected radionuclide library. If a spectral line is detected within the user defined energy tolerance range, a match will be declared. If more than one spectral line is identified within the energy tolerance range, the closest match is chosen.

The following equation is used to calculate the activity concentration of a radionuclide in the sample:

$$A_d = \frac{P}{q \times \varepsilon_d \times b \times E_l} \times e^{\lambda T_s}$$

The efficiency value, ε_d, is a variable dependent on a sample density.
The equation used to calculate the density correction factor is shown below:

$$dcf = \frac{\varepsilon_u}{\varepsilon_d}$$

The minimum detectable activity concentration (MDC) is calculated using the following equation utilized by the application software:

$$MDC = \frac{\left(2.71 + 4.65 \times \sqrt{B}\right)}{q \times \varepsilon_u \times b \times E_l} \times e^{\lambda T_s}$$

Here, the MDC value is prior to the density correction. The result obtained is further processed by taking into account of matrix density effect for MDC.

The Limit of Quantification in activity concentration (LOQ) is calculated using the following equation:

$$LOQ = \frac{50\left\{1 + \left[1 + \dfrac{B}{12.5}\right]^{\frac{1}{2}}\right\}}{q \times \varepsilon_d \times b \times E_l} \times e^{\lambda T_s}$$

where,

A_d = Activity concentration (Bq/kg) corrected for sample density
q = Sample quantity (kg)
d = Sample packing density (kg/l); $d = q/V$
V = container fill volume; $V = 400$ ml or 0.4 l
ε_u = Uncorrected counting efficiency
ε_d = Density adjusted counting efficiency; the uncorrected counting efficiency/dcf
b = gamma-ray abundance
E_l = Elapsed live time (seconds)
Λ = decay constant (ln2/$T_{1/2}$); seconds^{-1}
$T_{1/2}$ = half-life of radionuclide; seconds
T_s = sample date – acquisition date; seconds
P = Net Peak Area introduced by a sample after subtraction of environmental background
dcf = density correction factor

$B = B_{SC} + N_B$; *The background counts used for the MDC and LOQ calculations in the region of the radionuclide key-line energy*

B_{SC} = *The continuum counts in the region of the radionuclide key-line energy in the sample spectrum*

MDC = *Minimum Detectable Activity Concentration*

LOQ = *Limit of Quantification*

Sr-90 Analysis of the TDS Samples

Because of the nature of food matrices, Sr-90 analysis is a lengthy and labor-intensive process. A brief summary of the procedure is described below [3]:

After completion of gamma-ray analysis of a sample, the sample is used for Sr-90 analysis. The sample is ashed first and then digested in nitric acid. The resultant sample solution is mixed with nitric acid equilibrated tributylphosphate in a separatory funnel where yttrium 90 (Y-90) is separated from Sr-90 and the sample matrix. After removal of iron and rare earths by fluoride ion and hydroxide ion precipitations, the purified Y-90 is deposited onto a glass fiber filter as yttrium oxalate and the beta emission from the Y-90 is counted using a low-background internal gas-flow proportional counter. The Sr-90 concentration in a sample is equal to the Y-90 concentration calculated with its respective attenuation-corrected counting efficiency, chemical yield, decay correction factor, and sample weight.

Quality Control of the Sample Analysis

Gamma-Ray Analysis

Gamma counting efficiency is sample specific and must be determined with the same geometry that is used for the sample. Whenever possible, a matrix and geometry specific efficiency should be established. Efficiencies for mixed-gamma standards are determined annually or after a detector is repaired. An efficiency fit is considered acceptable when an analysis of a Laboratory Control Sample (LCS) using the new efficiency file yields results with an uncertainty that overlaps the certified uncertainties for each radionuclide declared in the certificate. This quality control is documented in a quality control logbook.

Prior to sample analysis, a check standard shall be counted and evaluated to demonstrate that the instrument is suitable to collect sample data. During periods of time when no samples are being analyzed, this check must be performed at least weekly. After the standard is counted and passed quality control criterion, the spectrum is analyzed to demonstrate that the instrument is meeting specifications for energy, resolution and efficiency.

Background Checks

The background check spectrum is collected in conjunction with food sample analysis. This check analysis is conducted daily. During periods when no samples are being analyzed, a daily background check must be performed at least weekly. The counting of a daily background should be reported on the function verification/preventative maintenance chart.

Strontium 90

The quality control for analysis of Sr-90 in foods involves insuring instrument quality control and method procedures quality control. For instrument quality control, it basically requires routine instrument calibration, which includes establishing operating voltages for alpha and beta particle counting and corresponding efficiencies; making sure both alpha and beta counting efficiencies meet established criteria. Continuing quality control steps are also implemented, which involves: monitoring background; counting both alpha and beta standard sources and insuring the source activities are within the established quality control boundary; and monitoring the quality control chart trend. The method quality control procedures basically require the analysis of LCS, analysis of method blank sample with each batch of TDS samples. The results of both LCS and method blank samples need to meet established criteria. The quality control criteria, i.e. the warning and control limits, are preestablished according to the corresponding historical data or standard reference value(s) for each quality control element. The laboratory corrective action procedures are followed if there are any quality control violations.

Key Findings

WEAC sample analysis results of past decades indicated that the levels of analyzed radioisotopes in the foods collected for the analysis have been minimal, or notdetected for most samples. In rare cases, trace results were found from certain samples. A non-detected result was assigned if the detected level is below the minimum detected activity (MDA) per kilogram of a sample; trace was assigned if a detected level was above the MDA and below the LOQ of the detection system used for the analysis. It is worth noting, however, that the detected trace levels were far below the FDA's derived intervention levels (DILs). For instance, the DIL for Cs-134 and Cs-137 together is 1,200 Bq/kg, whereas a typical MDA for Cs-134 is at the scale of 1 Bq/kg and the same holds true for Cs-137. The Cs-134 and Cs-137 activity levels in the samples have been below the MDA values. The DIL for Sr-90 is 160 Bq/kg, whereas the MDA values have been mostly below 0.1 Bq/kg. The Sr-90 activities of the samples have been mostly below the MDA values. In rare cases, the Sr-90 activity of certain samples was detected at a level above the MDA.

For instance, the highest Sr-90 activity of 2004 TDS samples was found at 0.28 Bq/kg with the 0.08 Bq/kg MDA value and 0.38 LOQ value. The data collected in the last decade also showed that there have not been variations in the analytical results of the samples collected in different years.

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Chapter 13
Quality Control and Assurance Issues Relating to Sampling and Analysis in a Total Diet Study

Pieter Scheelings

Introduction

Given that the overall cost of total diet study (TDS) programs can be significant, it is prudent to ensure that the integrity of such programs are not compromised because of inadequate analytical quality control and assurance. Furthermore, the public health cost of unreliable or inaccurate data applied to dietary exposures and associated community health impacts are likely to be much more considerable although difficult to quantify. These cost considerations apply equally to national TDS programs as to community health studies, which underpin environmental policies associated with regional mining operations or industrial activities. The cost of using incorrect data will be magnified where public health interventions are based on flawed data.

The integrity of TDS data is a function of the comprehensiveness of the sampling strategy and the reliability of the laboratory operations. Laboratory activities require particular care as the analytical data impacts on the health assessment of specific populations in regard to dietary exposure to environmental and other contaminant chemicals. Data integrity may have other impacts where, for example, the data is used as a baseline for comparison with new follow-up studies or where the data is incorporated into an international database, which may be used to compare the global health of communities against the chemical intake through diet. Since analytical laboratories are a key component of any TDS, laboratory personnel should be involved in the planning of TDS programs.

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Factors That Influence Data Quality

Representativeness and Integrity of Samples

While the selection and purchase of samples falls outside the traditional role of the analytical facility, laboratory staff will likely be consulted in the design stages of the TDS program. This may include scheduling of sampling, sample packaging, transport and storage, minimum size for processing and analysis and optimum sample submission batches, particularly for food samples that require rapid laboratory processing to minimize deterioration.

Although it is not uncommon for laboratory staff to be involved in the collection of food samples, the traditional role of the laboratory commences when samples are received in the laboratory. As the quality of laboratory data is intrinsically linked to the identity and integrity of the samples, it is critical that the sample submission information is checked against the samples provided. Discrepancies should be recorded and communicated to the program coordinator. All food samples should have clear and detailed labels with client reference numbers. Sample reception staff in the laboratory need to verify the integrity or 'consumption quality' of fresh fruit, vegetables, raw meat, fish and eggs and check the packaging of processed foods for breakage, mold, insect infestation or other possible foreign matter. Foods with short shelf lives should be processed as soon as practical or stored at appropriate temperatures to minimize loss of quality.

Preparation and Cooking of Food Samples

Other than foods and beverages consumed as purchased, most foods will need to be prepared and cooked in accordance with strict protocols, which are prescribed in the TDS Procedures Manual normally prepared and supplied by the TDS coordinator. Food preparation may be undertaken by a third party such as a home economics school or contract kitchen, prior to receipt by the laboratory. The responsibility for verifying the integrity of samples received from samplers then transfers to the third party. In Australia it is now more common to contract the laboratory to undertake food preparation and cooking provided it has the facilities and relevant staff experience to prepare cooked samples. Receipt, preparation and cooking at one site minimizes problems relating to relabeling, repackaging, transport and storage of samples prior to analysis.

Preparation of Laboratory Samples

The preparation of laboratory test samples generally involves the sub-sampling, compositing, mixing and homogenization of primary foods in accordance with the

TDS sample preparation instructions. Sample compositing may be based on set volumes or weights of the individual samples and care needs to be taken that the accuracy of sub-sample weights or volumes is within the protocol specifications. Samples of dry powders may require cone and quartering while others may require grinding prior to sub-sampling for composites. Some high sugar confectionery foods may require cryogenic grinding to facilitate homogenous preparation. It is important that laboratories adhere closely to the sample preparation protocol to minimize bias towards unrepresentative samples.

When the composite has been prepared, it is recommended that a number of sub-samples be packaged in individual glass or inert plastic sample bottles and stored cold or frozen prior to analysis. Analysis for organic residues and contaminant metals are normally undertaken by different sections of the laboratory and it is advisable that at least a spare sample is available in case of some operational mishap. It is also good practice to repeat the analysis on a new sample to verify unusual or unexpected analytical values. Where analyses are sub-contracted to other laboratories due to lack of in-house expertise, or instrumentation or for quality assurance purposes, additional test samples need to be packaged and stored.

Preparation of Analytical Test Samples

An analytical test sample is simply defined as a sample that undergoes chemical analysis. Composite laboratory samples, when stored frozen, should be allowed to attain ambient temperatures prior to sub-sampling. Some further mixing with an omni-mixer or similar may be required where 'settling' of the matrix has occurred. After taking a weighed test sample, the composite sample should be returned to storage to minimize deterioration. Analyses should be planned and undertaken in optimum batch sizes allowing for a number of reagent blanks, sample duplicates, Quality Control (QC) samples and, where available, Certified Reference Materials (CRMs).

Laboratory Competence and Quality Systems

The technical competence of an analytical laboratory can in part be judged by the formal adoption of a quality management system, compliance with the principles of good laboratory practice or technical accreditation to ISO/IEC 17025. Whether the laboratory holds formal accreditation or quality systems certification, it is essential that the laboratory has a proven reputation in organic residue and contaminant metal analysis in foods. Ideally the laboratory should hold technical accreditation for such methods and can demonstrate its ongoing competence in relevant inter-laboratory proficiency studies.

Laboratory Infrastructure

Analytical laboratories should be located in dedicated buildings, designed and fitted out to comply with appropriate standards for workplace health and safety. Of particular importance is that laboratory operations are sufficiently segregated to avoid cross-contamination between samples or from the working environment. Laboratories in developing countries may be more susceptible to contamination problems when located in non-laboratory designed buildings, for example, possible heavy metal contamination from airborne dust, elevated levels of iron due to corrosion of laboratory fittings, or sodium contamination where located in close proximity to seawater. Care should also be taken where laboratory areas including outside areas are sprayed with insecticides, which are likely to result in high background levels of organic contaminants.

Methods and Instrumentation

Methodology

It is highly preferable that the analytical methods employed are standard or official methods which have stated validation parameters and have undergone inter-laboratory collaborative studies. It is even more crucial for a TDS, where the sensitivity of the methods may be several orders of magnitude higher than those required for routine regulatory or monitoring programs. It is incumbent on laboratories and analysts, therefore, to verify their capabilities to replicate the key method characteristics, including precision, bias, limit of detection (LOD), limit of quantification (LOQ) and analyte specificity, prior to use of a method as well as on-going monitoring of accuracy and precision during use.

For a TDS where trace levels of residues, that is, those levels lying between the LOD and LOQ, may be reported, it is important that there is a consistent or agreed approach to the establishment of LOD and LOQ for the target analytes in the matrices being analyzed. Vogelgesang and Hädrich [1] have provided a statistical approach for practitioners for the establishment of LOD and LOQ.

In previous Australian TDS studies, it has been common practice to report trace levels for residues observed between the method LOD and LOQ. Depending on how the LOD and LOQ is established, this practice may give rise to some false positives as well as lower concentrations of trace components where the identity of the analyte may not be readily confirmed. In order to provide some consistency in the lower level reporting procedures, TDS program designers should consult with laboratory managers or analytical scientists to establish a common procedure for the determination of LOD and LOQ. Note that confidence indicators for both identification and confirmation of organic residues will likely be different for banned substances than for compliance testing for permitted residues in foods. WHO GEMS/Food has developed guidance for the reliable evaluation of low-level contamination

of food [2]. The issue of reporting and modeling of results below the LOD is covered in Chap. 16 – Reporting and Modeling of Results Below the Limit of Detection.

Metals

For trace and contaminant metal analyses, common procedures include initial acid digestion using open hot plate, hot block or microwave techniques followed by metal determination using atomic absorption spectrometry (AAS), graphite furnace atomic absorption spectrometry (GFAAS), inductively coupled plasma atomic emission spectrometry (ICP-AES), or inductively coupled plasma mass spectrometry (ICPMS). These methodologies are described in more detail in Chap. 11 – Analyzing Food Samples—Inorganic Chemicals.

Trace metal laboratories for multi-element residues in foods are increasingly adopting microwave digestion combined with ICPMS. Microwave digestions are rapid and incur minimal loss of volatile metals. Considerable care is required in the acid cleaning of the heavy duty Teflon-based digestion vessels after use as they have a propensity to absorb lead from highly contaminated samples which can then migrate back into subsequent digests leading to false positive or elevated lead levels. The inclusion of reagent blanks in TDS programs is critical in verifying that the laboratory environment, reagents and re-useable vessels do not contaminate program samples, particularly where very low levels of metal residues are expected.

Open digestion blocks are now designed to operate with disposable digestion tubes that minimize the potential of cross-contamination from previous digestion steps. Open hot-block digestions, however, are not well suited to the more volatile metals such as mercury and its organic analogues. Hot-block digestions are relatively simple to undertake, cost-effective in regards to equipment investment and labor use and well suited to large batch analyses. The inclusion of a number of control samples, spiked samples, and, where available, CRMs is highly recommended in underpinning the analytical quality assurance.

Modern ICPMS instruments combine high sensitivity and selectivity with simultaneous multi-element quantitation. The interfacing of liquid chromatographs to ICPMS instruments has facilitated the resolution of metal species of arsenic and mercury, which, in due course, will enable TDS programs to focus on the more toxic species of these and other elements in foods. The availability of relevant standards and CRMs of these compounds will be essential in the subsequent speciation studies and collection of data.

Organic Residues

The determination of organic residue levels and profiles in foods and beverages is considerably more complex than metal profiles due to the greater variety and diverse chemical properties of organic residues derived from agriculture and industry use.

Sample extraction and clean-up of food extracts for low-level pesticide residues is a considerable technical challenge and a number of standard methods of the Association of Official Analytical Chemists and other organizations are available which have been developed primarily for compliance with international Codex or national Maximum Residue Limits (MRLs). This is described in detail in Chap. 10 – Analyzing Food Samples—Organic Chemicals. The desire to identify and report, at a reasonable level of confidence, residues between the LOD and LOQ for TDS samples provides an additional challenge for the analyst and the laboratory.

The QuEChERS-based methods [5], which are finding increasing application in the extraction of pesticide residues from fruit and vegetables, are well suited to smaller laboratories in developing countries as the procedure is comparatively cheap, quick, uses minimal quantities of high purity solvents and has been extensively validated particularly for high water containing matrices. The methodology is currently under investigation for suitability for TDS samples by the Kansas City Food and Drug Administration laboratory (see Chap. 10 – Analyzing Food Samples—Organic Chemicals). The use of QC samples, matrix-spiked samples and, where available CRMs or remaining proficiency testing samples is a key quality assurance (QA) activity.

Although gas chromatography (GC) combined with a range of selective detectors have been the 'core' of residue programs, the interfacing of GC with mass selective detectors (GC-MS) and tandem mass spectrometers (GC-MS/MS) has provided considerable improvements in sensitivity, selectivity and structure identity. GC-MS and GC-MS/MS are now essential tools for trace residue laboratories. In addition, the development and availability of liquid chromatography/mass spectrometry (LC-MS) technology has meant that the LC-MS has a complementary role to GC-MS. The application of state-of-the-art liquid chromatography/mass spectrometry is well suited to TDS studies where trace levels, particularly of ubiquitous chemicals, may well be important in establishing the overall dietary exposure to organic residues.

The application of mass spectrometry to the identification and quantitation of trace organic residues, however, requires considerable skill and the application of some rules in confirming the presence of organic residues. Methods need to be fit-for-purpose and fully validated, preferably by collaborative studies involving competent laboratories. The rapidly changing technology of hyphenated chromatography/mass spectrometry, as well as the increasing variety of agricultural residues means that there will be an increasing reliance and acceptance of single-laboratory validation to monitor residue levels of food in trade. In order to assist laboratories in the interpretation of low-level residues established by mass spectrometry, a Codex Committee on Pesticide Residues (CCPR) working group prepared a guideline paper for identification and confirmation for pesticides in traded commodities [3]. The validation requirements for residue methods and the fitness-for-purpose approach to determining the criteria for qualitative identification of analytes by mass spectrometry are expertly discussed by Boyd [4] and others [5].

Qualifications and Training of Staff

Consistent with the general principles of good laboratory practice, staff responsible for implementing TDS programs should be appropriately qualified and trained in residue analysis and have a detailed understanding of analytical quality control and assurance. Under the technical requirements for ISO/IEC 17025 laboratory accreditation, laboratory management needs to provide evidence on continuing staff development and maintain a register of staff competence which may be audited during laboratory re-assessments. It might not be unreasonable for such registers of staff competence to be available from laboratories prior to analytical contracts being finalized, particularly where there is some uncertainty about the laboratory's overall technical competence to undertake the challenges of the TDS program.

Calibration Standards and Reference Materials

Analytical and calibration standards need to be purchased from reputable suppliers with details on source, lot number and expiry date and certificates of analysis traceable to ISO standards. Likewise appropriate CRMs should be sourced from accredited reference material suppliers with relevant traceability certificates. The storage of calibration standards and the preparation of calibration solutions should be well separated from sample preparation work areas to avoid cross-contamination.

Calibration of Instruments

It is generally acknowledged that analytical instruments require periodic calibration. Under technical accreditation, all measurement instruments including balances, volumetric measurement devices such as piston operated volumetric apparatus and syringes, reference thermometers, digestion hot blocks, ovens, furnaces as well as chromatography equipment are listed for regular calibration. New volumetric glassware, such as pipettes, burettes and volumetric flasks, require accuracy verification prior to use. Volumetric glassware not meeting specifications should be discarded or returned to the supplier. Balance calibrations should be undertaken with standard weights with traceability back to ISO standards. Calibration of mass spectrometers, including tandem and triple quadruple instruments, should comply with instrument specifications. Detailed logbooks of calibrations as well as records of failure and repairs should be maintained.

Analytical Quality Control

Use of Analytical Duplicates

Test sample duplicates are strongly recommended and should be mandatory for empirical methods and where control samples or reference materials are not readily available. For other methods, it is good laboratory practice to employ a minimum of 10 % duplicate test samples for large batch analysis with a higher number of duplicates for smaller (<10) sample batches. Where duplicate results exceed the repeatability value established during method validation, consideration should be given to re-testing the batch, although some professional judgement may be applied.

Internal Standards

Internal standards, which mimic the chemistry of the target analyte, should routinely be used in pesticide residue work to 'compensate' for loss of residues during sample clean-up.

Matrix-Based QC Samples and Charts

The routine use of matrix-based QC samples in chemical analysis has been actively promoted in the publications, texts and training courses of the US National Institute of Standards and Technology [6], which has generally been recognized as one of the leading institutions in QC in chemical analysis. From the application of QC samples and charts, the laboratory should be able to demonstrate statistical control of the analytical operation, thereby reducing the need for duplicate sample analyses. As the availability and cost of reference materials and CRMs is likely to be prohibitive for routine use, suitable QC samples can be prepared in-house from incurred laboratory samples. Alternatively, these can be prepared by carefully spiking a representative food matrix, followed by homogenization and packaging a sufficient number of test portions in individual vials for use over a set period of say 3–6 months. After establishing acceptable homogeneity from a minimum of seven replicate analyses, a QC chart is set up and subsequent QC results are plotted in real-time. The results of batched samples where the QC has been judged as an outlier may be rejected and all the samples re-tested. There are circumstances, however, where professional judgement may override the initial decision to re-analyze.

As the identification and development of suitable laboratory QC samples is time consuming, it would be beneficial for the TDS laboratory community to share information on availability of suitable reference foods and QC samples. These may be commercially available from reference material providers, proficiency testing study organizers, or leading analytical laboratories, which may prepare larger lots of QC samples.

Spiked Samples

The use of samples spiked with standards is essential, particularly where matrix-based CRMs are unavailable and/or too costly for use in routine analysis. The recovery of the spiked standard(s) provides a best estimate of the accuracy or bias of the method in routine use. Recoveries of spiked standards from the range of foods under investigation are established during the validation of the method. Recoveries of 80–110 % are generally considered acceptable for pesticide residues in foods at around 0.1–1.0 mg/kg, although some reports suggest 70–125 % recoveries may be acceptable. Lower recoveries may be acceptable for some chemicals in foods at lower concentrations, especially those on the front or tail end of multiresidue methods with known and consistent, albeit lower recoveries. In particular, the extraction of lipophilic residues from foods with high water content may be problematic. Given the diverse range of residues, which may accumulate in foods arising from agriculture and industry use, it is normal practice for laboratories to prepare spiked samples with 8–10 standards, which are representative of the chemical entities which may arise. Additional spiked samples containing a different suite of standards may be required for broad multi-residue programs.

Proficiency Testing Studies

Routine participation in proficiency testing schemes provides an excellent analytical performance benchmark. Consistent good performance in relevant studies together with a well-defined quality assurance program should provide clients with a high level of confidence in the quality output of a laboratory. While there are a number of reputable providers who offer certain schemes relevant to TDS, the specific needs of TDS analyses has not yet been addressed. It may be worthwhile if the TDS community approached a provider of proficiency testing, such as the UK Central Science Laboratory's Food Analysis Proficiency Assessment Scheme (FAPAS), to design and offer a proficiency testing program for laboratories involved in TDS programs. This would be particularly useful for new laboratories commencing TDS programs. The technical capability of laboratories to identify and provide a quantitative estimate of trace contaminants could be an initial aim.

Uncertainty Estimates of Laboratory Data

There is an increasing expectation from laboratory accreditation agencies that laboratories should be able to provide an estimate of the uncertainty associated with the data derived from the analytical measurement process. Measurement uncertainty (MU) reflects the summation of random and systematic errors associated with the analytical process and can be important in compliance decision-making where analytical results are close to the compliance limit. The MU estimate is reported as a range within

which the true value lies. It is likely to have important commercial as well as legal implications where the value of the commodity in trade is based on a particular specification, such as the protein value in wheat or the oil content of seeds, or whether a drug seizure represents a threshold quantity which can trigger prosecution

MU has as yet not been incorporated into nutritional values in food composition tables nor in the TDS data used to calculate dietary exposures and the associated toxicological assessments. It is anticipated that in future the uncertainty estimates associated with laboratory operations will be considered in the overall risk assessment of chemical intake through diet. Likewise, consideration may also be given to the estimation of measurement uncertainty associated with sampling as is being proposed by some Codex Alimentarius Commission committees.

There are a large number of guidelines and procedures for the estimation of measurement uncertainty, which are too numerous to list here. A paper by Cuadros-Rodriguez and co-workers [7] deals specifically with the assessment of uncertainty associated with pesticide residue analysis, which may provide some assistance to residue laboratories dealing with measurement uncertainty estimates for results derived from complex residue determinations. Uncertainty and variability in TDS data are also addressed in Chap. 18 – Addressing Uncertainty and Variability in Total Diet Studies.

MU data generated by laboratories should be benchmarked against the Horwitz [8] relationship between concentration and variance to ensure that MU values are not over- or underestimated.

Analytical QC/QA Indicators

As summarized in Table 13.1, this chapter has presented many components within the analytical process that need to be considered when evaluating the reliability of laboratory data. Associated with these are indicators which reflect various aspects

Table 13.1 Analytical quality control/quality assurance indicators

Quality control/assurance activity	Quality indicator
Good data correlation between sample duplicates	Good control of repeatability precision
High recovery of matrix spikes	Good measure of method bias for the spiked analyte
Consistent recovery of matrix spike	Good measure of reproducibility precision of method
High analyte(s) recovery of CRM	Good measure of method accuracy (lack of bias)
No outlying data in relevant proficiency testing studies	Good overall measure of analytical competence measured against peer laboratories
No results outside the QC chart warning limit (+/−3 SD)	Analytical operation (method + analyst + instrumentation) in statistical control
Technical accreditation in relevant TDS methods	Independent assessment of technical competence
MU estimates consistent with the Horwitz predictive model	Good estimate of random (and possibly systematic) errors

of data quality. The reliability of TDS data can be enhanced by providing a detailed protocol for sample preparation activities associated with laboratory operations as well as a detailed sampling plan for selection and sample purchase that are generally outside the control of laboratory staff.

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Chapter 14
Commercial Analytical Laboratories—Tendering, Selecting, Contracting and Managing Performance

Janice L. Abbey and Carolyn Mooney

A total diet study (TDS) requires an analytical laboratory to determine the level of chemical compounds in the food samples collected. Some food regulatory agencies may have analytical laboratories directly associated with their organization, whereas others may not. In addition, for some specialized analyses, agencies may elect to outsource the analyses instead of developing their own in-house capabilities. For those regulatory agencies that use commercial analytical laboratory services, it is important to engage a competent laboratory for the food analyses prior to the sample collection stage of the TDS commencing. Such laboratory services may be located locally, in another part of the country or possibly in another country.

Procurement Guidelines

To engage an analytical laboratory, it is essential to determine whether there are any procurement procedures which must be adhered to within the specific country. For example, in Australia, Food Standards Australia New Zealand (FSANZ) is a food regulatory agency that does not have an analytical laboratory directly associated with the organization. Therefore, in order to conduct a TDS, a laboratory, or in some cases, multiple laboratories, must be contracted to perform the analytical component of the project using a selection process that adheres to the Australian Commonwealth Procurement Guidelines [1]. Traditionally, the process by which analytical laboratories are engaged for the Australian TDS (ATDS) has been through a process that seeks a formal written proposal describing the laboratories analytical capability as well as a formal quotation of costs incurred to conduct the laboratory

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analyses. In recent years, FSANZ has used a widely advertised open competitive tender process through a *Panel of Analytical Laboratories*, which establishes specific *Deeds of Standing Offer* with each laboratory. The advantages of establishing a panel is that an analytical laboratory can be sourced directly from the panel to conduct analyses for the ATDS, following a request for quotation from the panel members. This expedites the procurement process, which is vital if analyses are required urgently, for example in the case of a food safety incident. Establishing a panel does not preclude FSANZ from using laboratories outside the panel, although a formal open competitive request for tender to the marketplace may need to be conducted depending on the value of the work. Therefore, this chapter will focus on the tender process in depth and subsequent contract development. Additional information on establishing a panel in Australia is available elsewhere [2].

Engaging an Analytical Laboratory

To engage a laboratory to conduct analyses for a TDS, a formal selection process should be followed. However, the type and details of the process used may vary among countries. Therefore, the information herein is only as a guide and should not supersede any formal procurement guidelines within a specific country.

Tendering for a Total Diet Study

Preparing a Tender Document: What Should Be Included?

Tender documents can generally be divided into three main sections, although other information may be necessary in individual countries according to their specific procurement guidelines:

1. Conditions of tender
2. Statement of requirement
3. Response format

A tender may also include the attachment of additional documents, such as a draft list of foods and analytes to be tested in the survey, a draft copy of the procedures manual (see Chap. 8 – Preparing a Procedures Manual for a Total Diet Study) including relevant preparation instructions for food samples and a copy of the draft proposed contract. This documentation aims to assist laboratories in understanding the scope and content of a TDS which may influence the laboratories' response to the tender.

Conditions of the Tender

This part of the tender document includes the invitation to tender and a variety of procedural matters, such as where to direct enquiries regarding the tender, where to submit responses to tender documents and the process for managing late tender submissions. Also addressed in this section of the tender document is the responsibility of the tenderers, which may vary depending on the countries procurement requirements. It may address topics such as, who absorbs the costs of the response to the tender, declaration of potential or perceived conflicts of interest and other aspects such as the ownership of submitted tender documents.

Statement of Requirement

TDSs are complex and therefore it is essential that the tender document clearly states the services that are required in a logical and comprehensive manner. This will assist the tenderers in preparing their responses to the request, which will enable a fair assessment and comparison of the costs/benefits presented by each tenderer. Provision of additional information on the background and purpose/objectives of the study are also useful to the prospective tenderers, as it provides context to the required services. If the major requirements are for analytical services and capacity to successfully conduct the large-scale survey within the expected time-frames, information on the prospective analytes and food samples, as well as any specific reporting requirements, should be detailed. Any other services that may also be required such as sample collection, sample preparation and sample compositing, as well as provision of sample containers for products that are purchased in an unsealed container (e.g. cold meats from a delicatessen), should also be listed.

Indicative timelines should also be provided in the tender document to give the tenderers an indication of the overall length of the project and the timeframes for the completion of each individual stage. It is important to include indicative timelines for the services requested in the tender document as it allows laboratories to consider other work commitments and to assess whether they have the capacity to participate in the large-scale study. For laboratories which may not have the capability to analyze for a specific analyte, it also provides an indication of the timeframe for when the development of the required analytical methodology will need to be completed. Alternatively, laboratories can be given the option to tender for only part of the analyses or subcontract those analyses to a secondary laboratory that can complete the analyses.

Specific information which should be sought in the tender includes:

- Analytical methodology for all proposed analytes.
- Level of detection that can be achieved and quantified for each analyte (i.e. Limit of Detection [LOD] and Limit of Quantification [LOQ] or Limits of Reporting [LOR]) (see Chap. 15 – Managing Concentration Data—Validation, Security, and Interpretation).

- Method validation including any accreditation.
- Quality assurance and quality control measures.
- Measurement uncertainty associated with the analyses and the basis for its determination.
- Sample collection and transportation capabilities.
- Quantity of sample required for analysis.
- Method of sample storage of both primary and composite samples.
- Management information such as:

  – Detailed timeline for the project
  – Details of current, pending and proposed accreditation
  – Details of relevant inter-laboratory proficiency testing recently undertaken
  – The contact details for a minimum of two referees

The expected outputs of the successful tenderer should also be detailed and may include:

- Coordinating the transport of samples to the laboratory
- Recording sample details on a spreadsheet or in a database
- Preparing primary and composite samples to a 'ready to eat' state
- Conducting analytical services
- Storing samples for a specified period of time
- Provision of analytical results as they become available, including detailed information regarding measurement uncertainty
- Submission of a final report of all sample analysis and product details

Response Format

The tender documents may request that responses are submitted in a specific format. A uniform format with clear instructions should assist potential tenderers and reduce any uncertainty or ambiguity in preparing their responses. This approach will also assist the organization in the evaluation of responses to the tender.

In their response, the tenderer should demonstrate the company's ability to provide the requested services, fully address all specified criteria as well as provide any additional information requested. A failure to do so may compromise the quality of the tender and its further consideration in the evaluation process. This decision, however, is at the discretion of the organization seeking the required services.

Selecting a Tender

Evaluation Process

Prior to conducting the tender evaluation process for the provision of analytical services for a TDS, it is important that compulsory and desirable criteria are used as a point of reference when evaluating each tender document and that

these are already established and approved by the organizations' legal team prior to advertising the tender. Similarly, it is recommended that a project team consisting of representatives from relevant areas of the organization be formed to evaluate each tender. Once all of the tender documents have been lodged by the specified closing date, the evaluation and selection process can commence.

Compulsory Criteria

As a first step, it is advised that each tender document is comprehensively cross-checked against each of the compulsory criteria. Examples of potential compulsory criteria that may be used as part of this process include:

- Lodgement of the tender by the specified closing date
- Declaration of any potential conflicts of interest
- Appropriate accreditation for performing the analytical services required
- Any issues in relation to confidentiality have been noted and explained
- Provision of business details, e.g. registered name, registered business number (if applicable), address, telephone and facsimile numbers and email address
- Contact details of an authorized business representative and their signature are provided
- Insurance details are provided, e.g. public liability and worker's compensation or similar
- A business continuity plan in place that guarantees full provision of required analytical services

It is at this stage, and at the discretion of the tender evaluation team, that any tender documents, which are considered to be non-compliant with the compulsory criteria, may be removed and not progressed for further evaluation.

Desirable Criteria and Ranking

Following the initial evaluation of tender documents against the compulsory criteria, the documents may be evaluated against a list of desirable criteria with an assigned weighting in order to further facilitate the short listing of potential tenderers. The weighting assigned is not generic but dependent on the specific project and is at the discretion of the organization. Examples of desirable criteria used as part of the tender evaluation process may include:

- Demonstrated ability to meet the agency's statement of requirements for conducting a TDS (e.g. a thorough description of similar and/or recent analytical services performed by the tenderer)
- Evidence indicating a clear understanding of the food regulatory environment and pertinent legislation, where applicable

- Demonstrated ability of personnel who will be assigned to work on the analysis (e.g. provision of curriculum vitae outlining the skills and responsibilities of each person for performing the required analytical services)
- A comprehensive summary that demonstrates the tenderers ability to manage a large and complex project and to deliver successful outcomes within specified timelines

Once all of the tender documents have been evaluated against the desirable criteria, a ranking for each can be calculated based on the weightings and a short list generated. For example, achieving the requirements of the tender may be assigned a weighting of 30 %, the tenderer's capacity and infrastructure 30 % and value for money and potential risk 40 %. Weightings can be modified against the criteria in the "Request for Tender", if desired.

Assessment of Value for Money and Risk

The remaining short listed tender documents should be evaluated for value for money against relevant procurement policies where applicable. For example, when FSANZ is evaluating tender documents for engaging a laboratory for the analytical component of the ATDS, the process followed must be consistent with procurement principles around value for money as stipulated in the Australian Commonwealth Procurement Guidelines [1].

In terms of evaluating the overall potential risk to the agency in contracting any one of the short listed tenderers, it is advised that an assessment be conducted on each to address the following fundamental elements:

- Financial stability
- Accountability and transparency
- Security
- Flexibility

Following this assessment, an overall ranking can be assigned to each of the short listed tenderers. This process will assist the tender evaluation team in selecting the successful tenderer who will be awarded the contract for the TDS.

Establishing the Analytical Contract

Establishing a contract between the selected tenderer and the organization conducting the TDS is essential in ensuring complete understanding of the expectations of the services required. The contract (or letter of agreement or memorandum of understanding) is a legally binding agreement between the selected analytical

Table 14.1 An example of a payment schedule for a TDS

Milestone	Detail	Fee amount[a]
1	On execution of the contract	x % of total fees payable
2	On completion of all analysis for the first sampling period and presentation of interim data report in electronic and hard data copies to the organization	y % of total fees payable
3	On completion of all analysis and presentation of the final data report in electronic and hard data copies and acceptance of the final report by the organization	The remaining fees payable

[a]Where 'x & y' are the numerical value determined by the organization seeking the analytical services

laboratory and the organization conducting the TDS, which outlines all agreed services and associated costs. The agreed services may not be limited to sample analysis and may also include the following:

- Coordinating sample transportation
- Provision of portable food coolers (chilly bins) and cold bricks
- Sample preparation and compositing
- Sample storage for a specified period of time following the completion of the project

The agreed LOD and LOQ or LOR for each analyte in the various food matrices should also be listed. The agreed cost for all services and a final overall cost for the entire service should be detailed. An agreed payment schedule, including specific details around what stage in the project payments will be made, should be outlined. As the TDS is a large-scale survey which can be conducted over a long period of time, it may be worthwhile scheduling payments throughout the course of the project when significant milestones have been reached. The schedule would be dependent on the range of services provided by the analytical laboratory. However a simplified example is shown in Table 14.1.

The example in Table 14.1 may be even more specific where required with the payments broken down further. For example, milestone 2 could be specified payments to include (1) completion of sample coordination, (2) sample preparation and (3) compositing.

The analytical contract should also include the specific details that the organization requires in each invoice to make the relevant payments for each milestone. Information such as, 'Title of Agreed Services', the name of the project manager and an itemized list of fees and expenses should be included. A timeframe for payment following receipt of the invoice by the organization should also be included so the laboratory can account for when payments will be received.

Managing Performance

The TDS may require the analytical laboratory to be engaged for up to 2 years, depending on the sampling schedule, number of samples and timeframe for analysis. Therefore, it is important to maintain regular contact with the laboratory to monitor the progress of the study, ensure interactions between the sampling officers and laboratory is occurring, and to provide regular feedback to manage the laboratory's performance. Regular contact could be made at significant stages within the project, such as dispatch of transport containers, completion of sampling, receipt of samples at the laboratory and completion of analytical results. If more than one sampling period is required, it is useful to contact the laboratory prior to subsequent sampling periods to critically assess how the previous sampling period was performed and determine whether there is anything that could be incorporated into the next period to improve the study. Alternatively, it may be useful to establish a regular meeting, for example monthly, to discuss any issues that may have arisen. Frequent contact between the project manager and the laboratory builds and maintains communication and encourages contact in the event of any issues arising which require prompt resolution.

Summary

The planning and management of the analytical component of a TDS is a comprehensive process. Therefore, thorough consideration should be given to the analytical services required to successfully conduct the study and to ensure that these are documented in a clear, detailed and logical manner. It is important that any country's specific procurement guidelines as well as organization specific guidelines are adhered to throughout the procurement process from the release of request for tender, to evaluation, selection and contracting of the analytical laboratory. In addition, effectively managing the performance of the contracted analytical laboratory for the duration of the analytical component is critical to the success of the study. Maintaining regular contact with the laboratory is recommended in order to foster a positive and productive working relationship that achieves agreed outputs.

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Chapter 15
Managing Concentration Data—Validation, Security, and Interpretation

Carolyn Mooney, Janice L. Abbey, and Leanne Laajoki

Introduction

The effective management of food chemical concentration data is critical when conducting a large-scale project such as a total diet study (TDS). Data validation, maintaining data security and the accurate interpretation of concentration data are all interrelated procedures required to ensure the data generated from a TDS is of high quality, accurate and representative of the food supply for the chemicals under investigation. The concentration data will underpin the subsequent estimates of dietary exposure derived for each food chemical included in the study and therefore it is important that a comprehensive data management process is followed. The approach for estimating dietary exposure will not be discussed here in any detail and is covered in depth in Chap. 17 – Dietary Exposure Assessment in a Total Diet Study.

Validation of Analytical Data

Validation of the food chemical concentration data is a process that should be conducted when the data is initially received from the analytical laboratory. This process involves scrutinizing the concentration data that is provided, often in a Microsoft Excel spreadsheet, along with all certificates of analysis to check for any errors and/or anomalies. It is important to cross-check the data recorded in the spreadsheet with all certificates of analysis to ensure consistency of reporting.

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The identification of errors in the concentration data can be challenging, particularly when working with the large number of data points generated from a TDS. To assist with the accuracy of this process, the following list of errors that may be identified in analytical data can be used as a reference:

- Analytical result does not make sense:

    - An order of magnitude different to that expected
    - Unpredicted high or low values
    - Unexpected chemical for that food matrix

- Limit of Detection (LOD) or Limit of Quantification (LOQ) not low enough to provide subsequent meaningful exposure estimates for TDS purposes.
- No results reported when analysis was conducted.
- Absence of 'less than' sign as it relates to the LOQ or the Limit of Reporting (LOR), which is a trace amount between the LOQ and the LOD (see below).
- Values reported that are less than the LOQ/LOR.
- Reporting of dry weight results instead of fresh or as consumed weight results and vice versa.
- Use of incorrect units or units not reported.
- Transposition or calculation from raw instrumental data to analytical result spreadsheet.

It is recommended that two project team members working independently conduct the process outlined above in order to reduce the likelihood of errors being overlooked. Any errors or questionable results that are identified should be brought to the attention of the analytical laboratory to seek clarification. If the laboratory confirms that an error has been made in reporting, it is important that the errors are corrected by the laboratory and a revised data set forwarded to the project manager. By the laboratory making all the relevant changes, the number of individuals altering the data sheets is limited and the potential of introducing additional errors is reduced.

If the laboratory confirms that the results have been correctly reported in both the spreadsheet and the certificates of analysis, it is recommended that any available Quality Assurance (QA) information, including Quality Control (QC) data be obtained from the laboratory (See Chap. 13 – Quality Control and Assurance Issues Relating to Sampling and Analysis in a Total Diet Study). QA data provides information on the repeatability of the data on a given day using the same instrumentation (i.e. replicate analysis on the same day) and the reproducibility of the data under standard conditions (i.e. reproducibility of the data on different days by different analysts and using some altered conditions, such as reagent batches). Recovery efficiency information could also be sought from the laboratory. Recovery efficiency of food samples spiked with a known amount of the analyte, gives a good indication of the method's ability to accurately extract and detect the analyte in the food sample matrix. The concentration determined from the method is compared with the known amount that the sample was spiked with to generate a recovery efficiency. If Certified Reference Materials (CRMs) have been analyzed these results should also be checked to confirm analytical accuracy.

FOOD ANALYZED	FOOD MAPPING		
Apples e.g. Red Delicious	To all types of apples e.g. Granny Smith	To all pome fruits e.g. Nashi pear	To foods/recipes containing pome fruits e.g. apple pie
	CONCENTRATION DATA		
Determined quantitatively by analytical methods	Quantitative concentration of analyte is extrapolated to similar foods which were not analyzed	Quantitave concentration of analyte is extrapolated to foods of a similar group which were not analyzed	A percentage of the concentration of the analyte is extrapolated to foods containing the relevant fruit (e.g. canned fruit, fruit pie and fruit juice). The percentage of the concentration used is equivalent to the percentage of the fruit in the final product. These products were not analyzed

Fig. 15.1 An illustration of validation of analytical data

After considering all QA/QC data, if there are still reservations about the results, re-analysis of the same sample by the same laboratory and/or arranging an alternate laboratory to conduct inter-laboratory check tests of the relevant samples may be appropriate. The purpose of this exercise is to reduce uncertainty around the validity of results and to allow interpretation of the data with confidence. It is important to ensure a provision is included in the contract with the analytical laboratory that requires questionable results to be re-tested and a proportion of samples to be made available for inter-laboratory check testing if considered necessary. The potential for re-analysis and inter-laboratory check testing of samples during the study should be taken into account during the sample collection stage, thus ensuring sufficient sample is collected and stored (See Chap. 9 – Food Sampling and Preparation in a Total Diet Study). Once all of the data has been checked and any errors and questionable results have been addressed, it is advised that the names of those involved in the data validation process and the date of completion are clearly documented together with any notes to the data.

Careful management of the data validation process is critical to ensure errors are not carried over into the dietary exposure assessment component of the total diet study, where their effects may be potentially amplified. For example, if *Red Delicious apples* are analyzed as part of a TDS, these values may be logically mapped to other types of apples, similar types of fruits (pome) as well as recipes containing these fruits, as illustrated in Fig. 15.1. This simple example demonstrates the importance of data validation, accurate reporting and the potential follow-on effects of an error in analyte concentration.

Security

Following completion of the data validation process, it is crucial that the spreadsheet is locked (protected) to preserve the integrity of the data. The password used to protect the spreadsheet should be created by the recipient of the original analytical data from the laboratory, generally the project manager. Protecting the spreadsheet will prevent manipulation of the raw concentration data and the potential for the introduction of errors. It is also important that the spreadsheet is appropriately named and dated, and the file is saved in a location agreed by the project team.

The TDS project team is likely to include representatives from other discipline areas within an organization, in particular the dietary exposure assessment area or equivalent. In this instance, the validated analytical data will need to be provided to the team members in this area that are responsible for completing the estimates of dietary exposure for the food chemicals investigated. It is recommended that a clearly named source spreadsheet is generated from the original validated data spreadsheet and provided electronically to the team members completing the dietary exposure assessment. By doing this, any adjustments to the spreadsheet format that are required for the purposes of calculating the estimates of dietary exposure will not affect the original data spreadsheet. This practice should preclude any issues from arising in relation to version control. It is encouraged that the procedures outlined above are clearly documented and referred to as a guide by the project team to ensure the security of the data is maintained.

Interpretation

Understanding the data and how it is obtained is essential to the interpretation process. Information such as sample composition is important, and whether the data was derived from individual or composite samples should be known. For example, if the data is derived from a composite of three primary samples and a high level of the food chemical is reported, further analysis will need to be conducted to determine whether one, two or all three primary samples are contributing to the measurement.

Understanding and subsequent interpretation of concentration data generated from the TDS is fundamental to achieving an accurate representation of the dietary exposure to chemicals from food. On occasion, the analytical data set will report results as 'notdetected' (ND) and 'trace amounts' (tr) for the analytical method. Non-detect results do not always indicate that the food chemical being analyzed is absent. In fact the chemical may be present, but its detection is limited by the sensitivity of the analytical instrument. In these cases, the food chemical would be considered as being below the LOD (Fig. 15.2). The LOD refers to the lowest concentration of a chemical that can be qualitatively detected using a specified laboratory method and/or item of laboratory equipment but cannot be accurately quantified. In contrast, trace amounts, is the term used where the food chemical has been detected by the analytical instrument (above the LOD) although the concentration cannot be quantified accurately (below the LOQ) (Fig. 15.2).
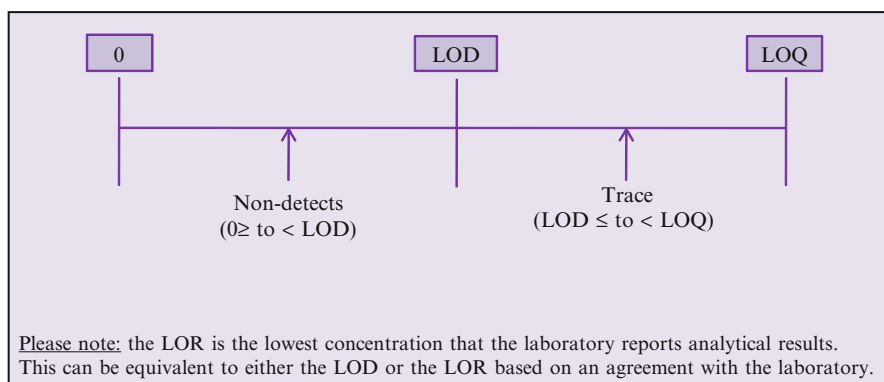
Fig. 15.2 Interpretation of non-detects and trace results in relation to the LOD and LOQ

The LOR is also a term used widely in the TDS. The LOR refers to the level of reporting which has been agreed between the project manager of the TDS and the laboratory conducting the analyses, and recorded in the contract for analytical services (see Chap. 14 – Commercial Analytical Laboratories—Tendering, Selecting, Contracting and Managing Performance). It is important to know the relationship between the LOR, LOD and LOQ, as this provides information regarding the certainty of the results. Understanding this relationship is invaluable when assigning numerical values to non-detects or trace results in order to calculate estimates of dietary exposure.

For the purposes of deriving summary statistics (e.g. minimum, mean or median and maximum concentrations) to facilitate the data interpretation process, and to allow these concentration values to inform the dietary exposure assessment, consideration needs to be given to the treatment of these results. In other words, a decision needs to be made as to what numerical concentration value to apply to non-detects and to trace results. Typically, one of the following scenarios would be applied to non-detects or trace results:

- Assigning a zero value (referred to as the lower bound)
- Assigning a value equal to half the LOQ/LOR* or LOD (referred to as the middle bound)
- Assigning a value equal to the LOQ/LOR* or LOD (referred to as upper bound)
- Assigning a range of values based on a parametric or a non-parametric method (see also Chap. 16 – Reporting and Modeling of Results Below the Limit of Detection)
  *Assumes LOQ=LOR

It is important to note that the treatment of non-detects and trace results may differ depending on the type of food chemical analyzed. Factors to consider include whether the food chemical is intentionally added to food or if it is naturally present, whether both adequacy of intake and safety are being investigated (e.g. nutrients), the number of non-detect results reported and the LOQ assigned to the specific food chemical. Table 15.1 describes some of the methods used to treat non-detects in

Table 15.1 Treatment of non-detects in national total diet studies

TDS	Chemicals	Non-detects (ND)[a]
20th Australian Total Diet Study [1]	Pesticides	Reported results <LOR were included in calculation of the mean. Values <LOD were assigned 0 as pesticides are selectively applied to crops
	Metals	For values <LOR a lower bound (=0) and upper bound (ND=LOR) approach was taken and the range presented
21st Australian Total Diet Study [2]	Sorbates, sulphites, benzoates	If <LOD, ND=0 as these additives are intentionally added to food
22nd Australian Total Diet Study [3]	*Micronutrients* – iodine, selenium, molybdenum, chromium and nickel	For values <LOR, ND=1/2 LOR (middle bound) was assigned
1st French Total Diet Study [4]	Mycotoxins	For values <LOQ, ND=1/2 LOQ (middle bound) was assigned
6th New Zealand Total Diet Study [5]	*Contaminant elements* – arsenic, cadmium, lead and mercury	As contaminant and nutrient elements are naturally occurring, ND=½ LOD was allocated
	Nutrient elements – Iodine, iron, selenium and sodium	

[a]Definition of ND in this context ND=<LOD or LOR, assuming LOD=LOR

national TDS reports. For example, when dealing with non-detect results, it would not be considered appropriate to apply a zero value to the food chemical if it is known to be naturally occurring in the food analyzed, as this could potentially result in an underestimation of actual concentration. For this scenario, it may be appropriate to assign a value of ½ LOQ or LOD. This is the approach that was used in the 6th New Zealand Total Diet Study for contaminant elements [5]. In relation to the treatment of trace results, for example, in the case of a nutrient for which adequacy is being assessed, applying a value equal to the LOQ could significantly overestimate the actual concentration in the foods analyzed and generate a corresponding overestimate of dietary intake. In this situation, it may be appropriate to assign a value equal to ½ LOQ. This is the approach that has been used in the 22nd Australian Total Diet Study [3].

When addressing non-detects and trace results, it is important to consider their use in exposure assessments on a case-by-case basis and ensure that any assumptions made are applied consistently and clearly documented. This will be important when preparing the final report. Once all non-detect and trace results have been considered and values assigned where necessary, summary statistics can be calculated. Reporting the median value (the statistical middle value) for the food chemicals analyzed, in addition to the mean value, may be useful where there are a large number of results below the LOD or LOR (assuming LOD=LOR) since the median is not affected by results outside the expected range. However, when there are a large number of results ($n > 50$) and many are below the LOD or LOR, the median

cannot be calculated. In this instance, the mean is reported and the resulting assessment is conservative given the mean is higher than the median. Where there are a good number of results reported and few results reported as <LOD or LOR, it would be considered appropriate to report either the mean or median value, however the mean is more conservative. The data set is now collated and summarized and can be used to calculate estimates of dietary exposure to the food chemicals analyzed.

Summary

The management of concentration data generated from a TDS as it relates to validation, security and interpretation is vital to the quality and reliability of the study. It is recommended that procedures in relation to the format and validation of the analytical results from the laboratory should be agreed upon and stipulated in writing. Similarly, clear and detailed procedures should be in place for the project team to follow to ensure that the integrity of the data is maintained. Given that the concentration data will ultimately inform the dietary exposure assessment component of the TDS, guidance on data interpretation should be provided and consistently applied. Because conclusions regarding public health and safety will be made on the basis of analytical results, the methodical handling of such data is critical to the accuracy and representativeness of the study.

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Chapter 16
Reporting and Modeling of Results Below the Limit of Detection

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Introduction

Conducting dietary exposure assessment (E) consists in combining deterministically or probabilistically food consumption figures (Q) with concentrations (C) of a given chemical substance in a number of foods or food categories. To be compared with the acceptable daily intake or another health-based reference value, the exposure is then divided by the number of days of the survey (n) and by the body weight for individuals (bw). The basic formula is therefore:

$$E_i = \frac{1}{n_i bw_i} \sum_k \sum_t Q_{i,t,k} C_{i,t,k}$$

Occurrence data can be obtained either from control and monitoring programs or from a total diet study (TDS). In both cases, data reported to be below the limit of

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detection (LOD), often called 'non-detects' or 'left-censored data', are likely to have a critical influence on the results of the assessment. The LOD and limit of quantification (LOQ) also known as "limit of determination" are of special importance for exposure estimations in risk assessments as they determine the minimum value that can be detected and quantified, respectively. It should be noticed that many definitions of LOD and LOQ have been suggested over time in different analytical areas. The LOD represents the minimum concentration or mass of an analyte that can be detected with a given confidence for a given analytical procedure. More formally, the LOD can be defined as the lowest concentration level that can be determined to be statistically different from a blank [1], customarily set using confidence levels equal to 95 % or 99 %. Similarly, the LOQ is the minimum concentration or mass of the analyte that can be quantified with acceptable accuracy and precision [1], given that at this level the analyte is considered to be present. In the Australian TDS, this has been defined with slightly different criteria as the limit of reporting (LOR) (see Chap. 20 – The Australian Experience in Total Diet Studies).

The objective of TDS is to provide concentration data for dietary exposure assessment, which are analyzed in food as consumed and obtained from composite samples expected to represent an average value for a food, food group of interest or even the whole diet. In theory, the dietary exposure to a chemical could, therefore, be based on a unique sample including a weighted mix of all food of the diet in which the chemical is expected to occur. At the other end of the spectrum of possibilities, a TDS can be based on each relevant food item, such as fish, or on a composite of various species available on the market. Finally composite samples can be prepared locally and repeated in various areas of a country or region and in various seasons to capture the variability of the analyte content regarding these parameters.

In the current practice of TDS, a low number of composite samples (generally 1–4) are prepared for relevant single food items or food groups (e.g. bread, fish, beef, etc.). In the case of food group samples, generally weighted composites are made up from different foods from the food group according to the ratio in which they are consumed (e.g. different types of bread or species of fish). The pooling of different foods in composite samples has several drawbacks: Firstly, it introduces considerable uncertainty about the variability of the concentrations of the individual foods present in the food groups. Moreover, compositing may dilute individual food samples having high concentrations when the remaining samples have much lower concentrations. The dilution effect may even prevent the determination of a chemical if it occurs at very low levels and/or if it occurs in only one or a few of the foods within a composite [2]. In addition, the analysis of weighted food composites allows only one mixture of foods (i.e. representation of only one age-sex group of the population or of the whole population) to be evaluated. Analysis of individual foods allows greater coverage of population subgroups, because the daily consumption of foods for different groups can then be simulated and calculated [2]. For the reasons mentioned above, the analysis of single food items is preferred over composite samples, although this approach has different advantages and disadvantages (see Chap. 9 – Food Sampling and Preparation in a Total Diet Study).

This chapter covers the handling of non-detects in TDS studies. It is based on a review of the literature included in a recent report of the European Food Safety

Authority dedicated to this topic [3]. While none of these works were specific to the TDS, many were based on realistic datasets in the field of chemical occurrence in food.

Dealing with Non-detects in Dietary Exposure Assessment

An important factor for the evaluation of the presence of chemical substances is the possibility of distinguishing between non-detects and true zero values. For persistent organic pollutants, such as dioxins, PCBs (polychlorinated biphenyls) and PBDEs (polybrominated diphenylethers) and naturally occurring heavy metals such as lead and cadmium, it seems accepted that there are no true zero values in food: these substances are ubiquitous and will be consistently present in foodstuffs, although sometimes in extremely low concentrations. On the other hand, for process contaminants, like acrylamide, 3-monochloropropane-1,2-diol (3-MCPD) and also for most pesticides, true zero values can occur if the contaminant is not formed in the food, or the pesticide is not used on a crop. When dealing with non-detects, it should be kept in mind to which group the substance of interest belongs.

Communication with the analytical laboratory that measures TDS samples is very important. The laboratory analyzing the samples should be able to reach the lowest LODs and/or LOQs possible and at the same time have good performance of other important QC factors (high reproducibility, low blanks, high recoveries). The definitions of the LOD and LOQ used by the laboratories should be available. In the contact with the analytical laboratories, it is recommended to emphasize the need for the correct reporting of the LOD and LOQ. Analytical laboratories are often not aware of how exposure assessors use their reported values, so usually not much effort is put into accurate reporting of the LOD or LOQ. Depending on how strict the LOD and LOQ are defined by the analytical laboratory, it may be decided to use different definitions, or to report values between LOD and LOQ, such as the LOR.

Methods for Handling Non-detects

There are a variety of statistical methods to deal with non-detects. The most commonly used are: deletion, substitution, maximum likelihood estimation (MLE), log-probit regression, and non-parametric methods.

Deletion

Within the methods available to deal with non-detect samples, deletion represents the elimination of all non-detected data from the dataset. For TDS, in the case that more than one single sample for a food or food group is available, depending on the number of non-detects in this food or food group, this solution is likely to result in a considerable overestimation in terms of the frequency of occurrence of a chemical

Table 16.1 Statistical treatment of data sets containing various proportions of non-quantified results

Proportion of results < LOD	Simple estimate of mean	Estimation of statistical mean, median, standard deviation
None, all quantified	True mean	
≤ 60 % non-quantified	Use LOD/2 for all results less than LOD[a]	Use methods in [12, 13] and/or graphical methods[b, c]
> 60 but ≤ 80 % non-quantified and with at least 25 results quantified	Produce two estimates using 0 and LOD for all the results less than LOD[a, d]	Use methods in [12, 13] and/or graphical methods[b, c]. Use with caution if total number of measurements is < 100
> 80 % non-quantified, or if > 60 % but ≤ 80 % non-quantified and with < 25 results quantified	Produce two estimates using 0 and LOD for all the results less than LOD[a, c]	None practicable

[a] Provided the distribution is not highly skewed and only one LOD exists in the data set (or the LODs are not very different)

[b] Plot data on log-probability paper and produce best estimates of median and standard deviation, and thus arithmetic mean. See also [14, 15]

[c] If different LODs are in the data set, use only the quantified results above the highest LOD

[d] In cases where the LOD is not equal to the LOQ, the upper bound is calculated by setting all non-detectable results equal to the LOD and all non-quantified results (<LOQ) equal to LOQ; the lower bound is calculated by setting all non-detectable and non-quantified results equal to zero

substance in a set of foods (in case of removal of true zero values), and in terms of levels of contamination (all the values below the LOD are excluded). When only one single sample is available, the exposure from the total diet may be underestimated when food groups with concentrations below LOD are deleted. For these reasons, this approach is not further considered in this chapter.

Substitution Method

In the field of food safety, the most commonly used recommendations to handle left-censored data are the ones from the GEMS/Food-EURO workshop in 1995 [4]. In practice, depending on the proportion of positive values and the overall sample size, for results below the LOD, a value equal to the LOD, zero or LOD/2 is used as a surrogate for the unknown non-detected value (see Table 16.1). This method is referred to as the substitution method, whereby the substitution of the non-detect with zero, LOD/2 or LOD is customarily defined, respectively, as the lower-, middle-, and upper-bound scenario. It is important to note that the GEMS/Food-EURO workshop recommended that for the purpose of dietary exposure assessments, laboratories and analysts should report as quantified results the data between the LOD and LOQ as this would promote the best use of available data. If this is done, only the LOD remains.

The substitution of non-detects with other values is widely recognized to be biased, with the bias a function of the true variability in the data, the percentage of censored observations, and the sample size [5]. Another disadvantage of substitution is that it does not work well when the number of detected samples exceeds 60 % of the results. In other words, when the dataset contains 1 % or 60 % of non-detect samples, it is likely that the two datasets have different underlying distributions. The most critical situation for the substitution method is when there are multiple LOD values. The reason for this is that substituted values depend on the conditions, which determined the detection limit, such as the laboratory sensitivity and precision and sample matrix interferences. These factors do not necessarily bear a relation to the true value [6].

A WHO publication recognizes the impact of left censored data on the overall uncertainty in chemical exposure assessment and recommends using statistical methods to provide more accurate estimates of a fitted distribution and its statistics than the classical method of substitution [7]. Despite its drawbacks, the substitution method is easy to implement, widely understood, and the upper-bound practice leads to conservative estimates for exposure assessment calculations, i.e. overestimation of the mean and underestimation of the variability.

Statistical Methods Available

There are a variety of statistical methods to deal with non-detects. The most commonly used are parametric maximum likelihood estimation (MLE), log-probit regression and non-parametric methods. It is important to note that both for TDS data and other sets of data, when the occurrence of a chemical in a food or food group is below the LOD/LOQ, based on a single or a very low number of analytical results, none of the statistical techniques described below can be used. The only possibility is, therefore, to employ the WHO recommendation and, more precisely, with the last row of Table 16.1, i.e. conduct lower bound and upper bound estimations.

The parametric maximum likelihood estimation (MLE) method is often considered as the preferred approach because the distribution of concentration values in food products can be expected to be log-normal if the food product is grown/made in a 'homogeneous environment'. Data both below and above the detection limit are assumed to follow a log-normal distribution. The parameters of the chosen distribution are estimated so to best fit the distribution of the observed values above the detection limit, compatibly with the percentage of data below the limit. The estimated parameters are the ones that maximize the likelihood function. It is also possible to use other distributions, such as the Weibull and the gamma distributions. However the reported data often does not fit with a parametric model, particularly when they are collected in an international environment. A variety of point sources are likely to be present, leading to different

background levels in different regions/countries and in different foods. In addition, true zero concentration values may be present, and the concentration in a food or food group may be better described by a combination of more than one distribution, e.g. binomial and a log-normal. According to Helsel [6], for data sets of at least 50 observations and where the percent of censored observations is small, the MLE method is usually considered as the method of choice. Some improvements of the MLE method are possible, for example by accounting for different sources of heterogeneity and by forcing the distribution in such a way that the observed fraction of non-detects is equal to the predicted fraction of non-detects.

In the log-probit regression method the data are sorted, and a linear relationship is assumed between the logarithm of concentration values and the inverse cumulative normal distribution of the observations' plotting position. It has been suggested that the log-probit regression should not be applied to data-sets with multiple LOD values [8].

The standard non-parametric technique for censored data is the Kaplan-Meier (KM) method. The advantage of such an approach is the possibility of estimating the mean, together with the median and other quantiles, in the presence of non-detect values, without relying upon distributional assumptions [9]. With the KM method, the weight of the censored data is distributed over the different observed values below the censoring values, i.e. LODs and LOQs, and zero. It is therefore not interesting to apply the KM method when there is only one LOD value, as it would be equivalent to substituting the censored values with zero or the largest observed value below the LOD. Because it is non-parametric, the KM method tends to be insensitive to outliers, which occur frequently in environmental data [10].

Bayesian statistics are fundamentally based on a different paradigm from "frequentist" statistics used for MLE methods. In summary, model parameters are not assumed to be fixed unknown constants to be estimated but instead are seen as random variables. All models fitted by MLE approaches could be, in general, also fitted using Bayesian approaches. In the case where no prior information is available, Bayesian methods will theoretically lead to very similar (if not identical) results as those obtained by MLE methods, when the same underlying model is used. An example of Bayesian modeling of left-censored data can be found in a paper of Paulo [11], which shows that application of Bayesian modeling to pesticide risk assessment is feasible, and that in a data-rich situation, the model compares well with empirical Monte Carlo modeling.

Several publications have evaluated the performance of statistical treatments of left-censored data [6, 8, 10]. The authors used various procedures and relied on different indicators to evaluate the performance of the proposed approaches. A

complete analysis of the papers is included in the EFSA report [3]. In summary, the choice of the method depends, on the one hand, on the characteristics of the dataset under consideration, and on the other, on the resources for an accurate statistical analysis and modeling.

Because most dietary assessments employ a tiered approach, a sophisticated analysis of the data should be performed only when necessary and after a clarification of the issues above. Then, the following steps should be followed:

1. *Initial analysis*
   The main quantities to be evaluated are the size of the dataset, its potential sources of heterogeneity, the number of distinct LODs and the percentage of non-detects. In practice the analyses could be conducted following these preliminary steps, separately for each food or food group analyzed.

2. *Sensitivity of concentration data*
   The sensitivity of concentration distributions can be estimated by calculating the lower bound and the upper bound of dietary exposure based on the substitution of non-detects respectively by 0 and by the LOD. The substitution should be applied on the mean and/or the high percentile(s). If the effect is negligible then the dietary exposure assessment can rely on the upper bound approach without need for modeling. On the contrary if the difference between the lower and the upper bounds is important, i.e. if the health-based guidance value is between the two estimations, a modeling of left-censored data is needed.

3. *Treating left-censored data*
   As mentioned above, the TDS usually involves consideration of a food category with a single or very few analytical results, e.g. one to four analytical results per food group. Under such circumstances there is no robust way to deal with censored data. Based on the available literature and on the recommendations both from WHO and EFSA, the only possibility is to estimate the lower and the upper bound. However, because the use of TDS at regional level represents an important and valuable trend, it is likely that in the future, TDS will aim to include more samples for each food or food group to capture the variability in occurrence. As an example, on the basis of four samples analyzed for a country, a regional TDS involving 15 countries would result in 60 analytical results to describe the distribution of occurrence in a single food item at regional level. Such a number would allow for a statistical analysis. Moreover, the introduction of uncertainty analysis in the risk analysis process will require a more accurate picture of the distribution of occurrence than a single average value.

When the dataset is more than 50 observations and the percentage of censoring is between 50 % and 80 %: the parametric (MLE) approach is recommended. A set of candidate parametric models, such as log-normal, gamma, and Weibull, should

WHEN:

- **NOT negligible difference between lower-and upper-bound substation estimates, AND**

- **upper-bound estimates are "in the range" of toxicological reference dose**

< 50 samples or
< 25 positive samples or
> 80 % censoring

> 50 samples or
> 25 positive samples and
< 80 % censoring

STOP
Request
additional
data

< 50%
censoring
and
> one LOD

< 50 %
censoring
and
one LOD

> 50 %
censoring

Parametric
modeling
or
Kaplan
Meier

Parametric
modeling

Fig. 16.1 Flowchart of the overall strategy for the treatment of left-censored observations proposed by EFSA

be considered and the best final model should be checked for goodness of fit. When the dataset is more than 50 observations and the percentage censoring is lower than 50 % with a single LOD, a parametric approach (MLE) is recommended.

When the dataset is more than 50 observations and the percentage censoring is lower than 50 % with multiple LODs, both the parametric approach and the KM method can be performed; the latter has the advantage that it avoids making any assumptions about the form of the underlying distribution (see Fig. 16.1).

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Chapter 17
Dietary Exposure Assessment in a Total Diet Study

Julie L. Boorman, Janis Baines, Tracy L. Hambridge, and Janice L. Abbey

Introduction

The main purpose of conducting a dietary exposure assessment for a total diet study (TDS) is to estimate likely levels of exposure to food chemicals for the population and/or population sub-groups from the diet and the associated level of risk to public health and safety. Dietary exposure assessment forms an essential part of the risk assessment process and is a quantitative base from which risk management and public health decisions can be made if necessary [1] (see Chap. 4 – Overview of Dietary Exposure). While the formula for calculating dietary exposures is simple, the techniques and considerations for its application are more complex.

$$Dietary\ Exposure = \ \Sigma\left(Food\ Consumption \times Food\ Chemical\ Concentration\right)$$

Before commencing a dietary exposure assessment for a total diet study, it is important to determine the purpose of the assessment and the questions that need to be answered. This will help to guide the choices of dietary exposure assessment methodology, food chemical concentrations, food consumption data and the population group and/or sub-groups to examine. Figure 17.1 provides an overview of the inputs required for a dietary exposure assessment for a total diet study. Each of these inputs will be discussed in detail in this chapter. The preparation of data for the dietary exposure assessment and the interpretation of the results from the assessment often take a significant proportion of time, with the actual dietary exposure calculations taking a much shorter time. The accuracy of these dietary exposure

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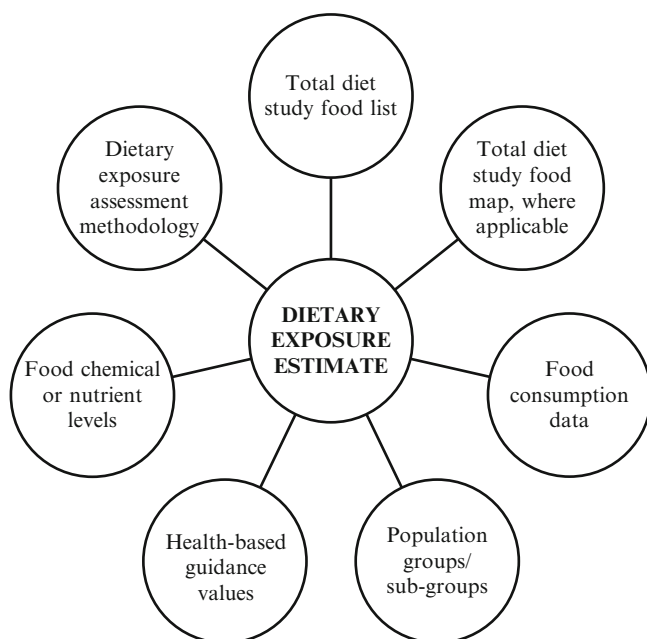
Fig. 17.1 Overview of inputs for a dietary exposure assessment

estimates depends on the quality of the data used in the calculations. The uncertainty and variability associated with dietary exposure estimates are further discussed in Chap. 18 – Addressing Uncertainty and Variability in Total Diet Studies.

Dietary Exposure Assessment Methodologies

The dietary exposure assessment methodology used in a TDS will depend on the goals for the study and the data, time and financial resources available [2]. Total diet studies are usually designed to estimate long-term dietary exposures to chemicals in food rather than short-term dietary exposures. When the analytical results for the study are derived from composite samples, the analytical results can only be used in a long-term dietary exposure estimate. Short-term dietary exposure estimates have different analytical data requirements, such as the analysis must be conducted on individual food commodity units and not composites.

Long-term dietary exposure can be estimated using three different methodologies:

1. Deterministic (point-estimate of concentration and food consumption for each food analyzed)
2. Semi-distributional (point estimate of concentration, distribution of food consumption)
3. Probabilistic distributional (distributions of food consumption and food chemical concentrations)

The deterministic method provides mean dietary exposure estimates only and may be the only option available; for example, when model diets are used to describe average food consumption amounts for each population group studied. The use of distributions of individual data (semi-distributional and probabilistic distributional) has the advantage of allowing a distribution of exposures to food chemicals and nutrients to be estimated so information on high exposure to food chemicals and nutrients and low exposures to nutrients can be obtained, but has the disadvantage of being more resource intensive (see Chap. 4 – Overview of Dietary Exposure). The data required for each of the methodologies are discussed below.

Food Chemical Concentrations

Representative chemical concentrations need to be determined for each food analyzed in the TDS. It is important to know how the samples were prepared, whether the analytical data were generated from individual or composite samples (see Chap. 8 – Preparing a Procedures Manual for a Total Diet Study and Chap. 9 – Food Sampling and Preparation in a Total Diet Study), the potential contribution of water that was used in the preparation of samples and the sensitivity of the analytical methods used to determine the concentrations (Limit of Quantification (LOQ) and Limit of Detection (LOD)) – refer to Chap. 15 – Managing Concentration Data—Validation, Security, and Interpretation and Chap. 16 – Reporting and Modeling of Results Below the Limit of Detection.

In food chemical analysis, 'trace' and 'non-detect' results are sometimes reported by the laboratory. A 'non-detect' result may occur because the chemical is either not present at all or is present in amounts that are below the LOD. Results reported as 'trace' can occur where the concentration of the chemical in the food is above the LOD (i.e. can be detected) but is below the Limit of Quantification (LOQ), i.e. the amount cannot be quantified. To enable a representative concentration for each food analyzed to be calculated, decisions about assigning numerical values to the 'non-detect' and 'trace' analytical results need to be made. Therefore, it is important for the exposure assessor and the laboratory analyst to discuss how 'non-detect' and 'trace' values are defined. Depending on the nature and likely distribution of the chemical in the food, there are a number of options available for assigning a numerical value to 'non-detect' or 'trace' result for use in the dietary exposure assessment (see Table 17.1). Note that these default assumptions apply to nutrients when potential toxicity is be assessed, but not when adequacy of intake is being estimated.

The types of food chemicals assessed in a total diet study may include many different categories, including contaminants (e.g. mercury, aflatoxins), agricultural chemical residues (e.g. DDT, aldrin), nutrients (e.g. iodine) and food additives (e.g. sulphites). Sometimes the chemical could be classified into a number of categories (e.g. zinc could be considered as a nutrient or as a contaminant) and therefore, a case-by-case approach is required for each chemical.

Table 17.1 Options for 'non-detect' analytical results

Result type	Options	Comments
Non-detect (ND)	ND=0	Assigned when chemicals are used intentionally in foods, and known in this case not to be used in the food of interest (e.g. food additives, pesticides and veterinary drugs)
	ND=½ LOD or ½ LOQ ND=LOD or LOQ ND expressed as range (e.g. 0 – LOD or 0 – LOQ)	Food chemical where presence on food is likely (e.g. naturally occurring, or ubiquitous contaminant)
	Statistical treatment	See Chap. 16 – Reporting and Modeling of Results Below the Limit of Detection for details on this approach
Trace (Tr)	Tr=½ LOQ Tr=(LOD+LOQ)÷2 Tr=LOQ Tr expressed as a range, e.g. LOD – LOQ	
	Statistical treatment	See Chap. 16 – Reporting and Modeling of Results Below the Limit of Detection for details on this approach

For a chemical not permitted for use in food, such as an unapproved food additive or an agricultural chemical, a 'non-detect' value would likely mean that the chemical was not added to the food and that a concentration of zero can be assigned. However, if use is permitted in national food standards, a non-detect may be assigned ½LOD or a range from zero to LOD. Since contaminants are generally not intentionally added to foods, a 'non-detect' value could mean that the contaminant is present in the food but at levels that cannot be detected. Therefore, it is assumed that the contaminant may be present in the food anywhere between a zero concentration and the LOD concentration, either by assigning ½LOD to the 'non-detect' result or using a range from zero to the LOD. For nutrients, there are often two health-based guidance values to consider– a lower one for essentiality/adequacy and a higher one for potential adverse health effects. In this situation, the dietary exposure estimation should not be an underestimate of intake for nutritional adequacy and overestimate of exposure in the case of potential toxicity. When 'non-detect' values are not assigned numerical values, similar options are available for results below LOQ, e.g. assign a value equal to ½LOQ. For assigning a numerical value to trace results, a value between the LOD and LOQ is assigned.

If statistical expertise is available, a numerical value for 'non-detect' results can be estimated from the distribution of positive results (see Chap. 16 – Reporting and Modeling of Results Below the Limit of Detection).

After decisions have been made about 'non-detect' and 'trace' values for each sample analyzed, representative chemical concentrations can be determined for those foods where more than one sample was analyzed. Depending on the food chemical being examined and the dietary exposure assessment methodology chosen, the selected concentration may be a mean, a median or a distribution of concentrations. If the analyzed samples are composites, then mean food chemical concentrations should be used rather than the median as an 'averaging' effect on the food chemical concentration has already occurred due to the compositing process. Where individual samples were analyzed, a mean or median concentration could be used in a deterministic or semi-distributional methodology, depending on the nature of the food chemical and the data available. The median is more valid when dealing with a significant number of samples, i.e. $n > 50$. However, in most total diet studies, there are usually only 1–10 samples and therefore, the mean is more representative of the results. In a probabilistic distributional dietary exposure assessment, the distribution of all chemical concentrations is used.

Food Consumption Data

Food consumption data are a key component in dietary exposure assessment and may be sourced from per capita data (apparent consumption data, food supply data, disappearance data, WHO GEMS/Food Consumption Cluster Diets), food frequency questionnaires, household economic surveys, duplicate diets and national nutrition surveys (see Table 17.2). In some countries, model diets are developed from a variety of these information sources on food consumption patterns and are used to represent food consumption for specific populations or sub-groups (see Chap. 4 – Overview of Dietary Exposure and Chap. 43 – GEMS/Food Consumption Cluster Diets).

The first step in selecting food consumption data is to assess what is available. The data must be relevant to the country or region(s) that the TDS is being conducted for and include data for the population group or sub-groups of interest. If no data are available for the country/region, consideration should be given to whether data available in another country/region that has similar dietary patterns can be used. Since the TDS analyses foods in their 'ready-to-eat' form, the food consumption data should ideally include foods that were consumed in a 'ready-to-eat' state; however this is not essential. In 2006, the fourth International Total Diet Study Workshop recommended that the WHO GEMS/Food Consumption Cluster Diets be used where no other data are available [3].

Where food consumption data for individuals (i.e. national nutrition surveys) are used, the number of food items reported as consumed is usually much greater than the number of foods that can be analyzed in the total diet study. Consequently, a system needs to be devised to 'map' the foods analyzed to the foods as consumed. This is discussed in Chap. 44 – Food Mapping in a Total Diet Study.

Table 17.2 Food consumption data that can be used with the different dietary exposure assessment methodologies

Food consumption data that can be used	Dietary exposure assessment methodology		
	Deterministic	Semi-distributional	Probabilistic
Per capita data (e.g. FAO food balance sheet data, GEMS/Food Cluster Diets)	✓		
Model diets	✓		
Household economic surveys	✓		
Food frequency questionnaire[a]	✓		
Duplicate diets	✓		
National surveys	✓	✓	✓

[a]Food frequency questionnaire data may be used as the sole source of food consumption data to derive a model diet if that is the only source of information on food consumption patterns available, but these data are best used in conjunction with another source of food consumption data

Population Groups/Sub-groups

Since the total diet study examines long-term dietary exposures, all age groups in the population should be covered in the dietary exposure assessment, if possible. An alternative approach is to identify key age groups that are of interest for the food chemicals considered and report on those same groups each time these chemicals are included in subsequent total diet studies. The population groups who are at particular risk of exceeding the upper health-based guidance values should be included in the assessment. Children can have higher dietary exposures to food chemicals in comparison to adults due to the amount of food that they consume relative to their body weight. This is because they need more energy for growth and development. Population sub-groups with different health-based guidance values should be considered in the assessment along with population sub-groups who have distinct differences in food consumption patterns due to gender differences, geographical location, ethnic background or religious practices. For each population sub-group identified, a separate dietary exposure assessment is required to be undertaken and reported. Examples of population groups and sub-groups used in the Australian and New Zealand TDSs are provided in Examples 1 and 2, respectively, as follows.

Example 1

Population groups and sub-groups used in the 22nd Australian Total Diet Study

　　Since nutrients were selected as the analytes for the 22nd Australian Total Diet Study, the age-gender groups chosen for the dietary exposure assessment were selected to match the Nutrient Reference Value age-gender groups for Australia and New Zealand [4].

Age Group	Gender		
	Male	Females	Both genders
9 months			✓
2–3 years	✓	✓	
4–8 years	✓	✓	
9–13 years	✓	✓	
14–18 years	✓	✓	
19–29 years	✓	✓	
30–49 years	✓	✓	
50–69 years	✓	✓	
70 years & above	✓	✓	

Example 2

Population groups and sub-groups used in the 2003/04 New Zealand Total Diet Study

The 2003/2004 New Zealand TDS examined agricultural compound residues, contaminant elements and selected nutrient elements. The age-gender groups for the dietary exposure assessment were selected to represent key groups of interest and to achieve consistency with past total diet study reports on these food chemicals [5].

Age Group	Gender		
	Male	Females	Both genders
6–12 months			✓
1–3 years			✓
5–6 years			✓
11–14 years	✓	✓	
19–24 years	✓		
25 + years	✓	✓	

Health-Based Guidance Values

A health based guidance value is generally defined as the amount of a food chemical that can be consumed on a daily, weekly or monthly basis over a lifetime without appreciable risk to health. Most health-based guidance values are expressed on a per kilogram body weight basis. Health based guidance values are used to determine if the level of dietary exposure is a potential risk to the health of a population or population sub-group (risk characterization), which is an integral component of risk analysis (see Chap. 3 – Risk Analysis Paradigm and Total Diet Studies).

The health-based guidance value chosen for risk characterization will depend on the nature of the chemical being examined, the data available and the goals of the dietary exposure assessment. Nutrients differ from many other food chemicals in that exposures are compared to both an upper level and an estimated average requirement. Once the health-based guidance value for the chemical of interest has been determined, the estimated dietary exposures are compared to the health-based guidance value and expressed as a percentage of the health-based guidance value.

Body Weight

Where it is necessary for dietary exposures to be expressed in units per kilogram of body weight (units/kg bw), it is important to have representative body weight data to use in the dietary exposure assessment. National nutrition surveys for individuals may have data on the body weights for each individual respondent in the survey. Where these data are available, the dietary exposures for each individual in the survey can be calculated and converted to units/kg body weight using the individual's own body weight. Alternatively, mean body weights for each population group and sub-group of interest can be derived from these data. If body weight data are not available from national nutrition surveys, the mean body weight for each population group and sub-group can be determined using other surveys, studies or published literature.

Calculating Dietary Exposures

Prior to commencing the dietary exposure calculations, it is important to check the units of food consumption with the units of the food chemical concentration and to make adjustments in the calculations to convert to the same units. Nutrient content is usually reported by laboratories in units per 100 g of food, whereas other food chemical concentrations (e.g. for pesticide residues) are usually reported in units per kilogram of food.

Dietary exposure to a chemical is calculated using the formula below and is then compared to the health-based guidance value:

$$Dietary\ Exposure = \ \Sigma\left(Food\ Consumption \times Food\ Chemical\ Concentration\right)$$

If the health-based guidance value is in units per kilogram of body weight per day (units/kg bw/day) then the dietary exposure estimate will need to be converted from units/day to units/kg bw/day. In a deterministic method, the mean dietary exposure is divided by the average body weight for the population group/sub-group of interest. If using a semi-distributional or probabilistic method based on individual dietary records, the dietary exposure for each individual in the population group/

sub-group is divided by their individual body weight and compared to their individual health-based guidance value. Then the individual results are ranked and the mean and low or high percentile dietary exposures for the whole population or population sub-group of interest are derived. However, these calculations require computer programs as there are usually thousands of people in a national nutrition survey who have each reported consuming a variety of foods in a variety of amounts (see Chap. 45 – Automated Programs for Calculating Dietary Exposure).

Before commencing the dietary exposure calculations, it is important for all inputs to be crosschecked. This can be a time consuming process but is a critical step in the dietary exposure assessment process. The quality of the dietary exposure output is dependent on the quality of the input data. All meta-data (data about data) should be recorded with the calculations and should include how the data were compiled, the sources of the data and the methodology used (see Example 3 for additional considerations). This is helpful for future reference since, over time, important details can be forgotten or lost.

Example 3

Meta-data recorded for a total diet study
- Methodology used by the laboratory to analyze the food samples for each chemical.
- The form of the chemical that was analyzed.
- How the food samples were prepared prior to analysis.
- How samples were composited.
- Where the food consumption data came from.
- Assumptions made in the food mapping process.

Compiling and Reporting Results

The data from the dietary exposure assessment should be compiled in a way that allows the risk assessment questions to be answered. However, care must be taken that the data are not extrapolated beyond their limitations (e.g. it is not valid to extrapolate 97.5th percentile dietary exposures using data from only a few individuals). The information on dietary exposure that may be compiled and reported for total diet studies include:

- Mean dietary exposures for each population group/sub-group.
- High percentile dietary exposures for each population group/sub-group (where individual dietary records have been used).
- Low percentile dietary exposures for each population group/sub-group (nutrients only, where individual dietary records have been used).
- Comparison to the health-based guidance value (e.g. % health-based guidance value; proportion of population above or below the health-based guidance value when individual dietary records have been used).

- Foods that are major contributors to the estimated dietary exposures.
- Summary of food consumption data (e.g. the model diet used; average food consumption amounts).

Case Study 1 below provides an example of a deterministic dietary exposure calculation and the outputs that this calculation can provide.

Case Study 1: Deterministic Dietary Exposure Assessment

Step 1: Calculating mean dietary exposure (mg/day)

Food	Mean consumption (g/day) of food that may contain Chemical X	Mean concentration of Chemical X (mg/kg)	Estimated contribution to dietary exposure to Chemical X (mg/day)
Rice	15	80	1.2
Oat Porridge	8	100	0.8
Milk	600	5	3.0
Beef	70	50	3.5
Tomato	50	10	0.5
Total			*9.0*

Step 2: Calculating mean dietary exposure (units/kg bw/day)
   If the mean body weight $= 67$ kg

Estimated mean dietary exposure to Chemical X (mg/kg bw/day)	$=$	$\dfrac{9.0 \text{ mg / day}}{67 \text{ kg}}$
	$=$	0.13 mg/kg bw/day

Step 3: Calculating mean dietary exposure as a percentage of the health-based guidance value
   If the acceptable daily intake (ADI) for the chemical of interest is 5.0 mg/kg body weight per day

Estimated mean dietary exposure to Chemical X (%ADI)	$=$	$\dfrac{0.13 \text{ mg / kgbw / day}}{5.0 \text{ mg / kgbw / day}}$	$\times$	100 %
	$=$	Approximately 3 % ADI		

Step 4: Calculating contributors to dietary exposure

Food	Estimated dietary exposure to Chemical X (from Step 1) (mg/day)	% contribution to dietary exposures
Rice	1.2	13 (= 1.2 ÷ 9.0 × 100 %)
Oat Porridge	0.8	9
Milk	3.0	33
Beef	3.5	39
Tomato	0.5	6
Total	*9.0*	*100 %*

When reporting dietary exposure assessment results from semi-distributional or probabilistic assessments (i.e. using nutrition survey data for individuals), it is important to consider whether the results should be reported for:

1. The whole population group/sub-group, irrespective of whether the individual respondents were exposed to the chemical or not ('all respondents'); or
2. Only those respondents exposed to the chemical ('consumers only').

The choice of 'all respondents' versus 'consumers only' may not make much of a difference for nutrients and contaminants that are widely distributed in the food supply and are usually consumed by all people in the population every day. However, it may make a difference for a food additive or contaminant, for example, where the food chemical may only be found in specific foods that not everyone in a population may have eaten. Traditionally in a TDS approach, dietary exposures are reported for the whole population only.

The data from a dietary exposure assessment can be presented in many forms including:

- Text
- Graphs
- Diagrams (e.g. flow diagrams, schematics)
- Photographs and drawings
- Tables (numbers and/or text).

The ways in which the data are presented in the TDS report need to take into account the questions that the study was trying to answer and the intended audience for the report (e.g. risk managers, scientists only or the general public).

Before compiling and reporting the results of the dietary exposure assessment in a final report, it is important to crosscheck all calculations and formulas used. All outputs from the dietary exposure calculations should be crosschecked against the data inputs. For example, if apples had a detection of pesticide residue X, then there should be a percentage contribution of apples to the dietary exposure to pesticide residue X. If not, then there is either an error in the calculations or apples were not consumed by the population group. The dietary exposure results can also be crosschecked against other dietary exposure estimates (national or international) that are available. If the results differ significantly from other published results, it is

important to consider whether that was what was expected from known differences in food consumption patterns, conditions of use of the food chemical or permitted levels of use and, if not, the inputs to the calculations and the calculations themselves may need to be rechecked.

Assumptions, Limitations, Uncertainties

The aim of conducting a dietary exposure assessment is to make an estimate that is as realistic as possible with the resources available. Each dietary exposure assessment requires decisions to be made about how to set the food consumption and food chemical concentration parameters and what assumptions to make. Different decisions may result in different answers. The decisions made will be guided by the questions that are to be answered by the assessment and the data and resources that are available. Uncertainty can come from many sources, including survey design, sample collection, transport and preparation, analysis, food chemical concentration derivations, food consumption, health-based guidance values, assumptions and reporting (see Chap. 18 – Addressing Uncertainty and Variability in Total Diet Studies). To enable the results of the dietary exposure assessment to be put into context, the methodology used for the assessment, the assumptions made and the uncertainties in the data need to be clearly documented. This will allow informed decisions to be made about the outcomes of the dietary exposure assessment.

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Chapter 18
Addressing Uncertainty and Variability in Total Diet Studies

Christel Leemhuis, Judy Cunningham, and Amélie Crépet

Introduction

Total diet studies (TDSs) are powerful tools for collecting data on the concentration of chemicals in food, estimating dietary exposure and undertaking risk assessments for these chemicals for population groups of interest. As with all scientific studies, uncertainty and variability that are encountered when conducting a TDS need to be considered when reporting and interpreting the findings.

Uncertainty in a TDS arises when there is insufficient information available to accurately determine the value of a particular parameter being investigated [1]. Uncertainty can, in principle, be reduced through additional research and more accurate data [2]. *Variability* in a TDS refers to the inherent variation in the parameters being investigated; it contributes to total uncertainty in an exposure assessment. Variability cannot be reduced through further research but can be better understood [1, 3]. It is important to document both the uncertainty and the variability in the data sources used in a TDS and to make some judgment regarding their impact on the dietary exposure estimates and overall risk assessment associated with the study.

The specific consideration of uncertainty in diet-related risk assessments is a developing science. Some recent publications in this area provide detailed discussion on uncertainty and variability in exposure assessments [1–3]. This chapter does not aim to summarize the comprehensive information provided in these publications

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or to discuss every area where uncertainty may be encountered. Instead, it aims to provide a brief consideration of the main areas of uncertainty for the purpose of conducting a TDS.

Three key principles have been identified for the consideration of uncertainty in exposure assessments [2]:

- Uncertainty analysis should be an integral part of risk assessments including dietary exposure assessments associated with a TDS.
- The level of detail of the uncertainty analysis should be based on a tiered approach and consistent with the overall scope and purpose of the assessment.
- Sources of uncertainty and variability should be systematically identified and evaluated in the risk assessment.

Where Do Uncertainty and Variability Occur in Total Diet Studies?

Uncertainty and variability can affect every aspect of a TDS, starting with the formulation of the objectives through to the characterization of the risk. In practice, when planning a TDS, the project manager needs to focus carefully on the sampling, measurement and dietary exposure assessment phases of a TDS, assuming that they are already clear on the objectives of the study and how the proposed survey design will achieve these objectives. The project manager should also consider, at the planning stage, how to incorporate detailed checking and review processes throughout the project to minimize errors, such as calculation and programming mistakes.

One of the challenges of conducting a TDS is to minimize uncertainty as far as possible within practical limits and to understand the major areas of expected variability. Acknowledging the limitations of the study and identifying and addressing areas where uncertainty and variability exist is seen as good practice in reporting TDSs. It also provides risk managers with important information to assist with the interpretation of the study's findings [4].

One of the key outputs of a TDS is the risk characterization. The risk characterization allows the comparison of exposure estimates with relevant established health-based guidance values, such as the Acceptable Daily Intake (ADI), Recommended Dietary Intake (RDI), Provisional Tolerable Weekly Intake (PTWI), acute Reference Doses (ARfD), etc. In comparing exposure assessments with health-based guidance values, it is important to note that there is also uncertainty in the establishment of the guidance value including the use of safety factors to account for inter- and intra-species variability. This chapter does not explore the uncertainty of health-based guidance values in detail; however a number of documents are available which address this area [5, 6].

Variability

Variability is an inherent property of biological systems. Levels of chemicals in foods can be highly variable, even within the same type of food. Many factors affect this variation including season, location of sample, soil types, agricultural practices, breed or cultivar, maturity of plants or animals, production and cooking methods, batch-to-batch variation in processed foods, and many others [7]. Due to the limited number of samples usually collected for analysis, a TDS can never capture all the variability that occurs in foods, but understanding the sources of variation can help in the design of the sampling frame and in the interpretation of results. Uncertainty associated with variability is likely to be most significant in the sampling phase and therefore a well-designed sampling plan is vital to capture the most representative sample of foods practicable.

Sampling Considerations Related to Variability

A key component of TDSs is the identification and collection of foods upon which analytical measurements are undertaken. Representative foods are first identified via a food list (see Chap. 6 – Preparing a Food List for a Total Diet Study). Each of the foods selected as being representative of total diet patterns will vary in chemical concentration over time. In addition, the pattern of variation in food chemical levels may differ according to the chemical being investigated. Therefore, before planning sampling, it is important to research the factors that may affect variation in levels of the chemicals being investigated in your TDS. Then the sampling plan can be designed to at least take account of the major sources of variation.

For example, for an unprocessed food, such as lettuce, it may be important to ensure that more than one variety of lettuce is collected, that samples cover the major growing practices (e.g. hydroponic production as well as traditional 'in ground' production), that samples were collected from different production regions (where relevant) and that samples are collected at different times of the year. For a manufactured food such as breakfast cereal, purchase location may be less relevant than for a fresh product, as there may be a limited range of producers who distribute their product nationwide. In this case consideration may be given to sampling products with varying formulations, with different batch numbers and/or packaged in different materials.

When levels of a food chemical are highly variable, it is preferable to draw on a large primary sample to generate a more robust estimate of the mean concentration of the chemicals in question. In addition, analysis of as many individual samples as possible will allow a better understanding of the magnitude of the variation in chemical levels around the mean. However where different samples are aggregated or composited prior to analysis, as a means of reducing costs and analysis time, additional uncertainty may arise because information on sample variability is reduced.

Sample Preparation and Variability

A key element of a TDS is the preparation of samples to a 'as consumed' state before analysis is undertaken. The preparation steps will vary according to the type of food and should reflect food preparation practices within each country. There is considerable variation in how people prepare foods, such as variation in cooking time, storage practices before cooking, cooking equipment used, etc. While the aim of preparation practices is to use what is assumed to be the most common cooking method, the chosen method will not cover all possibilities and therefore will not reflect the full variation in preparation techniques.

Variability and Selection of an Analytical Aliquot

Adequate homogenization of analytical samples is required to ensure that aliquots removed for analysis will be representative of the original samples. This may be difficult to achieve when deal with large bulk samples. For example, aflatoxin sampling plans require an initial 20 kg sample be ground to a fine powder.

Variability in Food Consumption Data Used to Estimate Dietary Exposure

Dietary exposure assessments conducted as part of a TDS require not only the chemical concentration data measured in the study, but also representative food consumption data for the population being studied. In the same way that a sample of foods can never capture the full variability of the food supply, a survey of food consumption will not cover the full variability in consumption patterns that an individual, group or population might follow, particularly where consumption data are collected over a short period of time (typically 24 h). However if a large, well designed food consumption survey is used as a basis for estimating dietary exposure to the chemicals measured in a TDS, this source of variability is likely to be minimized, at least in terms of the mean amounts of each food consumed in a population.

Uncertainty

In this section, sources of uncertainty are considered, aside from considerations associated with the innate variability of foods and food consumption patterns.

Uncertainty Associated with Sampling

Sampling uncertainty or error can arise for a number of reasons, such as when the wrong samples have been purchased or the samples have not been prepared or stored correctly. Each sampling step can introduce errors from a range of mechanisms, such as loss of analyte, contamination of samples within and/or from containers, spoilage of samples or inadequate detail to identify samples for analysis. To address these areas of uncertainty it is important to develop robust sampling plans and provide clear instructions on the collection, packing, recording and transportation associated with the foods being collected as part of the TDS. It is important to recognize that sampling protocols can never describe the action required by the sampler for every eventuality that may arise in the real world of selecting samples [8]. However protocols should be clear and concise to reduce the sampling uncertainty, as explained in Chap. 8 – Preparing a Procedures Manual for a Total Diet Study.

Measurement Uncertainty

There are many excellent references on measurement uncertainty and approaches to estimating it for any given analysis [1], for those readers who need more detailed information than that provided here. Analytical measurement uncertainty is an important consideration in TDSs. Measurement uncertainty may arise from many possible sources including sample preparation, matrix effects and interferences, environmental conditions, uncertainties of masses and volumetric equipment, reference values, approximations, instrument maintenance and calibration, experience of the analyst and assumptions incorporated in the measurement method and procedure. To address measurement uncertainty in TDSs, it is important to ensure that the laboratory selected to undertake the analysis work is accredited or to ensure that analytical methods are validated.

Random errors are present in all measurements and cause replicate results to fall on either side of the mean value. The random error of a measurement cannot be compensated for, but increasing the number of observations may reduce the magnitude of such errors. Systematic errors occur in most experiments. The sum of all the systematic errors in an experiment is referred to as the bias. They may go undetected unless appropriate precautions (e.g. validating the analytical method by use of standard reference materials) are taken [2]. Both random and systematic errors will affect measurement uncertainty.

The selection of instrument and method validation is an important consideration in a TDS. Measurement uncertainty can arise in analytical results if the instrument and method selected are not suitable to the analyte of interest. In practice the fitness for purpose of analytical methods applied for routine testing is most commonly assessed through method validation studies [1]. Laboratories should have established the measurement uncertainty associated with each analyte for the methods of analysis they are using and be able to report this uncertainty with the analytical results.

Dealing with Non-detects

Within analytical data sets there may be concentrations of a food chemical that are shown as 'not detected' or are below the Limit of Quantification (LOQ) or Reporting (LOR) for the analytical method. For the purposes of the dietary exposure assessment, a numerical value needs to be assigned to these. There are a number of techniques for doing this, but whatever method is chosen there will be associated uncertainty. For example, if a 'worst case' approach is taken of assigning the LOQ to non-detect values, dietary exposure is likely to be overestimated, particularly where a large proportion of the analytical results were non-detect results (see Chap. 16 – Reporting and Modeling of Results Below the Limit of Detection and Chap. 17 – Dietary Exposure Assessment in a Total Diet Study). Conversely, assigning a zero value could underestimate dietary exposure, particularly for food chemicals such as contaminants that are not intentionally added to foods but are naturally occurring and therefore likely to be present, albeit below the limit of detection. It is important to document any assumptions made in the treatment of non-detect values, including noting the likely direction of the uncertainty. Other techniques are available for the treatment of non-detects [9].

Assigning Measured Concentrations to Other Foods

Another source of uncertainty is the extrapolation of concentration data measured in one food to individual foods reported as consumed in the population being studied. For example, the chemicals that are the subject of the study may have been measured in wheat-based bread; these values may also be applied to rye- and maize-based breads and flatbreads if there are no analytical data for these breads. Clearly this introduces further uncertainty. It is difficult to quantify the magnitude of this uncertainty but it is reduced by a well-designed sampling plan that includes the most important foods for your population. It is also reduced through careful extrapolation by trained staff by a 'mapping' process that assigns concentration levels to a wider number of foods than that analyzed (see Chap. 45 – Food Mapping in a Total Diet Study).

Uncertainty in Food Consumption Data

The quality of the food consumption data is an important aspect to consider in undertaking dietary exposure assessments for the purposes of a TDS and other assessments [10]. Uncertainty exists in food consumption data due to the methods used to collect, collate and report those data.

In addition to variability, uncertainty occurs in the collection and reporting of food consumption data. This uncertainty may include factors such as reporting errors (under- or overreporting consumption of foods) and errors in estimation of

portion size, food categorization and data entry. There is additional uncertainty for some obscure or occasionally consumed foods where there may not be sufficient consumers of the food in a survey population to enable a robust estimate of the amount of food consumed to be made [2].

Using short-term food consumption surveys may capture an unusual eating occasion for an individual that does not describe how they normally eat. This could potentially over- or underestimate their typical food consumption and in turn exaggerates the reported extremes of food consumption across the survey group. The distribution of food consumption amounts for a survey of one 24-h duration is much broader than that of two or more days. Therefore, the number of days of food consumption data affects the predicted high food consumption amount [9]. This in turn affects estimated high consumer dietary exposure (typically represented by the 90th percentile of exposure where only 1 day of food consumption data are available) particularly for food chemicals in occasionally consumed foods. Uncertainty in the estimates of dietary exposure for high consumers will be greater than for the population mean dietary exposure.

In many countries, specific 'model diets' are developed to represent usual patterns of consumption for each population sub-group of interest; these may be derived from individual dietary records or other sources of information (see Chap. 17 – Dietary Exposure Assessment in a Total Diet Study). There will be uncertainties in the food consumption amounts in 'model diets' due to the assumptions made in formulating the 'model diet'.

Documenting Sources of Variability and Uncertainty

Even though it is challenging to quantify uncertainty associated with a TDS, it is generally possible to make a qualitative assessment of the major sources of uncertainty (including that originating from variability). It is important to note both the significance of the uncertainty and its direction (i.e. whether it would be likely to lead to an over- or underestimation of dietary exposure). In some cases a degree of overestimation of exposure is preferred so as to provide a 'worst case' scenario and to ensure that risk is not underestimated. However in relation to dietary exposure to nutrients, where a minimum intake (exposure) is required to assess the risk of nutritional inadequacy, underestimation is preferred as this will better identify areas for further work in relation to public health objectives including meeting relevant recommended dietary intakes. An example of a way to report uncertainty is provided in Table 18.1; in these examples, the assessments of the direction and magnitude were made for specific investigations being conducted and may differ in other assessments.

Depending on the circumstances of the assessment, a quantitative or semi- quantitative assessment of uncertainty may be important for interpreting results in a particular situation, especially if considering risk management options to address an apparent problem, for example if estimated population dietary exposure to a chemical is close to a health-based reference value, but there is considerable measurement or sampling uncertainty that could have led to a conservative assessment of risk.

Table 18.1 Examples of the impact of uncertainties and variability on dietary exposure assessment for a food chemical

Sources of uncertainty and variability	Direction and magnitude
Measurement uncertainty in analytical results, particularly at low analyte concentrations (may be possible to quantify this for some or all analytes)	+++/−−−
Number of sub-samples collected for each food	++/−−
Size and variability of analytical data set	++/−−
Influence of non-detects in analysis	from +/− to +++/−−−
Uncertainty in assigning foods to concentration categories and developing analyte concentrations for mixed foods	++/−
Use of 24-h food consumption recall data to assess usual food consumption amounts and subsequent food chemical dietary exposure	++/−
Overall evaluation of total uncertainty	+ *(whole population)*

+, ++, +++ represent uncertainty with potential to cause small, medium or large overestimation of dietary exposure to food chemical

−, −−, −−− represent uncertainty with potential to cause small, medium or large under-estimation of analyte intake

Conclusion

Significant areas of uncertainty and variability exist in the sampling, measurement and dietary exposure estimate phases of a TDS. In undertaking a TDS, it is necessary to recognize areas of uncertainty and variability and to address these where possible. It is also important to clearly document the uncertainties associated with a TDS as this assists in interpreting any risk assessment outcomes and the development of risk management options if required.

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Chapter 19
Communicating Results in a Total Diet Study

Cherie A. Flynn

The focus of a total diet study (TDS) is to estimate the chemical exposure, through the diet, of a population or population sub-group to contaminants and nutrients (both naturally occurring and introduced). While determining the concentrations of these chemicals in individual foods or a particular food group is not the primary objective of a TDS, nevertheless both types of information are generated by a TDS and both are of interest to many stakeholders – how many will depend on what particular foods are sampled and which particular analyses are being undertaken. Ensuring that communication of results is performed within the context of the overall TDS, which includes explaining what such a study is (and in some cases, what it is not) is, therefore, an important consideration when determining how and when such communication is to be undertaken.

Introduction

There are essentially two aspects to the results for a TDS; these being the dietary exposures, which are the main focus of a TDS, and the analytical results of the foods that are sampled. Both of these aspects are of interest and given the nature of a TDS, are received at different stages of the overall project. Communicating the results of a TDS is, therefore, not necessarily a single event. Rather, communication of results may be undertaken at several points and to a range of involved or interested parties.

A TDS does not produce a single result of interest or value to only a limited number of parties. Government, industry, academia, consumer organizations and

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consumers themselves will all be interested in the results of a TDS. Using the results of a TDS to influence various stakeholders is presented in Chap. 47 – Involving and Influencing Key Stakeholders and Interest Groups in a Total Diet Study. The levels of interest from these various parties are linked to the actual planning and design of the TDS. The wider the range of foods sampled and chemicals analyzed, the wider will be the range of parties that will be interested in the results.

This fact reinforces the importance of considering how results are to be communicated in the planning and design of a TDS. Developing a plan that captures the release of results as well as communication on other aspects of the entire study is an integral component in the design of a TDS (See Chap. 5 – Scope, Planning and Practicalities of a Total Diet Study). The key features of such a plan should answer the following questions:

- How should the communication be undertaken, and if more than one communication mechanism is available, which is the best in each circumstance?
- Who needs to be communicated with?
- What needs to be communicated?
- When does such communication need to occur?

The development and implementation of such a communication plan is the topic of discussion in the remainder of this chapter.

How Should the Communication Be Undertaken?

How results are to be communicated and who has the responsibility for undertaking such communication, will be influenced by the objectives or goals of the particular TDS. What is the focus of the study? Is the study to encompass the whole country or only a particular region? Will dietary exposures be estimated for more than one age or ethnic group? Is there a particular health concern that is being targeted (e.g. a nutrient deficiency or an environmental contaminant)? Is the study looking to see if a previously implemented risk management decision has been effective? For example, such decisions may relate to: fortifying salt with iodine to address iodine deficiency; stopping the use of lead solder in canned products to reduce dietary exposure to lead; or addressing a previously identified environmental issue such as a discharge of industrial waste into water that is used to irrigate food crops.

When undertaking a TDS for the first time, the design components and goals of the study can guide identification of those likely to be interested in the results. If a TDS had already been undertaken in the past, then an analysis of how that study was reported and the results communicated, and the response or reaction to that communication, should influence how and when the results of the new study are communicated. If the past communication was well received, then a similar approach can be followed. If not, then it will be important to look at why there was dissatisfaction and to consider how this could be addressed and the communication improved. For example, were all the interested parties or organizations aware that

the TDS was being undertaken and that the information would be or was available? If not, can a contact list of such parties be developed and used to keep them informed. Also, how long did it take for the results to be available? If this was a concern, could the timetable be improved or can some interim results or the food sample analysis results be made available? This approach is discussed later in this chapter.

Communication about a TDS and the publication of the results allows a wide range of people and parties to access the information and data that is produced. This communication and publication can occur in a range of ways. However, advances in electronic technology and increased access to the Internet now mean that the available options are not as limited as in the past. An example of a dedicated webpage containing a wide range of information about a country's TDS is on the New Zealand government's food safety website [1].

Production of a full final report in the form of a printed stand alone paper or submitting of some or all of the results for publication as one or more articles in a scientific journal are options that should be considered. However, release of the results on the Internet can mean that such information and data can be made available faster and at less cost. Electronic publication also does not prevent publication in other forms as time and resources permit.

Preparation and issue of a press or media release when results are published can also help to advise the general public and interested parties that such results are available. If there is interest, giving media interviews can be a way of further explaining what a TDS is, why it was undertaken and what the results mean for consumers and other interested parties. Similarly, presentation of results at conferences or seminars is also an effective way to share the information. These also provide an opportunity to focus on a specific aspect of the TDS that is of interest to the particular audience and allow for questions and discussion.

Who Will Be Interested in the Results of a Total Diet Study?

The government agency or research institute that funds a TDS clearly has an interest in the results and may well have processes and protocols that need to be followed in reporting results. Over and above such official or formal reporting requirements, those undertaking the study should also be mindful of the wider range of people, organizations and institutions that will be interested in the results. The results of a TDS will not only be of interest nationally but also regionally and internationally.

Given that a TDS considers what it is that consumers are exposed to through the food they eat, consumers will be one of the main groups that will have an interest in the results. As well as consumers, others in the country who will be interested can include:

- Growers, producers or sellers of the foods, as well as any industry organizations or associations representing those businesses
- Various industries whose chemicals may have been analyzed for in the foods (e.g. agri-chemicals, food additives, and dietary supplements)

- Academic researchers and scientists engaged in a wide range of areas including, public health, nutrition, food technology, animal husbandry, and horticulture
- Government agencies responsible for control and/or monitoring of the food supply (including food ingredients and packaging) from production or importation through processing, manufacturing and distribution to the sale of foods and food ingredients, and
- Those agencies responsible for the wider public health and those involved in environmental management.

Regional or international interest will also be wide ranging and can include those in other countries that undertake TDSs, trading partners (in that a TDS can contribute to the demonstration of food safety controls within a country), and international agencies, such as, the World Health Organization (WHO) through its GEMS/Food Program, the Codex Alimentarius Commission, and the Food and Agriculture Organization of the United Nations (FAO) through the Joint FAO/WHO Joint Expert Committee on Food Additives and the Joint FAO/WHO Joint Meetings on Pesticide Residues.

What Results to Make Available, and When

Although the primary focus of a TDS is the estimation of chemical exposure through the diet and not what concentrations of contaminants or nutrients are present in individual foods or a particular food group, by its nature a TDS does produce data on both these aspects. It is, therefore, important when considering how to communicate the results for both these aspects to ensure that the context of the entire TDS is provided. Setting out the context should include being clear about what a TDS is and what it is not. A TDS normally provides estimates relating to an average consumer. It is not a commodity-based surveillance or monitoring survey, which analyze foods as they are available for sale or 'as produced' and compares the results with regulatory limits. Nor is a TDS a nutrition survey – in that the foods within a national nutrition survey are in the thousands rather than the much smaller number of representative foods that is normal in a TDS (refer also to Chap. 1 – Total Diet Studies—What They Are and Why They Are Important).

A TDS provides a snapshot in time of the dietary exposure of a population or population sub-group to contaminants and nutrients (both naturally occurring and introduced) and should not be extrapolated as doing more than this. This snapshot relates to the time when the foods were sampled. When first undertaking a TDS, this information can provide an assurance to consumers that there are no concerns in respect of their food supply, or can indicate areas that need further investigation. However, when a series of TDSs is undertaken, then the results can also provide information on trends over time. This information can help in preparing advice to government as to where resources need to be focused to address a concern or, when risk management actions have been taken previously, can show what impact such actions have achieved.

A full report on a TDS should include all the relevant information about the entire study or at the least, advise where such information is available. An outline of the content of a full report would include:

- An introduction, including an explanation of what a TDS is, why this particular study has been undertaken (the goals or objectives); if relevant the history of TDSs for the country; and an explanation of any changes between this TDS and any previous studies.
- An explanation of the various methodologies used: what foods were sampled (the food list) and why these particular foods were selected; the locations and dates on which foods were collected or purchased; the sample preparation; the population group or groups for whom dietary exposure estimates have been made and how the diets for the group or groups were determined (for example were simulated diets developed); the particular analyses that were undertaken and why these were selected.
- The results of the dietary exposure assessments will also need to be placed in context – what are the results being assessed against; is a comparison also being made against the results in other countries; if there have been previous TDSs in the country; and what are the trends over time.

When presenting the results from a TDS, it is important to consider how the information is formulated and who the target audience is. The reporting of results should be meaningful, relevant and accurate and be done in a way that is clear and understandable. Consideration should be given to the use of figures and diagrams (such as trend graphs and pie charts) as these can greatly assist in presenting numerical and percentage information. The report of the New Zealand TDS uses such an approach and this can be viewed on the New Zealand government's food safety website [1].

While the food sample analytical results of a TDS can only provide a snapshot of what contaminants and nutrients are in the diet of the population, this data can be useful when added to other data sets. For example, the results for particular chemical/food combinations (e.g. nitrates in preserved meats and mercury in fish and seafood), or for a particular element or chemical (e.g. iodine, lead, and persistent organic pollutants) can be added to food chemical concentration databases, including the WHO GEMS/Food Programme database for dietary exposure (See Chap. 46 – OPAL —A Program to Manage Data on Chemicals in Food and the Diet), or to a study that may have looked at the presence of that chemical in the wider environment. If moisture analysis is also undertaken, then data relating to nutrients can usefully be added to a food composition database.

One of the concerns that sometimes has been expressed about access to the results of a TDS is the length of time between the collection of food samples and the release of the analytical data and the dietary exposures. Where more than one round of sampling is undertaken, consideration can also be given to releasing the sample analysis results after each sampling round, once they have been checked for accuracy and the appropriate laboratory quality controls completed.

In making available the results of the food sample analyses, it is important to ensure that such information is placed in the proper context. A TDS, by its nature,

provide results for a moment in time depending on the period of time over which the food samples were collected, and the number of occasions the same food was sampled. For example, the collection or purchase of a sample of each food twice in a 1-year period (each 6 months apart) can provide information that captures seasonal variation.

The limited number of samples collected and the random nature of the brands collected (i.e. while the sample collectors may be instructed to purchase particular commonly available brands of a product, what is actually available in the marketplace at the time of sampling may dictate that only some brands are purchased), are also a reason for not specifically releasing brand or product identity information when the analysis results show that the levels of a particular chemical or chemical residue are within the expected or allowable range. The results of a TDS should not be used to either endorse or denigrate a particular supplier or brand of a product just because it happened to be the one that was purchased on a particular day. However, there may be instances when a result from a TDS indicates a potential risk to consumers that requires timely investigation and assessment by the relevant government agency and this may result in the identification of a product.

Communicating Unusual or Unexpected Results Identified During Sample Analysis in a Total Diet Study

A TDS is not usually considered useful as a compliance monitoring or surveillance tool. The primary purpose is to estimate population average dietary exposures to selected chemicals, contaminants and nutrient elements, and to identify trends over time. As a result, sampling in a TDS is traditionally not as extensive or statistically robust as most international recognized compliance monitoring or surveillance programs. Furthermore, the food samples in a TDS are analyzed after being prepared as for normal consumption; so bananas are peeled, meats cooked, etc. Generally, this extra sample preparation will lower the measured levels of many analytes compared to those found in the raw agricultural commodity state that is usually measured in a monitoring or surveillance program. The foods sampled are also composited within or across regions, brands and/or seasons depending on the particular analysis being undertaken and the resources available.

One of the decisions that needs to be made during the planning of a TDS is, therefore, what to do if a single result is outside the norm or what would reasonably be expected, or is at or above a regulatory limit that may apply. In some instances such a result may indicate a possible public health risk. However, this will need to be confirmed by extra means. Provision needs to be made for ensuring that results of this nature are able to be passed to the relevant government agencies in a timely manner so that any risk can be appropriately assessed, which may involve collection and analysis of additional samples outside the TDS itself and a decision made on what, if any, is the appropriate action. It is, therefore, important to ensure that provision for such notification is included in the design and planning of a TDS.

The government agency responsible for the control of the food supply will also need to have considered how it will deal with any such results from the TDS, including how and when it would expect to receive notification and whom in the agency will take responsibility for assessing the information, seeking additional information as necessary and deciding on the appropriate response, if any.

During the 2003–2004 New Zealand TDS, an analytical result identified an unacceptably high concentration of lead in an infant food. The product was recalled and it was identified that the source of the contamination was corn flour used in the product. Subsequent investigation identified that three batches of corn flour had lead contamination; all had been milled from one shipment of imported corn, which had been contaminated with lead during shipping. Packaged corn flour and products that used the corn flour as an ingredient were assessed and products with unacceptable levels of lead were recalled. Information communicating this event and how it was dealt with by the responsible government agency[1], including the risk assessment (relating to the various products and the dietary exposure risk for children and adults), the products recalled, and the various media announcements were also published on the agency's website as well as being communicated directly to relevant affected or interested parties in New Zealand and internationally (See also Chap. 35 – New Zealand's Experience in Total Diet Studies).

Conclusion

While a TDS is a key tool in exposure assessment and risk assessment, which can then help guide the selection of risk management options, the effective communication of a TDS, its results and their significance is just as pivotal in the risk analysis context.

To be effective, the communication of TDS results needs to consider how the communication should be undertaken, and if more than one mechanism is available, which is the best option in differing circumstances. It should also consider who needs to be communicated with, what needs to be communicated and when such communication should occur.

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[1] At that time the responsible agency was the New Zealand Food Safety Authority (NZFSA). The NZFSA was established in 2002. From 1 July 2010 NZFSA was amalgamated with the New Zealand Ministry of Agriculture and Forestry (MAF), and on 1 July 2011, the Ministry of Fisheries was also merged into MAF. On the 30 April 2012, the new ministry became the Ministry for Primary Industries (MPI).

Part II
Total Diet Studies in Countries

Chapter 20
The Australian Experience in Total Diet Studies

Janice L. Abbey, Janis Baines, Leanne Laajoki, and Tracy L. Hambridge

Introduction

The purpose of the Australian Total Diet Study (ATDS) is to estimate the dietary exposure (intake in the case of nutrients) for the Australian population to a range of chemicals that may be found in the food supply and determine whether there are any concerns for public health and safety. Australia has conducted a number of ATDS over the last 40 years and intends continuing this national survey in future years.

Traditionally, the ATDS has estimated dietary exposure for the Australian population to a range of pesticide residues and contaminants. In recent years, however, the scope of the ATDS has evolved with food chemicals of concern, such as additives and nutrients, which are now included.

History of the ATDS

In May 1969, at its Sixty-Eighth session, the Australian National Health and Medical Research Council (NHMRC) recognized the need for Australia to conduct a national "market basket' survey" to examine the levels of agricultural and veterinary chemical residues and contaminants in foods that constitute a significant part of the normal diet. The NHMRC recommended that the Commonwealth and State Departments of Health should cooperate in the organization and execution of the survey, with the Commonwealth assuming overall responsibility. This recommendation resulted in

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the first Australian market basket survey in 1970, conducted by the NHMRC. The NHMRC conducted a further 15 surveys before responsibility and oversight of the survey was passed to Food Standards Australia New Zealand (FSANZ), formerly known as the National Food Authority and Australia New Zealand Food Authority (ANZFA). This study, now more commonly referred to as the Australian Total Diet Study (ATDS), continues to be managed by FSANZ.

The ATDS: A Collaborative Approach to Food Regulation in Australia

FSANZ is one element of the Australian and New Zealand food regulatory system that has as its source of policy advice, the Council of Australian Governments Legislative and Governance Forum on Food Regulation (the Forum), formerly known as the Australia and New Zealand Food Regulation Ministerial Council, a body comprised of representatives from the Australian and New Zealand Governments and each of the Australian State and Territory Governments. A whole-of-government approach is taken in developing food standards, with health, agriculture, trade and other portfolios being consulted before policy advice is issued or decisions made. The Food Regulation Standing Committee (FRSC) is composed of the department heads of those portfolios represented on the Forum and supports the Forum by providing advice on policy development. FRSC's to implementation subcommittee on food regulation (ISFR) is responsible for the consistent implementation and enforcement of food standards within Australia and New Zealand (Fig. 20.1). A representative from the Australian local government authorities is an observer on the ISFR.

The ISFR Workplan is divided into eight components considered important in effective and consistent implementation in food regulation. As part of Component 1, '*Surveillance and Monitoring*', a 3-year forward 'Coordinated Food Survey Plan' (the Plan) was developed for Australian jurisdictions and New Zealand, with the aim being to develop efficiencies and enhance the quality of national or bi-national surveys through greater collaboration in the planning, implementation and consistent management of the outcomes. The 22nd ATDS commenced prior to the establishment of ISFR and was placed on the Plan while in progress. The 23rd ATDS is the first ATDS to go through the full cycle of planning and implementation through the ISFR process and continues to be a collaborative project with all Australian jurisdictions [1]. Almost 40 years since its inception, the ATDS continues to receive high-level support and commitment within the Australia New Zealand food regulatory system and is well recognized internationally. This high-level support for the ATDS was re-affirmed in 2008 with agreement to ensure full and timely national participation in all future ATDSs, including sufficient resourcing.

In addition to surveillance activities undertaken as part of the ISFR Plan, State and Territory health and agriculture authorities also conduct food surveys investigating a variety of food chemicals (e.g. pesticide residues, additives and contaminants). These surveys are usually targeted at specific food types or chemicals, and are used
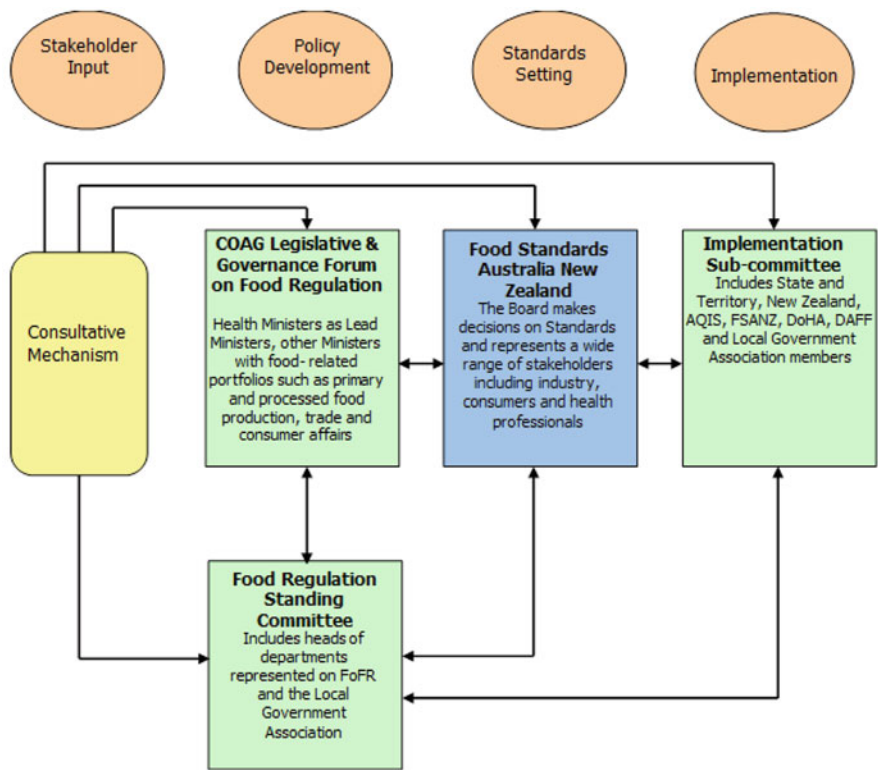
Fig. 20.1 Overview of the food regulatory framework in Australia and New Zealand

to assess compliance of primary producers and food manufacturers with relevant food regulations. The data generated from these surveys provide supplementary information on the chemical status of foods in Australia and serve as a valuable resource. The results of these surveys are shared with other State and Territory health and agricultural authorities through a Food Surveillance Network, a technical forum for collaboration on food surveillance issues in Australia and New Zealand, including the ISFR-related surveys, such as the ATDS. This network is chaired and managed by FSANZ.

Other Food Chemical Surveillance Activities in Australia

The Australian Government, through the Department of Agriculture, Fisheries and Forestry, conducts two ongoing surveillance programs that examine the level of specific chemicals in selected exported and imported foods, rather than

investigate a whole of diet exposure to food chemicals. These programs are known as:

- The National Residue Survey, which focuses on foods exported from Australia.
- The Imported Food Program, which is conducted by the Department of Agriculture, Fisheries and Forestry (DAFF) Biosecurity to ensure compliance with the *Imported Food Control Act 1992* and the *Australia New Zealand Food Standards Code*.

Comparison of ATDS with Other Studies

The ATDS is the only national survey that monitors the level of food chemicals in the total diet to determine their significance in the overall Australian diet and any associated risks to human health. The ATDS is also the only comprehensive national survey that analyses representative food samples as they are consumed. This is in line with the TDS approach but in contrast to most other food analytical surveys conducted in Australia. All food samples in an ATDS are prepared to a 'ready to eat' state prior to laboratory analysis, that is, they are subjected to typical preparation or processing steps (e.g. peeling, frying, baking etc.) (see Chap. 9 – Food Sampling and Preparation in a Total Diet Study). The type of preparation or processing required varies with the type of food. For example, vegetables may be peeled if they are usually eaten without their skins, while chicken is grilled as this food is consumed after cooking in this manner. By analyzing foods that have been prepared as customary, factors such as storage and preparation that can affect the concentration of some food chemicals can be accounted for. This results in more accurate and representative estimations of dietary exposure to food chemicals or dietary intakes of nutrients for the Australian population.

The Focus of the Australian Total Diet Study

The focus of the ATDS was primarily to estimate dietary exposure to agricultural and veterinary residues and contaminants every 2 years up to and including the 20th ATDS [2]. In general, the results from these studies consistently showed that dietary exposure of Australians to residues from a range of agricultural and veterinary chemicals and contaminants were low, that is below relevant health-based guidance values (HBGV), and therefore did not represent a public health and safety risk.

In 2003 FSANZ and the State and Territory government food regulatory agencies, agreed to diversify the scope and format of the ATDS to include other food chemicals, such as additives and nutrients. Residues from a range of agricultural and veterinary chemicals and contaminants would still be investigated but less frequently. The diversification of the ATDS has enabled data to be collected for a wider

Table 20.1 Summary of the analytes included in 19th–23rd Australian total diet studies

ATDS number	Sampled	Published	Number of foods	Analytes
19th	1998	2001	69	*Agricultural chemical residue screen:* chlorinated organic pesticides, organophosphorus pesticides, synthetic pyrethroid, fungicides, selected carbamates, piperonyl butoxide
				Contaminants: antimony, total arsenic, cadmium, copper, lead, mercury, selenium, tin, zinc, aflatoxins, polychlorinated biphenyls
20th	2000/2001	2003	65	*Agricultural chemical residue screen:* chlorinated organic pesticides, organophosphorus pesticides, synthetic pyrethroids, carbamates & fungicides
				Contaminants: antimony, arsenic, cadmium, copper, lead, mercury, selenium, tin, zinc
				Natural toxicants: aflatoxins & ochratoxin A[a]
				Inhibitory substances: penicillin G, streptomycin, oxytetracycline[a]
21st	2003	2005	60	*Additives:* sulphites, nitrates, nitrites, benzoates, sorbates
22nd	2004	2008	96	*Essential trace elements:* iodine, chromium, molybdenum, selenium and copper
				Additional survey activity on ATDS samples: e.g. polybrominated diphenyl ethers (PBDE) and polycyclic aromatic hydrocarbons (PAHs)[a]
23rd	2008	2011	93	*Agricultural chemical residue screen*
				Metals & other elements
				Natural toxicants

Please refer to the reference list for the details of each published ATDS
[a]Certain foods only

range of food chemicals. This has provided significant public health information about the Australian diet and allowed further investigation into concerns around some population groups exceeding (or not meeting in the case of nutrients) the required HBGV. The focus of the 21st and 22nd ATDSs reflected this change and evaluated food additives and nutrients (trace elements), respectively [3, 4]. The value of this new approach was demonstrated in relation to Australian's dietary exposure to sulphites (21st ATDS) and informing the status of dietary intake of iodine (22nd ATDS) in the Australian population. These findings prompted decisions to review relevant food regulations. A summary of the analytes examined in the more recent ATDS (19th–23rd ATDSs) is presented in Table 20.1.

How Is the ATDS Conducted?

The ATDS is managed by FSANZ in collaboration with all Australian States and Territories. The participation of all Australian States and Territories in the ATDS is necessary to ensure that high quality, nationally representative data are produced through the collection of representative national and regional samples. Sampling and analysis of food usually occurs over a 12 month period, for some foods up to four times a year to capture seasonal variation in the food supply. As the ATDS manager, FSANZ meets all costs associated with sample transport, preparation and analysis, with the States and Territories covering the cost of obtaining the samples. Food sample analysis is conducted by a commercial laboratory selected by an open and competitive tender process according to the Australian Government Procurement Guidelines (see Chap. 14 – Commercial Analytical Laboratories—Tendering, Selecting, Contracting and Managing Performance).

Following analysis, States and Territories receive the analytical data specific to their region. The ATDS is not undertaken for the purpose of assessing compliance with relevant food regulations, although cases of potential non-compliance are highlighted. From the concentration data obtained, FSANZ generates a dietary exposure estimate using DIAMOND (Dietary Modelling of Nutritional Data), a computer program developed by FSANZ to automate dietary exposure calculations (see Chap. 45 – Automated Programs for Calculating Dietary Exposure). DIAMOND combines food consumption data from the Australian 1995 National Nutrition Survey (NNS) [5] and more recently, the 2007 the Australian Children's Nutrition and Physical Activity Survey [6], also known as Kids Eats Kids Play (KEKP), with chemical concentration data to estimate the dietary exposure for that compound for a range of population groups. The 1995 NNS surveyed 13,858 Australians aged 2 years and above using a 24-h dietary recall survey. The KEKP surveyed 4,487 children aged 2–16 years also using a 24-h recall survey with a second 24-h survey on a non-consecutive day. As neither survey includes children less than 2 years of age, a theoretical diet was constructed for infants at 9 months of age. The theoretical infant diet is extrapolated from the diet of a child at 2 years for solid foods, with an adjustment for the proportion of the total diet made up of milk (e.g. breast milk or infant formula). While dietary modelling is a scientific systematic method for estimating the amounts of chemicals a person or population may be eating, the accuracy of these dietary exposures depend on the quality of the data used in the dietary models. These issues are addressed in the 22nd ATDS [4].

To assess whether the dietary exposure of each particular chemical from food is of concern to public health and safety, dietary exposure estimates are compared to the respective relevant HBGV and a risk characterization conducted. The outcomes of the survey and the final report are published in a hardcopy booklet, and in recent years, the reports have also been published on the FSANZ website (http://www.foodstandards.gov.au/monitoringandsurveillance/australiantotaldiets1914.cfm).

The Flexibility of ATDS Samples

While the ATDS is a resource intensive study, the value of the national samples, collected for this study is several fold. Over recent years, FSANZ has made a number of changes to the procedures, aimed at further minimizing the burden of sample preparation and collection, and maximizing the extent to which the samples are used. For example, ATDS samples collected from the States and Territories are stored for a period of time by the laboratory following the completion of the analytical component of the survey. These samples can then be used for additional analysis and the estimation of national dietary exposure to other chemicals. An example where this has been successfully used is with the samples collected for the 22nd ATDS, where the analysis of selected foods for polybrominated diphenyl ethers (PBDEs) [7] and polycyclic aromatic hydrocarbons (PAHs) [8] was undertaken in a subsequent survey activity (See Chap. 51 – Polybrominated Diphenyl Ethers in Food in Australia—An Additional Use of the Australian Total Diet Study).

Usefulness of Data Collected from the ATDS

It is essential to have a robust national total diet study that can produce the best scientific evidence available to inform the standards development process and other regulatory decisions. The ATDS provides quantitative information on concentrations of chemicals of interest in the food supply and estimates 'actual' dietary exposure.

Although there are recognized limitations of the sampling and methods of total diet studies, the ATDS produces a variety of useful and relevant data, which are often utilized internally by FSANZ for other purposes, including establishing priorities for further investigation, to identify or confirm potential areas of concern and contributing to FSANZ composition databases (Fig. 20.2). This information is used broadly in the work of FSANZ, providing information to fill data gaps in knowledge.

International Relevance of Information Collected from the ATDS

The ATDS is undertaken in accordance with international best practice for conducting total diet studies with the findings contributing to the international evidence base where possible. The ATDS generates data which are shared internationally via the World Health Organization (WHO) Global Environmental Monitoring System for food (GEMS/Food), which collects, compiles, and
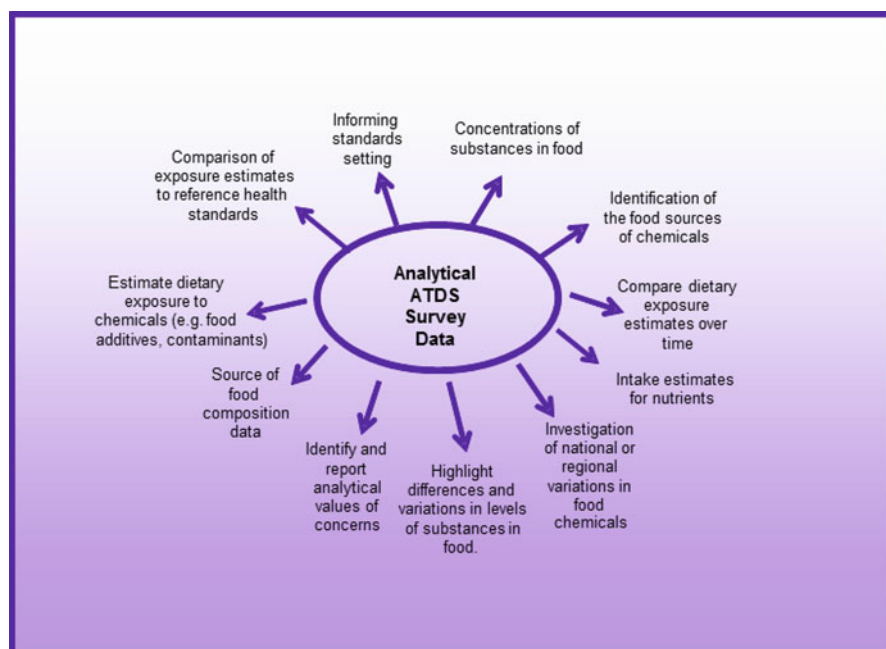
Fig. 20.2 Application of data collected for the Australian total diet study

disseminates food contamination data internationally, the Joint Food and Agriculture Organization (FAO)/WHO Expert Committee on Food Additives (JECFA), the Joint FAO/WHO Meetings on Pesticide Residues (JMPR), the relevant Codex Alimentarius Commission Committees, e.g. Codex Committees on Food Additives, Contaminants in Food and Pesticide Residues, and independent researchers in both government and non-government agencies.

Summary

Australia has considerable experience in conducting total diet studies, accumulated over a 40-year period. The ATDS is a unique study in Australia, being the only study to estimate the level of dietary exposure of the Australian population to a range of substances in food prepared as normally consumed over time. The study is a key element of the food regulatory system in Australia, and is an effective collaboration between food regulatory partners in State and Territory governments. The recent expansion of the scope of the ATDS to better inform potential developments in food regulation has proven successful in addressing key data gaps. Data collected as part of the ATDS are used in international food safety risk analysis and standards setting making regular and significant contributions to these processes.

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Chapter 21
Total Diet Study in Cameroon—A Sub-Saharan African Perspective

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Introduction

Little is known about the acute or chronic dietary exposure to toxic chemicals in sub-Saharan Africa. In these countries, except for some high-value exported products, few foods are regularly monitored for toxic chemicals, and no country has an operational monitoring program for chemicals in food. There is an obvious interest of the authorities to protect consumers faced with various food hazards. However, the means and mechanisms of implementation are not very efficient and do not always meet international requirements for exportation of foodstuffs. The following difficulties are often encountered: (i) inadequacy of the legislative authority which do not meet current international recommendations, (ii) absence of a disease alert

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and surveillance system, (iii) absence of a communication and promotion system, (iv) little or no application of good practices such as Good Manufacturing Practices and Good Agricultural Practices, (v) weak technical and analytical capabilities and capacities of laboratories, and (vi) absence of risk analysis-based approaches for food safety issues for the national population. All these difficulties contribute to ineffective coordination of food safety management actions. Moreover, rapid urbanization, industrialization and development in Africa have contributed to the emergence of man-made environmental hazards with harmful effects on the environment, food and health. These critical contributors to the continent's disease burden have to be addressed.

According to United Nations Environmental Programme (UNEP) and World Health Organization (WHO), the main sources in Africa of such persistent hazards are agriculture, artisanal or industrial mining, manufacturing, electricity and electronic production, certain imported products, vector-control purposes, stockpiles of obsolete pesticides, and uncontrolled combustion processes. These new and emerging environmental threats, including persistent organic pollutants (POPs), such as polychlorinated biphenyls (PCBs), dioxins and furans, as well as heavy metals, need to be better managed [1, 2].

Nweke et al. in 2009 [3] reviewed published data related to heavy metals (mercury and lead), pesticides, and industrial air pollutants, and pointed out the serious implication of these environmental health hazard releases for Africa's disease burden.

Large quantities of electrical devices and other electronic waste (e-waste) end up dumped in developing countries. According to Frazzoli et al. in 2010, [4] e-waste scenarios such as illicit dumping may impact on the environment and the food chain, thus eliciting a widespread and repeated exposure of the general population to mixtures of toxicants, mainly POPs, heavy metals, brominated flame retardants, and polycyclic aromatic hydrocarbons. The authors conducted a diagnostic risk assessment, which demonstrated how e-waste exposure poses an actual public health emergency for present and future generations to come.

Some sub-Saharan Africa countries, such as Senegal, Burkina Faso and Cameroon, have undertaken identification and quantification of their dioxins and furans releases. The results obtained showed the need to assess human exposure to these POPs and also to take necessary measures to reduce and eliminate these pollutants through a monitoring program. The level of dioxins, PCBs and hexachlorobenzene (HCB) was assessed in egg samples collected from free-ranging chickens in the neighborhood of the waste discharge, suspected as a potential source of POPs in Senegal. The results showed a dioxin content 11 times higher and PCB content 1.7 times higher than the European normal background values [5]. This raises the question of the level of exposure of people living in such an environment.

Several African countries have undertaken actions to eliminate and/or manage obsolete pesticides and POPs, according to recommendations of UNEP [6–8]. The major problems that arise include the identification of stockpiles, their safe storage and transport and their destruction in accordance with environmental and human health protection requirements.

Another potential source of human exposure to toxic chemicals is the use of DDT in malaria vector control, notably in Africa where use has doubled between 2000 and 2006. The Conference of the Parties to the Stockholm Convention on POPs continues to allow the use of this persistent organic pesticide. However, in areas where DDT and related pesticides have been used for disease vector control in Africa, high residue levels of these pesticides have been found in human milk. Considering the potential risks to infants through breastfeeding, the incorporation of such a risk assessment into the WHO Pesticide Evaluation Scheme has been suggested [9].

The WHO, through its Global Environmental Monitoring System/Food Contamination Monitoring and Assessment Programme (GEMS/Food), collects information on levels of POPs in foods, including human milk. According to their report, biomonitoring of human milk data can provide important information on the exposure of mothers through food as only traces of POPs appear in air and water [10]. Moreover, it has been reported in some African countries that mosquitoes have developed resistance to DDT. Considering the above reasons, it is important to develop alternatives to DDT that can effectively control vector disease [11].

In sub-Saharan Africa, pesticides are mostly used in plantations for export crops. Formal or informal agriculture has increased in urban and peri-urban areas with a growing use of chemical inputs, which could have harmful effects for human health and environment [12]. According to the agricultural experts, risks linked to the use of pesticides could be attributed to: (a) not following correct applications procedures, (b) off-label use of pesticides to treat food others than those registered for use for that product, (c) the use of pesticides for hunting or fishing, (d) the reuse of pesticide packages, (e) disregard for withholding periods prior to harvesting of crops, and (f) the circulation of fraudulent imitations of approved pesticides. They also argued that the half-lives of almost all approved pesticides are short, approximately 2 months; therefore, these compounds should not be easily found in food as consumed. Furthermore, the experts suggest that acute exposure to pesticides is most probably due to cases of dermal uptake and/or inhalation during application because of poor agricultural practices. It may also be due to accidental, intentional or criminal ingestion.

In a concrete way, studies on commonly consumed beverages were conducted in Nigeria to investigate their concentration of heavy metals. The results showed high concentrations (in mg/L) of copper (0.04–3.55), selenium (0.07–1.67), arsenic (0.002–0.261), total chromium (0.01–0.59), cadmium (0.003–0.081), and lead (0.001–0.092). The resulting mean and median concentration values of copper, selenium, cadmium, and lead, exceeded the Maximum Contaminant Level set by the United States Environmental Protection Agency (USEPA) [13–15]. This finding highlights the need to estimate the dietary exposure of the population and to implement a monitoring system to reduce and eliminate such contaminants in beverages.

Natural occurring food toxins are other threats to human health. An outbreak of Konzo Disease, which causes paralysis in both legs, has been attributed to dietary exposure from insufficiently processed cassava, containing high concentrations of cyanogenic compounds. Such outbreaks have been reported in some regions of

Cameroon and the Central African Republic [16]. The extent of chronic dietary exposure of the population has been raised and needs to be studied, especially in African regions where the dietary staple is cassava tubers.

In addition, concerning trade of food products originating from Africa, some of them have caused economic losses as a result of rejected food exports due to short-comings in food safety [17]. Groundnuts coming from Africa were frequently rejected at the European border due to their contamination with mycotoxins. The World Trade Organization (WTO) framework for international trade, under its Agreement on the Application of Sanitary and Phytosanitary Measures, now requires that health and food safety decisions be based on sound scientific risk assessments, including food products exported from African countries or from other regions of the world.

These few examples collected in various sub-Saharan Africa reveal that food may contain toxic substances, which have potential adverse health effects. Given these concerns, the African countries have to implement means and necessary mechanisms to assess these potential risks, manage such risks, and effectively communicate any risk; the main purpose being to prevent and reduce it, both nationally and internationally.

A total diet study (TDS) is a key risk assessment tool, enabling estimates of chronic dietary human exposure to chemicals in a most cost-effective way. The WHO recommends the implementation of a TDS in developing countries and encourages it via inter-country collaborations to ensure a safe food supply and a nutritionally adequate diet [18]. A TDS can also include the intake assessment of selected nutrients, especially micronutrients like iodine, iron, and zinc, which may be deficient in the diet and are known to cause numerous health disorders in African countries. The results thus obtained would provide pertinent information for various programs, notably in food fortification and supplementation.

Yaoundé-Cameroonian Experience on TDS

The Third International TDS Training Course and Workshop in Paris in 2004 targeted French-speaking participants from sub-Saharan Africa [19]. Following this training course, a TDS was initiated in 2006 by the Centre Pasteur du Cameroun in Yaoundé, Cameroon, with the support of the Food and Agriculture Organization of the United Nations (FAO) and the French Food Safety Agency (Agence Française de Sécurité Sanitaire des Aliments, AFSSA) [20]. The objective of the Cameroonian TDS was to assess the chronic dietary exposure of the inhabitants of Yaoundé to residues of the main pesticides used in the country. Yaoundé, the capital, is supplied with foods coming from all regions of the country and thus offers good sampling facilities representing the country's food supply. In addition, it is characterized by a heterogeneous population with a very high diversity in terms of food origin and habits.

Methods

Consumption Data

In Cameroon, as in some other sub-Saharan countries, data from household budget surveys are available. The Second Cameroonian Household Budget Survey [21] was used to derive the food consumption data needed for the TDS. Expenditures for 223 food products of households from Yaoundé (1,095 households) were extracted and transformed to 'foods as purchased' per adult equivalent (ae) using a price database and age and sex specific ae factors [22]. The amount of 'foods as consumed' expressed in g/day/ae was obtained by applying additionally edible and yield factors, which were obtained either from literature data or from measurements obtained during the study. In order to eliminate biases caused by an under- or over-reporting, only households for which the energy intake per ae was estimated as being within 1,200–3,500 kcal/day were included in the study population. When taking into account the sampling weights from the original database, 557 households remained in the analysis which corresponded to the 142,185 households of Yaoundé.

Food Selection

The foods for the TDS were selected if the food was consumed in amounts over 1 g/day/ae in the overall population or by 15 % of the household consuming this food; or if it was consumed only seasonally; or if it represented a high potential risk regarding pesticide contamination due to known local practices. For examples, fishing with pesticides or preservation of Kola nuts or dried fish with pesticides have been reported. Initially, a food list of 86 food products was selected, which were further clustered into 63 food items by grouping similar agricultural practices or processing methods in respect to pesticide usage.

Sample Collection and Preparation of Foods 'As Consumed'

A specific sampling plan for food was elaborated, which was refined after pretesting and peer review. For fresh and semi-processed foods, representativeness of food samples was ensured by considering the origin of production, the markets and the usual form for consumption. Seven wholesale or intermediate markets distributed all over Yaoundé, representing the city's major food outlets, were selected to obtain fresh, processed or frozen foods from all origins, including local, provincial and foreign sources. Peri-urban and urban farming products were purchased directly from producers in and around Yaoundé. Manufactured products and bakery products were purchased in the main supermarkets and bakeries of the city. A composite sample of tap drinking water from 12 districts distributed over the city was prepared. The same was done with drinking water collected from 12 underground sources. An individual food approach method was used to prepare food samples 'as

consumed' using local habits and recipes, but without added salt and spices. Due to budgetary constraints, some foods were combined into one composited sample. Stainless steel tools were mainly used, except for large aluminum cooking pots for leafy vegetables preparation. Vegetables and fruits were not systematically washed, as this is the observed norm in the vast majority of households where tap water is not available. Tap water was used for cooking. Samples were homogenized, and then stored at −20 °C in plastic containers for solid foods or in glass bottle for liquids, until their transport at low temperature to the laboratory for chemical analysis.

Purchased food samples were put together in several steps to obtain the final composite sample for analysis. They were grouped according to purchase site, market share and variety distribution before preparation. In most cases, another composite mixture was prepared based on the proportion of consumption of each preparation type. In the absence of information about market share or ratio of consumption data, equal portions of samples were combined within a composite sample.

Pesticides Selection

The pesticides for the TDS were selected if they were part of the GEMS/Food comprehensive list, including banned pesticides and other organochlorine compounds [23]; or on the list of approved and marketed pesticides in Cameroon in 2002, 2003 or 2004 (Ministère de l'Agriculture et du Développement Rural, MINADER); or on the list of approved pesticides of 2005 (MINADER); or if they have a low Acceptable Daily Intake (ADI). In all, 46 pesticides were selected for the TDS. Most of the selected pesticide residues were analyzed in all composite samples. Dithiocarbamates (DTC) (= mancozeb, maneb, ethylenethiourea, etc.) were analyzed only in vegetables and fruit consumed raw, such as tomatoes, cabbages, carrots, lettuces, cucumbers, aromatic herbs, bananas, mangoes, papaws, oranges, tangerines and pineapples. Glyphosate was analyzed only in the composite samples of rice, cassava tubers, cassava flour, and desiccated cassavas, unripe plantains, potatoes, cocoyam, yam, tomato, pineapple, and aromatic herbs. Chlordecone was analyzed in nine composite samples, i.e. tomato, carrot, cassava tubers, sweet potato, cocoyam, yam, taro tuber, and dried shelled groundnuts, all of which have been known to be potentially contaminated with this pesticide.

Chemical Analysis

The pesticides analyses were carried out by the French laboratory Qualtech accredited by the French Accreditation Committee (COFRAC) for the 99.2 'pesticides residues' program according to the standards NF EN ISO/CEI 17025. In-house methods were based on French and European standard (NF EN 12,393; NF EN 12,396–3). These operating conditions allowed a limit of detection (LOD) of 0.005 mg/kg and a limit of quantification (LOQ) of 0.010 mg/kg for the multiresidue

method; for glyphosate and its metabolite (AMPA), LOD and LOQ were 0.005 and 0.010 mg/kg, respectively; for dithiocarbamate residues, LOD and LOQ were 0.050 and 0.100 mg/kg, respectively; for chlordecone, the LOD was 0.0008 mg/kg and the LOQ was 0.0020 mg/kg. Samples were analyzed in duplicate.

Dietary Exposure Estimation

For the exposure assessment, it is necessary to assign a numerical value to contamination data that are less than the LOD (i.e. non-detectable) and to 'trace' contamination data between the LOD and the LOQ. Two estimates are provided according to international recommendations [24], the first resulting in a lower bound exposure and the second in the more conservative estimate of exposure. The lower bound estimate assigns for each sample a zero value if below the LOD and the LOD value if between LOD and LOQ. The upper bound estimate assigns each sample the LOD value if below the LOD and the LOQ value if between LOD and LOQ. Dietary exposures were calculated by multiplying the TDS food consumption data (including ready-to-eat foods and light meal consumption) obtained from the 557 adult-equivalents with the TDS food concentration data (including the estimated concentrations of ready-to-eat foods and light meals), leading to 557 data of exposure to the 46 tested residues. The mean and quantiles were calculated for each pesticide residue using the sampling weight of each household from the original database. The estimates were finally reported in µg/kg bw/day assuming a 60 kg body weight basis.

Results

Food Consumption

The amount of foods 'as consumed' without drinks is estimated on average to be 863 g/day/ae. Cooked rice is by far the most consumed food with 201 g/day/ae, followed by boiled fresh cassava tubers (73 g/day/ae), boiled unripe plantain (47 g/day/ae), bread (47 g/day/ae) and others foods.

Pesticide Residue Data

Of the 46 pesticides analyzed, only nine pesticides were detected, namely atrazine, chlorothalonil, cypermethrin, deltamethrin, endosulfan, malathion, pirimiphos-methyl, DTC and chlordecone. These pesticides were detected in nine

Table 21.1 Estimated exposure to pesticide residues of the Yaoundé population based on the 2006 Cameroon total diet study (lower and upper bound estimates in µg/kg bw/day)

Pesticides residues	Mean	95th percentiles	Acceptable daily intake
Atrazine	0.001–0.098	0.002–0.163	35[a]
Chlorothalonil	0.001–0.098	0.004–0.165	15[b]
Cypermethrin	0.027–0.121	0.074–0.211	50[c]
Deltamethrin	0.006–0.103	0.018–0.170	10[c]
Endosulfan	0.011–0.105	0.031–0.174	6[c]
Malathion	0.008–0.169	0.228–0.346	30[d]
Pirimiphos methyl	0.031–0.121	0.086–0.206	4[e]
Chlordecone[f]	0.002–0.005	0.006–0.012	0.5[g]
Other residues[h]	0.000–0.097	0.000–0.163	–
Dithiocarbamates[f] (DTC)	0.298–0.342	0.941–0.973	50[b]

[a] US Environmental Protection Agency, 2007

[b] Agence Française de Sécurité Sanitaire des Aliments, 2006

[c] International Programme on Chemical Safety (IPCS) (2007)

[d] European Food Safety Agency, 2006

[e] European Food Safety Agency, 2005

[f] Analyses performed on selected composite samples

[g] Agence Française de Sécurité Sanitaire des Aliments, 2003

[h] Aldrin, azoxyistrobine, bitertanol, cadusafos, carbofuran, chlorpyrifos ethyl, chlorpyrifos methyl, cyproconazole, DDT complex, diazinon, dieldrin, dimethoate, ethoprophos, fenamiphos, fipronil, HCH, heptachlor, heptachlor epoxide, hexachlorobenzene HCB, lambda-cyhalothrin, metalaxyl, methyl-parathion, monocrotophos, parathion, pendimethalin, permethrin, profenofos, propiconazole, pyrimethanil, spiroxamine, tebuconazole, terbufos, triadimefon, tridemorph, trifloxystrobine

of the 63 composite samples. These were the raw or cooked aromatic herbs, a composite of basil, parsley and celery (atrazine 0.02 mg/kg and DTC 8.66 mg/kg), boiled Ndole/Keleng Keleng which are local leaves (chlorothalonil 0.02 mg/kg and endosulfan<LOQ), raw and cooked fresh tomatoes (cypermethrin 0.05 mg/kg, endosulfan 0.02 mg/kg and Chlordecone 0.004 mg/kg), bread (deltamethrin<LOQ, malathion 0.05 mg/kg and pirimiphos-methyl 0.02 mg/kg), wheat doughnut (malathion 0.04 mg/kg and pirimiphos-methyl 0.02 mg/kg), cakes and pastries (malathion 0.05 mg/kg and pirimiphos-methyl<LOQ), boiled wheat pasta (pirimiphos-methyl<LOQ), pineapple (DTC<LOQ), papaya (DTC 0.14 mg/kg). No tested pesticide residue was detectable in drinking water.

Dietary Exposure Assessment

Multiplying the TDS food consumption with the TDS food concentration data provides the estimates of the dietary exposure to pesticide residues in the population of Yaoundé. The results are shown in Table 21.1.

Risk Characterization

The highest dietary exposure estimate was 0.941–0.973 μg/kg bw/day at the 95th percentile of exposure to DTC, which is well below the ADI of 30 μg/kg bw/day, [25] equivalent to 3.24 % of the ADI. For the pesticides for which at least one analysis was > LOD, the mean exposures using the 'upper bound estimate represent from 0.24 % (cypermethrin) to 3.03 % (pirimiphos methyl) of their respective ADIs. Using the 95th percentile ('upper bound' estimates), these relative proportions reached 0.42 and 5.1 % of their ADIs, respectively.

Discussion

While the study conclusions are limited to the population of Yaoundé, this city is a melting pot of the numerous ethnic groups of the country and is supplied with food sourced from the whole country. It can, therefore, be regarded as an indicator of the likely mean level of pesticide residue exposure of Cameroon in general. For this TDS, there was no valid individual food consumption survey available. Therefore, a household budget survey database with expenditure data was used to estimate individual food consumption, after several assumptions and transformations. However, because of the very low level of contamination observed, these approximations have little significance on the final conclusions of the study.

Pesticide residues were generally undetectable with the analytical methods used in this study. Only 9 samples out of 63 showed a result greater than the LOD for at least one pesticide residue. Among these nine composite foods, four were wheat-based (bread, wheat doughnuts, cakes and pastries, and pasta) and gave quantified levels of pirimiphos methyl or malathion. Wheat is not cultivated in Cameroon, and thus the contamination occurred probably abroad (agricultural crops or post-harvest grain treatment) or during storage after importation. The five other foods for which at least one result was greater than LOD (i.e. Ndole/Keleng Keleng, fresh tomatoes, papayas, pineapples, and aromatics herbs) were produced locally, notably in urban and peri-urban areas.

In the present TDS, no systematic bias was observed that could explain the low levels of pesticide residues (e.g. the destruction of pesticides residues due to an improper preservation before analysis). The rare residue levels found in the present study could also be explained by the overall low pesticide use in agriculture in Cameroon, in particular because of the lack of awareness and/or probably high price of these substances according to users. The observed low level of contamination levels resulted in an estimated exposure far below most ADIs, even for the highly consumed foods and using the most conservative 'upper bound' residue assumption. In conclusion, the chronic dietary exposure to the various pesticides evaluated within the framework of this TDS is low for the inhabitants of Yaoundé. These results are reassuring and seem to be in concordance with the opinions of the experts of the agricultural sector in Cameroon.

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Chapter 22
Canadian Total Diet Study Experiences

**Robert W. Dabeka, Dorothea F.K. Rawn, Xu-Liang Cao,
and John Moisey**

Introduction

Health Canada is responsible for ensuring that the risks associated with human exposure to toxic chemicals, such as lead, mercury, arsenic, cadmium, polychlorinated biphenyls (PCBs), polychlorinated dibenzodioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs) (PCDDs and PCDFs are commonly referred to as "dioxins") and pesticides, are minimal and that intakes of nutrients are adequate but not so high as to pose a risk to health. Assessing dietary exposure to chemicals is the responsibility of the Food Directorate, and the Canadian Total Diet Study (TDS) is an ongoing research program started 1969 [1] designed to address this responsibility. The most recent Canadian TDS phase began in 2006 and is currently in progress.

Methods

Sampling and Composite Preparation

In the Canadian TDS, food composites (159 in 2009) are prepared once a year from foods purchased in various cities. Samples are taken in each city over a 5-week period. The cities (see Fig. 22.1) are selected to represent the largest population centers as well as to address potential dietary differences associated with geographical location within the country. The foods and food composites are selected

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Fig. 22.1 Cities selected for TDS sampling between 1999 and 2006

according to the amounts consumed by average Canadians, based on 24-h recall food consumption studies. Some of the composites, such as meat organs, are also selected for their potential to concentrate specific groups of toxicants. The 159 composites prepared represent over 90 % of the Canadian diet.

Each of the individual foods going into a composite is purchased at the retail level from four different stores by the Canadian Food Inspection Agency, and shipped to the Department of Food Science, Kemptville Campus, University of Guelph, where they are immediately processed as for consumption in the "average household kitchen" using standard recipes. The processed foods are combined into 157 food composites, homogenized, bottled, and stored frozen at −20 °C until distribution for analysis. For example, raw carrots, purchased in four supermarkets, are combined, then half are cooked and half are shredded raw. These are the common ways carrots are consumed in Canada. Both the raw and cooked halves are combined, homogenized together, and bottled to form one composite. Recently the storage temperature for TDS composites was lowered to −35 °C. However, only small amounts of the composites are archived.

Two additional composites consist of tap water from the city being sampled and tap water from the preparation kitchen in Kemptville Community College. Water from the target city and Kemptville is also sampled independently by the Healthy Environments and Consumer Safety Branch of Health Canada, specially preserved and analyzed for disinfection by-products.

Each year, an evaluation is made on whether new foods need to be added to the list of food composites to better reflect the eating habits of the population. The list of composites for 2009 is presented in Table 22.1.

Table 22.1 List of 2009 total diet study food composites

Food category and composites			
Dairy products	*Soups*	*Vegetables*	*Miscellaneous*
Milk, whole	Soups, meat, canned	Baked beans, canned	Condiments
Milk, 2 %	Soups, creamed, canned	Beans, string	Salt
Milk, 1 %	Soups, broth, canned	Beets	Baking powder
Milk, skim	Soups, dehydrated	Broccoli	Yeast
Evaporated milk, canned		Cabbage	Vanilla extract
Cream	*Cereal and bakery*	Carrots	Herbs and spices
Ice cream	Bread, white	Cauliflowers	Soya sauce
Yogurt	Bread, whole wheat	Celery	Tap water, kitchen
Cheese	Bread, rye	Corn	Tap water, sample area
Cheese, cottage	Cake	Cucumbers	Water, natural spring
Cheese, processed	Cereal, cooked wheat	Lettuce	Water, natural mineral
Butter	Cereal, corn	Mushrooms	
Chocolate milk, 1 %	Cereals, oatmeal	Onions	*Baby foods*
Butter milk, 1 %	Cereals, rice and bran	Peas	Cereals, mixed
	Cookies	Peppers	Desserts
Fruit and juices	Crackers	Potatoes, peeled and boiled	Dinners, cereal + vegetable + meat
Apple juice, canned	Danish, donuts and croissants		
Applesauce, canned		Potatoes chips	Dinners, meat or poultry + vegetable
Apples, raw	Flour, white (wheat)	Rutabagas	
Bananas	Muffins	Vegetable juice, canned	Formulae, milk base
Blueberries	Pancakes and waffles	Tomatoes	Formulae, soya base
Cherries	Pasta, mixed dishes	Tomatoes and tomato sauce, canned	Fruit, apple or peach
Citrus fruit, raw	Pasta, plain		Meat, poultry or eggs
Citrus juice, frozen	Pie, apple	Spinach	Vegetables, peas
Citrus juice, canned	Pie, other	Asparagus	
Grape juice, bottled	Rice	Brussels sprouts	*Meat and poultry*
Grapes	Buns and rolls	Potatoes, baked with skins	Beef, steak
Melons	Breads, other		Beef, roast
Peaches		Corn chips	Beef, ground
Pears	*Snacks, sweets*		Pork, fresh

(continued)

Table 22.1 (continued)

Food category and composites			
Pineapple, canned	Chocolate bars	*Fast foods*	Pork, cured
Plums and prunes	Candy	Popcorn, microwave	Veal, cutlets
Raisins	Gelatin dessert	Frozen entrees	Lamb
Raspberries	Honey, bottled	Pizza	Luncheon meats, cold cuts
Strawberries	Jams	French fries	Luncheon meats, canned
Kiwi fruit	Peanut butter	Hamburger	Organ meats
Apricot	Puddings	Chicken burger	Wieners and sausages
Fruit drinks (cocktails)	Sugar, white	Hot dogs	Eggs
	Syrup	Chicken nuggets	Poultry, chicken and turkey
Beverages	Seeds, shelled	Beef chow mein, carry-out	Poultry, liver pate
Alcoholic drinks, beer	Nuts		
Alcoholic drinks, wine	Chewing gum	Fried rice (chicken)	*Fats and oils*
Coffee		Prepared breakfast sandwiches	Cooking fats and salad oils
Soft drinks, canned	*Fish and shellfish*		Margarine
Tea	Fish, marine	Fast food sandwiches	Mayonnaise
Soy beverage, fortified	Fish, fresh water		
	Fish, canned		
	Shellfish		

Analysis of Food Samples

Food composite samples are analyzed in the laboratories of Food Research Division and Health Canada Regional Laboratories, although for specific areas of expertise, analyses are also conducted in the laboratories of the Healthy Environments and Consumer Safety Branch of Health Canada. On a regular basis, the chemical groups measured include pesticides [2]; PCBs, PCDDs and PCDFs [3], polybrominated diphenyl ethers mostly used as flame retardants [4], toxic trace elements [5], radionuclides [6], and disinfection by-products (in drinking water). Recently, ochratoxin A was added to the list of chemicals being analyzed.

The methods of analyses selected are those that give the lowest limits of detection, so that background concentrations of the chemicals in the foods can be measured. These are research methods in nature, requiring elaborate contamination control and separation and pre-concentration steps, a high degree of expertise, and sophisticated instrumentation, such as high-resolution mass spectrometry. Thus, these methods differ substantially from normal surveillance methods, which are usually focused on regulatory levels.

Dietary Exposure Calculations

The dietary exposure to each chemical by average Canadians of various age and sex groups is estimated by multiplying the concentration of the chemical in each composite by the average amount of composite consumed by individuals in the group. The exposures to the chemical are then summed for all food composites to give the total exposure to the chemical by each specific age-sex group. The dietary exposure for each chemical is expressed in µg/day or µg/kg body weight/day. The food consumption data used for calculating dietary exposure are based on 24-h recall information from the Nutrition Canada Survey of 12,796 individuals in the national Nutrition Canada Survey [7]. Currently, food consumption data from the Canadian Health Measures Survey conducted by Health Canada and Statistics Canada in 2005 [8] are being developed as the basis for dietary exposure estimations. The dietary exposures calculated for the Canadian TDS include the contribution of water used to process the composites, but does not include water consumed directly as drinking water.

Results

TDS results, as they become available, are posted on the Health Canada website [9]. A list of publications on TDS results is also available at the same site. The design of the Canadian TDS has enabled collecting data on background concentrations of the chemicals in the most widely consumed foods, identifying potential contamination of public health significance; following trends in concentrations and dietary exposures with time, and making a direct comparison about the safety of the diet for different age/sex groups. Some examples of these are given below.

Direct Measure of the Safety of the Diet for Different Age/Sex Groups

Estimated dietary exposure is a direct measure of the safety of the average diet. The results obtained can be compared directly with internationally recognized safety reference values, such as those of the World Health Organization (WHO) to directly provide an assessment of whether exposures of toxicants exceed maximum safety levels, and whether intakes of nutrients are sufficient to confer benefits without exceeding safety thresholds. For example, the dietary exposures to all tested pesticides (approximately 70) were well below their respective acceptable daily intakes (ADIs). Some of these results are presented in Table 22.2.

Table 22.2 Estimated dietary exposures (µg/kg body weight/day) of selected pesticides in 2005 and comparison with WHO ADIs

Compound	Age/sex group					
	5–12 years M/F	12–19 years, M	12–19 years, F	40–64 years, M	40–64 years, F	WHO ADI
Captan	0.040	0.016	0.013	0.011	0.015	100
Chlorpropham	1.60	1.40	1.00	0.46	0.33	30
Iprodione	0.26	0.12	0.13	0.22	0.12	60
Malathion	0.015	0.008	0.008	0.005	0.004	300
Phosmet	0.015	0.005	0.006	0.005	0.005	10
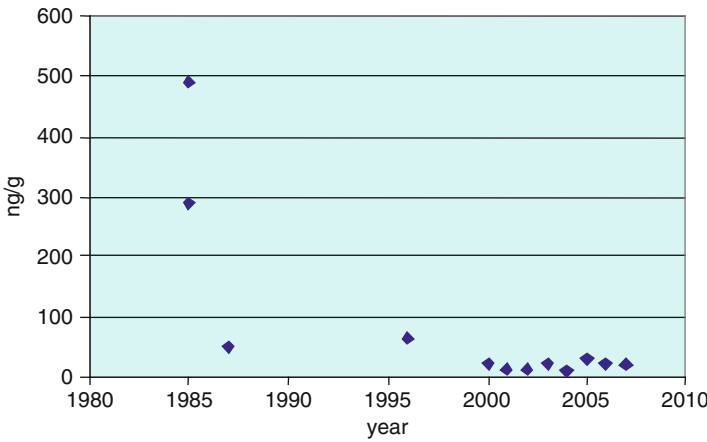
Fig. 22.2 Lead concentrations in total diet study raisin composites

Identification of Contaminated Foods

The relatively large number of food composites in the Canadian TDS facilitates the identification of adventitiously contaminated foods. In the Spring and Fall of 1985, high levels of lead were discovered in the raisin pie TDS composites from Ottawa, and follow-up targeted analyses found that some imported raisins containing up to 4 mg/kg lead were being sold [10]. The source of the lead was traced to lead contamination of the copper fungicide applied to grapes. Figure 22.2 demonstrates how stopping importation of the contaminated raisins and permanently removing the lead source impacted on the reduction of lead concentrations in TDS raisin composites.

Fig. 22.3 Dietary intakes
(µg/kg body weight/day) of
lead and cadmium by average
Canadians over time
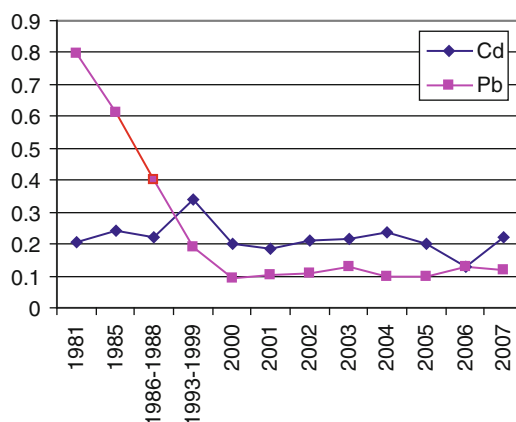
Monitoring Trends with Time and the Impact of Risk Management Strategies

For many years, it was recognized that a major source of dietary lead was the use of lead-soldered cans for storing foods. Beginning in 1975, Health Canada began pressuring industry to convert from lead-soldered cans to lead-free ones, and all Canadian manufacturers completed this process around 1982. In addition, the use of lead additives in automotive gasoline was gradually phased out beginning in 1975, and since 1990, the use of leaded gasoline in motor vehicles has been prohibited in Canada, under the Canadian Environmental Protection Act. Figure 22.3 illustrates with real data how these risk management strategies resulted in a dramatic decrease in dietary exposure to lead between 1981 and 2007.

Cadmium concentrations in foods are considered to be at or near background levels, and, as would be expected, dietary exposure of cadmium has remained relatively constant over this same time period.

Prioritization

With over 23,000 chemicals on the Domestic Substances List of the Canadian Environmental Protection Act, [11] it is important to prioritize the investigation of chemicals in foods. The Canadian TDS provides the information to allow researchers to focus resources on those food groups contributing most to the dietary intake of individual chemicals. For example, Table 22.3 gives the percent contribution of different food groups to the total dietary intake of mercury and dioxin TEQs (WHO Toxic Equivalents) [12] by 1–4 year-old children. Fish contributed 40 % of the dietary mercury intake [13], demonstrating that surveillance resources for mercury

Table 22.3 Percent contribution of food groups to total mercury and dioxin TEQ dietary exposures by 1–4-year-olds

Food category	Mercury (%)	Dioxin TEQ (%)
Milk, dairy products	22	62
Meat products	8	17
Poultry products	8	13
Fish	40	1.1
Soups	1.7	1.5
Fats and oils	0.3	2.2

should be targeted toward fish. The major dietary sources of dioxins and dioxin-like PCBs are milk, dairy, meat and poultry products, together contributing to 92 % of total intake in 2005. Fish, on the other hand, contributed only 1.1 % of the TEQ exposure. As a result, some of the concerns that farmed fish contain higher levels of dioxins than wild fish [14] are of little consequence because fish consumption has little impact on dietary TEQ intake of dioxins. Thus, targeted surveys for dioxins should be focused on meat, poultry and dairy products.

Identification of Compliance Monitoring Issues

Pesticides are the only group of chemicals with specific regulatory levels for a large number of foods because they are intentionally added. The Canadian TDS, with a large number of food composites, facilitates the identification of foods with specific pesticides nearing or exceeding their maximum residue limits (MRLs), and perhaps requiring more intensive targeted monitoring. In the period between 1993 and 1998, captan was the only pesticide that exceeded the MRL in strawberries (see Table 22.4). While the maximum level of 6,928 ng/g does not exceed the MRL of 5,000 ng/g by much, it is important to recognize that in general, TDS composites represent an average of foods from four different sources (stores), and that one of the four different sources may have been very contaminated while the other three may have been moderately low. Alternately, all four sources may have had approximately the same captan concentration. These high levels were observed despite the fact that strawberries in the TDS composite were washed prior to compositing. The MRL is applicable to the unwashed strawberries sold as the raw agricultural commodity, not as processed fruit. It is expected that captan in the TDS strawberries would have been even higher prior to washing [15].

Investigation of New Chemicals

Occasionally, analytical methods are developed for new chemicals, and archived TDS food composites can be used to find if the specific chemicals are or were present in the foods. For example, perfluorinated organics, such as perfluorooctanyl

Table 22.4 High levels of pesticide residues in some food composites from total diet studies in various cities during 1993–1999

City	Pesticide	Food	MRL (ng/g)	Concentration (ng/g)	% of MRL
Halifax	Dichloran	Potatoes, raw	5,000	3,422	68.4
Winnipeg	Dichloran	Peaches	15,000	2,558	17.1
	Dicofol	Strawberries	3,000	891	29.7
Vancouver	Captan	Blueberries	5,000	505	10.1
		Raspberries	5,000	4,720	94.5
Whitehorse	Captan	Blueberries	5,000	803	16.1
		Raspberries	5	2,890	57.9
		Strawberries	5	6,930	138.6
	Iprodione	Strawberries	5	1,990	39.8
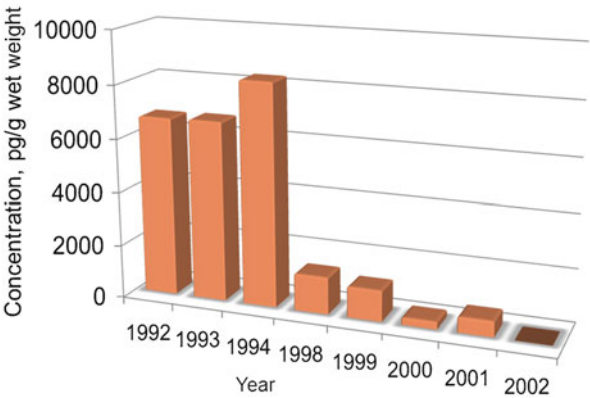
Fig. 22.4 Levels of *N*-EtPFOSA in archived French fry composites

sulfonate (PFOS) precursors, were used to protect cardboard food packages from fat and moisture, but their production was phased out in 2002. By analyzing archived TDS French fry composites, it was possible to demonstrate the sharp reduction of *N*-ethylperfluorooctanesulfonamide (*N*-EtPFOSA) levels with time (Fig. 22.4), [16] demonstrating the effectiveness of the abatement measures.

Also, the TDS can sometimes point to new areas of investigation, as when, for the first time ever, bisphenol A (BPA) was measured in TDS composites [17]. Compared to other food composites, higher levels of BPA were found in canned foods, as would be expected from its use in the production of epoxy resin can liners. Unexpectedly, results also revealed BPA present in uncanned foods, such as yeast (8.52 ng/g), baking powder (0.64 ng/g), hamburger (10.9 ng/g) and other fast foods (1.1–2.32 ng/g), and further investigations are needed to trace the sources of BPA in these samples.

Conclusions

The TDS continues to be a critical core component of food safety policy formulation in Canada, providing information on background concentrations of priority chemicals in the food supply and dietary exposures to chemicals that can be directly compared with WHO health-based reference values. It identified major sources of chemicals, thus facilitating the prioritization for more targeted surveillance, and it has revealed unexpected instances of food contamination having international impact. Finally, it has provided a direct measure of the impact of food safety as well as environmental risk mitigation policies introduced by Health Canada and Environment Canada.

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Chapter 23
The Chinese Experience in Total Diet Studies

Junshi Chen

Introduction

Since 1990, five nationwide total diet studies (TDSs) have been conducted in China. The general objective of conducting a TDS in China is to monitor the overall safety and nutritional quality of representative Chinese diets, with the following specific objectives: to estimate the dietary intakes of chemical contaminants by the Chinese population; monitor the trends of chemical contamination of Chinese diets; and, provide scientific data for specific food safety risk assessment projects and the development of food safety regulations and standards.

The Institute of Nutrition and Food Safety, Chinese Center for Disease Control and Prevention conducted all the TDSs with the administrative support from the Ministry of Health, People's Republic of China. Beginning as a research program, the Chinese TDS is now a key part of the regular national food contamination monitoring network, which provides important data for making risk management decisions in food safety in China as well as useful data for international risk assessment bodies, such as the Joint FAO/WHO Expert Committee on Food Additives (JECFA). On the technical side, the food sampling scheme is moving from the composite food group approach toward the individual food approach and the number of analytes is increasing from basic contaminants to include emerging contaminants.

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Methodology Development

The Chinese TDS covers 12 provinces, which represent various geographical regions (see Fig. 23.1) and dietary patterns in China. Covering about 50 % of the total Chinese population, the 12 provinces are divided into four TDS regions (market baskets) based on their geographical locations, namely, North 1, North 2, South 1, and South 2.

The working scheme of the Chinese TDS is shown in Fig. 23.2. In conducting the food consumption survey, three survey sites (two rural sites and one urban site) were selected and 30 households with middle level economic status were randomly selected in each site. In total, 1,080 households with approximately 4,300 subjects (> 2 years old) were selected from the 144 survey sites in 12 provinces. Drinking water was included in the food consumption survey and in the TDS food sample collection.

The food consumption data collected from the 3-day household survey (including weighing and recording) and three nonconsecutive 24-h recall surveys of individuals were grouped into 13 food categories (see Table 23.1). Foods samples (approximately 620 individual foods) collected from survey sites were combined, prepared and cooked based on local representative recipes. Cooking oils and
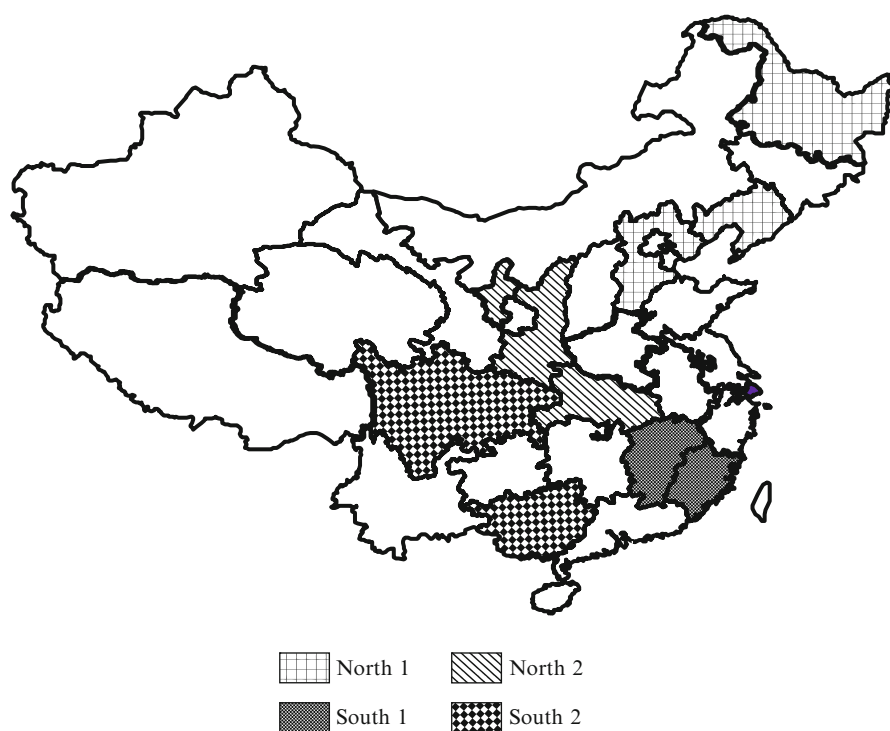
Fig. 23.1 Regions of the total diet study in China
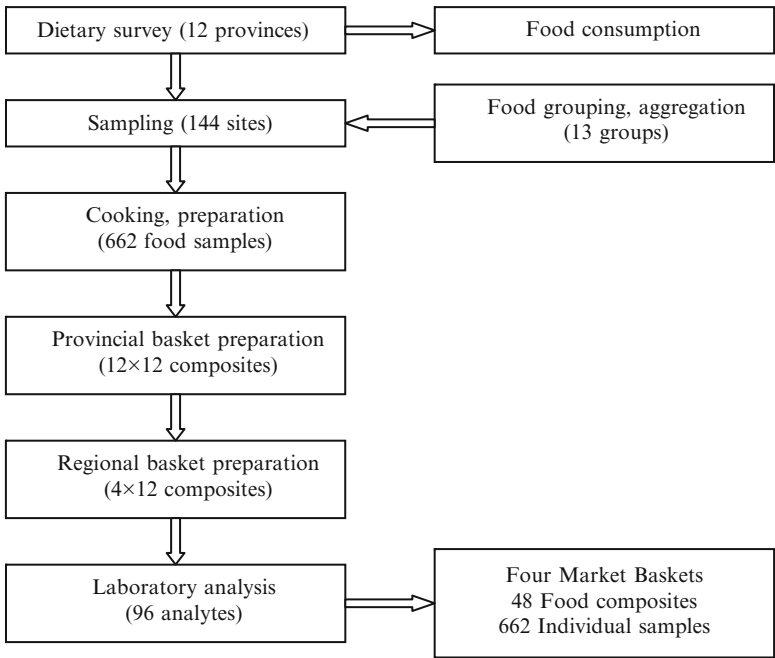
Fig. 23.2 Working scheme of the 2000 Chinese total diet study

Table 23.1 Food group composites
in Chinese total diet study

Cereals and products
Legumes, nuts, and products
Meats and products
Eggs and products
Aquatic foods and products
Milk and products
Vegetables and products
Fruits and products
Sugar
Beverages and water
Alcohol beverages
Condiments
Cooking oils

condiments (salt, soy sauce, etc.) were added into individual foods during preparation and cooking.

In the first Chinese TDS (1990), only the composite food group approach was used. Therefore, 12 composite food samples were made for each province ($12 \times 12 = 144$ provincial composites), which were further integrated into four regional market baskets ($4 \times 12 = 48$ regional composites). In this case, only the dietary exposure of analytes for one age-sex group (i.e. average Chinese adult male) could be obtained.

In the second Chinese TDS (1992), food consumption data was made available for four additional age and sex groups (i.e. 2–7 year old, 8–12 year old, 20–50 year old male, and 20–50 year old female), in addition to the average Chinese adult male group. Correspondingly, the number of food composite sample increased from 48 to 120, which greatly increased the laboratory workload as well as the data obtained.

Since the third TDS in 2000, an integrated composite and individual food sample approach was used. In this new approach, the use of 12 composites per province and per region was retained for trend analysis and new analytes were added, which required sophisticated analytical methods. At the same time, those 620 individual food samples feeding into the composite were kept stored separately in case analyte concentration data for individual food samples were needed, such as for tracing the source of high contamination, and distribution studies on dietary exposure for probabilistic assessment. In the third TDS, food consumption data was made available for ten age-sex groups, in addition to the average male adult group. This combined composite food group and individual food sample approach has both the advantages of the composite food group sample approach (fewer number of samples and less laboratory resources) and the individual food sample approach (more age-sex groups and ability to track the source of contamination and to study the distribution of dietary exposure at individual level). This approach could be seen as a transition from the composite food group sample approach to the individual food sample approach.

Analytes

The analytes included in the Chinese TDS are based on the GEMS/Food Core List. Radionuclides (e.g. ^{210}Pb, ^{210}Po, ^{226}Ra, ^{228}Ra, ^{90}Sr, ^{137}Cs) were analyzed only in the first two TDSs as basic information on these chemicals was not available. Analytes of emerging contaminants (e.g. dioxins, chloropropanols, acrylamide, organic tin, etc.) were added to the list in the latest TDS (see Chap. 49 – Emerging Chemical Contaminants in Total Diet Studies in China). Certain nutrients (e.g. lipids, minerals, and vitamins) were included in some TDSs (see Chap. 48 – Linking Nutrition Surveys with Total Diet Studies). Table 23.2 presents a list of major analytes in the Chinese TDSs.

Table 23.2 Analytes in the Chinese total diet study

Heavy metals and harmful elements		Lead, cadmium, mercury, arsenic
Pesticides	Organochlorine pesticides	HCH, DDT
	Organophosphorus pesticides	Methamidophos, dichlorvos, parathion, parathion-methyl, trichlorfon, dimethoate, acephate, disulfoton, fenitrothion, malathion, fenthion, phosmet
Dioxins and PCBs, chloropropanols, acrylamides, organic tin		
Aflatoxins		B1, B2, G1, G2, and M1
Minerals and trace elements		Potassium, sodium, calcium, magnesium, phosphorus, iron, zinc, copper, manganese, selenium
Lipids		Fat, cholesterol, fatty acids

Examples of Results from the Chinese TDS

Organophosphorus Pesticides

In the 1990 TDS, five of the 12 organophosphorus pesticides included in the study were detected in the fruit and vegetable composite samples. Among the four regions, only the vegetable samples in the North 1 region were negative for organophosphorus pesticides, although dietary exposures in the other regions were quite low. The finding of concern is the occurrence of methamidophos, which is a highly toxic pesticide and not permitted for use in edible crops. Further analysis showed that methamidophos accounted for 71 % of the total organophosphorus pesticide exposure by an average Chinese adult man, although it only accounted for a small percentage of the ADI. Based on these findings, intensive regulatory control measures for pesticide use, in particular organophosphorus pesticides, was implemented. As a result, in respect to all the organophosphorus pesticides analyzed in the year 2000 Chinese TDS, vegetable and fruit composite samples were below the detection limit.

Organochlorine Pesticides

Before organochlorine pesticides were banned in China in 1985, DDT and hexachlorocyclohexane (HCH) were the major pesticides used in agriculture. Considering the persistence of these pesticides in the environment, DDT and HCH are regular analytes in the Chinese TDS. When compared with the 1970 national survey (not a TDS), the dietary exposures of DDT and HCH per Chinese adult male in the TDS has been significantly reduced (see Fig. 23.3), although the exposures being still much higher than in Australia, Japan, and USA, which had banned the use of pesticides much earlier [1]. These results indicated that DDT and HCH should be included in the nationwide food contamination program, although it may not be necessary to study them in every TDS, since the degradation of DDT and HCH in the environment is rather slow.

Lead

Lead became a regular analyte in the Chinese TDS after several studies showed that a considerable proportion of Chinese children had high blood lead levels. In the 1990 and 1992 TDSs, the average lead exposure in preschool children exceeded the JECFA Provisional Tolerable Weekly Intake (PTWI) (see Fig. 23.4). When compared to developed countries, the dietary exposures of lead were much higher in China [2]. These results have resulted in a systematic review of the maximum limits for lead in various food categories.
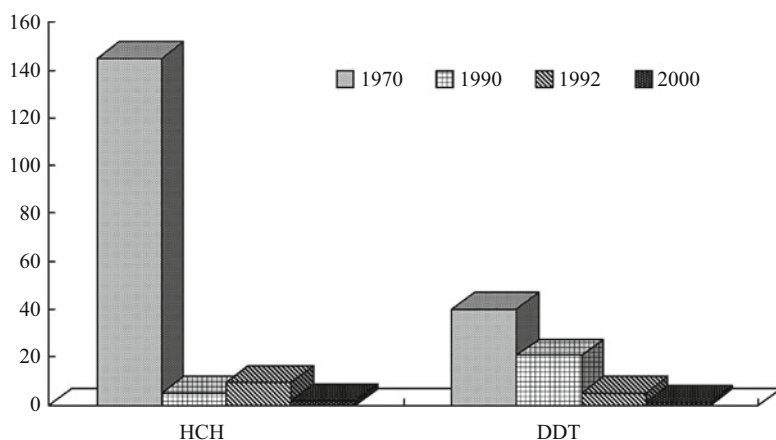
Fig. 23.3 Dietary exposures of organochlorine pesticides by average adult Chinese males (mg/person/day) from various total diet studies
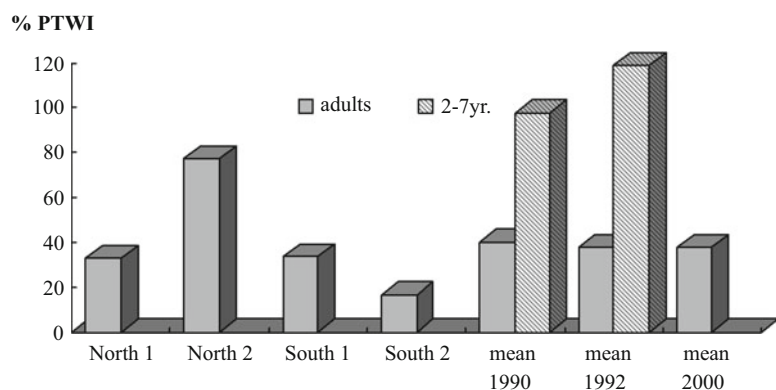
Fig. 23.4 Dietary exposure of lead by Chinese adults and children in the total diet study

Tracing the Source of Contamination in Exceptional Findings in TDSs

The current methodology of TDS can be effectively used to identify the source of contamination when a high level of a chemical was found in a food composite sample. In one example, a high level of cadmium (Cd) contamination of 149 μg/kg was found in the aquatic foods composite from the North 1 region. Based on the scheme in Fig. 23.5, Cd was further analyzed in the aquatic food group composite from the three individual provinces, and the results showed that the aquatic food sample from
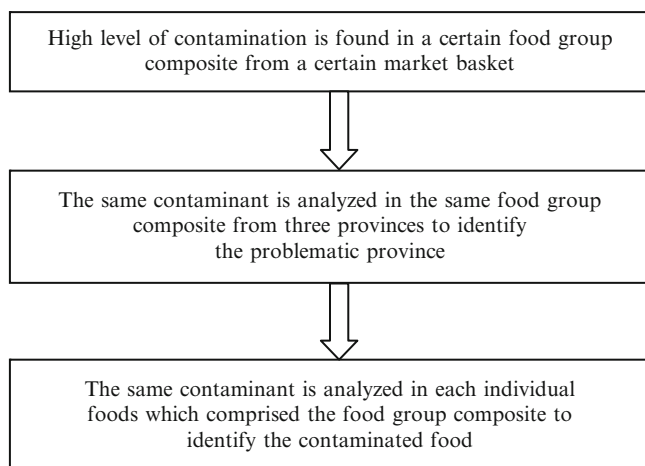
Fig. 23.5 Procedures for identifying source of high contamination in food composite

Liaoning Province had the highest Cd concentration (594.3 µg/kg) as compared with those from Heilongjiang (29.7 µg/kg) and Hebei (259.7 µg/kg). Cadmium was then analyzed in the seven individual aquatic foods which comprised of the Liaoning aquatic food group composite and results clearly showed that sea crab (Cd 1,498 µg/kg) was the source of the high Cd contamination.

In another example, high concentrations of HCH were found in the aquatic food group composite from North 1 and South 2 regions (25.1 and 79.2 µg/kg, respectively). Further analysis found that gamma-HCH (lindane) was the major isomer and alpha and beta-HCH were present in very low concentrations. Since only technical grade HCH, which consists of all three isomers, was used in China before the ban of organochlorine pesticides, the lindane finding indicated an illegal use of the pesticide rather than persistent residues from previous use of technical HCH. Subsequently, the aquatic food group composites from Heilongjiang Province (300 µg/kg gamma-HCH) and Hubei Province (200 µg/kg gamma-HCH) were identified as the source of contamination from North 1 region and South 2 region, respectively. When gamma-HCH was analyzed in three individual aquatic foods (river fish, sea fish, and river shrimp) that comprised the composites, the results clearly showed that river fish was the source of the high gamma-HCH contamination (Heilongjiang 302.3 µg/kg and Hubei 546.4 µg/kg).

Summary

The first TDS in China was started in 1990 and covered four geographical regions comprised of the 12 most populous provinces. TDSs have become an important part of the national food contamination monitoring network. The methodology of

Chinese TDS is a combination of the composite food group sample approach (48 regional composites) and the individual food sample approach (approximately 620 foods). Current results showed that this methodology currently suits the Chinese situation but the practice is gradually moving toward the individual food sample approach. The results of Chinese TDSs have provided valuable data for food contamination trend analysis, identified sources of high-level contamination, and assisted in food safety risk assessment and risk management, including regulatory decision-making.

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Chapter 24
The First Total Diet Study in Hong Kong, China

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Introduction

Hong Kong is a special administrative region of China with a total area of about 1,000 km^2, and home to about seven million people. With few domestic agricultural activities, Hong Kong is in a unique situation that over 95 % of its food supply is imported, with Mainland China by far the major source. In recent years, Hong Kong has not been short of food incidents, such as Sudan Red in duck's eggs, malachite green in fish, and more recently melamine in dairy products, to name just a few. Understandably, consumers have been concerned about food safety. In addition, they are increasingly interested in diet, nutrition, and health. Accurate information on people's dietary exposures to chemicals is important for assessing possible risks and for setting priorities for public health action. To address these issues, the Food and Environmental Hygiene Department (FEHD) was formed in 2000. In 2006, the Centre for Food Safety (CFS) was set up under the FEHD responds to growing consumer concerns about the safety of food.

Road to a Total Diet Study

Hong Kong has been conducting risk assessment studies for some time. Initially, these studies focused on individual food hazards but were hampered, to a certain extent, by the lack of appropriate food consumption data. The only data on food consumption was from a survey conducted in 2000 on about 1,000 secondary school

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students by means of a self-administered food frequency questionnaire, which covered 93 commonly consumed food items. One of the aims of establishing the FEHD was to build up the capability and capacity of the food safety regulatory authority in Hong Kong. Political commitment and funding were secured early to attain these aims.

To strengthen the quantitative assessment of population exposure to chemicals, the FEHD conducted the first population-based food consumption survey in 2005. With the availability of food consumption data for the local population, dietary exposure studies could be expanded incorporating the total diet study (TDS) approach, which is considered to be one of the best ways for dietary exposure estimation for a population.

Capability and Capacity Building for a Total Diet Study

A TDS is a large and complex project with many components, which include purchasing foods commonly consumed, processing them as for consumption, combining the foods into food composites, homogenizing and analyzing them for chemical contaminants and selected nutrients. Finally, the dietary exposures of the contaminants and nutrients are estimated by combining the analytical results with food consumption information for the population.

A team approach is necessary when conducting TDS. A Task Force on TDS comprising professionals of different backgrounds, including public health, food science, nutrition, and laboratory analysis was formed to plan and monitor the progress of the TDS in 2007. All team members, including those responsible for food sampling, food preparation, laboratory analysis, and risk assessment, were acquainted with the TDS principles and methodology. Team members had attended International Workshops on TDS organized by World Health Organization (WHO) since 1999. Moreover, in December 2008, the CFS, in collaboration with the WHO, organized a workshop in Hong Kong to equip the members with the knowledge and skills required for conducting a TDS.

Laboratory Facilities

To have better exposure estimations, sensitive analytical methods are needed to obtain the lowest achievable limits of quantification for the chemicals of interest in the dietary exposure assessment. In addition, a comprehensive quality assurance and quality control program is required to assure the quality of the analyses. Since no commercial laboratories in Hong Kong could provide testing services with sufficiently low detection limits, the Food Research Laboratory (FRL) of the CFS and the Government Laboratory (GL) conducted the analytical work. The substances to be included in the TDS were linked to the capabilities and capacities of FRL and GL.

Other factors, including the stability of the chemicals and availability of long-term and reliable storage facilities, were also considered in prioritizing the chemicals to be tested. Furthermore, retention and storage of reserve samples was considered important, in case reanalysis was required.

Kitchen Facilities

A TDS is different from other food commodity-based surveys in that a TDS is characterized by measuring chemicals in foods as normally consumed and therefore, food preparation is a key step in conducting a TDS. Since the operations of FRL and GL mainly focus on laboratory analysis, it is not possible for them to perform extensive food preparation with their existing facilities. In view of infrequent use of kitchen facilities, the food preparation work was outsourced. To ensure consistency in the preparation of food samples, a single kitchen facility was used for the whole project.

Dietary Exposure Estimation

The fieldwork for the first population-based food consumption survey was completed in 2007. A total of 5,008 Hong Kong individuals aged 20–84 years were interviewed by using two independent, nonconsecutive 24-h dietary recall methodology supplemented by a food frequency questionnaire. More than 1,400 food items as consumed have been captured by the 24-h dietary recall of this survey and the average daily consumption of solid food and liquid food were about 1.1 kg and 1.9 l (including about 1.1 l of water), respectively. The top 10 solid foods identified by the survey are listed in Table 24.1.

Table 24.1 Top 10 solid foods identified by the first population-based food consumption survey in Hong Kong (g per person per day)

Solid food	Average consumption
Rice (including white rice, brown rice, and cognee)	297
Leafy/stalk/shoot vegetables and brassica	121
Pasta/noodles	120
Fish	57
Oranges	56
Pork	54
Bread/rolls/buns	44
Chicken	33
Apples	21
Squash/gourds	17

Given the complexity of the food consumption dataset and exposure estimation, development of an in-house computer program enabled the dietary exposure assessments to be conducted more efficiently and accurately and the data to be managed more systematically.

The First Total Diet Study in Hong Kong

The first TDS in Hong Kong aims to estimate the dietary exposures of the Hong Kong population to a range of substances including chemical contaminants and nutrients, and thus assess their potential health risks. The study plan was developed as follows.

More than 1,400 food items were contained in the food consumption data from the first population-based food consumption survey of the local people. It was not feasible to carry out laboratory analysis of every single food item due to time and resource constraints. Therefore, a TDS food list was developed to select representative food items out of the more than 1,400 survey foods, to represent the key components of the local diet.

Food items in the TDS food list were selected based on the following criteria: (i) food commonly consumed by the population; and (ii) food that is likely to contain high concentration of certain chemicals even it is consumed in a low amount. To this end, a TDS food list with 150 food items was developed, including drinking water and bottled water, and covered 88 % of food consumed by the Hong Kong population in terms of weight of food consumed.

Owing to its small size, three regions across the territory have been identified for sampling purposes as shown in Fig. 24.1. However, it is expected that in terms of food supply, the differences are likely to be relatively small. The 150 TDS food items will be sampled from each of the three regions over four seasons of a year. In the end, a total of 1,800 samples will be collected for the entire TDS project.

Following the food sampling, samples from the three regions will be prepared separately as food normally consumed, i.e. ready-to-eat, in a manner consistent with cultural habits in Hong Kong. Three prepared samples of the same food items will then be mixed and homogenized to obtain a composite sample for laboratory testing. A total of 600 composite samples will be tested in the Hong Kong TDS. The composite samples will be kept frozen prior to testing. Portions of the three separate prepared samples making up each composite will be kept frozen individually as backup reserve samples, should follow up investigations of any composite be needed. The food preparation work will be carried out by a single kitchen facility and completed in a year.

When selecting the substances for the TDS project, the following criteria were considered in prioritizing the substances to be analyzed: (i) recommendation from international authorities, (ii) public health significance, and (iii) public concern. However, the inclusion of substances in the TDS project also hinges on the laboratory capability and capacity, such as the number of analyses that can be handled and
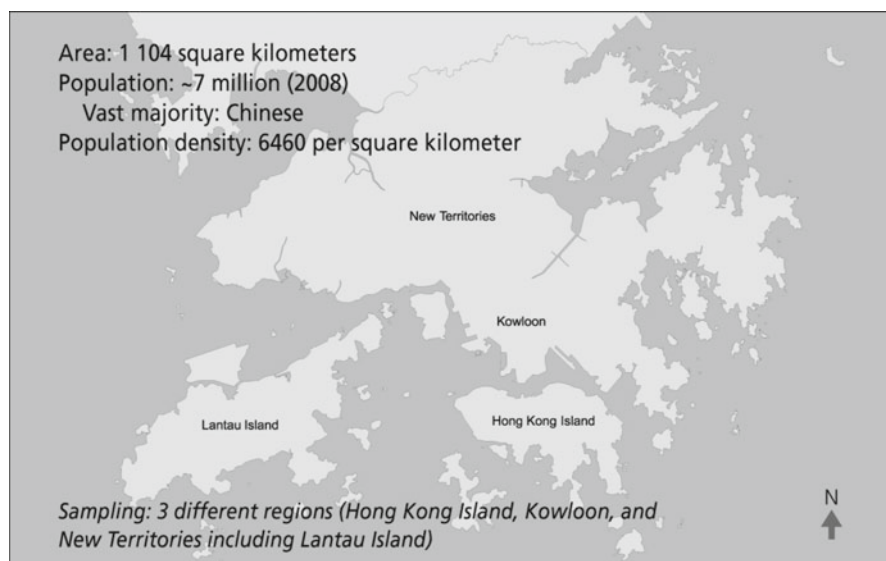
Fig. 24.1 Hong Kong total diet study sampling regions

the progress of analytical method development, which will be a key determinant in selecting substances for testing. To this end, over a hundred substances including persistent organic pollutants (POPs), pesticide residues, heavy metals, mycotoxins, processing contaminants and nutrients, will be analyzed.

Laboratory analysis will be mainly performed by FRL of the CFS. As some of the targeted substances may gradually decompose over time, become bound to the food matrix or change its oxidation state, such substances will be analyzed immediately upon delivery of the composite food sample to the laboratory. Other substances will then be analyzed in batches depending on the stability of substances. Substances, such as POPs and heavy metals, are relatively stable. Therefore, sufficient and reliable freezer storage space is necessary for keeping these composite samples.

Dietary exposures will be estimated by using a computer program for a point estimate approach, in which the TDS food items will be mapped with food consumption data, as far as possible, in estimating the dietary exposure. The resulting dietary exposure estimates will then be compared with the safety reference or nutritional reference values.

To ensure consistency of the procedures, sets of procedural manuals are being developed to explain the management structure and contact information, and detail the sampling and food preparation procedures. Prior to the fieldwork of food sampling and food preparation, a pilot run will be conducted for testing the workflow, which will be critical to the success of the fieldwork. Based on the experience obtained from the pilot run, the procedural manuals may need to be further modified.

Way Forward

It is anticipated that the fieldwork of food sampling and food preparation of the first Hong Kong TDS will be started in 2010, and that the laboratory analysis will take about 3 years to complete. Once the analytical results are available, the data analysis will be conducted, and a report will then be prepared and released in phases, as contaminant assessments are completed.

Chapter 25
Experiences in Total Diet Studies in the Czech Republic

Jiri Ruprich and Irena Rehurkova

Introduction

The objective of the national program of dietary exposure monitoring in the Czech Republic is to address scientific questions related to possible health risks from exposure of the population to selected chemical substances contained in foods. To achieve this, the total diet study approach has been used. The methodological principles involve defining the consumption of staple and other foods in a typical national diet and the subdividing of such foods into specific groups, purchase of defined foods in randomly selected shops in predefined geographical regions and during assigned periods representing four climatic seasons over an entire year. Purchased foods are immediately transported to one central processing facility in the country, cooked according to standardized procedures (recipes), and subsequently analyzed in the central chemical laboratory. The first total diet study started in 1991 by preparation of standard operation procedures and implementation of a quality assurance/quality control (QA/QC) system, followed by a pilot study. Routine monitoring activities have been ongoing since 1994. This longitudinal monitoring program is financed from the national budget. Summarized results and their primary interpretation are publicly available [1]. Conclusions are regularly used for communication with various stakeholders, for developing governmental programs on health protection and promotion, for regulatory work but also for the daily work of specialists operating the Czech part of the European Union Rapid Alert System for Food and Feed.

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Background

In early 1990s, the Czech Republic underwent rapid economic and social transformation. With a population of 10.5 million, this historically highly industrialized country has been confronted by many problems associated with the contamination of its environment. Domestic agricultural production has been subjected to increased contamination of certain foodstuffs by some chemicals, including persistent organic pollutants (POPs). Liberalization of the food market and various preexisting problems underlined the need for a newly designed, specialized monitoring system. It had to address society's basic concerns about what are the main health risks related to foods and consumer behavior. In addition, it also needed to provide data useful for effective risk management, taking into account not only health risks but also possible economic losses. For these reasons, a longitudinal monitoring program has been used to provide relevant data to estimate long-term, i.e. chronic, dietary exposure of the population and/or specific population groups. The system was developed as a part of the integrated monitoring program of the Czech Government that incorporated surveillance and monitoring activities carried out by the health, agriculture and environment sectors. Another key objective was to implement some recommendations and tasks promulgated by international organizations, such as the World Health Organization (WHO) and the Food and Agriculture Organization of the United Nations (FAO). Within national public health authorities, the National Institute for Public Health Prague (NIPH) and particularly, a specialized department located in Brno was commissioned to focus on dietary exposure monitoring. Its organization was defined in legal documents, based on decisions of the Czech Government. The dietary exposure monitoring was organized based on the principles of a total diet study (TDS) as recommended by WHO GEMS/Food. Previous national and international experiences with TDS were used to design national procedures describing a standard for a transparent and quality assurance/ quality control (QA/QC)-based organization and technical facilities. Preparation of standard procedures, implementation of the QA/QC system and a pilot study started in 1991.

Organizational Framework for the Czech Total Diet Study

The wider Czech national monitoring program is composed of four parts and is carried out in 12 selected cities and areas within the country. These sampling localities were selected to be representative of various country regions. An independent commission of experts took into account various scientific, socioeconomic, and political factors in the process of selection. The first part of the wider monitoring program is aimed at notifications of foodborne diseases, including both infections and intoxications. It utilizes the data collected routinely in the national epidemiological system (EPIDAT) [2] and data available in official reports of regional public health authorities.

The second part focuses on the monitoring of occurrence and qualitative and quantitative parameters of some prioritized pathogenic bacteria, such as *Salmonella*, *Campylobacter*, and *E. coli*, in raw food samples and food ingredients. The strains of bacteria isolated from foodstuffs undergo detailed qualitative/quantitative investigations, which is not usually done by the routine food control system. This includes their resistance to antibiotics, molecular-genetic characterization, and the number of total colony-forming bacterial cells (CFU) per food weight unit. The third part focuses on the incidence monitoring of toxigenic fungi (molds) in sampled food ingredients. Isolates of fungi are identified by their genus and species using traditional and molecular-genetic methods and for their potential to produce mycotoxins, such as aflatoxins and ochratoxins. The second and third parts have more characteristics of longitudinal scientific studies, as a part of wider surveillance, and are directly related to the fourth part of the program because it is an economic advantage to use the same food samples and/or the same logistics. In the fourth part of the program, the dietary exposure of the general population and population cohorts to selected chemical compounds is longitudinally monitored. This is the Czech TDS. Samples of foodstuffs are collected and transported to one place in the country where they are processed/cooked as consumed and analyzed for a broad spectrum of chemical substances. All the analytical results are used for calculations of exposure doses. Calculated exposures are then used for characterization of health risks resulting from the dietary patterns of the general population and population cohorts.

Principles of the Czech Total Diet Study

The primary objective of the monitoring program, as defined in government documents, is the assessment of the general population and population cohorts to exposures to known hazardous contaminants and residues, but also to possible deficiencies of some nutrients and micronutrients important for public health. The presence of contaminants in food may pose health risks of a carcinogenic and/or noncarcinogenic nature. For calculation of exposure doses, two sources of food consumption data were used. The first source is individual food or food group consumption data as measured in national epidemiological studies. Mean availability of foodstuffs at the level of each household member was used in the first two 5-year TDS periods, which commenced in 1994 and 1997, respectively. The second source is the standardized model of food consumption derived from food based dietary guidelines (FBDG). Since 2004, the Czech TDS has been using food consumption data collected at the individual level [3]. This data now serves both purposes: to calculate traditional point estimates of average exposure doses, but also for new distributional modeling and probabilistic evaluation of result uncertainties of chronic exposure of chemicals.

The defined sets of food samples covering specific food groups are collected in four regions of the country for subsequent analyses. Every region has three cities selected for sampling (see Fig. 25.1). The sampling schemes for the Czech TDSs to date are summarized in Table 25.1 and reflect how they have evolved over time.
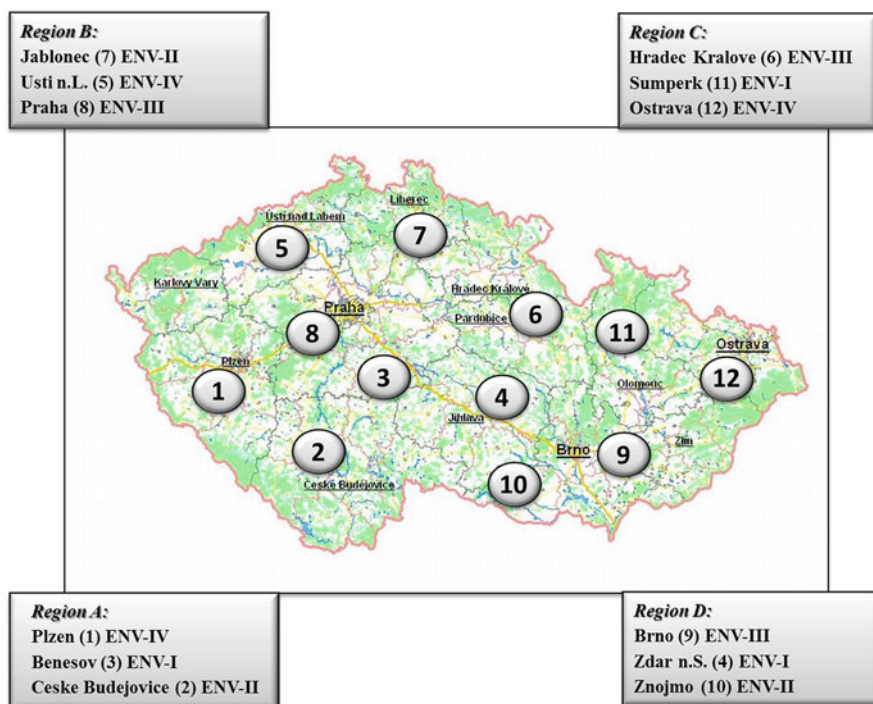
Fig. 25.1 Total diet study sampling locations in the four regions of the Czech Republic (Notes: Number in parentheses is identification number used in database. ENV–I to- IV indicates environment pollution and other factors according to national classification system for particular region with I being the least concern and IV being the most)

For economic reasons, purchased food samples are usually combined into composite (pooled) samples according to individual regions. The individual food items representing a particular region are cooked and/or prepared in compliance with standard recipes and then combined into composite samples for each of the four regions of the country. Composite samples are further specifically prepared for chemical analysis. This step is essential because various chemical substances need tailored procedures, such as homogenization to avoid artificial contamination of samples. For determination of some chemical substances, the composite samples from individual regions are mixed into so-called national composite samples where one sample represents the whole country. This approach is applied for some chemical substances where chronic exposure is expected and which play a crucial role in risk characterization, for example, toxic polychlorinated biphenyls (PCBs), dibenzofurans and dibenzodioxins for which chemical analyses are expensive.

Selection of chemical substances to be analyzed in TDS takes into account various criteria and factors. The most important are following: known toxicity, potential exposure, results from the national food control system, signals from the EU Rapid Alert System for Food and Feed, public/stakeholder concerns, international recommendations, such as those of WHO GEMS/Food [4]. All of these have to be considered in the light of budgetary constraints, and the capability and capacity of

Table 25.1 Summary of Czech Republic total diet studies (1994–2009)

Parameter	I	II	III
Year	1994–1998	1999–2003	2004–2009
Number of sampling places	12	12	12
Sample collection period	1 year	1 year	2 years
Number of regions	–	4	4
Number of sampling dates	5	4	8
Number of food composite samples	46/place	108/region	110/region
Total number of composite samples	$46 \times 12 = 552$/year	$108 \times 4 = 432$/year	$110 \times 8 = 880$/2years
Total number of individual food commodities purchased	$160 \times 12 = 1,920$	$195 \times 12 = 2,340$	$308 \times 12 = 3,696$
Number of country composites	46/year	108/year +16 (TCDD samples)	220/2years +40 (TCDD samples)
Total number of individual commodities analyzed			BA – 456; AA – 1,296 ADIT – 1,476 I – 144 (milk) DON – 264
Number of analytes	71	71 + 37	~100 + 37
Total number of analytical results	~20,000	~16,500 + 592	~10,000– 20,500 + 1,480
Consumption data used	SKP 91/ed.94	SKP94/ed.97 SKP97/ed.2000	SKP97/ed.2000 SISP 2004/since 2006–2007

TCDD dioxins and dioxin-like PCBS, *BA* biogenic amines, *ADIT* additives, *I* iodine, *DON* dexyni-valenol + other related fusaria mycotoxins, *SKP* household budget survey, *SISP* individual food consumption study (2×24 h recall)

appropriate analytical laboratories. The chemical substances are analyzed mostly in the central laboratory (NIPH Brno), which specialize in trace chemical analyzes of foods. In order to save time and money, contract laboratories are used in some specific cases mainly for emerging chemicals, which are not normally monitored. Most of substances are analyzed by accredited methods [5]. Since 1994 the spectrum of chemical substances analyzed includes organic compounds (PCBs and organochlorine pesticides), inorganic substances (nitrates, nitrites, cadmium, lead, mercury, arsenic, copper, calcium, sodium, potassium, phosphorus, zinc, manganese, selenium, magnesium, chromium, nickel, aluminum, iron, and iodine). Other groups of substances were included in the pilot, non-periodic, study. Those are substances with possible endocrine or carcinogenic effects (dioxin-like PCBs, dioxins, furans), polycyclic aromatic hydrocarbons, carbamate pesticides, biogenic amines, acrylamide and mycotoxins. In addition, certain nutrients, like vitamin C and fatty acids, are also measured. One important principle of the Czech TDS is to analyze all the selected substances in the same food composite sample. The total number of quantified chemical substances is in the range of 79–120 in every analytical food sample. This produces approximately 22,000 analytical results during each monitoring period.

The concentrations of chemical substances found in food samples are then used in the calculation of exposure. The point estimate of exposure levels is calculated as a simple average exposure for population. In some specific situations, the estimate of exposure levels is done also for specific cohorts. Since the third TDS, sophisticated methodology has been used to calculate the distribution of individual intakes for various age and gender groups of consumers. Probabilistic evaluation of acute intakes has been used to estimate the intake of some natural toxins, such as glycoalkaloids [6]. Since 1994, the model based on FBDG (also called "standardized recommended food consumption data for population groups") has been applied for the long-term comparison of dietary exposure levels. These results simply reflect trends in the content of chemicals in foods not masked by changes in food consumption. The model of FBDG is used for five population cohorts, namely children, adult males, adult females, pregnant or breast-feeding females, and subjects over 60 years of age.

Results of the Czech Total Diet Study

Results of TDSs in the Czech Republic reflect changes in concentrations of some chemical substances in foods available on the market. This is due to the relatively greater openness of the food trade in the EU, but also changes in dietary habits of consumers. For some persistent contaminants, such as non-dioxin-like PCBs (see Fig. 25.2), TDS results clearly document declining levels of environmental

Exposure doses : Sum of PCBs (ug/kg b.w./day)
(models according to the food guide pyramid)

Legend: Children 4-6 years — Adult Women 18+ years — Adult Men 18+ years — Older people 60+ years — Pregnancy/Lactation
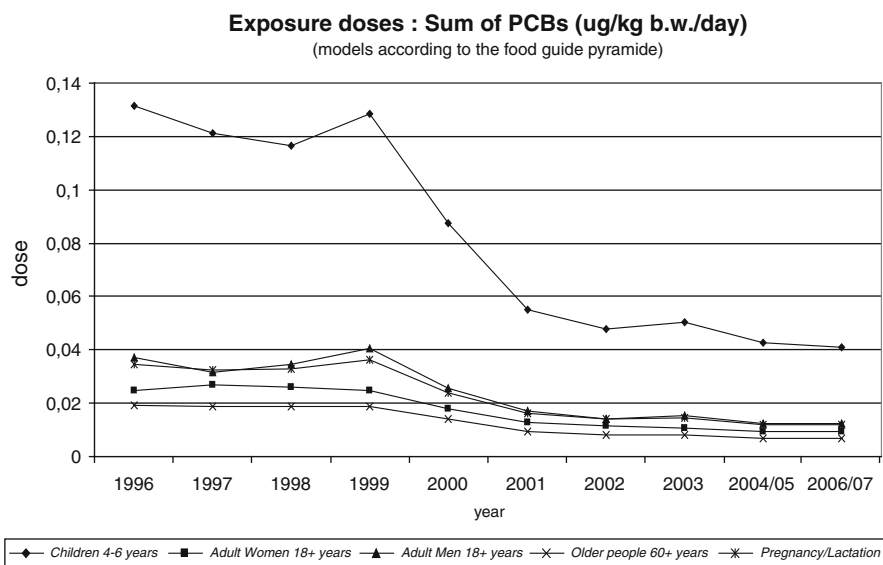
Fig. 25.2 Trends in exposure of various cohorts according to model for food based dietary guidelines for sum of six non-dioxin-like polychlorinated biphenyls

contamination. For some chemical substances, results are more or less constant. For some important micronutrients, like iodine and selenium, daily intakes are increasing. While dietary exposures in the Czech Republic to persistent contaminants, such as non-dioxin-like PCBs, is low and decreasing over time, visible increases in exposure levels in 1999 and 2003 were observed. These related directly to catastrophic floods, which moved soil sediments and caused pollution by wastes that then influenced all food chains.

In connection with changes in concentration levels, it is important to stress that the major factor influencing dietary exposure levels are the continuously changing dietary consumption patterns. Consumption of some foods decreased (e.g. red meat, mainly beef), consumption of some increased (e.g. white meat, mainly chicken), consumption of some is essentially the same (e.g. fruit and vegetable although a number of items are higher). Generally, there is a visible shift to buy more processed foods. The characterization of the dietary health risks thus far for the average Czech appears to be relatively low. However, the risk characterizations still need to be improved because they are still not precise enough and are missing for some priority population cohorts, like young children (< 4 years), the elderly (> 60 years), and pregnant and breast-feeding women. This is mainly due to missing or limited quality of food consumption data for these priority groups. Beginning in 2010, some modifications in the Czech TDS procedures were tested in a pilot phase. Detailed results from the Czech TDS are publicly available [7].

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Chapter 26
The Present and Future Use of Total Diet Studies by the European Food Safety Authority

Stefan U. Fabiansson and A.K. Djien Liem

The Formation of European Food Safety Authority

Following a series of food crises in the late 1990s, the European Food Safety Authority (EFSA) was set up in 2002 as an independent source of scientific advice and communication on risks associated with the food chain. EFSA was created as part of a comprehensive program to improve food safety in the European Union (EU), ensure a high level of consumer protection and restore and maintain confidence in the EU food supply.

EFSA's remit covers food and feed safety, nutrition, animal health and welfare, plant protection and plant health. In all these fields, EFSA's most critical commitment is to provide objective and independent science-based advice and clear communication grounded in the most up-to-date scientific information and knowledge possible. Here information from total diet studies (TDSs) has the potential to fill important knowledge gaps.

In the European food safety system, risk assessment is performed independently from risk management. As the risk assessor, EFSA produces scientific opinions and advice to provide a sound foundation for European policies and legislation and to support the European Commission, European Parliament and EU Member States in taking effective and timely risk management decisions. Risk assessment is a specialized field of applied science that involves reviewing scientific data and studies published in the literature in order to evaluate risks associated with certain hazards. The EFSA has an important role in collecting and analyzing scientific data on the presence and concentration of microbial or chemical hazards in food and feed from available sources to ensure that European risk

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assessment is supported by the most complete scientific information available. It does this by working with the EU Member States to gather, share and analyze EU-wide data, as well as launching public consultations and calls for data to gather information from external sources. A significant part of this information comes from TDSs.

EFSA's Future Strategic Direction

In 2008, the EFSA Management Board adopted a Strategic Plan for 2009–2013 [1]. The plan outlines how EFSA will maximize the benefits of the scientific expertise and results at its disposal across Europe and strengthen its integrated approach to risk assessment. Six key strategies have been identified:

1. Provide an integrated approach to delivering scientific advice, field to plate
2. Produce timely, high-quality evaluation of products, substances and claims subject to regulatory authorization
3. Collate, disseminate and analyze data in the fields within EFSA's remit
4. Position EFSA at the forefront of risk assessment in Europe and internationally
5. Reinforce confidence and trust in EFSA and the EU food safety system
6. Assure the responsiveness, efficiency and effectiveness of EFSA

Collection and analysis of scientific data on the presence and concentration of microbial or chemical hazards is a central task for EFSA and has now been elevated to one of six key strategies for the next 5 years. The task is also outlined in the EFSA founding regulation (EC) No 178/2002 of 28 January 2002 [2] where Article 33 states that:

1. The Authority shall search for, collect, collate, analyze and summarise relevant scientific and technical data in the fields within its mission. This shall involve in particular the collection of data relating to:

    (a) Food consumption and the exposure of individuals to risks related to the consumption of food
    (b) Incidences and prevalence of biological risk
    (c) Contaminants in food and feed
    (d) Residues

2. For the purposes of paragraph 1, the Authority shall work in close cooperation with all organizations operating in the field of data collection, including those from applicant countries, third countries or international bodies.
3. The Member States shall take the necessary measures to enable the data they collect in the fields referred to in paragraphs 1 and 2 to be transmitted to the Authority.

In simple terms the legislation calls for more information about what might be found in the food in Europe and details of the European population food consumption profile. The legislation goes on to request an inventory of data collection systems at Community level in the fields within the mission of EFSA and development of a strategy of how to improve the system.

Current Data Collection Activities

EFSA carries out much of its work in response to requests for scientific advice or so-called mandates from the European Commission, European Parliament and EU Member States, as well as initiating its own scientific activities. Risk assessments are currently carried out using occurrence data that are available at the time of addressing the mandate. Consequently, collection of available data, e.g. for a contaminant, is often undertaken on an *ad hoc* basis, when the need arises. Typically this involves a call for data issued by the EFSA or the Commission. In 2011, an annual data submission process for contaminant data was initiated for a specified range of more than 30 different chemicals or chemical groupings.

Member States often collect contaminant data as part of their surveillance according to existing Community legislation, now consolidated in Commission regulation (EC) No 1881/2006 as amended by regulation (EC) 629/2008 of 2 July 2008 [3]. Such surveillance is often targeted to problem areas and not random. The results will thus not necessarily be representative for the exposure of the general population.

European Commission regulation (EC) 1881/2006 specifies contaminants that should be regularly tested. However, the number of tests to be performed is not specified and reporting requirements differ. Thus implementation varies across Member States. Data from some contaminant testing has to be regularly reported to the Commission. For example, monitoring of nitrate in vegetables is compulsory with regular reporting, but the frequency of testing would vary between Member States. On the other hand the monitoring scheme in place for the furan data collection, as specified in Commission recommendation 2007/196/EC [4], outlines both the number of samples to be tested and reporting requirements. For other substances, an annual report of the surveillance results is produced by each Member State and no data are stored at a central level. It is thus difficult to access data for many contaminants.

Attempts to Harmonize Data Collection

An overview of the current initiatives to improve the efficiency and accuracy of exposure assessment for chemical substances and to harmonize data collection is given in Fig. 26.1.
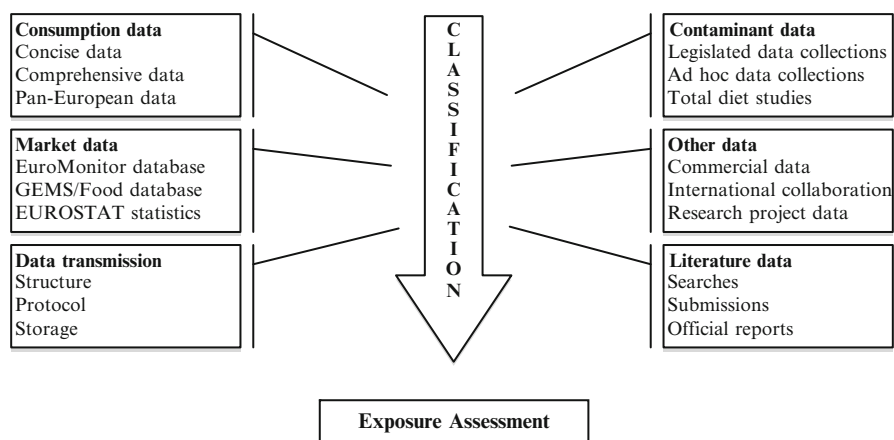
Fig. 26.1 Data sources, procedures and harmonization to enable calculation of exposure

Occurrence Data

Within the EU framework called Scientific Cooperation (SCOOP) studies (Council Directive 93/5 [5]), data for specified contaminants were collected amongst Member States in a coordinated way to assist the European Commission in developing European Legislation. With the formation of EFSA those activities were subsumed into the general EFSA program (see Article 33 of Commission Regulation 178/2002 [2]). Significant attempts are in place across the EU to harmonize methodology and analytical protocols for testing of hazardous substances. Regulation (EC) No 882/2004 [6] establishes Community Reference Laboratories in food and feed for this purpose for:

- Marine biotoxins
- Mycotoxins
- Heavy metals in food and feed
- Dioxins and PCBs
- Polycyclic aromatic hydrocarbons
- Residues of veterinary medicines and contaminants in food of animal origin

In addition, regulation (EC) No 882/2004 foresees a Community reference laboratory for food contact materials. There are also a number of Commission regulations specifying in detail sampling and analytical protocols to follow for the official control of selected contaminants:

- Commission regulation (EC) No 401/2006 [7] lays down methods of sampling and analysis for the official control of levels of mycotoxins in foodstuffs.
- Commission regulation (EC) No 1882/2006 [8] lays down methods of sampling and analysis for the official control of the levels of nitrates in certain foodstuffs.

- Commission regulation (EC) No 333/2007 [9] lays down methods of sampling and analysis of some heavy metals, 3-MCPD and benzo(a)pyrene in foodstuffs.
- Commission regulation (EC) No 1883/2006 [10] lays down methods of sampling and analysis of dioxins and dioxin-like PCBs in certain foodstuffs.

Despite these official specifications, there is still some incongruence in the reporting of analytes. Specificity and sensitivity of the methods used are not always given. Sensitivity is more commonly geared to maximum levels permitted in the legislation rather than the levels required for the exposure assessment, which may be orders of magnitude lower, as undertaken by TDSs. There is thus a need for further harmonization.

There is also a need at the European level for contaminant data reflecting the actual market situation facing the consumer – a market basket survey type activity typified by a TDS. However, such an activity is complex and should be planned carefully to avoid unnecessary cost. In this regard, it is particularly critical to consider the extent, frequency, accuracy and coverage of analytical data needed for risk assessment purposes.

Food Consumption Data

The availability of accurate and detailed food consumption information is fundamental to assess the exposure to hazardous substances within the risk assessment process or to estimate the intake of substances with potential beneficial effects. The need to standardize food consumption data was raised by the SCOOP Task 4.1 [11] and initially was addressed in projects like DAFNE, EPIC, the FLAIR Eurofoods-Enfant project, COST Action 99 and others. Building on these previous activities, the EU-funded EFCOSUM project worked toward the development of a method for a European food consumption survey that delivers internationally comparable data on a set of policy-relevant nutritional indicators. Its successor, EFCOVAL, continued the work initiated by EFCOSUM and further developed and validated a food consumption instrument necessary to assess dietary intake for studying associations with public health and food safety in future pan-European monitoring surveys.

In 2005, EFSA's Scientific Committee published an opinion on exposure assessment recommending the urgent collection of available consumption data at an aggregated level followed by an expanded collection of data at a detailed level [12]. A Scientific Colloquium was arranged to debate the state of the art of harmonized approaches to food consumption data collection at the pan-European and international levels. A report available on the EFSA website outlines future harmonized activities and recommends that EFSA takes a lead role in the coordination and completion of a pan-European initiative [13].

As a first response, EU Member States collaborated in the establishment of the "Concise European Food Consumption Database" containing food consumption information in broad food categories only, to be used for preliminary exposure assessments.

The Concise Database has been fully operational since the end of February 2008. By the end of 2008, EFSA started a project aimed to establish a "Comprehensive European Food Consumption Database". Twenty EU Member States provided EFSA with the latest dietary survey information available for adults at the most disaggregated level recorded at national level. At the same time a similar initiative collecting food consumption information for children was initiated involving 13 EU Member States. It is anticipated that when the Comprehensive Database is operational during 2010 it will greatly improve the accuracy of EFSA's exposure assessment calculations. However, data will still be affected by important methodological differences in their collection making them unsuitable for direct country-to-country comparisons. The collection of accurate and harmonized food consumption data at a pan-European level is therefore a primary long-term objective for EFSA and has been recognized as a top priority for collaboration with EU's Member States.

Food Classification

Food consumption and occurrence data collection systems do, implicitly or explicitly, rely on a certain categorization of foods. In order to permit the combining of food consumption and occurrence data for calculating exposure, it is therefore necessary that the food categories can be linked, even if the categories are not identical.

Already several different food classification systems exist. Codex food categories, the European Food Grouping (EFG) system, FAO food balance sheets, the WHO Global Environment Monitoring System / Food Contamination Monitoring and Assessment Programme (GEMS/Food), DAFNE, Eurocode 2, and EPIC are a few examples. The Eurostat F-5 unit has established a data dictionary for products subject to controls (Doc. ESTAT/F5/ES/156). It considers the areas of feed, animals, food, aggregates of food, contact materials, and water. Furthermore, Regulation 396/2005 [14] on maximum residue levels of pesticides in or on food and feed of plant and animal origin has also established a food classification system. In its zoonoses data collection system, the EFSA has already agreed with the Member States on yet another food categorization system.

The problem of food terminology is not so much the difficulty of finding the best terms or the best ways of classifying foods, but rather the fact that differing, inconsistent, and often incompatible terminologies are used. Each method has its own description language or code designed to satisfy the immediate requirements of the scientific work of the method initiator. Consequently, it is difficult to exchange data between countries, between organizations within the same country, or even between colleagues in the same institution. EFSA has already initiated an effort to harmonize food descriptions for gathering detailed food consumption information. Initiating collaboration around a TDS initiative would create a further incentive for the adoption of a common or at least compatible food description system so that meaningful linkages can be defined.

First Steps in Using Total Diet Study Information

Apart from recommending initiatives in harmonizing food consumption information across Europe, the Scientific Committee also recommended that future efforts should focus on harmful substances and agents present in food [12]. In 2008, EFSA completed a strategic review of existing data collection systems and future data collection needs to support its activities. For the first time, the TDS approach to collecting baseline and trend information on the presence and concentration of beneficial or harmful chemicals in food in a typical market basket setting ahead of an explicit need was raised. Already, nine EU Member States (Czech Republic, Finland, France, Ireland, Italy, Netherlands, Spain, Sweden, and United Kingdom) regularly or occasionally undertake TDSs to gather baseline information on nutrients and contaminants, at least partly encouraged by the efforts of the World Health Organization. Each study reflects the health concerns and resources of the country in which it is conducted. There is presently no EU-wide coordination of substances to be included or typical foods to be tested on an annual basis. By harmonizing the general approach it would be possible to use the information to create an EU-wide picture.

There is also no central data repository that could provide synergies of scale by combining similar data from several Member States. A case could be made for nominating preferred Community laboratories for each specific analyte to improve economies of scale and to standardize analytical protocols. This could overcome the massive challenge EFSA is facing to calculate occurrence of a substance by combining analytical results from many different laboratories across the EU Member States where detection limits often vary by three to four orders of magnitude or more. This issue is equally challenging irrespective of whether the data come from *ad hoc* or market basket surveys, but could more easily be harmonized when using a coordinated TDS approach.

Results collected through a TDS can be of great assistance when quantifying the exposure component of an EFSA risk assessment. The lack of baseline information for the presence and concentration of a compound in typical food commodities as normally consumed can restrain the universal applicability of exposure calculations. For example, in assessing nitrate exposure from vegetable consumption as requested by the Commission, the Panel for Contaminants in the Food Chain soon found that access to information on overall nitrate as well as nitrite exposure from the total diet was necessary [15]. Detailed information was only available from nitrate in vegetables, which was a data collection mandated by the Commission for some time [8]. Fortunately the Panel could access detailed information covering most of the food supply from two Member States, which collected such data within a TDS framework. Equally, when assessing aflatoxin contamination in almonds, hazelnuts and pistachios, a question was raised about the importance of such contamination in relation to overall aflatoxin exposure. Aflatoxin contamination information from worldwide TDSs was accessed, while also considering the impact of climatic factors endnote.

Challenges Ahead

EFSA's experience in using contaminant information from TDSs has so far been positive. The information has provided a baseline against which it has been possible to compare more detailed targeted survey information for the compound under study in specific products. However, the sensitivity of the methodology used has not always been sufficient. Sometimes a broad selection of products has been pooled for the analysis, which decreases sensitivity for individual food products and can make results difficult to compare with food consumption information from areas with different food consumption patterns.

Another major challenge in combining contaminant information from many different sources will be harmonization of the food classification system. This is a perennial problem in a multinational setting. The various systems for food contaminant data collection that exist often have disparate food categorization systems with incompatible terminologies. Consequently, exchange and use of data becomes difficult, if not impossible.

The TDS involves selecting a typical basket of foods that are common in the overall diet, randomly purchasing the nominated foods, processing them as for conventional food consumption, combining the foods into food composites or aggregates, homogenizing them, and analyzing them for an agreed range of chemicals. The analytical results are then combined with food consumption information for different population groups, and the dietary exposure to the chemicals by groups is estimated.

Although EFSA has already benefited from access to data gathered through TDSs from a few collaborating EU Member States, there has so far been no overall coordination of a joint pan-European initiative. As a first step, a feasibility study was initiated to investigate the possibility of coordinated efforts across several Member States. With a positive result, a joint Working Group of representatives from Member States, the Food and Agriculture Organization and the World Health Organization was charged with developing details of a coordinated TDS and issued recommendations for the following list of issues in their final report [16].

Selection of Foods

The first stage of any TDS is establishment of a list of foods to be sampled based on representative surveys of the population's diet. A complication in setting up a coordinated pan-European effort is the different food consumption profiles in different Member States. However, national surveys can also face regional dietary differences, although maybe less pronounced. There is also the issue of special-diet subpopulations, like different vegetarian diets. In France, creating three different regional diets and surveying three different vegetarian diets addressed this. The food choice was split into national and regional food groups and results merged according to the subpopulation profile. Such a flexible approach could be adapted to suit a pan-European TDS.

Food Descriptions

There is no common or uniform system in place between EU Member States for describing the multitude of foods available on the market. Standardized food identification would solve many of the problems arising from the possible misidentification of foods. This is further complicated by the need to use compatible food classification systems for occurrence and food consumption data in order to permit combining the two when calculating exposure. There is already a move in place by EFSA to harmonize food classification for the gathering of detailed food consumption information. Initiating collaboration around a TDS initiative would create a further incentive for the adoption of a common or at least compatible food description system so that meaningful linkages can be defined. When mapping between different classification systems that describe the same food (for example where there are already several existing food dictionaries), the EFSA food dictionary should be able to work as a mapping module between the different food dictionaries. A draft new system called FoodEx 2 was launched by EFSA in 2011 [17].

Selection of Substances

Substances to consider include chemical contaminants such as heavy metals and metal-organic compounds, persistent organic pollutants, processing contaminants, naturally occurring toxicants, mycotoxins and residues of non-authorized substances. There is some flexibility in the choice of substances to include in a testing scheme and it is also possible to target different substances in different years. It is impossible to foresee all the data that will be needed to carry out future panel mandates. Nevertheless, given the remit of a panel and provided there is sufficiently close liaison with the Commission and the Member States on multi-annual work plans by EFSA and by risk managers, it may be possible to anticipate future data needs and include these in the plan for the following year. The range of substances included in the surveys as well as the number of samples to be analyzed will be the main determinants for the annual cost of the initiative. A minimum range of tests and samples could be prescribed with the option of expanding the range for individual Member States should they so wish.

Food Preparation

In a TDS, foods are analyzed as prepared for consumption. Harmonization of food preparation must be an integral part of the survey methodology and extra attention should be given to the choice of experimental kitchen. Regional and seasonal differences in food composition and contamination levels as well as local food preparation habits will be considered if at all possible.

Harmonization of Analytical Methodology

Because of the detailed protocol for a TDS there is an unprecedented opportunity to standardize the analytical methodology. The possibility of using one dedicated laboratory for each substance or substance group will be explored to minimize analytical bias and cost. The dedicated laboratories could be spread uniformly across participating Member States.

Reporting, Storage, and Handling of Uncertainties

A standardized procedure should be available for reporting of analytical results. All results should preferably be stored in a common database with data access rights to the stakeholders as appropriate. A data submission protocol favoring electronic data transmission directly database-to-database would significantly assist the process. The creation of a data warehouse containing all valid study datasets is anticipated. Using fact and dimension tables for the data warehouse will create a data store that is simple to query with a complex combination of fields. Additionally this structure is sufficiently flexible to accommodate yearly data submissions from studies that evolve over time and incorporate historical data. Analytical results from a multinational setting are associated with uncertainty. The Scientific Committee reviewed sources and types of uncertainty affecting areas of dietary exposure assessment and issued an opinion recommending a tiered approach to analyze uncertainties [18]. This approach should be followed.

The European Consultation Process

There is an existing elaborate consultation process in place between EFSA, the Commission, and the Member States. For issues of chemical hazards, EFSA has set up an Expert Group on harmonization of chemical occurrence data collection in food and feed consisting of representatives from all EU Member States and the Commission. The Terms of Reference are to:

- Assist in data standardization and the design of EU occurrence surveys.
- Support online access to and transfer from existing chemical occurrence databases. A data warehousing system would provide connection between and search facilities for interrogation of disparate data systems across EU Member States.
- Build EFSA databases on chemical occurrence, as appropriate. It could also be of benefit to EFSA to start regularly collecting from Member States and the Commission contaminant data generated in the ongoing surveillance even if not fully suited to exposure assessment.
- Produce EU summary reports on chemical occurrence.

The use of TDSs as a means of providing a baseline for chemical occurrence data as recommended by the joint EFSA/FAO/WHO Working Group, was presented to and endorsed by the Expert Group. With the positive response, a TDS pilot project funded by the European Commission Directorate-General for Research and Innovation was initiated to explore and test optimal details for a collaborative TDS effort in the EU [19].

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Chapter 27
The First Total Diet Study in Fiji

William Aalbersberg

Introduction

The University of the South Pacific (USP) serves its 12 member countries of Solomon Islands, Vanuatu, Fiji, Marshall Islands, Tuvalu, Kiribati, Cook Islands, Tonga, Samoa, Nauru, Niue and Tokelau. The laboratory at its Institute of Applied Sciences (IAS) is one of the best equipped in this region. In 1986, the need for nutrient composition of locally produced and imported foods was identified as an analytical priority at a regional meeting and during the next decade, a food nutrient laboratory was developed at IAS and over 100 local foods were analyzed. These data were incorporated into an extensive Pacific Island Food Composition Table published in 1994. Follow-up workshops identified possible improvements in these tables and a Food and Agriculture Organization of the United Nations (FAO) technical cooperation project from 2002 to 2004 was funded by IAS to make these improvements, publish a second edition of the Pacific Island Food Composition Tables [1], and prepare for international accreditation of the nutrient laboratory. Support was also provided to further develop the food contaminant capability, especially heavy metals and pesticides, of the IAS laboratory. The IAS laboratory achieved international accreditation through *International Accreditation New Zealand* in 2004.

As Fiji has long developed annual national food balance sheets with FAO and through its National Food and Nutrition Centre conducts a national nutritional survey every 10 years that in 2004 included food consumption data, it was felt that it was possible to conduct a total diet study (TDS) for Fiji. In 2005, this became possible with support from the New Zealand Agency for International Development.

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Background

Indigenous Fijians, like most Pacific Islanders, have a traditional diet based on starchy staples, e.g. taro, cassava, sweet potatoes, yams, and breadfruit, combined with fish and edible greens, such as taro leaves, often cooked in coconut milk. Wild nuts and fruits supplement this basic diet. This diet, however, has been changing as people consume more easily prepared foods, such as rice, wheat, instant noodles and pulses. Thus an increasing amount of food is being imported. In Fiji there is also a significant population (36 %) of Indian origin, who have maintained typical food consumption patterns of rice, wheat, pulses, vegetables and milk products with some meat consumed by nonvegetarians.

The minimal industrial development in Fiji is localized to a few main urban centers. As a volcanic island, significant amounts of heavy metals, such as cadmium, occur naturally in the soil. Agriculture is mainly for subsistence reasons with little use of insecticides, but occasional use of herbicides for weed control. Commercial vegetable farmers do use pesticides and in some cases, it is suspected the required waiting period is not observed before marketing. The import of chlorinated pesticides, such as DDT, has been banned for some years.

For the first Fiji TDS, it was decided to include four heavy metals and pesticides already analyzed by the IAS laboratory (organochlorine and organophosphate screening methods). As a local issue, iron was also analyzed, as anemia is a major health problem in Fiji. It is recognized that there are additional contaminants, such as mycotoxins and ciguatoxins, which are likely to be present in a limited range of Fiji foods but potentially in high concentrations.

Approach

As New Zealand has a long history of conducting TDSs, the manager of these studies, Dr. Richard Vannoort, was engaged as a project adviser. Discussions were held with him as to the tasks to be undertaken, including protocols for:

- Selection of food groups and foods
- Sample collection
- Food handling and preparation
- Analyses

In addition, it was agreed that for some key foods, analyses would be carried out in an accredited New Zealand laboratory (Hill Laboratories) as well as the IAS laboratory, as a quality assurance measure. The lower detection limits in the New Zealand laboratory would also decrease the uncertainty in exposure estimates associated with assigning a default value, i.e. half of the limit of detection (LOD), to food group composites for samples in which no analyte was detected, often referred to as "non-detect". For each step of the process, all key activities to be undertaken were detailed in a TDS protocol document to help ensure proscribed actions were followed.

Methodology

The general approach taken was to divide all foods consumed into 11 groups, e.g. grains, root crops, oils, vegetables, etc. Meats were further divided into poultry and red meat. The most commonly eaten components of each group were collected and either analyzed separately, if they were thought to be a major dietary contributor, or made into a food group composite sample, which was analyzed to represent the level of the chemicals of interest in that food group. A list of food groups and component foods is given in Table 27.1. The chemical concentration of each group was determined from the laboratory and then multiplied by the estimated weekly consumption to give the weekly exposure of the chemical of interest in that food group. These group results were then summed to give the total weekly exposure.

In addition to the four heavy metals and iron, thirteen organochlorine and five organophosphate pesticides that could be detected by general screening methods were also included. Atomic absorption spectroscopy was used for metal determination and gas chromatography for pesticides at IAS, and inductively coupled plasma mass spectrometry for metals in the New Zealand laboratory.

Fiji annually prepares a Food Balance Sheet for submission to FAO. For commercial crops and fish, annual production data are collected as well as imports and exports. From this, the amount of the food consumed (after subtracting wastage) can be estimated for the year which, divided by 365 days and the population of Fiji, gives the per capita daily consumption. Unfortunately, noncommercial crops are not included. In 2004, Fiji had also completed a major National Nutritional Survey in which a large sample population was asked the frequency of consumption of a wide selection of foods. This provided the approximate number of times in a week a certain item was consumed but the amount still needed to be estimated. Average serving sizes are fairly well established but it was not clear if a frequency meant a full portion or less (for instance, adding milk to tea as opposed to a glass of milk). Another problem was estimating the composition of mixed foods. For some foods, data from main Fiji producers were obtained. Estimates were made using both Food Balance Sheet and National Nutrition Survey data. In some cases, like root crop consumption, the two methods gave similar results but for other foods less so. In general Food Balance Sheet data were more useful.

Foods in the Fiji TDS were purchased from retail outlets. In general several samples of a given food were collected and composited to allow for individual variation. For locally grown foods (called regional foods) collections were made in both Suva (eastern side of main island) and Lautoka (western side of main island) in the winter and summer seasons. The seasonal (warm and cool season) collections of regional foods were analyzed as a composite of the Suva and Lautoka collection but separate reserve samples were kept so that regional differences could be assessed. A sampling and analysis plan was developed and documented. All foods were brought to the laboratory and prepared ready for consumption before analysis.

For economic reasons, considerable compositing of samples was undertaken. For each food a composite was made incorporating equal amounts of all collections of that food. Where a food group was suspected to have a small amount of analyte,

Table 27.1 Food groups
included in the Fiji total diet
study

G	Grains	
	1	Grains, wheat flour
	2	Grains, rice
N	Nuts	
	3	Peanuts
	4	Ivi nuts
M	Poultry and meats	
	5	Poultry, chicken whole
	6	Poultry, eggs
	7	Meat, corned beef and mutton
	8	Meat, beef cuts
S	Seafood	
	9	Fish, tinned mackerel
	10	Fish, tinned tuna
	11	Fish, reef fish
	12	Fish, shellfish
B	Beverages	
	13	Beverage, beer
	14	Beverage, bottled water
	15	Beverage, tap water
	16	Beverage, well water
	17	Beverage, tank water
	18	Beverage, kava
O	Oil	
	19	Oil, soya bean
	20	Oil, canola
	21	Oil, ghee
	22	Oil, coconut cream
D	Dairy products	
	23	Dairy products, milk
	24	Dairy products, butter
	25	Dairy products, ice cream
R	Root crops	
	26	Roots, taro (dalo)
	27	Roots, cassava
F	Fruits	
	28	Fruits, pawpaw
	29	Fruits, bananas
	30	Fruits, pineapples
L	Legumes	
	31	Legumes, beans
	32	Legumes, split peas
V	Vegetables	
	33	Vegetables, taro leaves
	34	Vegetables, cabbages
	35	Vegetables, bhaji (Amaranth sp.)

a "group composite" was made by combining equal amounts of the individual food composites from that group.

Depending on the level of consumption and the expected contaminant concentration, some foods were analyzed individually, or the component foods of a given food group were composited before analysis. Key samples were sent to Hill Laboratories in New Zealand for heavy metal analysis and the results compared with those obtained by the IAS laboratory at the University of the South Pacific.

In the Fiji TDS, a large number of samples had contaminant levels below the limit of detection. For calculation purposes, the pragmatic practice is to use half the detection level as the "average" likely value for such samples in determining mean concentrations for use in subsequent exposure estimates. With more advanced analytical equipment available in Hill Laboratories, detection levels were sometimes one tenth of those at the IAS so more accurate calculations could be made for such "non-detect" samples. Calculations using the Hill data and USP data were in good agreement. The presence of "non-detects" suggests that besides the use of 50 % of the detection level in calculations, a range should also be given with the lower end of the range assuming the level is zero and the upper bound using the detection level itself.

Results

Exposures are normally expressed on a per body weight (bw) basis which for an adult in Fiji has been taken as 75 kg. The summary of the results is given below in Tables 27.2 and 27.3. Results are also expressed as percentage of the PTWI (Provisional Tolerable Weekly Intake) for heavy metals established by the World Health Organization (WHO), namely 25 µg/kg bw for lead [2], 7 µg/kg bw for cadmium [3] and 1.6 µg/kg bw for methylmercury [4] and 4 µg/kg bw for inorganic mercury [5]. For inorganic arsenic, WHO established a BMDL 0.5 (Benchmark Dose Lower Confidence Limit) for a 0.5 % increased incidence of lung cancer was determined from epidemiological studies to be 3.0 µg/kg bw/day (3–7 µg/kg bw/day based on the range of estimated total dietary exposure) [5]. A range of assumptions were used to estimate the total dietary exposure to inorganic arsenic from drinking water and food. However, for organoarsenic, which is the predominant form in marine products, WHO has noted that intakes of about 50 µg/kg bw/week did not appear to cause any health effects in populations so exposed. For iron, the situation is complex given the low and variable bioavailability of iron and the special needs of premenopausal and pregnant women. Recommended Dietary Allowances range from 8 mg/day for men, 18 mg/day for women of childbearing age and up to 27 mg/day for pregnant women [6].

Only one food had detectable levels of pesticides and so calculations were not done on pesticide intakes.

Table 27.4 compares the results obtained for samples collected in the summer and winter months.

Table 27.2 Dietary exposure to heavy metals and iron and comparison with corresponding health reference values

	Health reference value (HRV)	Fiji lab	% HRV	NZ lab	% HRV
Arsenic (total) (µg/ kg bw/week)	50	45.6 (40.4–50.9)	91 % (81–102 %)	56.8 (56.5–57.7)	114 % (113–115 %)
Cadmium	7	1.17 (1.01–1.35)	17 % (14–19 %)	1.15 (1.13–1.17)	16 % (16–17 %)
Mercury (total)	5	1.25 (0.02–1.88)	25 % (12–38 %)	0.85 (0.57–1.15)	17 % (11–23 %)
Lead	25	3.2 (0.93–5.5)	13 % (4–22 %)	1.9 (1.6–2.0)	8 % (7–8 %)
Iron (mg/week)	56–350	135	NA	–	–

Table 27.3 Heavy metals and iron in the food groups in warm season (mg/kg)

		As	Cd	Hg	Pb	Fe
Grains (G1)	Fiji	0.112 (0.094–0.130)	0.015	0.011 (0–0.022)	0.032 (0–0.064)	17.29
	NZ	0.063 (0.057-0.120)	0.013	0.007 (0–0.014)	0.010 (0.004–0.016)	–
Nuts (G2)	Fiji	0.0015 (0–0.003)	0.0034 (0.003–0.0035)	0.0005 (0–0.001)	0.0015 (0–0.0030)	11.40
	NZ	0.0004 (0.0002–0.0004)	0.0031 (0.003–0.0032)	0.0003 (0–0.0006)	0.0001 (0.00004–0.0001)	–
Meat (poultry) (G3$_a$)	Fiji	0.0196	0.0008 (0–0.0016)	0.0033 (0–0.0066)	0.0049 (0–0.0098)	4.60
	NZ	0.024	0.0002	0.0008	0.003	–
Meat (red) (G3$_b$)	Fiji	0.0055 (0–0.011)	0.0009 (0–0.0018)	0.0037 (0–0.0074)	0.0055 (0–0.011)	11.62
	NZ	0.0030	0.0013	0.0004 (0–0.0008)	0.0030	–
Seafood (G4)	Fiji	2.898	0.0103 (0.010–0.0143)	0.0462	0.031 (0.021–0.041)	17.41
	NZ	4.018	0.0204	0.0417	0.0145	–
Beverages (G5)	Fiji	0.307 (0–0.614)	0.0328	0.0031 (0–0.0062)	0.0862 (0.0442–0.128)	39.64
	NZ	0.103	0.0327	0.0041 (0–0.0810)	0.0724	–
Oils (G6)	Fiji	0.0169 (0–0.0338)	0.0028 (0–0.0056)	0.0056 (0–0.0112)	0.0169 (0–0.0338)	3.54
	NZ	0.0056 (0–0.0112)	0.0012 (0–0.0025)	0.0056 (0–0.0112)	0.0056 (0–0.0112)	–

Table 27.3 (continued)

		As	Cd	Hg	Pb	Fe
Dairy products (G7)	Fiji	0.006 (0–0.012)	0.001 (0–0.002)	0.0020 (0–0.004)	0.006 (0–0.012)	0.087
	NZ	0.0002 (0–0.0004)	0.0001 (0–0.0002)	0.0002 (0–0.0004)	0.0002 (0–0.0004)	–
Root crops (G8)	Fiji	0.0299 (0–0.0598)	0.0050 (0–0.01)	0.0099 (0–0.0198)	0.0298 (0–0.0596)	7.996
	NZ	0.0102 (0–0.0204)	0.0100	0.0020 (0–0.004)	0.0163	–
Fruits (G9)	Fiji	0.004 (0–0.008)	0.007 (0–0.0014)	0.0013 (0–0.0026)	0.004	0.79
	NZ	0.0003 (0–0.0006)	0.0002 (0–0.0004)	0.0003 (0–0.0006)	0.002	–
Legumes (G10)	Fiji	0.004 (0–0.008)	0.0007 (0–0.0014)	0.0010 (0–0.002)	0.004	2.027
	NZ	0.0003 (0–0.0006)	0.0004	0.0003 (0–0.0006)	0.002	–
Vegetables (G11)	Fiji	0.018 (0–0.036)	0.0144	0.0060 (0–0.012)	0.018 (0–0.036)	18.97
	NZ	0.0312	0.0035	0.0012 (0–0.0024)	0.0048	–
TOTAL	Fiji	3.4224 (3.0296–3.8152)	0.0941 (0.0755–0.1028)	0.0936 (0.0425–0.141)	0.2398 (0.0732–0.4062)	135.37
	NZ	4.2592 (4.2372–4.3309)	0.0861 (0.0845–0.0878)	0.0639 (0.0462–0.0860)	0.1339 (0.1224–0.1461)	–

Discussion

In general, the heavy metal values were about 20 % of PTWI. For arsenic, only total arsenic was determined and these values were close to the PTWI for inorganic arsenic, the more toxic form of arsenic. However, a majority of arsenic exposure came from seafood, which contains mainly organic forms of arsenic, which is less toxic.

Comparison of the results from samples analyzed in New Zealand and Fiji showed results in almost all cases to be within expected uncertainties. Values for arsenic in the New Zealand samples showed a bias to slightly higher values. As expected, with lower detection levels, the average dietary exposure values and range were lower for mercury and lead, which had a large number of "non-detects" in the Fiji laboratory. For total mercury, the Fiji range was 12–38 % of the PTWI, while the New Zealand laboratory results produced a range of 11–23 % of PTWI. For lead, the Fiji range was 4–22 %. The much lower LOD for lead obtained by the New

Table 27.4 Comparison of results in warm and cool seasons (mg/kg)

	Arsenic	Cadmium	Mercury	Lead	Iron
Meat (Fiji lab, cool season)	0.0125	0.0012	0.0022	0.0045	11.36
Meat (Fiji lab, warm season)	0.0055	0.0009	0.0037	0.0055	11.62
Seafood (Fiji lab, cool season)	2.4512	0.0083	0.1374	0.0297	16.00
(Fiji lab, warm season)	2.898	0.0103	0.0462	0.031	17.41
Beverages (Fiji lab, cool season)	0.0211	0.0232	0.0043	0.0442	37.27
Fiji lab, warm season	0.0307	0.0328	0.0031	0.0862	39.64
NZ lab, cool season	0.0201	0.0499	0.0043	0.0261	–
NZ lab, warm season	0.0103	0.0327	0.0041	0.0724	–
Root Crops (Fiji lab, cool season)	0.0299	0.0043	0.01	0.0299	10.56
Fiji lab, warm season	0.0299	0.0050	0.01	0.0298	8.00
NZ lab, cool season	0.0060	0.0086	0.002	0.0189	–
NZ lab, warm season	0.0102	0.0100	0.002	0.0163	–
Fruits (Fiji lab, cool season)	0.004	0.0007	0.0013	0.004	0.735
Fiji lab, warm season	0.004	0.0007	0.0013	0.004	0.79
NZ lab, cool season	0.0008	0.0002	0.0003	0.0003	–
NZ lab, warm season	0.0003	0.0002	0.0003	0.0002	–
Legumes (Fiji lab, cool season	0.0003	0.0007	0.001	0.004	3.315
Fiji Lab, warm season	0.004	0.0007	0.001	0.004	2.207
NZ lab, cool season	0.0003	0.002	0.0003	0.0003	–
NZ lab, warm season	0.0003	0.0004	0.0003	0.0024	–
Vegetables (Fiji lab, cool season)	0.018	0.011	0.006	0.018	17.64
Fiji lab, warm season	0.018	0.0144	0.0016	0.018	18.97
NZ Lab, cool season	0.0096	0.004	0.001	0.0008	–
NZ lab, warm season	0.0312	0.0035	0.0012	0.0048	–

Zealand laboratory dramatically reduced the uncertainty in the mean concentration calculations, and therefore the exposure estimates, so that the exposures had a much lower and a smaller range (7–8 % of PTWI). For iron daily intake amounts were within the broad range of recommended daily intake.

The most challenging part of the process was determination of weekly exposures. Data were available from national Food Balance Sheets and a national survey of food frequency consumption. These were fairly accurate and in good agreement for imported foods and major crops. The consumption of "wild foods", which may be a significant part of a rural diet when the food is in season, was likely not captured. It will be useful to have data from a 24-h recall survey in which serving size has also been estimated. This study has been done, but the data are still being analyzed.

Conclusions and Recommendations

The successful conduct of Fiji TDS was a major accomplishment. It confirmed preliminary data that exposure to heavy metals and pesticides is not a population-wide health concern. However, some commonly used pesticides were not tested and there

are some vegetables on which these are used. The steering committee for the project has recommended for the future that chemicals of known health effects in Fiji, such as ciguatoxins, should be measured. The study of mycotoxins, which are likely to thrive in Fiji's hot, humid conditions, is another group of contaminants to be considered.

The absence of significant differences in samples collected from different parts of the island and during the wet and dry seasons suggests that the costs of these added collections are not justified for an island the size of Fiji. These resources might be spent on looking at foods important to different age groups, especially infant weaning foods. The availability of food consumption for different age groups, sexes and ethnicity would also allow for disaggregated analysis by these groups.

These data can also be put to use for other purposes. When the issue of possible calcium deficiency in Fiji diets arose, food consumption data were combined with calcium concentration estimates for each food group based on local food composition tables to get a rough estimate of total calcium intake, which was less than 50 % of recommended values.

Another possible extension of the TDS would be to include other island countries of similar climate and geography. The food contaminant data could be used in concert with local food consumption information to estimate weekly heavy metal exposures. Perhaps a few key local foods might be analyzed to help confirm the assumption that these will not vary too much from island to island. Another similarity is that the increasing amount of food is being imported, usually from the same source country.

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Chapter 28
The French Total Diet Studies

Véronique Sirot and Jean-Charles Leblanc

Introduction

French national authorities carry the responsibility for checking that chemical substances are not present in food in quantities that may adversely affect public health. While food control and monitoring programs are essential for the surveillance of production practices and imports, the government has also to assess the public health and consumer risks associated with the presence in food of additives, pesticide residues, environmental contaminants, and other substances of possible concern.

The French Agency for Food, Environmental and Occupational Health and Safety (ANSES) is a public, independent risk assessment agency contributing, through surveillance, monitoring, alerts, research, and investigations, to the protection and improvement of human health and safety in the fields of environment, occupational health, food safety, animal health and welfare, and plant health. While biological and chemical safety issues are major challenges, ANSES's jurisdiction also covers the risks relative to human nutrition and foods of animal origin. To evaluate health and nutritional risks via collective expert assessments, the ANSES conducts and coordinates national studies, like the total diet study (TDS) to assess the occurrence of chemicals of interest in foods as consumed in order to perform accurate dietary exposure estimates to those substances for different population groups. A TDS is a key tool for French population exposure monitoring and is based on a standardized methodology recommended by the World Health Organization (WHO), Food and Agriculture Organization of the United Nations (FAO) and the European Food Safety Authority (EFSA) [1], and is the method used in many

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countries to evaluate food safety risks. The use of the TDS also facilitates international comparisons of consumer exposures. Conducted in 2000–2001 by the French National Institute for Agronomical Research in collaboration with ANSES (previously AFSSA), the first French TDS assessed population exposures to 30 substances, including mycotoxins, trace elements and minerals. Five years later, ANSES began implementing a new study over the 2006–2010 period, extended to more than 400 substances requiring updated or in-depth knowledge, such as plant protection product residues, environmental contaminants, emerging hazards, natural toxins, additives, trace elements and minerals. A TDS for infants was launched in 2010 to provide dietary exposure of children less than 3 years of age to more than 200 substances (see below).

The advantage of a TDS analyzing foods "as consumed" is that it provides a more realistic "background" concentrations of chemicals in foods and the actual diet and "background" dietary exposure data than other more conservative methods that are generally used to prioritize substances for monitoring, like theoretical exposure indicators. TDS results help direct health protection measures and guide French authorities in charge of food safety risk management. This exposure evaluation is useful when drafting and making decisions on the regulation of chemical products and the safety of food products consumed by the nation's population. It is necessary that member states of the World Trade Organization base their consumer protection regulations on sound scientific assessment of the risks using this type of methodology. And last but not least, TDSs represent the most comprehensive and accurate tool for risk assessors to follow and evaluate trends in "background" levels in food and exposure in order to better protect and inform consumers.

A TDS Based on the Individual Food Item Approach

Among the key points of TDS methodology and design, the choice in food grouping remains of high interest. Two main trends are described in the international literature: the food group composite approach and the individual food approach [2]. The French TDSs are based on the individual food item approach rather than on the food group sampling approach [3–5]. Taking into account cost constraints, the second French TDS focused on 212 different individual core foods representing about 20,000 products and covering approximately 90 % of the total diets of adult and children. Choices were made not to sample foods that were consumed in very small amounts and that were not significant contributors to the exposure of contaminants of interest.

Moreover, each sample is a composite sample. In the French TDSs, each sample is a composite sample of subsamples of equal weight of the same food (5 in the first TDS, 15 in the second one and 12 in the infant TDS). This increase in the number of subsamples was done to ensure a better representativeness of the market shares of the products and the purchasing habits of the population, and to allow consideration of the interindividual variability of composition or contamination between

subsamples without losing too much information. The ideal number of subsamples was assessed considering a maximum confidence interval of 15–25 % for the mean composition or contamination results, taking into account a standard deviation of 30–50 % for each subsample, based on usual "background" data, including data from the first French TDS.

A Combination of Different Data Sources to Design the Sampling Plan

The French TDS sampling plans use three main data sources to select the core foods and to design the sample composition. The first source is the updated national individual food consumption survey conducted by the ANSES every 5 years. The most current is the second "Enquête Individuelle Nationale de Consommation Alimentaire" (INCA2 survey), which is the main information source on consumption [6–8]. The latest 11-month survey was conducted by ANSES in 2006–2007 with two independent random samples of 3–17 year-old children ($n=1,444$) and 18–79 year-old adults ($n=1,918$), representative of the French population through stratification. Population consumption data (kind of foods, quantities, as well as consumption frequencies) were collected by a 7-day food record diary (consecutive days), including other questionnaires on anthropometrical and socioeconomic factors. The food record included questions on consumption details and food preparation. For instance, subjects were asked if they consume raw meat, such as steak tartar and carpaccio, and for cooked meat, they were asked for the cooking degree (rare, medium, etc.) and the use of added fat. This kind of information is essential to prepare the samples "as consumed" by the population and to be representative of consumption habits. Other types of information were collected, including which brands and purchasing locations. For the infant TDS, consumption data used were completed by an online survey targeting about 400 parents who were asked for details on the preparation of foods for their children (cooking methods, times, utensil material and uses, etc.).

When data were insufficient to build a representative sample of a consumed food, another source of information was used in the TDS sampling plan, namely the SECODIP-TNS purchase panel. This is a panel of 17,150 French households, which are followed every year and provide supply habit data and market share information for more than 400 different product groups (unpublished data). This panel also provides details on the purchased food products, such as origin or species for fruits or vegetables, conditioning and packaging for commercially prepared products, flavoring if any, etc. All this information can be merged and included in the sampling plan in order to be as representative as possible of the consumption of the population, maintain the variability of dietary habits, and be as close as possible to the real French food supply diet.

A third information source can be used for homemade foods. Part of the French TDS samples includes commercial foods, bought ready-to-eat foods or

ready-to-cook foods. For some products, the final preparation methodology only involved following the packaging instructions. But some samples are partly composed of homemade foods, such as cakes, pies, or mixed dishes. For these types of foods, it is necessary to provide recipes taking into account home-cooking habits. Some recipes used for the nutritional evaluation conducted by the ANSES can be used, i.e. validated recipes from cookbooks, some being recipes from the INCA2 survey. To be concordant with other national activities involving risk assessment and nutritional evaluations, all the recipes have to be taken from the national food survey. More than 600 recipes had been updated or created by the Agency taking into account European recommendations, and have to be concordant with the composition of foods provided by the national food nutrient database [9] on one hand, and to be used for contaminant risk assessment on the other hand. As TDS is included in the general hazard and risk assessment area, the concordance of the methodologies and tools used in this field have to be improved and the use of this new database should be one of the key tools of future French TDSs in conjunction with the use of the updated third national individual food consumption survey (INCA3 survey) and also the updated purchase panel of French households providing food supply habits data and market shares.

National and Regional Considerations

The sampling of the second French TDS (2006–2010) was performed in eight large regions for two reasons. The first reason was the need to tie in with the national consumption survey, which is used to build the sampling plan and which provides the consumption data used for the exposure evaluation. In this survey, the subject samples, adults as well as children, were made representative of the French population through stratification, notably by including regions of residence, which were comprised of eight large regions, including areas [6–8].

The second reason was the need to take into account the specificity of each region in France. France is known for the diversity of its foods and diets and there are important regional variations in dietary habits. Dietary habits are region-dependent and highlight the intermediate geographical position of France in Europe, between Northern and Mediterranean diets [6]. Northern French inhabitants eat more butter, margarine, potatoes, and pastries than southern inhabitants, who eat more fruit and vegetables. Some food consumption patterns are typical of the identified region and have to be taken into account in the French TDS food sampling. Consequently the sampling plan was tailored for each region. If some foods are consumed in enough regions, they were included in the sampling lists as core foods.

Seasonal variation in consumption also appeared in the national consumption survey, as well as in the data from household supply. These trends were also taken into account in the sampling strategy with two sampling periods were conducted for each region. Each period lasted 3 months at the most and the starting dates of the

two periods were spaced at least 6 months apart. This option allowed taking into account seasonal purchases, such as certain fruit or vegetables, as well as meat cuts, and covered potential variability in the contamination and composition levels between seasons, for instance in mycotoxin or pesticide residue contamination. For each region, samples were therefore collected in summer and winter, or in autumn and springtime.

Another specificity, ethnic foods, may also be integrated in future TDSs as already occurs in Canada. Ethnic foods are not yet included in the sampling plan for two reasons. The first is that in the national food survey, ethnic foods are not well covered by the individual sampling because of a low yearly consumption, despite a large population of foreign origins. Most ethnic foods are still considered to be occasional foods and are not available everywhere, except in the capital and in big cities. The second reason is that the consumption survey did not include categories, such as 'halal' or 'kosher', if those interviewed did not raise it themselves. It was only recorded if the interviewed person chose its foods mainly or partly according to production methods or followed a particular regime for "personal or religious reasons". However, these were without any details on the precise religious or ethnic preferences.

Using the French TDS Results and Methodology to Perform Risk Assessment

The results of the French TDS are used in food safety risk assessment. At a local level, they are used by the interregional groups of epidemiologists to perform risk assessments when they confront by a problem, such as local pollution. The TDS results can also be used to evaluate the total exposure to a contaminant and provide background exposures through food to augment environmental and occupational exposure assessments.

At the national level, ANSES uses the TDS results to conduct population-based risk assessments and to help risk managers implement or update European or international/Codex food standards and improve their monitoring and sampling of chemicals in the food supply. In a first round, from the risk assessment performed by scientific experts committees of ANSES, main conclusions and formulated recommendations addressed particularly risk management challenges or research requirements. Out of the overall analyzed substances and on the basis of available knowledge, it was concluded that risk could not be excluded for certain specific consumer groups in the general population to 13 substances or substance groups (lead, cadmium, inorganic arsenic, aluminum, methylmercury, sodium, dioxins and PCBs, bisphenol A, deoxynivalenol and its derivatives, acrylamide, sulfites, and dimethoate) [10, 11]. In a second round, and following request mandates received from risk managers on specific safety situations, updated TDS data are often used by the ANSES scientific panels to take into account general "background" exposure

in risk evaluation and before proposing recommendations to risk managers to better protect consumers. For instance, the results concerning the arsenic exposure have been used in 2009 in an ANSES scientific opinion on the recommended maximum inorganic arsenic content of *Laminaria* and consumption of these seaweeds in light of their high iodine content [12]. It was necessary to assess the population's "background" exposure to inorganic arsenic to allow assessment of the risk associated with supplementary exposure from the consumption of seaweeds. At the national level, contamination data on inorganic arsenic were insufficient to perform the calculations. Data on inorganic arsenic from monitoring plans mainly concern seafood and the rest of the diet was not well covered. Therefore inorganic arsenic exposure through food was evaluated by considering the total arsenic exposure from the first French TDS results and applying contribution factors from a WHO evaluation. It was considered that in meats and dairy products, 75 % of the arsenic was inorganic, 65 % in poultry and cereals, 10 % in fruit, and 5 % in vegetables and seafood/fish [13]. This work highlighted the fact that, even if seaweed is not a major contributor to exposure of inorganic arsenic for French consumers, its contribution is in the same range as some food groups. Given seaweed is not a food group but a single food item, even its low contribution should be considered with caution. By providing an overview of the exposure through the whole diet, French TDS results were a good comparative support tool. As another example, the results of cadmium exposure were used in a 2011 opinion on the revision of maximum content for cadmium in foodstuffs intended for human consumption [14]. The results were used to assess the safety impact on the exposure of the French population of proposed maximum levels (MLs), following the 2009 lowering of the health-based guidance value by EFSA. According to the model results, the experts concluded that the MLs under discussion at European level as well as MLs established according to the ALARA (as low as reasonably achievable) principle would neither have a significant impact on mean levels of foods, nor on consumer exposure.

The TDS methodology is also used in more specific studies. For instance, the sampling methodology was applied to the Calipso study, which was a fish and seafood consumption study using biomarkers of exposure to trace elements, pollutants and omega-3 fatty acids [15–17]. Due to the lack of representative data in the national consumption survey, the individual food consumption survey focused on high percentile of seafood consumers and was the first conducted around four coastal regions in France involving about 1,000 consumers in order to base the TDS sampling on representative data [18]. After that, fish and other seafood samples were collected in order to assess the exposure through seafood consumption to some specific contaminants for which seafood are known to be high contributors, such as methylmercury, dioxins, polychlorinated biphenyls and cadmium [13, 15, 19]. Based on the first French TDS methodology, composite samples of up to 5 subsamples of 200 g of the same species were prepared. Several criteria were taken into account to build the sampling plan, such as quantities consumed by the studied population and consumption frequencies to select the specific food, but also

preservation and processing methods, if any (fresh, semi-fresh, frozen, canned, etc.), supply source (beach fishing, purchase on the fish dock, at the market, from a fishmonger, in another type of shop, or consumption outside the home), and geographical origin of product (preferably local, regional, etc.). This kind of study also stresses the importance of adapting the food sampling to the studied contaminants that are not ubiquitous. For instance, TDS was not really adapted to assess the exposure of the general population to methylmercury. Actually, it has been shown that food and especially fish provided more than 90 % of exposure to methylmercury. Indeed, the main contributors are predatory fish, which are not generally consumed in France in terms of quantity or consumer frequency. In the French TDS, it was then decided not to include them in the sampling plan. Therefore studies, such as the Calipso study, which focus on particular contaminants in specifically identified food types, can be a complementary method to the TDS in risk assessment and reinforces the importance of a standardized and transportable methodology.

As explained previously, another TDS is currently on-going at the national level for the 2010–2014 period. It consists of an infant TDS (children aged 0–3 years), focusing on infant foods, including infant formulae and ready-to-eat infant foods. The sampling plan aims to be representative of the purchasing habits of the parents and the market shares of the different products. Foods will be prepared as consumed by the infant population. While the infant TDS methodology differs slightly from the general population TDS, it had to be adapted to this specific population for these specific foods. For example, for several products, the sampling plan does not include composite samples of all the different available brands according to the market shares for a same core food, but separates individual food brands to take into account brand loyalty that is common for infant foods. Twelve samples of the same product and the same brand were bought (one per month during 1 year to take account of the seasonal variations) and mixed together in a composite sample.

A specific 2005 consumption survey on infants of 0–3 years old has been used, excluding breast-feeding children, to assess the exposure of this particular population. To take into account the product market shares of this particular and dynamic sector, data from a national purchase panel have also been used. This new study will also be an example of adaptation of the sampling strategy in that not only in situ additives, persistent organic pollutants, pesticides residues, acrylamide, traces elements and minerals will be analyzed, but also other chemical known as endocrine disruptors substances that migrate from food contact and cookware, such as inks, bisphenol A, phthalates and phenols. For that purpose, the sampling plan integrates information to take into account different home-cooking methods using different cookware known to be a source of contamination, and separates not only brands but also packaging types (cans, plastic boxes, jars, etc.).

In conclusion, the work completed in France over the 12 years since the implementation of the first French TDS shows how progress has been made to achieve a comprehensive overview of the occurrence of chemical in foods and the diet and "background" exposures to these chemicals based on TDS methodologies in order to better assess and manage food safety risks of public health importance.

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Chapter 29
Total Diet Studies in the Indian Context

Kalpagam Polasa and V. Sudershan Rao

Introduction

Indian dietary patterns are extremely varied and are a reflection of India's diverse cultural and regional preferences. Eating habits are closely identified with religious practices and traditional customs, but are also influenced by local agricultural practices and climate. India ranks second only to China among the world's most populous countries. Divided into 28 states and 7 union territories, India's people are culturally diverse with religion playing an important role in the life of the country. About 83 % of the people practice Hinduism, a religion that originated in India [1]. Another 12 % are Muslims, and millions of others are Christians, Sikhs, Buddhists, and Jains. For instance, some Jain communities do not kill life to feed themselves – including plants. This means they only consume fruits, milk and leaves.

The food habits of the one billion Indians also varies by the availability of raw materials, cooking traditions, and local spices. Rice and wheat are the primary bases for Indian food. People in coastal areas prepare seafood dishes, while people living in desert areas have mastered cooking with minimal use of water. Dietary practices in many parts of India are also adapted to suit occupation, health and physiological status and the amount of physical activity.

Presently India is in a phase of rapid demographic transition. A major feature of the developmental change in India is rapid urbanization and large shifts in population from rural to urban areas. Due to an increase in per capita availability of food,

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there are rapid quantitative and qualitative changes in food consumption. Food balance data from the Food and Agricultural Organization of the United Nations indicate that there have been large increases in consumption of animal products, sugars and fats [2].

Food Consumption Patterns in India

The National Nutrition Monitoring Bureau (NNMB) [3] set up in 1972 as an integral part of National Institute of Nutrition, periodically collects data on food consumption based on multi-clustered samples from ten selected states from different regions of India. The staple is cereals, which gives rise to rice-, wheat- and millet-based diets. Legumes are a major source of protein. Consumption of milk, milk products and other animal products has increased.

The NNMB Rural Survey 3 (2006) reported that cereals formed the bulk of the diets for the populations surveyed in ten states. The consumption of nuts and oil seeds (mainly coconuts) was high in Kerala State while the State of Gujarat had the highest milk consumption. The average daily consumption of cereals and millets was about 396 g per person and ranged from a low of 320 g in Kerala to a high of 477 g in the State of West Bengal. The average daily per capita consumption of pulses and legumes was low (28 g) in all the states and was about 70 % of the Recommended Daily Allowance (RDA) and ranged from a low 18 g in West Bengal to a maximum 37 g in Tamil Nadu and Karnataka. The average daily per capita consumption of green leafy vegetables (16 g) was much below the suggested levels of 40 g in all the states, except in Orissa (43 g) and West Bengal (41 g). Consumption was very low in the states Andhra Pradesh (6 g), Kerala (7 g), Karnataka (8 g) and Gujarat (9 g). The average daily per capita consumption of other vegetables among all states was 49 g, with consumption lowest (23 g) in Karnataka and highest (78 g) in Gujarat. The consumption of roots and tubers varied in different states: Maharashtra (20 g), Andhra Pradesh (34 g), Karnataka (40 g) and Tamil Nadu (41 g). The average daily per capita consumption of milk and milk products was about 82 g, with consumption lowest in the State of Orissa (14 g), followed by Madhya Pradesh (59 g) and Kerala (66 g). The average daily per capita consumption of fats and oils was about 14 g. The consumption of sugar and jaggery was lowest in Orissa (7 g) and highest (29 g) in Maharashtra. In Kerala, consumption of green leafy vegetables was lower whereas consumption of chicken/meat/fish was higher. Consumption of eggs and meat products is low in the north and east where poverty levels are high, as in the States of Bihar [4]. The overall consumption of fruits is also noticeably lower in the central and eastern regions [5]. Many people have a mixed diet – combination of various vegetarian and nonvegetarian foods. About 60 % of Indians are nonvegetarians. Consumption of nonvegetarian food was highest (90 %) in south India followed by east (70 %), north-east (60 %), west (60 %) and least in north (40 %) [6].

Background to Indian Total Diet Studies

On one hand, governmental public health agencies are deeply concerned with the diseases of malnutrition that accompany scarcity and poverty. However, they now have to deal with fast rising rates of chronic diseases due to changes in dietary habits among the more affluent as well as changes in other population groups due to changes in agricultural practices and urbanization [7]. There are other factors, which are likely to contribute to the emerging burden of chronic diseases in India. Contamination of food sources by pesticides, chemical fertilizers and toxic metals is common and results in increased risk of exposure to deleterious chemicals that adversely affect human health.

Food security is not only availability of food to people but ensuring that the food is safe and free of contaminants. Assuring the safety of the food supply is one of the essential public health functions of any country. As it is impossible to totally eliminate contaminants in the food supply, which pass through various stages in the food chain, it is prudent to periodically assess exposures from food in the manner they are normally consumed and compare these exposures with their corresponding health-based guidance values, such as the acceptable daily intake (ADI) or provisional tolerable weekly intake (PTWI). In this context, total diet studies are one of the most cost-effective methods for assessing the safety of the food supply from chemical hazards.

Food Consumption

On average, Indians gets 90 % of their calories from basic commodities like rice, wheat, pulses, etc., and only 10 % from secondary and tertiary processed foods. Therefore a major part of the diet is home-cooked food, prepared from raw and semi-processed foods. Typical food habits of Indians do not provide much scope for consumption of a large variety of foods thereby limiting the number of foods for consideration in a total diet study.

Another essential requirement for conducting the total diet study is the availability of food consumption data. In India the National Sample Survey Organization undertakes periodic food consumption surveys across the country. The data are expressed in terms of per capita consumption, which do not provide information on different age and sex cohorts. The National Nutrition Monitoring Bureau (NNMB) is another agency that performs diet surveys and reports food consumption data in selected states by different age groups and physiological strata. But the limitation of NNMB food consumption data is that it is carried out only in rural areas. There is no authentic data of food consumption from urban India.

Food Safety Act 2006

The Indian Parliament passed the Food Safety and Standards Bill in 2006 [8]. According to this bill, all food items used for human consumption will be regulated by one agency, with updated and upgraded methodology that will be in consonance with the regulations of Codex Alimentarius Commission. In Chapter II of the Act, it is documented that scientific panels are to advise the Central Advisory Committee on potential risks.

Panels on pesticide residues, contaminants in food chain, and biological hazards have been constituted. Their major aims are to collect data on food consumption to assess risk in individuals in relation to food, incidence and prevalence of biological risks, contaminants in food and identification of emerging risks. The panels also ensure prevention of unfair trade practices that may harm consumers, and to prevent unsafe, contaminated or substandard food from being sold. They also detect the ongoing use of those chemicals, especially pesticides, even after they have been banned, which is a regular feature in many developing countries. A national total diet study is required by the authority to ensure the safety of the overall diet.

Food Safety Issues in India

The food safety concerns in India are different from other countries due to the fact that dietary habits are so different. The foremost food safety concern among Indians is food adulteration [9]. The concern for contaminants like pesticide residues and toxic metals in food is a more recent phenomenon. The type of contaminants to be included in the total diet study depends on foods selected and the possibility of the particular contaminant being present in that food. For example, with the introduction of partially hydrogenated fats as a cheap substitute for clarified butter, the consumption of partially hydrogenated fats has gone up in India. With the emerging evidence that trans fats formed during hydrogenation are harmful to health, there is a need also to include these in total diet studies. Similarly acrylamide formed during roasting and deep-frying [10] is another contaminant that needs special attention in the Indian context, as most of the snack foods consumed in India are prepared from cereal-pulse combinations that are known to favor acrylamide formation.

Andhra Pradesh Total Diet Study

A total diet study (TDS) has been conducted in Andhra Pradesh State in South India [11]. Similarly, at least one state from southern region, north, east and west should be covered to generate national TDS data. For carrying out this TDS, the major food groups needed to be identified, including their form, e.g. primary / secondary /

Table 29.1 Calories of the food items in diet (as % of total calories) [12]

Food Item	Rural		Urban	
	1987–1988	1999–2000	1987–1988	1999–2000
Rice	38	40	31	30
Wheat	22	22	24	23
Other cereals	13	7	5	2
Total cereals	*73*	*68*	*60*	*56*
Pulses	4.6	4.4	5.4	5.2
Dairy	5.0	6.4	7.5	9.4
Edible oils	4.4	6.5	7.6	9.4
Meat/fish/eggs	.7	.8	1.0	1.2
Vegetables/fruit	4.0	5.9	5.7	7.2
Sugar/spices	5.8	5.9	7.2	7.2
Processed food	2.0	1.4	5.2	4.2
Beverages	0.1	0.2	0.3	0.4

Adapted from [12]

Table 29.2 Food groups in the total diet study in Andhra Pradesh, India

1. Cereals and millet	5. Fruits	9. Spices and condiments
2. Pulses	6. Milk and milk products	10. Oils and fats
3. Green leafy vegetables	7. Fish	11. Sugar and confectionary
4. Other vegetables	8. Other flesh foods	

tertiary processing. A recent estimate of calorie share of various food items in India indicates that about 90 % of calories come through primary processed food [12] (see Table 29.1 above).

Andhra Pradesh is the fifth largest state of India, and is often referred to as "*The Rice Bowl of India*". Rice is the staple food, which is consumed in a wide variety of ways. A typical meal consists of cooked rice, vegetable curry, dhal and curd or buttermilk. Although more than 90 % of population is nonvegetarian [6], rural areas are essentially vegetarian except in some coastal districts [11].

TDS sampling followed a stratified random sampling design to cover the entire state of Andhra Pradesh. The state was divided into three natural regions, i.e. Telangana, Andhra and Rayalaseema. From each of the regions, two districts were randomly selected and from each of the two districts, two mandals, i.e. districts, were randomly chosen. From each mandal, two market samples of each of the selected foods were collected along with two water samples. These samples belong to one of the TDS food groups listed in Table 29.2.

Four samples of each food from each district were collected. However, depending on the availability, the number varied. Thus a total of 503 samples were taken for analysis of contaminants. The contaminants, namely heavy metals (lead, cadmium), fluoride, mycotoxins (aflatoxin B_1, fumonisin B_1, aflatoxin M_1 and T2 toxin) and pesticides were analyzed in food samples that were highly likely to

Table 29.3 Food-contaminant combinations for analysis [12]

Food	Pesticides	Heavy metals	Mycotoxins	Fluoride
Rice	√	√		√
Sorghum (flour)		√	√	√
Red gram dhal	√	√		√
Groundnut oil	√	√	√	
Buffalo milk	√	√	√	
Butter milk	√	√	√	
Tomato	√	√		
Brinjal (eggplant)	√	√		
Onion		√		
Potato	√	√		
Mango	√	√		
Banana		√		
Amaranth	√	√		√
Spinach	√	√		√
Chilies, dry		√	√	
Tamarind		√		
Cane sugar		√		
Eggs		√		
Chicken		√		
Mutton		√		
Catla (fish)		√		
Water	√	√		√

contain the particular contaminant. From the above food lists, specific food-contaminant combinations that might result in high exposure were identified for analysis (Table 29.3) [11].

Twenty-two types of foods belonging to eleven food categories were selected for the study. The choice was made on the basis of most commonly consumed foods in Andhra Pradesh as indicated by 2006 NNMB report [3]. The food samples were prepared as they are normally consumed, that is "ready-to-eat", before they were analyzed.

Methods of Analysis

For pesticide analysis, the QuEChERS method was followed [13, 14]. It is an emerging sample preparation technique for multi-residue pesticide analysis of food and agricultural produce. Twelve food items were taken up for analysis. A total of 19 residues were detected by a gas chromatograph equipped with electron capture detector with a limit of quantification of 0.003 and 0.025 mg/kg for organochlorines/organophosphates and synthetic pyrethroids, respectively. Representative samples were analyzed by gas chromatograph-mass spectrometer for characterization and confirmation. The selection of these pesticides was made on their reported common occurrence in foods.

The mycotoxins, namely aflatoxins B_1, fumonisin B_1, aflatoxin M_1 and T2 toxin, were analyzed in sorghum, groundnut oil, red chilies and milk by a liquid chromatography method. The results indicated that levels of mycotoxins analyzed in selected food items were below detectable level (LOD$=0.5$ ppb for aflatoxin B_1, 0.01 ppb for aflatoxin M_1, 12.5 ppb for fumonisin B_1 and 5 ppb for T2 toxin) and significantly be low concentrations that would give rise to exposures apporaching tolerable levels.

Fluoride was measured using an ion-selective electrode [11].

Toxic metals, namely lead and cadmium, were analyzed in all 22 selected food items and water. The determination of lead and cadmium were performed by atomic absorption spectrometry using graphite furnace after passing through immunoaffinity column.

Calculation of the Estimated Dietary Exposures to Contaminants

To assess the actual exposure of the contaminant, amounts ingested by all cohorts were calculated. The mean concentrations of contaminants are expressed as μg per kg of food for all contaminants except fluoride where the concentrations were expressed as mg per kg. The concentrations of contaminants in each foodstuff were an average of values from all the 12 mandals. Contaminant exposures were further expressed for each of the cohorts by multiplying the concentration in each food with the amounts of each food consumed. The exposures were expressed as mg per kg of body weight per week for toxic metals and μg per kg body weight per day for other contaminants. The estimated dietary exposures were then compared with the corresponding international health-based guidance value, such as the ADI and PTWI. Mean contaminant concentrations were used in the exposure calculations as it provides an appropriate estimate of long-term exposure.

Dietary Exposure for Selected Cohorts

Dietary exposure to a specific contaminant is dependent on the quantity of food consumed, which varies with age and sex. In order to assess the risk at different quantities of food consumed, dietary exposures were based on the following age and sex cohorts: 1–3 years, 4–6 years, 7–9 years, 10–12 years, 13–15 years, 16–17 years, sedentary worker (male), and pregnant women.

Food Composites and Dietary Exposure Assessment

The amount of foodstuff ingested directly determines the amount of contaminant exposure. Therefore, a percent contribution of all the foods to particular contaminants was assessed. The commonly consumed foods in Andhra Pradesh are very

limited (22 in total, see Table 29.3) and have been individually analyzed, but considered as part of 11 food groupings for the purpose of exposure assessment. The cereal and millet food group was the major contributor of total DDT, aldrin, chlorpyriphos, cypermethrin, fluoride and cadmium in all cohorts. Milk and milk products were the major contributors of γ-hexachlorocyclohexane in children 4–6 years, 7–9 years and also pregnant women. Milk and milk products, and cereals and millet made equal contributions (32 % each) to the γ-hexachlorocyclohexane exposure in 10–12-year children. Groundnut oil and milk were the sole contributors of aflatoxin B_1 and aflatoxin M_1, respectively, to the diets of all cohorts. Most of the cadmium in pregnant women's diet comes from green leafy vegetables. Milk and milk products are major contributors to dietary lead.

For accurate dietary exposure of the contaminants, the concentration of a contaminant present in a cooked food with many ingredients was calculated from the individual foodstuffs with the added amount of a contaminant present in the water needed for cooking the particular mixed food. This gave the final exposure of the contaminant from the mixed food as a whole.

Lead

The present study reports the highest mean concentration of lead (74 µg/kg) in sorghum, followed by rice (54 µg/kg), unlike fruits and green vegetables which had the highest levels in Egyptian foods [15] and in cereals, nonalcoholic beverages and sugars in French foods [16]. However in one mandal, namely Gangadhara of Kareemnagar districts, cane sugar was observed to have the highest lead level (165 µg/kg). More than 80 % of samples of red gram dhal, eggs, chicken, mutton, groundnut oil, red chilies and water had no detectable lead (limit of detection 1 µg/ kg).

In this study for average consumption levels, children in the age group of 1–3 years had the highest exposure (8.3 % of the PTWI) and the age group 13–15 years had the lowest (2.7 % of the PTWI). However, it is noted that JECFA has withdrawn the PTWI for lead.

Cadmium

Green leafy vegetables (amaranth) showed highest mean cadmium concentrations of 10 µg/kg when compared to other foods that were analyzed. Green leaves were followed by red chilies, which had concentrations of 4.6 µg/kg. Similar results were reported in the Egyptian total diet study [15], whereas, in the UK, the highest cadmium concentrations were found in offal (84 µg/kg) and nuts (60 µg/kg) [17] and in France, in offal (52 µg/kg) and shellfish (83 µg/kg) [16].

In Andhra Pradesh, more than 80 % of spinach and amaranth samples were contaminated with cadmium, with up to 227 and 82 µg/kg, respectively. Chicken samples

procured from Ramavaram mandal of East Godavari and red chilies from Dakkili, showed high concentrations of cadmium, with 69.4 and 58.8 µg/kg, respectively. The reasons for these high concentrations of cadmium need further investigation. The 4–6-year-old age group had the lowest level of cadmium exposure of 0.11 µg/kg bw/day (11 % of PTWI). This is unlike the UK, where the highest exposure was seen in 1–4-year-olds. A Canadian study had an average exposure higher than the Andhra Pradesh population, being 0.21 µg of cadmium/kg bw/day [18]. In the French TDS, the 97.5th percentile exposure in adults aged >15years was 0.7 µg/kg bw/wk (10 % PTWI) whereas, it was 1.2 µg/kg bw/day for children aged 3–15 years, with leafy vegetables and starchy foods contributing the most [19]. Amaranth is the highest contributor for cadmium in the diet in this study.

Among all the food items, the maximum contributor for toxic metal consumption seemed to be leafy vegetables. In a study conducted in Delhi, it was revealed that spinach had more than 5 mg/kg of lead and more than 0.2 mg/kg of cadmium [20] with the high concentrations reported in the study possibly attributed to highly contaminated water. Another study from Bangalore showed that 4 mg/kg of cadmium was detected in spinach [21]. A study conducted in the suburban areas of Varanasi showed that cadmium and lead in spinach exceeded the safety limits, cadmium being highest in summer season and lead being high in both summer and winter seasons [22].

Fluoride

Fluorosis is caused by excessive exposure to fluoride through food and water. In food, the fluoride may be organically bound or inorganic. Toxicity of the inorganic form is much greater than the organic form. In water most of the fluoride present is inorganic, thus making it more harmful than dietary fluoride. Fluoride content is higher in plants and vegetables grown in soil and irrigated with water having high levels of fluoride.

On an average, exposure to fluoride from food ranges from 2 to 8 mg per day, depending on type of food consumed. However fluoride exposures higher than 6 mg/day increase the risk of bone effects and skeletal fluorosis results when the exposure is more than 14 mg/day [23].

In India, 50–100 % of districts in Andhra Pradesh, Tamil Nadu, Uttar Pradesh, Gujarat & Rajasthan, 30–50 % districts in Bihar, Haryana, Karnataka, Maharashtra, Madhya Pradesh, Punjab, Orissa and West Bengal and less than 30 % of districts in Jammu & Kashmir, Delhi and Kerala are affected by various degrees of fluoride toxicity [22]. According to WHO, 1.5 mg per liter is the safe limit of fluoride in drinking water for human consumption. However, several populations consume water and food with higher levels of fluoride. In Rajasthan, people consume water with fluoride levels up to 24 mg/l. In a study conducted in Nalgonda district of Andhra Pradesh, they reported the dietary exposure to fluoride through food and water as 2.2 mg/day in unaffected villages compared to 15.5 mg/day in fluorosis-affected areas [24].

In this study, fluoride was analyzed for five foods, namely sorghum, red gram dhal, amaranth, spinach and water. Among the food items, sorghum had the highest concentration of fluoride of 0.29 mg/kg. However the exposure values reported in the present study are much lower than those earlier reported [23].

Mycotoxins

Among the most commonly consumed foods that were selected for this study, groundnuts, red chilies and sorghum were found to be most susceptible for aflatoxin B_1 contamination and milk for aflatoxin M_1. Sorghum, in addition to aflatoxin B_1, may also be contaminated with fumonisin and T2 toxin. All the samples of groundnut oil, 18 out of 22 chili, 17 out of 20 sorghum were contaminated with aflatoxin B_1 at levels ranging from 0.33 to 50 µg/kg, 0.1 to 25 µg/kg, 0.1 to 1.2 µg/kg, respectively. Samples drawn from Dakkili, Nellore district had the highest concentration (50 µg/kg). A total of 24 buffalo milk samples were analyzed for aflatoxin M_1. Thirteen samples out of 24 had detectable levels of aflatoxin M_1, with a range from 0.007 to 0.09 µg/L. Out of the three food types which showed the presence of aflatoxin B_1, groundnut oil samples contained the highest concentrations whereas sorghum showed the least. This reduction could be due to the cooking procedure. None of the samples of sorghum were positive for fumonisin B_1, while 11 were positive for T2 toxin. The values ranged from 1.38 to 26.0 µg/kg [11].

Dietary exposure of aflatoxin B_1 ranged from 0.08 µg/kg bw/day in 1–3 years to 0.27 µg/kg bw/day in the age group of 16–17 years. Aflatoxin M_1 exposures ranged from 0.002 to 0.004 µg/kg bw/day. Similarly, the exposure to T2 toxin varied from 0.034 µg/kg bw/day (2–4 years) to 0.17 µg/kg bw/day (13–15 years). Earlier studies carried out in India showed that the exposure to aflatoxins was in the range of 0.25–78 µg/kg bw/day [25, 26]. Aflatoxins, being genotoxic carcinogens, do not have ADIs and it has been advised that levels in food should be reduced to as low as reasonably achievable, taking into account the availability of food [25, 27].

Pesticides

Among the eight cohorts, children of 1–3 years and 4–6 years were most at risk to aldrin, with exposures being 6 % and 4 % of ADIs, respectively. This was mainly due to their high consumption of rice and milk. Dietary exposure to total DDT was far less than the TDI in all the age groups, ranging from 0.01 % to 0.03 % of TDI. These values are far less than the average value of 0.4 % of TDI found in Canadian TDS during 1998 [18]. Also the exposures to γ-hexachlorocyclohexane and chlorpyriphos were 0.13 % and 0.08 % respectively in Canadian population during the same period, while exposures in Indian populations ranged from 0.003 % to 0.1 % ADI and 0.02 %,

respectively. However, it should be noted that meat and fish were not analyzed for pesticides where high levels of fat soluble pesticides, like aldrin, DDT, and γ-hexachlorocyclohexane, are often present.

Conclusions

The results of the total diet study reveal that the dietary exposures of contaminants investigated are generally much lower than the health-based guidance values for all the age groups with average consumption. In specific cases, where the concentrations of contaminants were high or where the consumption of a particular food was high, the risk for toxicity may be higher. At maximum food consumption levels in certain cohorts, exposure to contaminants, like cadmium, significantly exceeded safe or tolerable limits.

Risk assessment in vulnerable populations, like pregnant women, should be undertaken accurately, as even the lowest concentration of certain persistent organic pollutants may cause harm to the developing fetus or lead to adverse health outcomes later in life. Total diet studies are useful tools for assessing exposure to toxic chemicals in the diet and should be expanded to include other states in India.

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Chapter 30
Experiences in Total Diet Studies in Indonesia

Roy A. Sparringa, Winiati P. Rahayu, and Rina Puspitasari

Introduction

The National Agency for Drug and Food Control (NADFC), Republic of Indonesia, is responsible for the main food safety program associated with the Government Regulation on Food Safety, Quality, and Nutrition of Indonesia No. 28/2004. Several ministries, agencies and district governments share the authority for food safety control along the entire food chain from farm to table. The NADFC monitors and controls commercial foods on a regular basis as to whether or not they comply with limits set in the regulations and based on risk analysis principles in its food control program.

Risk assessment is essential in making effective scientific-based risk management decisions. However, exposure assessment of toxic chemicals in Indonesia has thus far not been part of the process in producing scientific data in chemical risk assessment. Therefore, the NADFC has been developing some pilot exposure assessment programs and related activities in preparation for a national total diet study (TDS) and to identify potential constraints which might exist in the implementation of a TDS, so that appropriate strategies and approaches to solving them could be determined.

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Challenges in the Indonesian Total Diet Study

The approach used by a country in undertaking a TDS should be in line with national concerns as well as those raised globally by the Codex Alimentarius Commission and GEMS/Food [1]. Dietary exposure assessment in Indonesia, as a developing country, is inadequate and challenged by a number of factors, such as a lack of databases required, infrastructure, resources, expertise, and experience. These challenges need to be addressed before implementing a national TDS in Indonesia [2].

Indonesia has more than 230 million people of diverse ethnic groupings living among thousands of islands, so the scope and coverage of food safety control in Indonesia is a very large challenge. Food consumption patterns are quite variable and may vary by age, sex, ethnic group, or availability and cost of the food. Besides food consumption habits, Indonesian society also has considerable variety in food recipes and preparation as well as cooking methods.

The accuracy of total diet studies relies on two fundamental data components: the quantity of each prepared food consumed by individuals, usually collected in national surveys, and the background concentrations of chemicals in the foods as ready for consumption. Estimates of the individual daily intake of food additives should only be undertaken when representative national dietary surveys are available [3]. Unfortunately, food consumption data based on individual dietary surveys are lacking in Indonesia. Therefore, Indonesia needs both individual food consumption data and chemical concentration data for the diets consumed by its population.

Foods usually consumed by Indonesians vary depending on ethnic groups and geographical distribution of the population and are characterized by different eating habits, recipes or food composition. The foods could be processed or prepared foods and distributed nationally and/or regionally. These factors make determination of a food list and shopping list for the Indonesia TDS more complicated and therefore a regional or cluster approach was developed [4].

Implementation of a national TDS should also be supported by facilities, such as a food preparation kitchen and laboratories for sample analysis. Indonesia is a large archipelago state with 34 provinces, so both its demography and geography present a challenge in implementing a national TDS. Kitchen and laboratory facilities will need to be well managed. For Indonesia, these facilities are available at the central as well as regional levels. Furthermore, implementation of a national TDS relies on competent staff with sufficient knowledge, and skills to conduct a TDS.

Development of Total Diet Studies in Indonesia

A step-by-step approach for the implementation of the national TDS in Indonesia has been carried out. This includes a number of pilot studies, such as development of exposure assessments of food additives based on maximum limits in 2002;

exposure assessment of primary school students in Malang to food additives with a TDS approach in 2002–2003; a pilot project for an integrated individual dietary intake survey for the purposes of exposure assessment and nutrition in 2003–2004; technical meetings, seminars, workshops on TDSs and implementation of a TDS in Indonesia, from 2004 through 2006; assessment of food consumption cluster diets in 2007; and exposure assessment of primary school students to cyclamate with a TDS in Surabaya during 2006–2007. Chemical risk assessment of heavy metals in fishery products consumed by vulnerable groups in Bandung, Semarang, and Mataram cities was undertaken in 2008–2009. Some of these experiences in conducting pilot exposure assessments are summarized below.

Exposure to Food Additives Based on Maximum Limits

A preliminary study of exposure assessment to food additives was conducted by the NADFC from October to December 2002 with the support of International Life Sciences Institute (ILSI) Southeast Asian Region. The objective of the study was to develop a self-assessment method using individual dietary records of food intake. There were 192 respondents from 15 provinces in Indonesia involved in the assessment. The food consumption survey was carried out using the 24-h food diary method while food additive concentrations were assumed based on maximum national limits. The result of this study showed the average intake of benzoate was 0.96 mg/kg body weight/day, which was 19 % Acceptable Daily Intake (ADI) established by the Joint FAO/WHO Expert Committee on Food Additives (JECFA). For the high (95th percentile) consumer, the exposure was 3.08 mg/kg body weight/day. It was also reported that the average intake of benzoate for the high consumers of young children (2–12 years) almost exceeded the ADI (5 mg/kg body weight/day) [5]. It was concluded that the self-assessment of food consumption could be applied in a broader survey.

Exposure Assessment of Cyclamate, Saccharin, and Benzoates Using a Total Diet Study Approach

The NADFC has regularly reported that foods sold in school areas by street food vendors across Indonesia contain artificial additives, such as sweeteners and preservative agents. However, it was not known whether or not these two classes of additives exceed their corresponding ADI levels. As young children are thought to be more susceptible to toxicological risk related to food additives, the NADFC extended its efforts to develop its exposure assessment of food additives by including cyclamate, saccharin, and benzoates in a total diet approach. It involved primary school students in Malang, East Java, Indonesia as respondents in a pilot project, which was conducted from December 2002 until December 2003 [6].

The objective of the study was to estimate the daily intake of various types of food products; to obtain basic data for the market-basket based study (total diet study); and to assess if the intake of cyclamate, saccharin, and benzoate by primary school children may be exceeding their respective ADIs. The outcome of this study was not only used as a model for the safety evaluation of food additives and toxic chemicals, but also as a model for the national TDS.

Seventy-two respondents who were 6–12-year-old male and female children were randomly selected from three primary schools representing low, middle, and high social-class schools in Malang, East Java, Indonesia. Each respondent was surveyed for his/her food intakes over six successive days. Food diary and dietary recall approaches were used to determine individual food consumption. The enumerator validated the respondent's record, which was combined with dietary recall by respondents during the interview. The interviews were conducted twice a day, before and after school, to obtain a 24-h individual intake record. The shopping list generated from the consumption data was utilized for a developing the market basket of food, which reflected the total diet of the consumers in the study.

For the analysis of samples, the food composite approach was used, in which individual food items were combined to represent groups of similar foods. One hundred and ninety seven food items were recorded in the consumption data and 81 food items were sampled and analyzed in the study. These accounted for 95 % of the total food intake by weight and consisted of 31 national food items, 6 local food items, 9 unregistered food items and 35 ready-to-eat food items. Ready-to-eat (RTE) foods were the highest contribution (70 %) of the total weight intake, and were dominated by the cereals food group, which accounted for 33 % of RTE foods consumed.

The average estimated intakes of cyclamate were about 240 % of the JECFA ADI, with main contributors being beverages and cereal-based snack foods. The daily intake of saccharin and benzoate was estimated to be about 12 % and 74 % of the JECFA ADIs, respectively [7–9]. It was suggested that an intervention for reducing cyclamate intakes among primary school children should be undertaken by the school community through school food safety programs and should involve the school commission, teachers, students, parents, food vendors, and the school canteen.

Exposure Assessment of Cyclamate Using a Total Diet Study

Given the previous findings among school children in Malang, cyclamate was considered as important additive to be assessed further. A similar study on exposure assessment of cyclamate was conducted in 2006–2007 and involved 716 respondents aged 6–12 years old in 30 primary schools but this time in Surabaya, East Java, Indonesia. Food consumption data was obtained by individual dietary intake survey using a food frequency questionnaire (FFQ). The food list in the FFQ was developed from a pre-survey using 24-h dietary recall data combined with data from food

diaries covering 3 consecutive days. The average estimated cyclamate exposure in this study was 260 % of the JECFA ADI. The important finding in the study was the excessive levels of cyclamate found in the foods consumed, which were well above the standards set for addition sweeteners to those foods. Using permitted maximum levels [10], the average estimated cyclamate exposure should have been only 27 % of JECFA ADI, and about 90 % of JECFA ADI for the highest consumer [11].

Lessons Learnt from the Experience

Indonesia has been learning some important technical and management lessons during the pilot projects undertaken as well as other preparation activities. Some important technical aspects needing attention are the validation of TDS procedures, method validation for food chemical analyses, pretesting of analytical systems, the sampling framework, food recipe and composition database, technical aspects in sample preparation, i.e. cooking, and especially laboratory proficiency testing.

Validation of procedures in TDS is important and includes testing the appropriateness of methods to be used, whether all preparation for TDS works well, and to identify potential problems that may need corrective action or improvement. As Indonesia's demography and food consumption patterns and habits are quite diverse, it may require a specific approach or adjustment in every region or cluster. However, the validation might best be conducted in only a selected site in each cluster or region to optimize project time and resources.

Selection of the location of survey and its supporting facilities as well as sampling points are an important step in establishing the sampling framework, as it will greatly influence sampling activity. Results of previous dietary intake surveys can be very useful to help shape a sampling plan. Food consumption cluster data is important to optimize the food purchasing and preparation of food samples. Cluster zoning is a possible approach to determine the best locations for sampling in a national TDS in Indonesia. It will also influence the selection and establishment of preparation and cooking facilities in each cluster because the sample would be prepared or cooked at the district level and composited at the central or national level.

Indonesia also should take into account the availability and variety of samples that must be collected in the market. Hence, it might need to include questions of where and how respondents obtain the food they usually consume. A database of food recipes or composition, especially for local or regional foods, should be available to develop a comprehensive food list and sampling protocol. For example, the food named "soto" (kind of clear soup) in Jakarta (*soto Betawi*) is very different in composition with "soto" in East Java (*soto Madura*). The local name of food should be defined along with its regional or national name so that food sampling in the market would be easier and accurate. For example, the food namely "utri" in Jakarta has same composition with "lemet" in West Java. Cooking methods are also

important information that should be gathered during consumption surveys. For example, rice cakes "lontong" and "arem-arem" have different cooking methods – "lontong" is made from uncooked rice (*beras*) without filling then steamed, while "arem-arem" is made from rice (*nasi*) with vegetable filling then steamed.

Food preparation facilities, including equipment and utensils, should be such that external contamination to the sample can be minimized. Laboratory proficiency testing is also important to check the competency of laboratories to measure chemicals at the low levels required by TDS criteria.

Future Preparation for the National Total Diet Study

The need for monitoring chemicals in the food supply is essential as consumers and regulators need to know what risks are posed by toxic chemicals and nutritional imbalances in foods consumed. Accurate information on people's actual total dietary exposure to chemicals is essential for risk assessment and can also be used in determining whether there may be a relationship between observed adverse effects in humans and exposure to a particular chemical. Indonesia therefore needs a TDS because it is an important basic activity that can reflect food safety status in a country, show trends and serve as basis for assessing the effectiveness of food safety control measures. Outputs from a TDS provide solid scientific data and information which can be used in developing national food safety programs, prevention and control, public health and nutrition programs, food safety regulations as well as standards, food safety intervention program priorities, targeted survey and monitoring programs, and as a contribution to international food safety programs, i.e. the Codex Alimentarius Commission and GEMS/Food.

A master plan for a national TDS should be developed and take into consideration Indonesia's needs and specific characteristics. A logical and proper framework for the national TDS program should be established to focus on the overall goal, the objectives and targeted outputs of the food safety program. Hence, advocacy of key stakeholders and appropriate policy makers should be organized to raise their awareness to the importance of a TDS and their support in setting priorities in the TDS.

Achieving a national TDS in Indonesia will require resources, expertise, and capacities from all involved ministries and agencies in a spirit of partnership throughout the planning and implementation process. A strong commitment by each organization is an imperative to make an effective TDS a reality, as each has specific strengths and roles. This will also minimize overlap or avoid gaps in TDS implementation [12]. The proposed steering committee for the management of a national TDS in Indonesia would be led by the Ministry of Health with the technical team consisting of relevant authorities in nutrient and food safety programs in Indonesia as well as other experts. Table 30.1 describes the proposed partners and their roles in a national TDS in more detail.

Table 30.1 Proposed management of a national total diet study program in Indonesia

Institution	Role/tasks
Ministry of Health (MoH)	Coordinator of National TDS Program, coordinator of nutrients assessment, management and processing of food consumption data, analysis of nutrients in ready-to-serve and processed foods
National Agency of Drug and Food Control (NADFC)	Coordinator of exposure assessment, coordinator of food sampling, analysis of food additives and contaminants in processed foods
Ministry of Agriculture (MoA)	Analysis of contaminants in fresh foods and ready-to-eat foods rather than processed foods, except the fish and seafood groups
Ministry of Fisheries and Marine Affairs	Similar to MoA but limited to the category of fish and seafood
Local governments (provincial/district/city level)	Food sampling
BPS-Statistics Indonesia	Support food consumption and TDS data analysis
National Food Safety Network	Coordinator of peer reviewer group including experts and resource persons in related fields, i.e. universities, research institutes, and competent authorities in health and food safety. The team will also facilitate data analysis and TDS results interpretation as well as develop recommendations to be followed up by relevant institutions based on the risk analysis framework

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Chapter 31
Total Diet Studies in Japan

**Fujio Kayama, Hiroshi Nitta, Satoshi Nakai, Satoshi Sasaki,
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Introduction

Two methods exist for directly assessing exposure to chemicals in food as consumed, namely by the total diet method and duplicate diet method. A total diet study (TDS) is suitable for assessment of contaminants and other chemical in populations, especially where individual food consumption data are available. Such data are useful for identifying high-risk populations and for risk management and surveillance planning. On the other hand, duplicate diet methods are less expensive and yield quicker results. While they include factors of real cooking and more precise portion size of the meals, the results of duplicate diet studies are often limited to the local area and cannot be used to estimate exposure of sex and age groups. The TDS based on market

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basket samples is greatly dependent both on surveillance data of contaminants in foods and food consumption data. In Japan, food consumption data used in the TDS have been obtained from the annual National Nutrition Survey (NNS).

National Nutrition Survey

After World War II, food shortages in Japan were very serious. General Headquarters of the Allied Powers conducted the first NNS in Japan in 1945 to assess the need for food aid from overseas. Food consumption of 6,000 families in Tokyo was monitored in December 1945. The purpose of the survey was to improve the management of the food supply to solve food shortages in the upheaval of the postwar period. In 1946, the survey was expanded to include 9 cities, 27 prefectures, and 4 mining areas. In 1948, a nationwide survey was conducted with study areas selected on the basis of a population-weighted random sampling method. The survey was modified in 1952 based on the Nutrition Improvement Law. Due to the rapid recovery of the Japanese economy, the new survey parameters, such as smoking, drinking and exercise habits, were added to the questionnaire.

Current NSS in Japan is conducted in November each year. First, 300 study areas are selected randomly and then 6,000 families or 20,000 individuals in the areas are asked to participate the survey. Participants of NSS are asked how much food was consumed on a certain day in November by the family and are requested to fill out an allocation table of food items consumed by each family member. A food composition table is used to calculate the intake amounts of energy and nutrients recorded on the sheets.

Method of Total Diet Study in Japan

The Ministry of Health, Labor, and Welfare (MHLW) has conducted total diet studies in Japan annually since 1977. Based on the methods of the Global Environmental Monitoring System/Food Contamination Monitoring and Assessment Programme (GEMS/Food), the TDS is used to estimate average Japanese dietary exposure to heavy metals and various chemical substances, such as pesticides, dioxins, food additives, and other potentially hazardous chemicals. The Division of Foods under the National Institute of Health Sciences (NIHS) in Tokyo orchestrates TDS in Japan. Twelve survey districts for the TDS are selected based on a population-size-weighed random sampling method. Food items are categorized into 14 groups (see Table 31.1). Samples of between 100 and 120 different food items are purchased at local markets in each sampling site and prepared as for consumption, i.e. 'as consumed'. Composite samples for each food category are prepared in proportion to regional food frequency questionnaire data collected during the NNS. The composite samples are sent to NIHS where concentrations of contaminants in the samples are measured.

Table 31.1 Food categories for Japanese total diet study

Category	Food items
1	Rice and processed rice products
2	Wheat, barley, rye, buckwheat and other cereals
3	Sugar and sweets, confectionary products
4	Oil and fats
5	Beans and bean products
6	Fruit
7	Green and yellow vegetables
8	Other vegetables and seaweed
9	Seasoning and condiments
10	Fish
11	Meat and eggs
12	Milk and dairy products
13	Processed foods
14	Water

The chemicals analyzed at NIHS are pesticides, including three isomers of hexachlorohexanes, four DDT analogues, three organophosphates, three other organochlorines and certain polychlorinated biphenyls (PCBs), and seven metals, namely cadmium, mercury, arsenic, lead, copper, manganese, and zinc. These are measured in 13 composite food samples from each sampling location.

Strengths and Limitations of the Current Total Diet Study

Food consumption data derived from the NNS conducted on one day in November annually consists of food items (1,194 food codes) and weights of each food ingredients collected from approximately 5,000 families, randomly sampled in all over the nation. The number of individuals included in the NNS is approximately 13,000 annually. Individual physical data, such as height and weight, physical activities and ratio of food consumption relative to the family members have been collected since 1995. This modification of the NNS enabled food consumption estimates to be made for 10 sex-age groups. Note that data on intakes by pregnant women were excluded to improve the precision of these estimates.

There are several limitations in using the current NNS data for TDS. Because the survey is based on 1-day study in November, it is impossible to evaluate seasonal changes of food items and individual daily variations of food intake. It is also impossible to evaluate intake assessment of sensitive subpopulations or high-risk groups. The family-based NNS has only limited information on dining-out as well as on composite and processed foods.

To partially address these limitations, NNS data covering several years are compiled for use of TDS exposure assessments of contaminants, such as cadmium, dioxins and dioxin-like PCBs and pesticide residues. Epidemiological studies

among high-risk subpopulations have been conducted in the several areas of Japan. At the same time, 150 pesticides were monitored in food for preparation before adopting a positive list system of residual pesticides in food in 2006.

Heavy and Other Metal Exposures from the Nationwide TDS

The average exposure to heavy metals, such as mercury, cadmium, lead and arsenic, was calculated based on the analysis of stored composite samples from the 2000, 2002, and 2004 TDSs [1]. The average intake of total mercury in the three TDSs was 8.9 µg/day, ranging 7.3–10.5 µg/day, which corresponds approximately to 38–55 % of PTWI. Exposure to total mercury was derived mainly from fish (Group 10) and rice (Group 1), but it should be noted that rice contains mainly inorganic mercury, as reported in early GEMS/Food data.

Average cadmium exposure ranged from 32.4 to 48.2 µg/day; the average is 42.0 µg/day; this corresponded to 65–96 % of PTWI. Cadmium exposure was derived from almost all the food categories. Cadmium intakes from rice (Group 1) and Groups 8 and 10 were fairly high. Average exposure from Group 1 was 0.033 mg/ day.

Average lead exposure ranged from 33.8 to 50.3 µg/day, which were 19–28 % of former PTWI (now withdrawn), and the average was 42.5 µg/day, lead from rice consist 50–60 % of total intake. Arsenic exposure ranged from 181 up to 350 µg/ day, equivalent to 7–15 % of former PTWI (now withdrawn), with an average of 243 µg/day. Arsenic is found in seafood, including seaweeds and fish and shellfish, with the major sources of arsenic were mainly from Groups 8 and 10.

Judging from longitudinal study of total diet study [2], cadmium exposures calculated from the data showed no changes in the last decade. In 2004, average cadmium exposure was 21.4 µg/day or 46 % of PTWI. Total mercury exposure is 8.5 µg/day is more than 50 % of the current PTWI of 1.6 µg/kg bw/week for methyl mercury. Arsenic exposure is high among the Japanese due to their higher intakes of marine products. However, there are some technical issues in extraction and measurement of chemical forms of organic arsenic in various food matrixes.

Arsenic Intake from Algae

Arsenic is ubiquitous in soil and sea sediments. It accumulates in food in varied concentrations and in several chemical forms. The most important from a toxicological point of view is inorganic arsenic compounds, such as arsenic trioxide, sodium arsenite, arsenic trichloride (i.e. trivalent forms), arsenic pentoxide, arsenic acid and arsenites (i.e. pentavalent forms). But marine organisms are well adapted to tolerate the metal and to accumulate arsenic as organic compounds. The major organic arsenic compounds are arsenobetaine, a water-soluble arsenical found in most of seafood, such as fish and shrimps. In contrast, the major organic arsenic

compounds in algae are arsenosugars. These organic arsenic compounds are less toxic than inorganic arsenic compounds. For risk assessment purposes, it is very important to collect concentration data on both organic and inorganic forms. Total diet studies provide very important information on total arsenic and inorganic arsenic exposures for risk assessment.

The Japanese people consume several kinds of edible species of algae such as "nori" or *Porphyra*, including most notably *P. yezoensis* and *P. tenera*, "kombu" or *Saccharina japonica* (*Laminaria japonica*), "wakame" or *Undaria pinnatifida*, "hijiki" or *Hizikia fusiforme,* and "mozuku" or *Cladosiphon okamuranus*. Most of these species contain arsenosugars, which are recognized as essentially nontoxic. But hijiki contains inorganic arsenic and is consumed regularly in Japanese dishes. This raised a question about whether dietary intake of hijiki is safe or not.

Matsuda and Watanabe [2, 3] reported the monitoring data of arsenic contents in three food groups as major sources of arsenic exposure in the Japanese diet. They are rice (Group 1) and composite samples of vegetables and seaweed (Group 8) and fish, cephalopods, and shellfish (Group 10). The 10 rice samples, collected from 10 districts all over Japan, were cooked and homogenized by food processors. The composite samples from the 10 different districts were used for determination of arsenic contents. Trivalent and pentavalent inorganic arsenic concentrations in the samples were determined by high performance liquid chromatography with inductively coupled plasma mass spectrometry (HPLC-ICPMS) by the method of Hamano-Nagaoka et al. [3, 4] Total arsenic contents were measured by atomic absorption spectrophotometry. Total and inorganic arsenic exposure was assessed by multiplication of the concentrations and food consumption data from NNS.

The results of the study revealed that total arsenic exposure was 245.7 μg/day, when zero was applied for non-detected (ND) samples, or 248.2 μg/day, when half the limit of quantification (LOQ) was used for ND samples. Inorganic arsenic intake was 15.7 μg/day (ND=0), and 30.4 μg/day (ND=½ LOQ). When units are converted using 50 kg for the average body weight, these values for inorganic arsenic were 14.7 % or 28.4 % of withdrawn PTWI. Contributions to total arsenic exposure from Groups 1, 8, and 10 were 6 %, 31 % and 59 %, respectively. On the other hand, inorganic arsenic exposure from Group 1, 8, and 10 were 42 %, 58 %, and 0 % (when ND=0), or 37 %, 47 %, and 16 % (when ND=½ LOQ). Even though the exposure is lower than the withdrawn PTWI, inorganic arsenic exposure from rice, as a staple food, is unexpectedly high, and dietary habit of eating certain algae elevates inorganic arsenic exposure in the Japanese diet.

Probabilistic Exposure Assessment on Cadmium Among Japanese by Monte Carlo Simulation

In 2005, the MHLW commissioned a probabilistic assessment of cadmium intake among the Japanese population. Datasets of cadmium concentrations in food were converted from surveillance data of cadmium in agricultural and fishery products
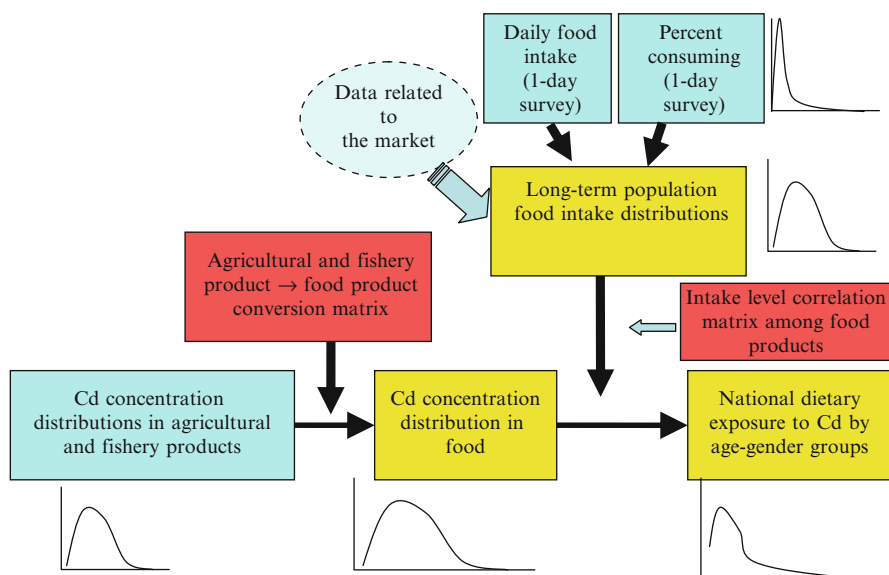
Fig. 31.1 Outline of the procedure for estimating exposure to cadmium in Japan

conducted by the Ministry of Agriculture, Forestry, and Fisheries (MAFF). As most of soybean and wheat consumed in Japan is imported, cadmium concentration data in soybean and wheat imported from the USA was used. Japanese Food Balance Sheets were used to estimate the consumption ratios of domestically produced and imported soybeans and wheat.

Average food intakes for the various food groups were obtained from the NNS database for the years 1995–2000. Age, sex, and body weight data was also obtained, but such data excluded individuals younger than 20 years and pregnant women in order to improve the precision of data. Data for approximately 53,000 adults were used for this analysis.

The outline of the procedure for estimating exposure to cadmium by age-sex groups in Japan is shown in Fig. 31.1. Although it is preferable to determine the mean long-term intake of food, 1-day data from the NNS were used without further treatment in the analyses. As food groups are interrelated in ordinary dietary habits, the following rank correlations were assumed: −0.32 for rice-wheat, 0.22 for rice-soybean, and −0.1 for wheat-soybean.

Approximately 36,000 cadmium concentration values in 130 agricultural and fishery products were obtained from the surveillance of cadmium concentrations performed by MAFF. However, as there was no one-to-one correspondence between these 130 surveillance items by MAFF and 1,000 food items included in NSS database by MHLW, cadmium concentrations of agricultural products were applied to grouped food categories for these calculations. In addition, previously determined coefficients for the retention of residual chemicals in food during cooking and food processing were used [5]. A conversion coefficient of 1 was applied for all fishery

products not indicated here on the assumption that cadmium remains in the fishery products after cooking and processing. The intake amounts of food groups were calculated by summing up values obtained through multiplication by the conversion coefficients.

The estimation of cadmium exposure distributions and factors involved in the estimations were examined by Monte Carlo simulations using the Japanese version of *Crystal Ball 2000*. The intake distributions of about 90 food groups were multiplied by the distributions of the cadmium concentrations in the agricultural products contained in the food groups. In practice, random numbers satisfying the distributions of the presence or absence of consumption, the amount of consumption (eaters only) and cadmium concentrations were generated; the product of the three random numbers is the cadmium exposure. The operation was repeated many times to estimate cadmium intake distribution. A binary distribution with 1 and 0 was assumed for the presence and absence of consumption; the expectation of the ratio of those whose consumption of a food group was not a zero in the NNS was set at 1 in the binary distribution. Lognormal distribution was presumed for the theoretical distribution of intake levels and cadmium concentrations. Distribution properties were determined based on the parameters estimated from mean values as well as standard deviations obtained by the NNS and the surveillance of cadmium in food.

Table 31.2 shows the different cadmium concentrations used in the three scenarios in the Monte Carlo simulation. In the scenarios, it is assumed that the food items containing cadmium concentrations at or exceeding the maximum level would be excluded from the food supply. By selecting the different cadmium concentrations in each scenario, Monte Carlo estimations were made by excluding any random numbers exceeding the maximum levels for the food. For food items fixed at median values due to their limited surveillance data, medians were calculated by excluding samples exceeding the set maximum levels.

Table 31.3 depicts the arithmetic means and values of cadmium intake at 25th, 50th, 75th, 90th, 95th, and 97.5th percentiles of cadmium exposure estimated in setting three different scenarios. By setting different maximum levels of cadmium in food, there were no large differences in distributions and the values at the 97.5th percentile, which in all the scenarios were above 7 μg/kg bw/week.

Contaminant Priorities for Surveillance in Food in Japan

Staple food and traditional cuisine among Japanese people consist of rice and many marine products. These dietary factors are thought to be beneficial for Japanese longevity. However, they also contribute to much higher exposures to cadmium, arsenic, methylmercury, PCBs, dioxins, and dibenzofurans. This may be called the "Japanese paradox". As a consequence, the Ministry of Health, Labor, and Welfare established a priority list for the surveillance for these contaminants, which will be included in future TDSs. These are shown in Table 31.4. Dioxins and dioxin-like PCBs are also prioritized contaminants especially in fish and other seafood as well as in agricultural products and meat and dairy products in Japan. Cadmium is one of the most

Table 31.2 Distribution maximum values for three Monte Carlo scenarios

| Item | Scenario (when data higher than or equal to each value were omitted) values in mg/kg | | |
	1	2	3
Cereals			
Polished rice	0.3	0.4	0.5
Wheat	0.2	0.2	0.2
Cereals other than rice and wheat	0.1	0.1	0.1
Beans (matured)			
Soybean	–	–	–
Beans other than soybean	0.1	0.1	0.1
Stem and root vegetables			
Burdock	0.1	0.1	0.1
Taro	0.1	0.1	0.1
Potato	0.1	0.1	0.1
Celeriac	–	–	–
Other than burdock, taro, and potato	0.1	0.1	0.1
Leafy vegetables			
Spinach	0.2	0.2	0.2
Other than spinach	0.2	0.2	0.2
Bulb vegetables (Alliums)			
Garlic	0.05	0.05	0.05
Other than garlic	0.05	0.05	0.05
Non-cucurbitaceous fruits and vegetables (including mushrooms and sweet corn)			
Eggplant	0.05	0.05	0.05
Okra	0.05	0.05	0.05
Tomato	–	–	–
Mushroom	–	–	–
Other than tomato, eggplant, and okra	0.05	0.05	0.05
Stalk vegetables			
Stalk vegetables	0.1	0.1	0.1
Cress (bulb-forming vegetables)			
Cress	0.05	0.05	0.05
Cucurbitaceous fruits and vegetables			
Cucurbitaceous fruits and vegetables	0.05	0.05	0.05
Beans and peas (immatured)			
Fabaceous vegetables	0.1	0.1	0.1
Peanut			
Peanut	–	–	–
Fruits			
Fruits	–	–	–
Mollusks (including cephalopods)			
Mollusks	1	1	1
Herbs			
Herbs	–	–	–

Table 31.3 Exposure to cadmium under three Monte Carlo scenarios

	Scenario 1	Scenario 2	Scenario 3
Arithmetic mean	3.29	3.33	3.35
25 percentile	2.10	2.10	2.11
50 percentile	2.85	2.86	2.86
75 percentile	3.94	3.97	3.98
90 percentile	5.45	5.54	5.57
95 percentile	6.67	6.85	6.93
97.5 percentile	8.01	8.32	8.46

Unit: µg/kg-bw/week

Table 31.4 Priority list of contaminants in food for total diet studies in Japan

Contaminants	Food items
PCDD/PCDFs and dioxin-like PCBs	Agricultural products
PCDD/PCDFs and dioxin-like PCBs	Meat and dairy products
PCDD/PCDFs and dioxin-like PCBs	Fish and other seafood
PCDD/PCDFs and dioxin-like PCBs	Feed
Deoxynivalenol and nivalenol	Agricultural products
Ochratoxin A	Agricultural products
Zearalenone	Agricultural products
Acrylamide	Processed foods
3-Methylchloropropane-1,2-diol-esters	Processed foods
1,3-Dimethlychloropropane	Processed foods
Cadmium	Rice, feed
Aflatoxin	Feed
Pesticides	16 major agricultural products
Pesticides	Imported foods on positive list
Pesticides	Feed

prioritized heavy metals in rice and feed. As for mycotoxins, aflatoxin, ochratoxin A, and zearalenone have been important contaminants in feed and agricultural products. In addition, mycotoxins from *Fusarium* fungi, such as deoxynivalenol and nivalenol, have been included as monitoring contaminants because of humid weather often occurs during the harvesting of barley and wheat. Contaminants recently evaluated in JECFA meeting, such as chloropropanols and acrylamide, are rather low in food, but these chemicals are also included in monitoring in response to changes of dietary habits of the younger generations, which includes increased consumption of imported processed foods.

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Chapter 32
Total Diet Studies in the Republic of Korea

Hae Jung Yoon

Introduction

The Korean Government attaches great importance to evaluating the exposure levels of the population to potentially hazardous chemicals in the food supply and providing various background data for risk assessment, which is the basis for risk management decision-making. The purpose of a total diet study (TDS) is to estimate the level of dietary exposure of the population to a range of food chemicals, including heavy metals and pesticides that can be found in the food supply. Dietary exposure is estimated by determining the level of chemicals in food from the laboratory analysis and then combining this with the amount of food consumed as determined in a separate study, such as a national health and nutritional survey.

Since the 1960s, monitoring in Korea has focused on gathering information on levels of chemicals in food in order to confirm food standard settings or justify maximum residue limits (MRLs). However, it was not possible to collect information on individual food consumption data until 1998. In that year the Korean National Health and Nutritional Survey was changed from basic household inventories to individual food consumption surveys. Although the academic researchers had experience with TDS for some time, the Korea Food and Drug Administration (KFDA) only began its first TDS in 2000.

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Identifying a Representative Food List

There are a number of considerations to be addressed as a part of defining the appropriate TDS procedures for one's own country. One of these regards which foods to sample. The food list should identify the most important foods to the general population, foods relevant to population subgroups, and those of specific concern for contaminant content. When examining existing food consumption data, the possible variations of food habits within the population must be considered. KFDA attempted the first TDS using regional menu tables based on the 1998 Korea National Health and Nutritional Survey. Considerations included how much and how often Koreans consumed the specific food or commodity and their geographical region, so that dietary patterns of the general population formed 45 kinds of regional menu tables, which in turn represented six regions' typical diets or consumption patterns. Each menu table contains five kinds of composite dishes were established and analyzed, after being prepared table-ready according to the local way of cooking, to provide heavy metal dietary exposure information. However, these regional menu tables could not provide information on the possible variation of dietary habits within the population in relation to gender and age.

Over several TDSs, a number of improvements have been made. A different approach for establishing consumption data has been implemented so that the representative food list was constructed and revamped based on Korea National Health and Nutritional Surveys from 1998, 2001, and 2005. Table 32.1 describes the evolution of the food lists for heavy metals in the Korean TDS, which attempted to accommodate the following directions:

– A move from composite foods to individual commodities
– An increased number of foods and food groups
– An increased number of population groups evaluated
– Combinations of common foods as well as high-risk foods

Commodities and composite foods that aggregated up to 80 % of the total food intake were selected from national health and nutritional survey data. In addition, commodities/composite foods that may have high levels of selected analyte(s), seasonal dishes and others that may have influence on the total dietary exposure

Table 32.1 Evolution of the Korean total diet study food list for heavy metals

TDS Year	Number of commodities on food list	Food consumption (% of total consumption, % total energy)
2001	116[a]	857 g/person/day (66.5 %, 58.9 %)
2004	101[b]	1,041 g/person/day (85.6 %, 84.9 %)
2007	113[c]	1,114 g/person/day (86.4 %, 89.3 %)

[a] National Health and Nutrition survey-1998 collected 496 food items (1,290 g/person)
[b] National Health and Nutrition survey-2001 collected 591 food items (1,215 g/person)
[c] National Health and Nutrition survey-2005 collected 553 food items (1,281 g/person)

```
        ┌─────────────────────────────┐
        │ 2005 National Health &      │
        │ Nutrition survey data       │
        └─────────────────────────────┘

        ┌─────────────────────────────┐
        │ Major Foods : 67 Foods      │
        │ (Intake Ratio : 80.0%)      │
        └─────────────────────────────┘

┌──────────────┐                              (  High intake food  )
│ 2005 National│
│ Nutrition    │
│ survey       │
│ by seasonal  │
│ data         │       (  High          )     (  Foods with       )
└──────────────┘       ( Intake food by )      ( high potency of  )
                       ( season,        )      ( heavy metals     )
                       ( region, sex,   )
                       ( age            )

        ┌─────────────────────────────────────┐
        │ Heavy Metals Analysis Final Target :│
        │ 113 Foods                           │
        │ (Food Intake 86.4%, Energy Intake 86.3%)│
        └─────────────────────────────────────┘
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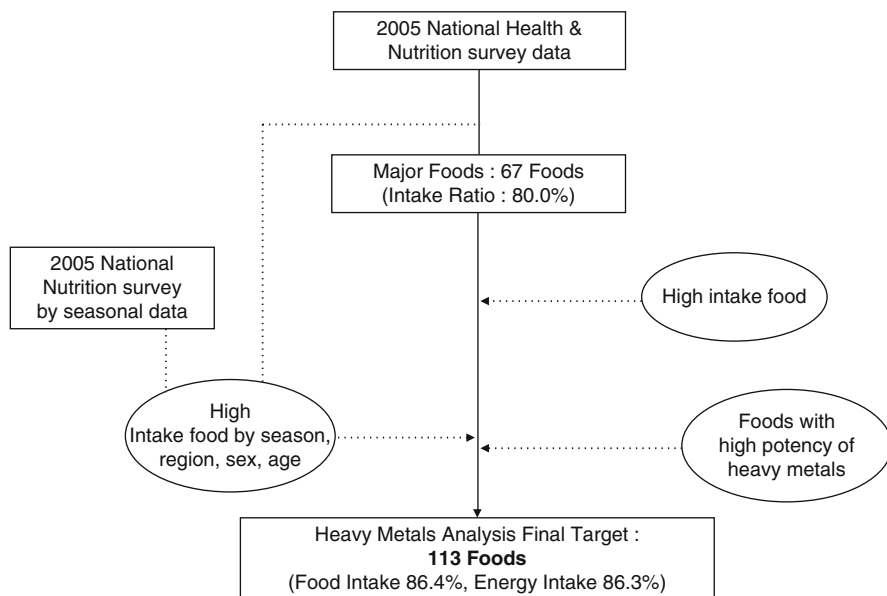
Fig. 32.1 Flow chart of food selection procedure

were also included. The energy intakes were also calculated to confirm the validity of the selected diets. A flow chart of the selection procedure is given in Fig. 32.1.

Sample Preparation

Sampling is a critical part of any successful TDS and it must be planned and managed effectively. Sample collection should be coordinated with sample preparation and analyses. KFDA included in its TDS sampling regionally as well as nationally produced and distributed food, except for certain imported products, such as beef and banana. Samples representing three different origins or manufacturers were purchased from major retailers in Seoul and Gyeonggi Province during May to October every year.

To ensure consistency, standard operating procedures (SOPs) were developed for preparing table-ready foods. Korean cuisine is richly endowed with fermented foods, like kimchi, and seasonings, like doenjang paste (soybean paste) and soy sauce. Therefore, knowledge of cooking methods for various Korean cuisines is necessary to reflect Korean dietary habits. Dishes may be boiled, blanched, broiled (or toasted), steamed, stir-fried or pan-fried with vegetable oil and prepared accordingly. More than one sample preparation method for a commodity could be applied if the commodity is contributed more than 1 % from total content of a specific dish. For example, boiling and stir-frying were applied in preparing zucchini.

Korean TDS Results

The KFDA TDS has provided assurances that foods in Korea are safe and nutritious. The TDS has evolved to reflect changes in food consumption patterns. As of July 2010, KFDA is implementing TDS for pesticide residues and mycotoxins as well as food contaminants, recognizing that assumptions and occurrence and food consumption data should be selected with care.

Heavy Metals

The representative food list is divided into 16 categories, based on 12 categories of Food Balance Sheets of the Food and Agriculture Organization of the United Nations (FAO), but including four categories of specific Korean commodities, like laver (seaweed). Samples of these foods were prepared as table-ready dishes and heavy metals were analyzed using Korean Food Code methods or those of the Association of Official Analytical Chemists (AOAC). The 16 food categories are: cereals and legumes, potatoes and starch, nuts, soybean and soybean products, sugar and sugar products, vegetables, fruits, meats and meat products, eggs, fish and shellfish, sea algae, milk and dairy products, mushrooms, vegetable oils, beverages including alcohols, and seasonings.

Total Arsenic

The seventy-second meeting of joint FAO/WHO Expert Committee on Food Additives (JECFA) withdrew the previous Provision Tolerable Weekly Intake (PTWI) for inorganic arsenic and noted that more accurate information on the inorganic arsenic content of foods as they are consumed is needed [1]. Because the proportion of inorganic versus the less toxic organic arsenic in foods are highly variable, data for inorganic arsenic in different food are being developed. In the interim, KFDA has assessed the risk to human health of dietary arsenic through the TDS where occurrence data are still reported as total arsenic. Because fish and shellfish group and sea algae group are consumed in large amounts in the Korean diet, these two food groups made a significant contribution to dietary arsenic intake that contributed 93 % to arsenic exposure in the 2007 TDS (see Fig. 32.2). Level of arsenic in toasted laver, which Korean children (1–6 years old) consumed the most on a body weight basis, was detected as high as 21.4 mg/kg in 2004 TDS and contributed 70 % of arsenic (total) exposure. The results from the 2007 TDS indicate that the total dietary exposure of the general population and children (3–6 years old) fell to 0.47 μg/kg bw/day and 1.0 μg/kg bw/day, respectively. In comparison, the JECFA set the benchmark dose level ($BMDL_{0.5}$) at 3.0 μg/kg bw/day for just
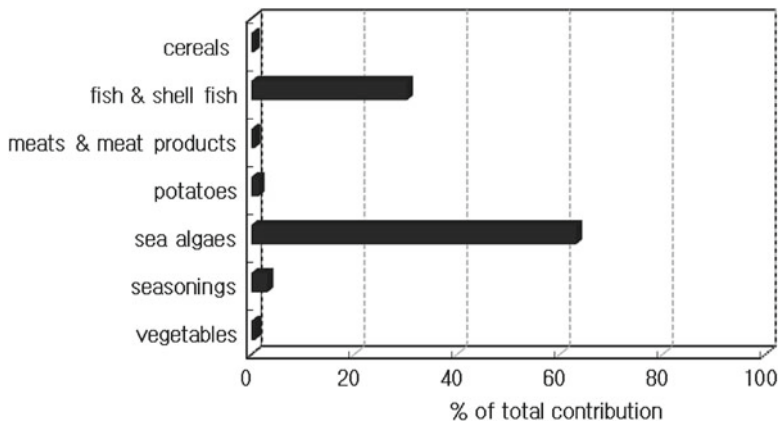
Fig. 32.2 Relative contribution to total arsenic exposure from food groups
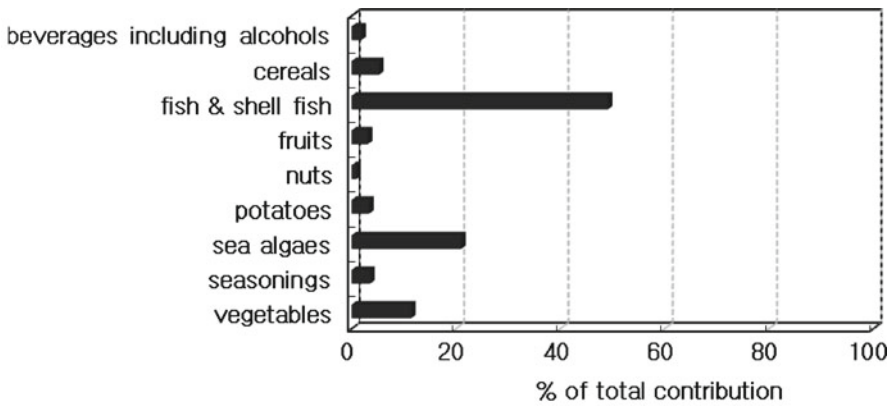
Fig. 32.3 Relative contribution to cadmium exposure from food groups

inorganic arsenic. However, it is known that naturally occurring arsenic in laver and sea mustard is largely in the organoarsenic form [2], which has not caused ill effects even among high consumers [3].

Cadmium

Cadmium is present at low concentrations in most foods. Like dietary arsenic exposure, the fish and shellfish group and the sea algae group made a significant contribution to most of the dietary cadmium exposure (see Fig. 32.3). The levels of cadmium from toasted laver, oysters, boiled cuttlefish, and boiled crab were higher than other foods with concentrations of 0.99 mg/kg, 0.47 mg/kg, 0.45 mg/kg, and 0.34 mg/kg,
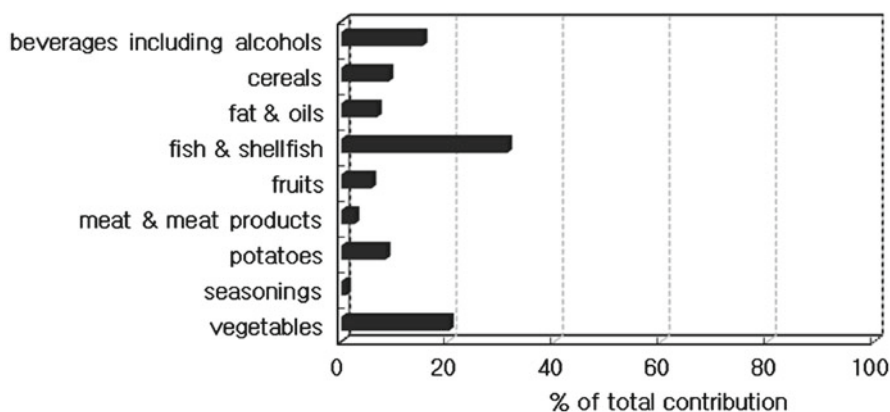
Fig. 32.4 Relative contribution to lead exposure from food groups

respectively, in the 2007 TDS. Total cadmium dietary exposure was 11–24 % of JECFA PTWI (0.007 mg/kg bw/week) depending on the gender/age group. Given these high cadmium dietary exposures, KFDA has endeavored to minimize the exposure to cadmium by establishing a national limit of cadmium in fresh molluscs and other shellfish at not more than 2.0 mg/kg. Compliance monitoring is being implemented, with both imported and domestic products being regularly tested.

Lead

Like some other inorganic contaminants, the dietary exposure to lead in food is well below the international health limits. In the 2007 TDS, the average total lead dietary exposure for the general population fell to 0.001 mg/kg bw/week, which was equivalent to 3.3 % of JECFA PTWI of 0.025 mg/kg bw/week. The largest contributing commodity groups to lead exposure were the fish and shellfish group that contributed 31 %, followed by vegetable group with 21 % (see Fig. 32.4). The highest lead concentration ever detected was in boiled radish leaf, which was as high as 0.76 mg/kg in the 2003 TDS.

Total Mercury

The food commodities making the largest contribution to total mercury exposure (0.0003 mg/kg bw/week) in the average Korean diet were from the fish and shellfish groups, which contributed 84.5 % of the exposure in the 2007 TDS (see Fig. 32.5). Highest levels of mercury were detected in baked hairtail and yellow corbina, which contributed 40 % of the total mercury exposure (0.0005 mg/bw/week) of children
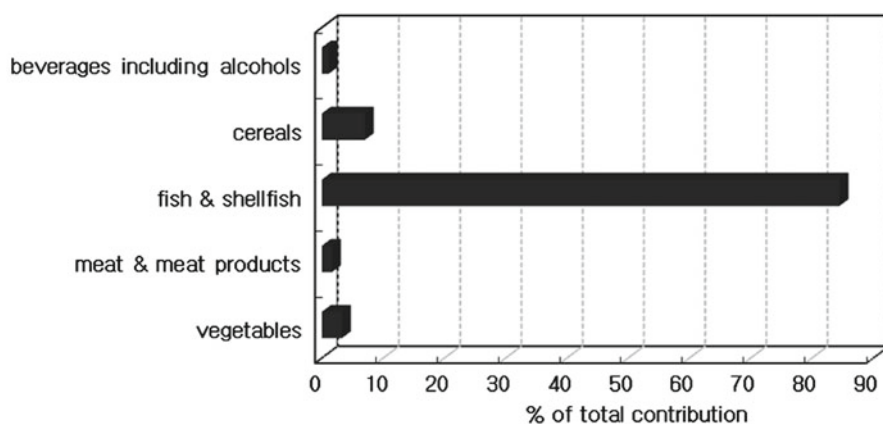
Fig. 32.5 Relative contribution to total mercury exposure from food groups

(ages 3–6 years). In noting the lack of data on the investigation of methylmercury levels in fish and shellfish group and reflecting on apparent high exposure to mercury, KFDA set a national limit of not more than 0.5 mg/kg of methylmercury in fish, including shellfish and molluscs, so that exposure to mercury would be minimized.

Aluminum

Aluminum is present in most foods and many approved food additives contain aluminum. Concern about the toxicity of aluminum was raised when JECFA lowered PTWI by a factor of seven to 1 mg/kg bw/week [4]. The inclusion of aluminum in Korean TDS began in 2004. Depending on the age group, the exposure estimated in the 2007 TDS ranged between 28 % and 65 % of the PTWI. As a result of high consumption, cooked rice contributed 24 % of the dietary exposure to aluminum, while dried anchovy had the highest concentration of aluminum (41.5 mg/kg) and contributed 13 % of the exposure. The remaining food groups contributed less than 5 % of the dietary exposure to aluminum (see Fig. 32.6).

Pesticide Residues

The 2004 TDS assessed pesticide exposure based on 84 core foods from the food list with 23 additional commodities that might contain pesticide residues (representing 86 % of the average food consumption). Chlorpyriphos from blanched aster leaf was the only pesticide detected out of 103 pesticides screened by gas chromatography, but the exposure to chlorpyriphos by the general population in Korea was well below international health limits. In another study, the national pesticide residue
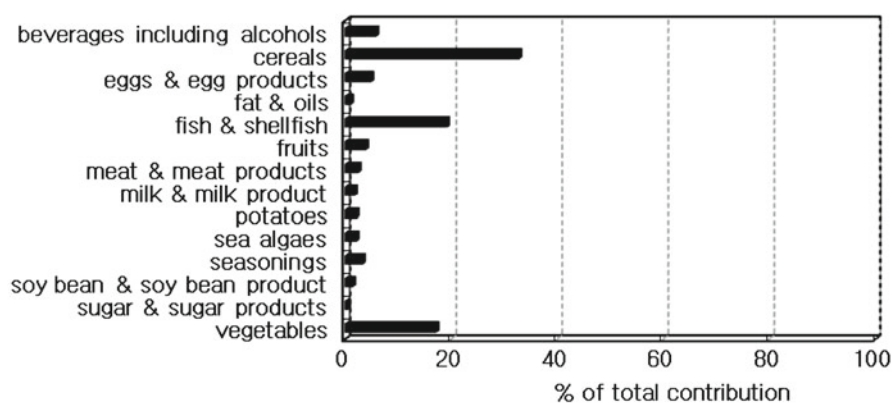
Fig. 32.6 Relative contribution to aluminum exposure from food groups

Table 32.2 Exposure to pesticide residues by Korean population compared to reference safety values

Pesticide	Exposure (ug/kg body weight[a]/day)	ADI[b] (mg/kg body weight/day)
Acetamiprid	0.033	0.07[c]
Benzoximate	0.027	4[d]
Boscalid	0.092	0.044
Cyazofamid	0.011	0.17
Dimethoate	0.089	0.002
Dimethomorph	0.004	0.2
Endosulfan	0.002	0.006
Fenobucarb	0.422	0.012[e]
Fenothiocarb	0.004	0.0075
Fenoxycarb	0.001	0.055
Flufenoxuron	0.028	0.03[f]
Iprovalicarb	0.002	0.027[e]
Isoprocarb	0.251	0.004[e]
Lufenuron	0.001	0.01
Methoxyfenozide	0.043	0.1
Prochloraz	0.001	0.01
Pyraclostrobin	0.050	0.034
Pyrimethanil	0.156	0.17
Pyroquilon	0.294	0.015[b]
Tebufenozide	0.031	0.02
Thiacloprid	0.004	0.012
Thiamethoxam	0.136	0.018
Tricyclazole	1.255	0.03[b]
Trifloxystrobin	0.002	0.038

[a] Average body weight: 54.1 kg per person
[b] Acceptable Daily Intake (ADI) from the Joint FAO/WHO Meetings on Pesticide Residues unless otherwise indicated
[c] Japanese Ministry of Health and Welfare ADI
[d] NOEL/100
[e] National Health and Nutrition survey-2005 collected 553 food items (1,281 g/person)
[f] Pesticide Manual, British Crop Production Council, 15th edition, 2009

compliance monitoring program in 2003 indicated that 11 % of aster leaf samples had not met the MRL for that pesticide. Therefore, various actions, including prohibiting chlorpyriphos use on leafy vegetables had been implemented based on these results.

The results from the 2008 TDS indicated that the dietary exposure of 24 pesticide residues by general population in Korea were well below international health limits (See Table 32.2).

Conclusions

The KFDA TDS differs from other government surveys and monitoring programs for food chemicals, which examine the levels of chemicals in raw agricultural commodities to determine compliance with food legislation. In contrast, the TDS carries out a comprehensive examination of total diet to determine whether there are any associated risks to human health. The TDS food samples are prepared to a 'table-ready' state before they are analyzed, which results in a more accurate estimation of dietary exposure. In conjunction with data from other sources, the TDS provides unique information to be considered when reviewing, developing or amending food regulatory measures.

The Korean TDS is a large and complex project with many components. The accuracy of exposure assessments depends, among other things, on the representativeness of the food list. This requires that the increased demand for convenience foods and for year-round availability of seasonal foods need to be taken into account. Despite these uncertainties, the exposure assessments presented in TDS represents a reliable estimate of dietary exposure for the Korean population using the available data.

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Chapter 33
Dietary Exposure to Heavy Metals and Radionuclides in Lebanon: A Total Diet Study Approach

Lara Nasreddine

Introduction

The continuous surveillance of food safety has lagged behind in Lebanon, a Mediterranean country with a territory of 10,452 km^2 and a population estimated to be around four million. Limited reports are available suggesting the presence of particular contaminants in specific food items [1]. However, the magnitude and the severity of the dietary exposure of the population to food chemicals have not been appropriately addressed.

   The estimation of dietary exposure to food contaminants combines data on the levels of the contaminant in particular foods with data on the quantities of those foods consumed by the population in question. The World Health Organization (WHO) supports the use of the total diet study (TDS) as one of the most cost-effective means of achieving accurate dietary exposure estimates, and the WHO's GEMS/Food Programme has encouraged all countries, and particularly developing ones, to conduct a TDS as a matter of public health significance. A TDS provides a first step exposure assessment based on food consumption surveys and point towards priority nutrients or contaminants that need to be further investigated. In this context, a TDS has been initiated in 2004 in Lebanon and has provided the first estimates of the dietary exposure of the population to heavy metals (lead, cadmium, and mercury) and to gamma-emitting radionuclides, the results of which are related below. In addition a TDS was performed to estimate the dietary exposure of children to mycotoxins [2] and to certain food additives [3].

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Source of Food Consumption Data

The first step in a dietary exposure assessment study is the generation of data on the types and amounts of foods typically consumed in the population under study. In theory, food consumption data can be generated by three different means: (1) Food Balance Sheets (FBS), (2) household budget or consumption surveys, and (3) individual food consumption surveys. Because the data provided by both FBS and household-based surveys represent food availability rather than actual food consumption data, individual food consumption surveys more closely reflect actual dietary habits and practices within a country or a region.

In Lebanon, the last comprehensive individual food consumption survey was conducted in 1961 by the Interdepartmental Committee on Nutrition for National Defense [4]. Afterwards studies on the dietary habits of the Lebanese population were only sparsely described in the scientific literature. In order to generate individual-based food consumption data that more closely reflect consumption patterns in the country, an individual dietary survey was conducted in 2001 on a representative sample of the population of Beirut, which has been called the "melting pot" of the country. The survey provided data on 210 men and 234 women aged 25–54 years. The age and sex distribution of this sample was proportionate to the baseline population according to the Lebanese Central Administration for Statistics [5]. Food consumption data were collected by means of a quantitative food frequency questionnaire (QFFQ) specifically designed for the study. It consisted of a list of 112 culture-specific food items/beverages and included a number of composite dishes that may contain multiple ingredients. The questionnaire permitted not only the estimation of the frequency of consumption of each food item, but also the identification of the portion size that the individual usually consumes [6].

Total Diet Study Design

Selection of Food Items

The selection of food items to be included in the TDS was based on two criteria. First, foods were selected based on their ranking in consumption by adults: the food items with a mean consumption >1 g/day per person were included. Second, foods identified by the WHO GEMS/Food Programme in its comprehensive list [7] as potential sources of lead (Pb), cadmium (Cd), and mercury (Hg) were selected. The second criterion has thus led to the exclusion of certain food items from the total diet list. The excluded food items comprised soft drinks, coffee, tea and infusions, nuts, added fats and oils (except for those incorporated in the cooked recipes), olives, alcoholic beverages, chocolate, added white sugar, jam, honey and candies. By combining the two selection criteria, 77 food items, including drinking water, were selected for the analytical determination of Pb, Cd, Hg, and radioisotopes (see Table 33.1). These foods

Table 33.1 Aggregation of the 77 food items into 21 food groups, weight of each item as consumed (g/day) and percentage weight of each food item in its group

Food group	Daily intake (g/day)	% weight	Food group	Daily intake (g/day)	% weight
1. Bread and Toast			*7. Fruit juices*		
Traditional bread	136.8	93.6	Juice, canned	65.2	50.1
Traditional crackers (Ka'ak)	6.2	4.2	Juice, fresh	65.0	49.9
Toast	3.2	2.2	*Total*	*130.2*	*100.0*
Total	*146.2*	*100.0*			
			8. Fruits		
2. Biscuits and croissants			Oranges	75.3	32.7
Biscuits	13.6	68.7	Apples	61.0	26.5
Croissant	4.9	24.7	Bananas	20.7	8.9
Doughnuts	1.3	6.6	Watermelon	15.0	6.5
Total	*19.8*	*100.0*	Fruit-based deserts	10.9	4.8
			Grapes	10.0	4.4
3. Cakes and pastries			Cherries	5.6	2.4
Cakes	11.8	46.3	Peaches	5.3	2.3
Traditional pastry (Knefah)	8.2	32.2	Pears	5.2	2.3
Other traditional pastry	5.5	21.6	Fruit salad	4.7	2.1
Total	*25.5*	*100.0*	Melon	4.2	1.8
			Strawberry	3.5	1.5
4. Pasta and other cereals			Exotic fruits	2.7	1.2
Pasta, cooked	23.9	74.0	Apricots	2.1	0.9
Burghol, cooked	5.5	17.0	Canned fruits	2.2	1.0
Burghol, raw	2.8	9.0	Prunes	1.4	0.6
Total	*32.2*	*100.0*	*Total*	*230.0*	*100.0*
5. Pizzas and pies			*9. Cheese*		
Pies, type Manaeesh	32.1	64.0	Cheese Akkawi	9.8	28.0
Pizza	11.3	23.0	Cheese Halloum	9.8	28.0
Other traditional pies	6.6	13.0	Cheese Kashkawal	8.1	23.0
Total	*50.0*	*100.0*	Packaged cheese	7.4	21.0
			Total	*35.1*	*100.0*
6. Rice and rice-based					
products	50.1	100.0	*10. Milk*		
Rice, cooked			Milk, reconstituted		
			from powder	69.8	70.0
			Milk liquid	29.9	30.0
			Total	*99.7*	*100.0*

(continued)

Table 33.1 (continued)

Food group	Daily intake (g/day)	% weight	Food group	Daily intake (g/day)	% weight
11. Milk-based ice cream and pudding			*15. Vegetables, raw and salads*		
Pudding	6.1	50.2	Other salads	56.6	42.1
Milk-based ice cream	6.0	49.8	Vegetables, raw	49.4	36.7
Total	*12.1*	*100.0*	Traditional salad, type Fattouch	15.5	11.6
			Traditional salad, type Tabbouli	12.9	9.6
12. Yogurt and yogurt-based products			*Total*	*134.5*	*100.0*
Yogurt	68.3	71.1	*16. Potatoes*		
Strained yogurt, type Lebneh	27.8	28.9	Potatoes, boiled	57.8	91.0
Total	*96.2*	*100.0*	Potato chips	5.7	9.0
			Total	*63.5*	*100.0*
13. Vegetables, canned					
Corn	4.6	39.8			
Mixed vegetables	3.2	27.8	*17. Pulses*		
Artichoke	1.5	12.6	Chickpeas	12.7	32.1
Mushrooms	1.2	10.3	Lentils	9.8	24.7
Asparagus	1.1	9.4	Fava beans	9.1	22.9
Total	*11.6*	*100.0*	Beans	5.3	13.4
			Fava bean-based falafel	2.7	6.8
14. Vegetables, cooked			*Total*	*39.5*	*100.0*
Green beans, stew	13.7	13.8			
Mixed vegetables, stew	13.7	13.8	*18. Fish*		
Zucchini, stuffed	12.9	13.1	Fish, fresh or frozen	11.2	62.4
Eggplant	8.7	8.8	Tuna, canned	6.7	37.6
Jews mallow, stew	7.0	7.1	*Total*	*17.9*	*100.0*
Peas, stew	6.9	6.9			
Cauliflower	6.7	6.8	*19. Meat, cooked and cured*		
Grape leaves, stuffed	6.3	6.3			
Cabbage, stuffed	4.5	4.6	Meat, cooked	47.6	91.5
Spinach, stew	4.5	4.5	Cured meat	4.4	8.5
Okra, stew	4.4	4.4	*Total*	*52.0*	*100.0*
Eggplant, stuffed	3.9	3.9			
Chicory	3.3	3.4	*20. Poultry*		
Artichoke	2.3	2.3	Chicken, grilled	36.1	96.1
Total	*98.9*	*100.0*	Chicken liver, fried	1.5	3.9
			Total	*37.6*	*100.0*
			21. Drinking water[a]	985.9	100.0

[a]Drinking water is a composite of water collected from the nine districts that were included in the dietary survey

represented approximately 80 %, on a weight basis, of the daily ration of the average individual. For the evaluation of the dietary exposure to Hg, only fish and fish products were included.

Food Collection, Preparation and Aggregation

The composite approach, as recommended by the WHO, has been applied. Accordingly, for each of the 77 foods listed, five subsamples, i.e. five different brands or varieties, were purchased and combined into one composite sample. Since market shares of the different brands are not determined in Lebanon, the contribution of each subsample to total weight was equal to 20 %. Individual samples were collected from different retail outlets in the city of Beirut. Food items were transported to one central laboratory where they were prepared and cooked in a manner similar to local cooking practices. To take into account the occurrence of changeable contamination, five complete sets of foods (market baskets) were collected during 2004 [8].

For each market basket, the 77 food items were aggregated into 21 groups of similar foods (see Table 33.1). For practical reasons, these 21 food groups were further combined into 12 aggregates for the analytical determination of radionuclides. Food items of each group were combined and blended and homogenized using an ordinary domestic mixer. Samples were then stored at −18 °C prior to analysis.

Source of Food Contamination Data

The analytical quantification of Pb, Cd and Hg was performed using inductively coupled plasma mass spectrometry (ICPMS). For quality control, each test run included spiked test samples and certified reference materials for the comparison of measured and certified concentrations of the elements of interest. All samples were analyzed in duplicate, which were digested and measured in separate batches to eliminate any batch specific error.

The quantitative determination of radionuclides was performed using two gamma ray spectrometry systems (Canberra) equipped with two high purity coaxial germanium detectors with relative efficiency of 30 % and 40 %, respectively, and of high resolution [1.85 and 2.0 keV (FWHM) at 1,332 keV, respectively] [9].

Dietary Exposure Assessment

In the Lebanese TDS, the calculation of dietary exposure was performed using a deterministic model in which the average value for food consumption was

multiplied by the average concentration of the contaminant and the exposures from all food sources were then summed to provide the average dietary exposure value. For foods containing levels of elements below the limit of quantification (LOQ), a value equal to half the LOQ was assigned and used for calculation purposes [10]. Consumer exposure estimates to Pb, Cd and Hg were then expressed in mg/kg body weight/week to allow comparison with the respective Provisional Tolerable Weekly Intake (PTWI) values. For this purpose, a body weight of 72.8 kg was used, which is the average body weight of the participants in the dietary survey.

Findings from the Lebanese Total Diet Study

Dietary Exposure to Lead and Cadmium

The highest levels of Pb and Cd were found in cereal-based products with bread presenting the highest concentrations of both elements (35.4 µg/kg for Pb and 17.5 µg/kg for Cd). However, when compared with the Maximum Levels (ML) proposed by the Codex Alimentarius Commission [11], none of the food samples analyzed within the Lebanese TDS were found to exceed these limits. The Lebanese TDS showed that the average dietary exposures to Pb and Cd represented 7 % and 17 %, respectively, of their corresponding PTWIs [12], [13] and thus did not, at least for Cd, represent a risk for the average consumer. Because the PTWI for Pb has been withdrawn, a further evaluation of Pb exposure is necessary. The TDS showed that the food groups that contributed most to the dietary exposure to Pb and Cd were cereals and cereal-based products (45.3 % and 36 % respectively), vegetables and potatoes (17.6 % and 28.5 % respectively) and drinking water (16.2 % and 24 % respectively) (see Table 33.2). The contribution of a food group to the dietary exposure depends not only on the contamination level of that particular food but also on the consumption level of this food by the population under study. In Lebanon, the diet relies heavily on cereals and vegetables. In fact, breads and cereals alone were found to provide 35.0 % of the total energy intake of the average Lebanese urban adult [6]. In addition, the mean consumption of fresh fruits and vegetables by the average Lebanese urban adult was reported at 367 g person/day, a value approaching the WHO/FAO minimum recommended value of 400 g daily. This plant-centered diet, which is a characteristic shared by other Mediterranean countries, partly explains the fact that cereals and other plant-based food products were the main dietary sources of Pb and Cd in Lebanon.

The TDS findings suggest that, in Lebanon, the dietary exposure to the potentially toxic elements Pb and Cd is low, and that for the average consumer, there is no risk of exceeding their respective PTWIs. However, it is important to keep in mind that the exposure assessment conducted in the present study was based on the analysis of the Lebanese total diet food list that represented 80 % of the average daily energy intake of the average individual. It might thus be argued that some food items that typically contain high levels of heavy metals may have been excluded

Table 33.2 Lead and cadmium concentrations (µg/kg) in food samples and mean daily exposures (µg/person/day) from "total diet" food groups

Food group	Lead			Cadmium		
	Range (µg/kg)	Mean[a] (µg/kg)	Mean exposure (µg/day)	Range (µg/kg)	Mean[a] (µg/kg)	Mean exposure (µg/day)
1. Bread and toast	23–47.1	35.4	5.2	14.2–19.8	17.5	2.6
2. Biscuits and croissant	6.9–23.3	14.0	0.3	8.7–16.7	10.7	0.2
3. Cakes and traditional pastry	27.9–40.5	35.2	0.9	3.6–5.5	4.4	0.1
4. Pasta and other cereal products	6.7–12.3	9.4	0.3	13.8–19.2	15.8	0.5
5. Pizzas and pies	21.6–41.8	27.3	1.4	10.2–14.8	12.5	0.6
6. Rice and rice-based products	4.1–5.5	4.6	0.2	3.2–8.8	6.6	0.3
7. Fruits and fruit-based products	2.6–14.6	6.1	1.4	0.4–0.9	0.6	0.1
8. Fruit juices	<6–<6	3.0	0.4	<6–<6	3.0	0.4
9. Pulses	3.9–11.3	5.9	0.2	0.9–2.1	1.6	0.1
10. Vegetables, canned	13.4–16.0	14.8	0.2	5.7–8.4	7.1	0.1
11. Vegetables, cooked	12.7–22.5	16.0	1.6	8.5–21.2	13.1	1.3
12. Vegetables, raw and salads	5.7–15.5	7.9	1.1	6.8–22.0	10.4	1.4
13. Potatoes	1.6–4.5	2.8	0.2	5.0–15.7	10.0	0.6
14. Cheese	14.8–22.3	17.6	0.6	1.4–1.5	1.4	0.1
15. Milk and milk-based beverages	<6–<6	3.0	0.3	<6–<6	3	0.3
16. Milk-based ice cream and pudding	4.1–6.3	4.8	0.1	1.1–3.3	2.0	0.02
17. Yogurt and yogurt-based products	1.7–3.0	2.1	0.2	0.4–0.5	0.5	0.1
18. Meat and meat-based products	6.2–11.8	9.0	0.5	1.2–3.4	2.0	0.1
19. Poultry	5.2–9.9	6.8	0.3	3.8–16.6	6.6	0.3
20. Fish and fish-based products	4.4–8.8	5.9	0.1	3.8–6.5	5.0	0.1
21. Drinking water	<6–<6	3.0	3	<6–<6	3.0	3.0
Total			18.5			12.3

[a]Mean concentrations are calculated based on the concentrations determined in the five "total diet" sets

from the TDS. Examples of such foods would include mollusks and crustaceans, which accumulate high levels of Pb, oysters, which accumulate high levels of Cd, and kidneys, which may contain high amounts of both Pb and Cd. According to the individual food consumption survey data [4], the average dietary intake of these food items was very low and did not exceed 0.5 g/day for the typical consumer. This suggests that these types of foods, such as crustaceans, mollusks and kidneys, are very rarely consumed by the Lebanese population and that their contribution to dietary exposure would be rather limited. It would be of interest, however, to evaluate the dietary exposure of the excessive consumers of these types of foods since this group of the population may be exposed to higher levels of Pb and Cd than the average consumer.

Dietary Exposure to Mercury

Being the primary source of dietary Hg and particularly methylmercury (MeHg), the most toxic form of the element, fish was the only food group included in the dietary exposure of the population to Hg. Accordingly, the average concentration of total Hg in fish samples was 165 mg/kg, ranging between 140 mg/kg and 203 mg/kg, and the mean daily exposure to Hg was estimated as 3 mg/day, representing 5.6 % of the PTWI (5 mg/kg bw/week) [14]. Based on the assumption that 100 % of Hg in fish is in the MeHg form, the levels of MeHg in the analyzed fish samples were not found to exceed the Guideline Levels specified in the Codex Alimentarius of 0.5 mg/kg for non-predatory fish and 1.0 mg/kg for predatory fish [9]. Based on the same assumption, the mean dietary exposure to MeHg was found to represent 17.5 % of the PTWI of MeHg (1.6 mg/kg bw/week) [15], and thus did not represent a risk for the average consumer.

Dietary Exposure to Gamma-emitting Radionuclides

Since the primary factor contributing to the internal effective dose in the human organism is contaminated food, the control of radionuclides in food represents the most important means of protecting public health. In this context, the Lebanese TDS was also used to assess the dietary exposure of the consumer to gamma-emitting radionuclides and for determining baseline levels of these radionuclides in foods, especially given that in Lebanon, there were no previous evaluations of radioisotopes in foods. The selection of the TDS design for this purpose was linked to many reasons: the TDS allows the derivation of ingestion doses by combining measurements of radionuclides in different food groups with food consumption data; it differs from other food surveillance programs because it focuses on the diet as a whole and not on individual foods [16]. Most importantly, the TDS deals with
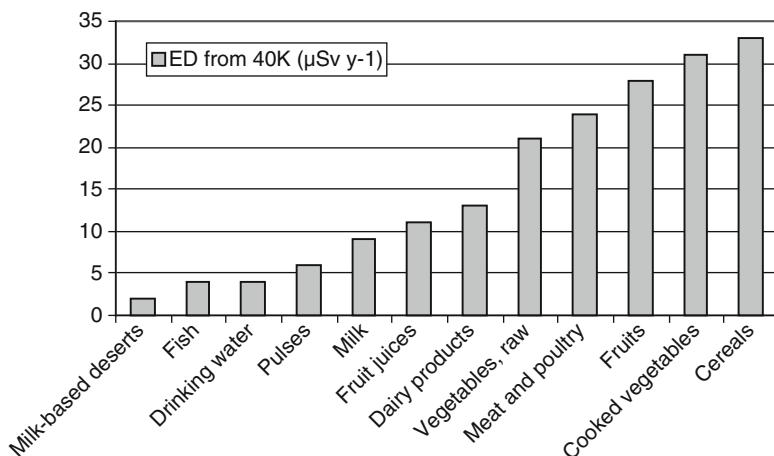
Fig. 33.1 Contribution of the different food groups to the effective dose (*ED*) from 40 K (µSv y^{-1}) in the reference typical diet of an adult urban population in Lebanon

foods that are processed as for normal consumption, thus taking into consideration the impact of home cooking and food processing on the levels of radionuclides.

Accordingly, the radioisotopes cesium-134 (Cs-134) and iodine-131 (I-131) were not detected in any of the food samples. The artificial radionuclide Cs-137 was measured above detection limits in only fish, meat and milk-based deserts, with the highest activity concentration being equal to 0.1 Bq/kg. In comparison, the maximum permitted levels of Cs-137 in foodstuffs (with the exception of foods for infants) are of 1,000 Bq/kg as specified by the Codex Alimentarius Commission [11] and the International Atomic Energy Agency [17].

The activity concentrations of the naturally occurring radionuclide potassium (K-40) varied between 31.1 and 120.9 Bq/kg in the analyzed food samples, which is in accordance with the range reported in different parts of the world (35–380 Bq/kg) [18]. By associating the activity concentrations of K-40 (in Bq/kg) in the different food groups with the consumption levels of these food groups (in g/person/day), the total daily exposure to K-40 was found to be equal to 81.86 Bq/person/day, a value that is comparable to estimates provided by other TDSs conducted in several other countries (42.79–94.8 Bq/person/day) [19]. The mean annual effective dose resulting from the dietary exposure to K-40 was estimated at 186 µSv/year for the average adult consumer (see Fig. 33.1), a value that is comparable to the world average value (178 µSv/year) and lies well within the range reported by other countries.

The applied TDS design has thus shown that the activity concentration of the gamma-emitting radionuclide K-40 in foodstuffs available on the Lebanese market is consistent with values reported in the literature and that the levels of Cs-137 in foods do not present any public health hazard.

Conclusion

The TDS that has been applied in Lebanon is a small-scale TDS, the findings of which may be limited by the fact that it was not a nationally representative study and by the use of the deterministic approach in the assessment of the dietary exposure. In fact, inherent to the deterministic model is the assumption that the average consumption of specified food(s) represents the average diet [20]. This approach therefore does not provide an insight into the range of possible exposures that may occur within a population or the main factors influencing the results of the assessment. However, while not excluding the possibility that the daily exposures determined in the present study may not be representative of the population as a whole, this TDS has provided a first estimate of consumers' exposure to heavy metals and radionuclides through the diet in Lebanon. The main output of this study, other than characterizing the risk for the consumer, is the fact that it has provided the framework for other total diet studies, which are currently ongoing and which target the dietary exposure of the Lebanese consumer to pesticide residues, mycotoxins and essential minerals

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Chapter 34
The Malaysian Experience in a Total Diet Study

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Introduction

Malaysia is one of the Southeast Asian countries that have conducted a total diet study (TDS) on a national basis. Malaysia is aware of the importance of the TDS as an assessment tool that can provide indicators of environmental contamination by toxic chemicals and generates a baseline for food safety and public health measures, including those that relate to nutritional adequacy.

In the past, the safety of the food supply was determined using the conventional approach of monitoring individual foods for compliance with national and international regulatory standards. However, this type of monitoring generally focused on individual chemicals in raw commodities to check compliance with good agricultural practice, and so was of limited value in assessing any potential health risks to the Malaysian population from their total diet, as normally consumed.

An alternative method for ensuring the safety of the national diet is a TDS. It provides a clear assessment of the safety and quality of the food supply. A key characteristic of such a study is that foods are prepared ready for consumption, and this provides the best means of assessing the risk to consumers, in contrast to raw commodity-based surveys. It measures the actual dietary exposure to chemicals by the population, and compares these exposures with health-based guidance values set by the World Health Organization (WHO), such as the Acceptable Daily Intake

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(ADI) and the Provisional Tolerable Weekly Intake (PTWI). These comparisons provide a direct link to the health of the population, and therefore, the TDS is the most reliable way to estimate the dietary exposure of toxicants in population subgroups. Therefore, periodic total diet studies are essential to answer the fundamental question whether the national diet is safe and to assess trends in exposure for the future.

The First Total Diet Study in Malaysia

The Food Safety and Quality Division (FSQD) in the Ministry of Health (MOH) is responsible for conducting the TDS in Malaysia. FSQD realized the importance of TDS through literature research and experiences from other countries that had established TDS programs. The planning to conduct the TDS was initiated in the year 2000 through the forum Research Dialogue, which was chaired by the Director General of Health, MOH. The most important requirements for conducting the TDS were identified as follows:

  (i) Obtaining appropriate food consumption data for Malaysia's population;
 (ii) Developing adequate TDS capability and capacity; and,
(iii) Implementing a pilot project on TDS.

   A TDS will provide estimates of the amount of food contaminants that are consumed by a population or population subgroup. Based on results of these exposure estimates and risk assessments, improved food safety standards and regulations, enforcement protocols and/or procedures, and health education materials can be developed with solid scientific justification. Robust risk assessments will not only benefit implementation of food safety management policies, but will also increase confidence of importing countries that trade with Malaysia.

Food Consumption Data

Food consumption data is one of the essential requirements of a TDS to assess the dietary exposure to contaminants for the population. WHO recommends that, if available, countries should use their own individual food consumption data. Because of this clear need, FSQD, in collaboration with Family Health and Development Division (FHDD), conducted the Food Consumption Survey (FCS) to collect the necessary data. Using a food frequency questionnaire, this survey was carried out from October 2002 until December 2003 throughout Malaysia and consisted of six zones covering all 13 states and the federal territory of Kuala Lumpur. This consumption data was collected on the general population aged between 18 and 59 years old, men and women from various ethnic groups, geographical areas and stratum.

   The outcome of the FCS for Malaysia's population was released in 2003 and played an important role in the conduct of Malaysia Total Diet Study (MTDS).

The Food Consumption Statistics (2003) provided individual food consumption data that was used to develop the MTDS food list. The data included 126 foods commonly consumed in Malaysia. The foods were grouped into 12 general categories which are cereals and cereal products, meat and meat products, fish and fish products, eggs and egg products, nuts and nut products, dairy products, vegetables and vegetable products, fruit and fruit products, drinks, alcoholic beverages, seasonings and, sweets and spreads.

Capability and Capacity Building

Training

Capacity building efforts in MTDS were enhanced by ensuring that personnel involved in MTDS are knowledgeable and skilled in this field. Attendance at international workshops, technical meetings, seminars, workshops and consultations, was essential. Some of these activities are presented below.

Japan International Cooperation Agency (JICA) Consultation (2003)

Japan International Cooperation Agency (JICA) consultant, Professor Dr. Hajimu Ishiwata (Department of Human Life and Culture, Faculty of Humanities, Seitoku University, Chiba, Japan) provided the technical expertise in the preparation of the protocol of MTDS for contaminants in 2003. The consultation included advice on planning and conducting of the dietary survey and the MTDS for food contaminants, which continued until the completion of the project.

Study Visit on TDS in Japan (2004)

In September 2004, three officers from FSQD, MOH participated in a 10-day visit to various departments involved in the TDS in Japan. The objectives of the visit were *inter alia* to learn firsthand how to conduct a TDS of contaminants and food additives. During this visit, the officers studied the administration of TDS in Japan, TDS methodology and preparation of TDS composite samples. They also obtained an overview of the Japanese nutrition survey and visited Yokohama Quarantine Station, National Institute of Health Science, Saitama Institute of Public Health and Seitoku Woman University. Following the study visit, FSQD developed its initial Standard Operation Procedures (SOPs) for the MTDS, and a pilot project was carried out in 2005.

FAO/WHO Consultation Program (2006)

In 2006, Dr Philippe Verger (National Institute for Agricultural Research, Paris) and Dr Josef Schlatter (Federal Office of Public Health, Food Safety Division, Nutritional and Toxicological Risks Section, Zürich), two consultants supported respectively by FAO and WHO, conducted training on practical methods of risk assessment of chemical hazards in food. They recommended that Malaysia be involved in the TDS training program conducted by WHO where the objective of the program was to improve the active and effective participation of countries in the elaboration of international standards by the Codex Alimentarius Commission.

WHO TDS Training and Workshop, Beijing (2006)

Malaysia attended the WHO TDS Training Course and Workshop in Beijing in 2006, which exposed the participants to relevant TDS procedures and information. Following this training, the SOPs for MTDS was improved [1].

WHO TDS Training Course, Hong Kong (2008)

Malaysia attended the WHO TDS Training Course in Hong Kong in 2008. The training course equipped the participants with the knowledge and skills required for conducting a TDS, including food consumption data sources, food mapping, sampling, food preparation methods, and types of dietary exposure estimates. Views on the challenges and benefits of conducting TDS were exchanged during a discussion panel, which included participants from Hong Kong, China, New Zealand and Australia [2].

WHO Consultation Program (2009)

In 2009, Dr. Richard Vannoort (Institute for Environmental Science and Research, New Zealand), a WHO consultant, provided technical input and support to FSQD. The consultancy focused on conducting a workshop on exposure and risk assessment of chemicals in the diet, as well as advice on the development of a Malaysian protocol on dietary exposure assessment of key chemicals, including heavy metals and pesticides. This included identifying essential requirements for conducting a TDS, evaluating capacity and capability for conducting a TDS, and developing expertise in terms of knowledge and practical skills in the evaluation of current exposure assessments.

Analytical Capabilities

There are 14 MOH food laboratories located throughout the country, which have been involved in the preparation of composited TDS samples. For the analysis of samples, four Public Health Laboratories were involved, of which one was the TDS reference laboratory.

Instrumentation

An atomic absorption spectrophotometry with a flow injection analysis system (AAS-FIAS) was used for the determination of mercury using the cold vapor technique. Lead and cadmium were determined using the inductive coupled plasma-optical emission spectrometer (ICP-OES). Lead and arsenic were also determined using a graphite furnace atomic absorption spectrophotometry (GFAAS) for low-level determination.

An inductively coupled plasma mass spectrometer (ICPMS) with clean room facility was set up in the TDS reference laboratory to enable more accurate analysis of metals for the TDS. In addition, the ICPMS will significantly reduce the limit of detection as greater sensitivity is important to ensure that exposure assessment calculations use actual data instead of theoretical default values.

Implementation

MTDS was implemented in Malaysia in 2005, where the implementation was divided into three phases, as follows:

Pilot Project (2005)

A small-scale pilot project, involving the central zone and one analytical laboratory, was initiated in 2005. It involved 39 food items based on individual food samples for heavy metal analysis, specifically for mercury, lead and cadmium. The objective of this pilot project was to determine and evaluate the readiness of MOH to carry out the MTDS project. The valuable experience gained during the pilot project was used to further improve the MTDS SOPs.

MTDS Project (2006)

The first MTDS project was conducted from August 2006 until February 2007, based on the food group composites approach, with 11 food groups and 23 sub-groups. The objective focused on mercury, lead, cadmium, and arsenic and implementation followed the MTDS SOPs. This project involved a total of 86 composite samples, involving 13 states and the federal territory of Kuala Lumpur in Malaysia. Analyses were only undertaken by the reference laboratory.

TDS Project (2007/2008)

Prior to this project, the MTDS SOPs were reviewed and minor adjustments were made. A committee was established to oversee the project. The MTDS project 2007/2008 was carried out from November 2007 until December 2008 and involved metal contaminants and pesticide residues using a food composite approach. All states in Malaysia, grouped into six zones, were involved in sample purchasing and sample preparation. A total of 105 food items were purchased and were combined into 57 composite samples for each of the six zones. The four Public Health Laboratories mentioned above analyzed the composite samples.

Having undertaken a pilot and two MTDS projects now, as well as the WHO Consultation Program (2009), Malaysia has strengthened its MTDS implementation capabilities, including its SOPs. To enhance further the MTDS, a master plan for conducting the MTDS is being developed as guidance. A special budget will be allocated and it has been proposed that the MTDS be conducted biennially.

Beginning with the MTDS 2010, food selection for the TDS will be based on the Food Consumption Statistics (2003), and an individual national and regional food approach will be used. Malaysia will utilize this individual food approach and composite individual foods on regional basis for analysis. This approach is more flexible and reliable for subsequent exposure estimates, and also important for traceability purposes. The number of sampling locations is also being reviewed to ensure efficiency of the project. The analytes for analysis will be expanded to include others substances, such as nutrients and dioxins. All samples will be maintained as reserve samples and archived for re-analysis and traceability purposes, if need be.

Conclusion

By carrying out a series of MTDS projects, Malaysia has gained a good deal of knowledge and experience in TDS procedures. Malaysia will continue to strengthen its TDS capacity and capability to ensure the effectiveness of MTDS implementation.

Malaysia now has the benefit of sound scientific risk assessments to protect the public from potentially toxic chemicals in food and in assuring trading partners that the food safety system in Malaysia meets international standards.

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Chapter 35
New Zealand's Experience in Total Diet Studies

Richard W. Vannoort and Cherie A. Flynn

Introduction

Situated in the South Pacific, New Zealand covers some 268,000 km² (slightly less than Japan), extending more than 1,600 km from the top of the North Island to the bottom of the South Island. Surrounded by seas and with extensive coastline, it has a temperate climate, which influences its need for use of certain chemicals in agricultural and horticultural food production. Located on the "rim of fire", New Zealand has associated mountain ranges and is geologically active, which contributes to the mineral content of its soils and foods.

New Zealand has a multicultural society, with a population of approximately 4.3 million, of which 67 % are of European descent, 15 % indigenous Maori, 8 % Polynesians and 10 % Asians. Consequently, New Zealand has a predominantly Western diet with additional ethnic influences and variety.

Almost 50 % of New Zealand's gross domestic product earnings come from food production, so it has a very strong emphasis on food safety and quality both domestically and for exports, with a comprehensive regulatory framework to support this. Meat, fish, dairy, cereals, fruit, and vegetables form the basis of the diet. New Zealand prides itself on its "clean and green" image, and also maintains high standards of health and wellbeing for its people. For these reasons, the New Zealand

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total diet study (NZTDS) was established in 1974 as a key part of its food safety program that complements its other food chemical surveillance and monitoring programs and provides a robust scientific basis for food safety risk management decisions.

New Zealand undertakes what the World Health Organization (WHO) considers to be an essential public health function [1] and achieves this in a highly cost-effective manner. Foods are sampled that represent the diet of the general population, or that are important for a particular cohort within the population, and are analyzed for chemicals on an 'as consumed' basis, e.g. meat is cooked, bananas peeled. By assessing foods at the point of consumption, the NZTDS provides the best means of assessing dietary exposures and any potential for risks to the consumer.

Goals and Objectives

The primary focus of the NZTDS, as with other TDSs undertaken by other countries, is to assess the dietary exposure of the population and specific cohorts within it to chemical compounds, such as contaminants and nutrients in food.

The NZTDS[1] enables New Zealand's food regulatory authority to assess the status of certain chemicals in the New Zealand food supply; indicate any potential exposure concerns and initiate any necessary risk management and/or risk communication interventions; demonstrate trends in dietary exposure; and, make comparisons with other countries.

The high quality scientific data that are generated by the NZTDS is fully documented and made available to all interested parties (see Chap. 47 – Involving and Influencing Key Stakeholders and Interest Groups in a Total Diet Study). Data outputs also inform national and international standard setting activities within Food Standards Australia New Zealand (FSANZ) and the Codex Alimentarius Commission (CAC), respectively. By also measuring moisture in the 'as consumed' NZTDS foods, useful nutrient concentration data can be provided to the New Zealand Food Composition Database (NZFCD).

NZTDS data are also fed into risk assessment and risk management by international bodies, such as the Joint Food and Agriculture Organization of the United Nations (FAO)/WHO Expert Committee on Food Additives (JECFA), Joint FAO/WHO Meetings on Pesticide Residues (JMPR), CAC subsidiary bodies and the WHO Global Environmental Monitoring System/Food Contamination Monitoring and Assessment Programme (GEMS/Food).

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[1] The NZTDS has in the past been known as the New Zealand Total Diet 'Survey', however internationally the term 'Study' is more usually used, which more accurately reflects the nature of the NZTDS in that the 'survey' component (the sampling and analysis of foods) is only one contributing element to the 'study' which has the primary aim of estimating dietary exposure using both analysis data from food samples and consumption information from the national nutrition surveys.

History

There have been six NZTDSs to date. These have been undertaken approximately every 5 years – the first in the mid 1970s and the most recent completed in 2009. The New Zealand Ministry of Health was responsible for the first five, and the New Zealand Food Safety Authority (NZFSA)[2] for the 2003/04 and 2009 NZTDS. Technical implementation of the NZTDSs was carried out for these agencies by the Institute of Environmental Science and Research Limited (ESR), or prior to 1992, by its predecessor, Department of Scientific and Industrial Research – Chemistry.

In initiating the first NZTDS, New Zealand used the food group composite approach. The 1974/75 NZTDS [2, 3] had a food list of 60 foods combined into eight food groups, i.e. grain and cereals; meat, fish and eggs; dairy products; vegetables; fruits; beverages and confectionery; imported foods; and canned foods, which were each sampled in four regions and at four times of the year. These were based on the diet of an adolescent male, the age-sex cohort with the highest consumption of food on a daily basis. Foods were analyzed for a limited number of pesticide residues, as well as a range of elements.

The 1982 NZTDS [4] also used the *food group composite* approach (83 foods, 33 subgroups, sampled in four cities over two seasons), which consisted of nine food group composites for analysis.

With New Zealand stakeholders increasingly recognizing the importance of the NZTDS based on its success in identifying key exposure risks and informing effective risk management, the 1987/88 NZTDS [5] was able to secure additional funding that allowed the redesign of the NZTDS to use the more flexible and robust *individual foods* approach. The TDS food list was extended to 105 foods, each sampled in four cities over two seasons, resulting in 105 individual food composites for analysis. The change to individual foods enabled the age/gender cohorts to include 1–3-year-old toddlers, 4–6 year children, 19–24 year males (constant throughout all NZTDSs), and 25+ year males and females. Point estimate exposures i.e. deterministic, were calculated by combining food consumption data from simulated 2-week diets for each of the respective age-sex cohorts with concentration data obtained after analysis of the TDS foods prepared 'as consumed'.

For the 1990/91 NZTDS [6, 7], the opportunity was taken to extend the range of analytes to include 11 nutrient elements and one vitamin, and categorize the 107 foods as either *Regional* or *National* foods. The 1990/91 NZTDS and 1997/98 NZTDS [8, 9] followed the *individual foods* approach with the food list extended to 114 foods for the latter, and a total of 460 samples analyzed for pesticide residues and 532 samples for contaminant and nutrients. The 1997/98 NZTDS returned to the more traditional contaminant focus with only selected priority nutrients included. The 2003/04 and 2009 NZTDSs [10, 11] also used the *individual foods* approach.

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[2] NZFSA was established in 2002. From 1 July 2010 NZFSA was amalgamated with the New Zealand Ministry of Agriculture and Forestry (MAF), and on 1 July 2011, the Ministry of Fisheries was also merged into MAF. On the 30 April 2012, the new ministry became the Ministry for Primary Industries (MPI).

Design of the Current NZTDS

Core and Add-on Components

The 2003/04 NZTDS and the 2009 NZTDS have been designed by the Ministry of Primary Industries (MPI) to have two parts, namely a core and add-ons components. This approach is intended to allow for both continuity with past NZTDSs and flexibility to include, on a less regular basis, chemicals of lesser priority. It also allows for the NZTDS to consider emerging or specific issues of interest to stakeholders.

NZTDS Food List

The number of foods sampled and analyzed in NZTDSs had initially increased over time, but now is relatively stable. For example, in the 2003/04 NZTDS, 121 foods spread across 14 food groups were included. Of these, 110 foods, including tap drinking water, were estimated to represent the most commonly consumed foods and amounted to >95 % by weight of the normal diet consumed. Three foods known to be potentially significant sources of certain contaminants were also included, namely, oysters, mussels and liver. The remaining foods were specific favorites with infants and children – baby food, snack bars and flavored drinks. The 2009 NZTDS used essentially the same food list, with only minor changes; adding one new food (an Indian takeaway dish) and separating water into tap and bottled, to give a total of 123 foods.

Population Cohorts

The particular population cohorts for whom dietary exposure estimates are calculated have increased over time. The young males (19–24 years) group was the only estimate made in the original (1974/75) NZTDS and it has been retained as a constant reference point in subsequent NZTDSs. Other age-sex groupings have been added over the years with the 2003/04 and 2009 NZTDSs including eight such cohorts. These are: adult males (25+ years); adult females (25+ years); young males (19–24 years); adolescent boys (11–14 years); adolescent girls (11–14 years); children (5–8 years); toddlers (1–3 years); and infants (6–12 months).

NZTDS Simulated Two-Week Diets

The foods selected for the NZTDS are intended to represent the average and typical diet of New Zealanders from a range of population cohorts. Dietary exposures are

estimated using consumption information from simulated 2-week diets. The simulated diets use only the foods on the NZTDS food list to reflect the consumption of the various population cohorts that those foods represent. In the interests of continuity, all foods from the previous NZTDS are usually considered for inclusion and any changes made are based on the most up-to-date available information about what foods are actually being consumed.

Food Consumption Data for Developing NZTDS Food List and Simulated Diets

The information used to develop the NZTDS foods list and the simulated diets is derived from a range of sources. The most important of these are the national nutrition surveys conducted by the Ministry of Health. There are two surveys undertaken at approximately 10 year intervals, one for adults 15 years and older, and one for children 5–14 years (recent surveys being the 1997 National Nutrition Survey [12] and the 2002 Children's Nutrition Survey [13], with another Adult's Nutrition Survey undertaken in 2010). Other sources of information include: retail sales data; specific nutrition surveys for age groups not included in the national nutrition surveys, particularly for those for children under 5 years of age; and advice from industry or academic experts.

Sampling in the NZTDS

There were 63 *National* foods and 58 *Regional* foods in the 2003/04 NZTDS, altered to 62 *National* foods and 61 *Regional* foods for the 2009 NZTDS. *National* foods are those that are expected to be the same no matter where in New Zealand they were purchased – that is they are manufactured or produced by a national or international company and distributed nationwide. Included in this group are imported foods such as bananas, and most beverages, oil, pasta, rice, and many processed foods such as biscuits, cheese etc. *Regional* foods are those foods that could change from region to region. They are grown or manufactured locally, so may be expected to have different agricultural chemical applications or soil contaminant/nutrient contents. This group covers most fresh fruit and vegetables, breads, meats, takeaways, milk products and tap water. The concept of *National* and *Regional* foods was introduced in the 1990/91 NZTDS and has been followed in each NZTDS since then. *Regional* foods have been sampled from four regional sites (two main cities/growing areas in each island – Auckland, Napier, Christchurch and Dunedin), while national foods are sampled from one nationally representative site. This has been Christchurch, the city where sample preparation occurs, thus facilitating transport and sample management (see Fig. 35.1).

Fig. 35.1 Sampling sites of
Regional and *National* foods
in 2009 NZTDS

Foods are sampled over a 12-month period in four sampling rounds. Each of the foods is sampled twice over the entire study. This allows for seasonal variations and also recognizes that some foods, or key ingredients in a food, are imported when not available from domestic production.

For each food, sampling officers are instructed on how much to purchase and, in some cases, brands are suggested. They are also instructed where to purchase the foods, for example from a local supermarket or from a specialist shop (i.e. green grocer, fruit shop, butcher, delicatessen).

Preparation of Samples

In the 2003/04 NZTDS, a total of 4,440 samples were purchased, and these were all prepared 'as consumed' by ESR at their laboratory in Christchurch (see Fig. 35.1).

The 2003/04 NZTDS used the *individual foods* approach. Multiple purchases of each *National* brand or *Regional* food type (i.e. multiple purchases of chocolate biscuits of one brand, or multiple tomato purchases in the Auckland region) were composited before analysis. In compositing the individual foods (e.g. chocolate biscuits, cracker biscuits, white rice, trim milk, etc.), each of the four *National* brands

or four *Regional* samples were kept separate in both seasons, resulting in eight analytical samples for each individual food over the course of the 2003/04 NZTDS. This was double the number of analytical samples for each food from the previous NZTDS. Wherever possible, *Regional* and/or seasonal sample information was retained. In total, 990 food samples were analyzed for agricultural compound residues, and 968 samples for specific contaminants and certain nutrient elements. The 2009 NZTDS has also used the *individual foods* approach with the numbers of samples purchased and analyzed increasing slightly to reflect the changes in the food list.

Analyses

To ensure the most cost-effective and robust analytical results would be obtained in the NZTDS, competing laboratories capable of providing an adequate analytical service (range of analytes, limits of detection/quantitation, quality control and assurance, capacity and throughput, timeliness, pricing, etc.) were asked to tender for the analytical services needed in the NZTDS. Use of commercial analytical laboratories is preferred, so that quality is maintained while capturing competitive cost savings (see Chap. 14 – Commercial Analytical Laboratories—Tendering, Selecting, Contracting and Managing Performance).

For agricultural compounds in the NZTDS, there are two specific screens that are currently considered to be core components of the NZTDS. The first is a multi-residue screen. This includes those pesticides on the WHO GEMS/Food priority list for TDSs [14]; compounds that are or have been registered for use in New Zealand; and those registered for use in other countries and may therefore be present on imported foods. The exact number of compounds included in such a screen has increased over time as technical capability as developed, such that for the 2003/04 NZTDS the multi-residue screen, over 200 compounds were included (well over twice that in the previous 1997/98 NZTDS). For the 2009 NZTDS the number increased to 240. The limit at which a residue can be detected has also lowered over that time as advances in technology have been made – these are now typically at the parts per billion or even parts per trillion levels compared to parts per million only about 10 years ago.

The second screen is for dithiocarbamates, which are the most commonly used fungicides in New Zealand and are also on the WHO GEMS/Food priority list for TDSs. In 2003/04 an additional screen for 18 acid herbicides was also included on a limited number of selected foods. In the 2009 NZTDS, the separate acid herbicides screen was not included because the 2003/04 NZTDS did not identify dietary exposure to these compounds in New Zealand as a public health concern.

The nutrient elements, iodine (I) and selenium (Se) are always included in the NZTDS. New Zealand soils are naturally deficient in these and associated intakes are low, so it is extremely important that the NZTDS is used to monitor trends in dietary intake. In the 2003/04 NZTDS the nutrient elements iron (Fe) and sodium

(Na) were also included. For the 2009 NZTDS sodium was again included to allow continued monitoring of New Zealanders intake levels.

Four contaminant elements, arsenic (As), lead (Pb), cadmium (Cd), and mercury (Hg) are currently considered as core for the NZTDS because of New Zealand's level of volcanic activity, historical fertilizer use, and soil make up. All have the potential for adverse health effects and are on the WHO GEMS/Food priority list for TDSs. Thus it is important for New Zealand to check that food concentrations of these elements are do give rise to adverse health effects and that trends are measured over extended time periods. This also requires careful control of the sampling and analytical procedures over time so that valid comparisons can be made. In the 2009 NZTDS, methylmercury (MeHg) was also analyzed in fish and seafood products, given this is the most toxic form of mercury and these foods are by far the dominant contributors to its dietary exposure.

Exposure Assessment and Risk Characterization

Dietary exposures in the NZTDS were estimated by combining the mean concentration data found in each of the individual foods with mean consumption information from simulated 2-week 'typical' diets for eight different age–sex cohorts in the population. Any potential risk to average consumers was characterized by comparing these dietary estimates to international health-based reference values, such as the Acceptable Daily Intake (ADI) for pesticides, Provisional Tolerable Weekly Intake (PTWI) for contaminants, or, in the case of nutrient elements, Estimated Average Requirement (EAR), Recommended Dietary Intake (RDI), or Upper Level of intake (UL).

Reporting

New Zealand places high importance in communicating the results of scientific research, such as the NZTDS (see Chap. 19 – Communicating Results in a Total Diet Study). Communicating results in a timely manner has consequently been one of the key goals for the NZTDS since 1997/98. For this reason, following each quarterly sampling round, a report containing the analytical results for each food/compound combination and for each region or national brand is released on the MPI [15] website. These results are anonymized as regards specific brand names and/or the business from which a food was purchased. This is because only a limited number of product brands are sampled and given the relatively small numbers per product, it is seen as unfair to identify these specifically when their selection may have been somewhat random. The analytical results should not be seen as endorsing a product because it has no residues, or denigrating it because residues (even within legal limits) are present.

The full NZTDS report on the dietary exposures for the various age-sex cohorts and the percentage contribution for each food group to that exposure is released approximately 12–18 months after the sampling and analysis of individual foods is completed. This is a comprehensive scientific report that is internationally peer reviewed before publication and is made available in both printed and electronic form.

Regulatory Action

Total diet studies, including the NZTDS, are not intended as enforcement or compliance tools. However, unusual or unexpected results are notified to the MPI as they are identified, that is, ahead of the presentation of full results. No regulatory action is expected to occur from a single result unless it is suggestive of a possible risk to public health, either alone or as representative of a particular class of product. Examples from the 2003/04 TDS were: very high iodine detected in a soy milk product that was indicative of a systemic product composition problem, and high levels of lead in an infant food which was identified as having been due to one-off contamination of a bulk-container shipment of maize. The latter incident resulted in products being recalled in New Zealand, Australia and Fiji.

Key NZTDS Findings

For pesticides, 97 % of the estimated dietary exposures for the eight age-sex cohorts in the 2009 NZTDS were less than 1 % of the ADIs for various agricultural compound residues, and the remaining 3 % were well below their respective ADIs. This is a key finding as it focuses on the exposures from the total diet. In contrast, if one were to focus on the frequency of residue detections, as some parties are occasionally inclined to do, then the TDS can be misrepresented as implying a health concern. In fact, finding more residues in more recent TDSs is not unexpected given the significant improvements in limits of detection over recent decades. Of the 982 food samples screened for agricultural compound residues in the 2009 NZTDS, 45 % (437 samples) were found to contain detectable residues, and residues of 75 different agricultural compounds were detected. That said, residues were detected in only 910 (0.4 %) of the approximately 237,000 individual analytical agricultural compound residue results. Clearly the focus for effective risk analysis needs to remain on dietary exposures, not maximum concentrations or frequency of detection. It is not so much what is in the food that counts but rather what the dose is from the total diet, i.e. for effective risk assessment. Consequently, the emphasis should not be on the mere presence of the hazard, but on the exposure.

For three contaminant elements (Cd, Hg and MeHg), the estimated dietary exposures were all well within their respective PTWIs (or the Provisional Tolerable Monthly Intake (PTMI) in the case of Cd). The PTWI/PTMI represents the
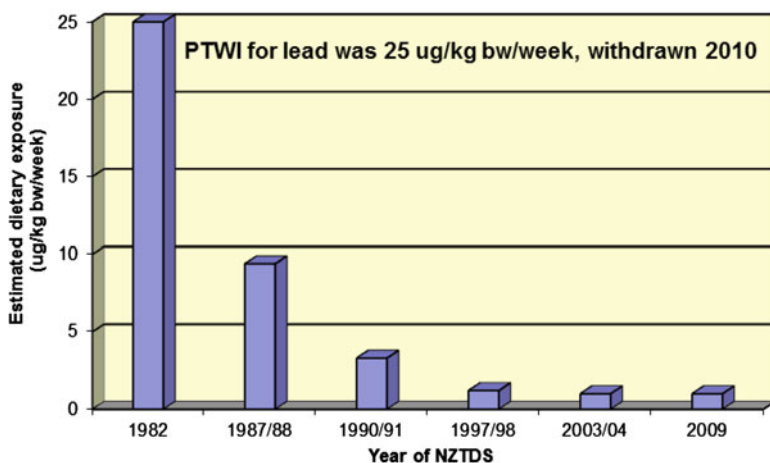
Fig. 35.2 Trends in dietary exposures to lead for 19–24 young males in NZTDSs

permissible human exposure to those contaminants unavoidably associated with consumption of otherwise wholesome and nutritious food i.e. a safe level of intake. Consequently, the contaminant dietary exposures in the 2009 NZTDS were considered to be unlikely to have any adverse health implications for the general New Zealand population. Even with the withdrawal of the international health-based reference values for inorganic arsenic and lead, NZTDS dietary exposures to these contaminants at current levels are unlikely to represent a significant risk to public health. Consequently, the consistency of 2009 NZTDS findings with previous NZTDSs is reassuring. However, it remains important to keep dietary exposures to these contaminants as low as reasonably achievable (ALARA).

Lead as a Case Study

The NZTDS not only has the ability to identify unacceptably high dietary exposures and the associated potential risks to public health, but also successive NZTDSs emphatically demonstrate the effectiveness of risk management strategies. Dietary lead exposure in New Zealand is a very good example. Risk management decisions have included discouraging the use of lead solder in canned foods, and phasing out of lead additives in fuel for vehicles, the benefits of which are clearly evident in the downward trend of estimated lead dietary exposures found over successive NZTDSs (see Fig. 35.2).

It is fair to say that a good proportion of the estimated dietary exposure to lead in 1982 and 1987/88 was associated with uncertainty due to the much higher limit of detection used then (LOD = 0.05 mg/kg) combined with the approach of assigning half of the LOD to 'not detected' results for deriving a mean concentration, and subsequently estimating the dietary exposures. In TDSs in 1997/98, 2003/04 and
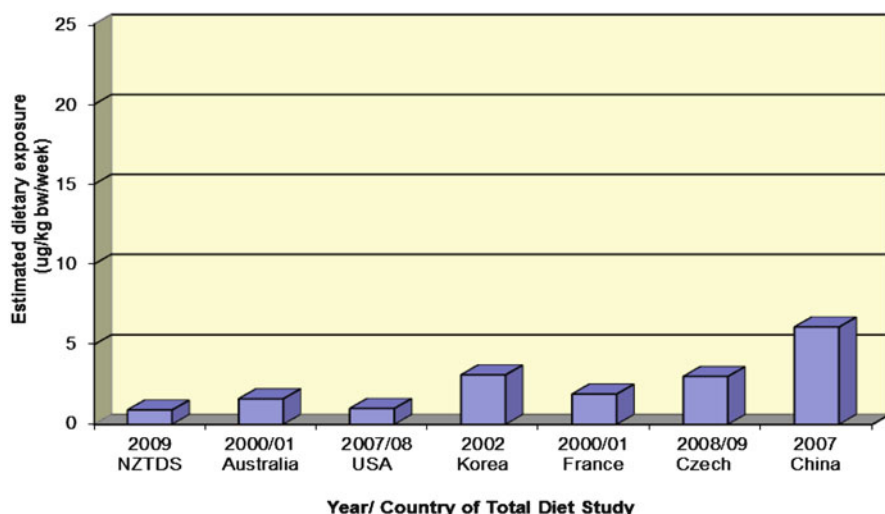
Fig. 35.3 Comparison of estimated weekly dietary exposures (μg/kg bw/week) to lead for 25+ year males in the 2009 NZTSDS with other TDSs

2009, the change of analytical methodology to inductively coupled plasma mass spectrometry (ICPMS) reduced the LOD emphatically to 0.0001 mg/kg in water, 0.001 mg/kg in liquids, 0.002–0.005 mg/kg in high moisture foods like fruit and vegetables, and 0.010 mg/kg in dry or fatty foods. So in 2009, this meant by assigning ND=0, the lower bound dietary exposure for a 19–24 year young male (YM) was 0.8 μg/kg bw/week, the upper bound (ND=LOD) was 1.1 μg/kg bw/week, and by assigning ND=1/2 LOD, the estimated dietary exposure to lead was 1.0 μg/kg bw/week.

From Fig. 35.3, it is clear that New Zealand dietary exposures to lead now compare very favorably with other countries around the world, recognizing that they do have different foods and consumption patterns, and they may have used different calculation methods, such as those for assigning concentrations to 'not-detected' analyses. The 2009 NZTDS lead exposure for an adult male (0.9 μg/kg bw/week) is one of the lowest when compared to Australia (1.6) [16], the USA (0.88) [17], France (1.9) [18], the Czech Republic (2.4) [19], the Republic of Korea (3.1) [20], and China (6.1) [21].

The individual foods contributing to the 2009 NZTDS dietary exposure to lead were spread fairly evenly over the food groups and reflected the ubiquitous environmental presence of residual lead in New Zealand.

While NZTDS dietary lead exposures are now very low, there is no room for complacency. Although not a compliance survey tool, the 2003/04 NZTDS identified a situation of major lead contamination in the New Zealand food supply, initially found in baby food (0.8 mg/kg) but traced back to contaminated corn flour. The level found was 23 mg/kg, which is much higher that the FSANZ Maximum Level in cereals of 0.2 mg/kg. It highlighted the need for prompt risk assessment, risk management and
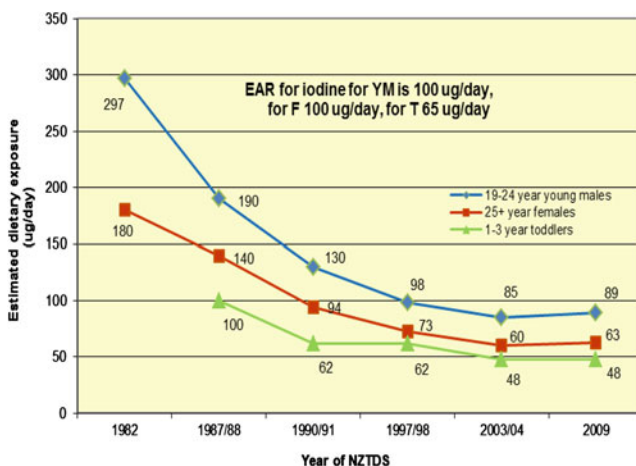
Fig. 35.4 Trends in dietary iodine intakes in NZTDSs

risk communication, as well as ongoing surveillance and monitoring of this and other ubiquitous environmental contaminants. This instance of lead contamination resulted in food recalls in New Zealand, Australia and Fiji [22].

Iodine as a Case Study

From a nutritional perspective, iodine is a key trace nutrient, which is deficient in New Zealand soils and the NZTDS has identified that iodine intakes have been dropping significantly over the last three decades, such that they are now well below Estimated Adequate Requirements (EARs) (see Fig. 35.4). These observations have been confirmed by complementary assessments involving urinary iodine excretion studies and also thyroid volume studies, where indications are that preclinical symptoms of goiter are beginning to re-emerge in New Zealand [23].

Iodine plays an integral part in thyroid and hormone function, and is essential for both mental and physical development, especially in infancy and early childhood. The current low levels of intake have been assessed and the risks of sufficient concern to public health that mandatory fortification of the food supply via iodized salt in breads has been regulated by FSANZ, effective from September 2009.

Sodium as a Case Study

Concentrations of sodium in NZTDS foods ranged from <10 mg/kg up to 35,000 mg/kg (in yeast extract). Higher sodium concentrations are found in processed foods

Fig. 35.5 Foods contributing
to estimated dietary intake of
sodium in 25+ year males in
the 2009 NZTDS
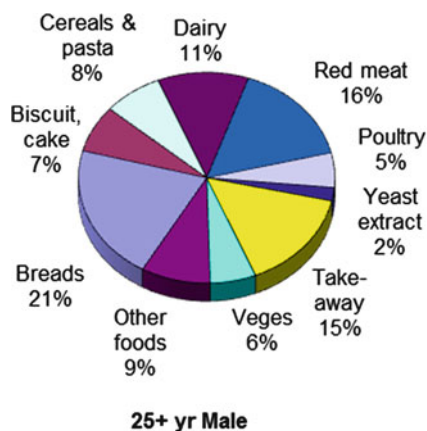
(e.g. breads, ham, sausages, etc.) than in unprocessed foods, such that the mean concentration of sodium in bacon was 16,911 mg/kg compared to 909 mg/kg in pork meat. Estimated mean sodium intakes in the 2009 NZTDS exceeded upper limits (ULs) by 116–148 % for all age-sex cohorts except the 25+ year females, whose intakes were below the UL, but still two to four times the adequate intake (AI).

A strength of the NZTDS is being able to identify which foods or food groups contribute most to dietary intakes/exposures (see Fig. 35.5). Processed foods contribute about 65–70 % of dietary sodium, and processed grain products collectively account for 27–48 % of dietary sodium intake. The sodium intake estimates in the 2009 NZTDS do not include the use of discretionary salt added at the time of cooking, or at the table for taste, and it has been estimated that this might add an additional 20 % to total sodium intake [24, 25]. Sodium intakes have not adequately fallen for New Zealand 25+ year males and females, 19–24 year young males and 1–3 year toddlers, decreasing by only 14–28 % for the period 1987–2009 in spite of education programs. It remains important to reduce dietary sodium intake, given it is probably one of the causative factors in New Zealand's high rates of hypertension and cardiovascular disease.

Conclusion

The NZTDS is an important exposure assessment tool for New Zealand's food regulatory authority, and provides essential scientific inputs to regulatory activities that range from risk communication to setting specific food control standards.

While perceived concerns about agricultural compound residues in food do exist among some consumers, the NZTDS has been able to clearly demonstrate such concerns are, in fact, incorrect, and that dietary exposures from agricultural compounds are highly unlikely to pose any adverse health risks for the New Zealand

population. Similar conclusions have been found for the contaminant element dietary exposures, including lead. That said, there is no room for complacency, as the lead contamination incident in baby food highlighted. The NZTDS has identified that the low dietary intakes of iodine in New Zealand are a public health concern, helped target appropriate follow-up studies, and contributed to development of regulations for the mandatory fortification of the New Zealand food supply. On the other hand, sodium dietary intakes in the NZTDS continue to exceed upper limits, and reinforce the Ministry of Health guidelines which support a reduction in sodium intake. The ability to also identify which foods are contributing to dietary exposures/intakes is a valuable attribute of the NZTDS. In addition, the NZTDS assesses temporal trends, which enable the effectiveness of risk management and risk communication strategies to be assessed. For all these reasons, future monitoring for agricultural chemicals, chemical contaminants and selected nutrients, such as iodine and sodium, are likely to continue in future NZTDSs.

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Chapter 36
Experiences in Total Diet Studies in Spain

Victoria Marcos

Introduction

The Spanish Food Safety and Nutrition Agency (AESAN) under the Ministry of Health and Social Policy is carrying out the first Spanish national total diet study. This total diet study (TDS) is to include the total Spanish population of nearly 47 million people. Considering the distribution of population and their different dietary habits, the country has been divided into four geographical areas: north, south, east, and center.

The TDS methodology was developed following World Health Organization (WHO) guidelines and recommendations stemming from the various expert groups organized by the European Food Safety Authority (EFSA). The first round of the study started in 2009. Food consumption data were taken from the latest available national survey carried out by the Ministry of Agriculture in 2007. The household survey method was used, which included about 6,000 households throughout the country [1].

In order to achieve as accurate exposure assessment as possible, AESAN is currently conducting a national food consumption survey based on both 3-day dietary records and food frequency questionnaires with a sample size of over 3,000 inhabitants. Results will be applied to the second round of the TDS.

Food Classification and Food Grouping

Using as a base the food classification system of the European Food Composition Database (EUROFIR), some of the initial 12 food categories have been subdivided giving a total of 21 categories and subcategories (Table 36.1).

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Table 36.1 Food classification by categories and subcategories of the spanish total diet study

I. Beverages (not including milk)	10. Seafood and related foods
Ia. Nonalcoholic beverages	10a. Fattfish
Ib. Alcoholic beverages	10b. Lean fish
2. Eggs and eggs products	10c. Crustaceans
3. Fats and oils	10d. Mollusks
4. Fruits and fruit products	10e. Processed seafood
5. Grain and grain products	11. Sugar and sugar products
6. Meat and meat products	12. Vegetables and vegetable products
7. Milk and milk products	12a. Pulses
7a. Milk and milk products (not including cheese)	12b. Potatoes and other starchy roots
7b. Cheese	12c. Vegetables (not including potatoes)
8. Miscellaneous	12d. Canned vegetables
9. Nuts, seeds, and kernels	

In order to make a detailed calculation of exposure, these 21 categories have been further subdivided, resulting in a total of 100 food groups, which contain a total number of 300 different food items, including drinking water. Besides the most commonly consumed foods, other products are considered of special interest based on their expected contaminants, such as nuts for the possible presence of mycotoxins and soup cubes for the possible presence of 3-monochloro-1,2-propanediol (3-MCPD). Seventy-three (73) of these food groups contain different food items (apples, pears, peaches, etc.). Criteria for grouping are: composition (% fat), expected type of contamination, seasonality, consumption rate and analytical procedures. The other 27 groups are made up of different types of the same food in the same group (hen eggs in its own group, potatoes in its own group, rice in its own group, etc.). Each of these 100 food groups is being analyzed independently.

Two types of foods were considered in the Spanish TDS: the first one being 'national' foods, such as processed products in which a relatively homogeneous level of contamination may be expected. 'National' foods include 175 items, such as drinks, dairy products and industrial bakery products. The second type of foods is 'regional' foodstuffs with 125 items, such as eggs, fruit, fish and meat. Considering the TDS as an ongoing activity, planning for TDS is organized on a yearly basis in terms of food sampling, number of samples and compounds to be analyzed.

Sampling

At the beginning of 2009, a pilot test was undertaken for sampling and transportation, in order to define conditions of purchase (shopping lists, shopping guide, etc.), packaging and transport. Purchase was made of a representative food for each of the most perishable food groups such as fish and mussels, or fragile items such as eggs.

Frozen foods were also included. At that time, criteria for acceptance of food samples in the kitchen/laboratory were also developed and adopted.

More than 300 nonperishable products (canned food, alcoholic and soft drinks, etc.) were sampled at the end of 2009. 'National' foods are being acquired in two locations near the place for sample preparation. 'Regional' foods are being acquired in a population center in each major geographical area. According to the capacity of the sample preparation laboratory/kitchen, the total amount of food products to be sampled in one area is divided into three stages of purchasing. Acquisition of such 'regional' products is carried out in a traditional store or supermarket. The TDS first round included a sampling plan of more than 1,200 individual food products.

Samples Preparation

Food preparation, including cooking, and sample compositing are being carried out in a kitchen/laboratory built for this purpose in the National Center for Food (CNA), belonging to AESAN. Based on other TDSs [2, 3] and recommendations, [4] a manual entitled "Standard Operation Procedure for Food Preparation, Cooking and Compositing" was developed and put into practice.

Two types of samples are being prepared "ready for consumption". Composite samples were formed by combining five different individual samples of the same food. This included foods with the highest consumption, such as eggs, milk, potatoes, etc. The second types of samples included aggregate food groups in which samples were formed by combining two to six different foods (two different individuals of each product) by weight depending of their consumption rates. These aggregate samples were comprised of foods belonging to the same food subcategory. The proportion of each food in the mixture was calculated on the basis of its respective consumption levels for an average 65 kg Spanish person.

Analyses

Analyses are being performed at the National Centre for Food (CNA), National Reference Laboratory of AESAN located in Majadahonda (Madrid). The laboratory has been accredited since 1999 by the national accreditation body (ENAC).

Substances analyzed in the first round include mycotoxins, pesticides, heavy metals, polycyclic aromatic hydrocarbons (PAHs), and 3-MCPD and its esters. Table 36.2 shows the respective determinations in the various food categories.

Analytical methods are validated according to the specific requirements for TDS, taking into account that in such studies, the lowest detection and quantification levels should be achieved. Each composite and aggregate sample is analyzed independently. Approximately 400 samples are being processed in the first round.

Table 36.2 Analytical determinations in the various food categories

Categories	Ia	Ib	2	3	4	5	6I	7a	7b	8	9	10a	10b	10c	10d	10e	11	12a	12b	12c	12d
PAHs	✓	✓		✓	✓	✓	✓	✓	✓	✓							✓				✓
Ochratoxin A	✓	✓		✓	✓	✓	✓	✓	✓	✓					✓	✓	✓	✓	✓	✓	✓
Aflatoxins		✓			✓		✓			✓	✓						✓				
Patulin	✓	✓			✓												✓				
Lead	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓			✓	✓	✓
Cadmium	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓			✓	✓	✓
Mercury	✓						✓				✓	✓	✓	✓	✓	✓					✓
Arsenic	✓	✓				✓	✓			✓	✓						✓		✓		
3-MCPD	✓					✓	✓	✓	✓	✓	✓					✓	✓				
3-MCPD esters				✓																	
1,3-DCP	✓			✓	✓	✓	✓	✓	✓	✓	✓					✓	✓	✓	✓	✓	
Pesticides	✓		✓	✓	✓	✓	✓	✓	✓							✓	✓	✓	✓	✓	
Dioxins			✓	✓		✓	✓	✓	✓			✓				✓				✓	✓

Results

Regarding preliminary results of this study, special attention was given to the presence of heavy metals. In most of the groups that have already been analyzed, including eggs, cereals, vegetables (including canned products), lean and fat fish, and nuts, concentrations are similar to those reported previously in the country [5] and in neighboring countries [6]. The protocol for assigning concentration values to "non-detected" (ND) or "not quantified" (NQ) analytical results is based on using lower and/or upper bound values (zero and LOD), [7] to calculate the mean food concentrations. For pesticides, which are non-detected in any of analyzed samples, only the lower bound value was applied.

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Chapter 37
Total Diet Study in the Basque Country, Spain

Mercedes Jalón, Inés Urieta, and M. Luz Macho

Introduction

The Basque Country is a small region in the north of Spain with an area of 7,261 km^2 and a population of 2.2 million. In 1990, the Basque Government initiated a total diet study (TDS) using the market basket approach as an important part of its monitoring program for chemical contaminants in the food supply [1]. This investigation pioneered TDSs in Spain and is still ongoing.

Design of the Basque Total Diet Study

The design of the Basque TDS has been described in detail previously [2]. The main features of the study (see Fig. 37.1) are summarized here. Using the information provided by the Basque Food Survey, the average diet of the population was established. The food list was then developed and the 91 food items included were purchased at monthly intervals at different locations having over 5,000 inhabitants each. After preparation and cooking, the 91 food items were combined into 16 food groups (see Table 37.1) and analyzed for the chemicals of interest. Finally, the

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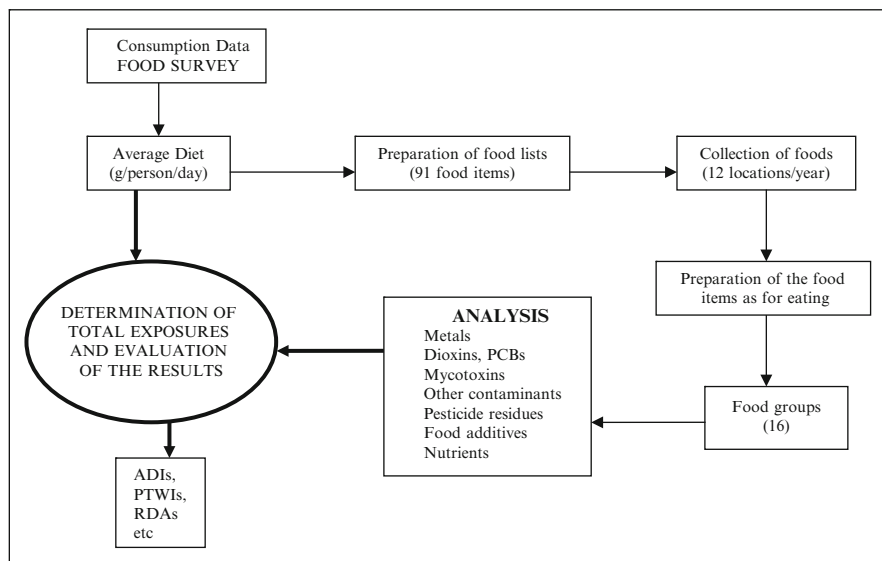
Fig. 37.1 Scheme of the Basque total diet study

dietary exposures were calculated by combining the concentration data with consumption data. These exposure estimates were compared with appropriate health-based guidance values and also with data from other countries. Annual dietary exposures were obtained by calculating the average of the appropriate 12 market baskets. Drinking water was not included in the estimated dietary exposures.

All analyses, except for those for dioxins and polychlorinated biphenyls (PCBs), were carried out in the Public Health Laboratory of the Basque Country, which has been accredited by ENAC since 1998. Dioxins and PCBs were analyzed in the Central Science Laboratory of the United Kingdom (now the Food and Environment Research Agency). None of the concentrations were corrected for the recovery percentage and all values were reported on a fresh weight basis. For calculating exposures, results quoted as less than the limit of determination/quantification are taken as being zero for pesticide residues and nutrients and as equal to the limit of determination/quantification for other chemical analytes. For calculating dietary exposures, a body weight of 68 kg was used, which is the average weight of the participants in the Basque Food Survey.

Summary of the Results

Initially, heavy metals (lead, cadmium, mercury and arsenic), organochlorine pesticides [HCB (hexachlorobenzene), HCH (α, β, γ, δ-hexachlorocyclohexanne)], DDT, DDE, DDD, dieldrin, aldrin, endrin, heptachlor, heptachlor epoxide, endosulfan

Table 37.1 Basque total diet study food groups

Food group		Average consumption (g/person/day)
1	Eggs	41
2	Meat	118
3	Meat products	45
4	Fish	89
5	Milk	294
6	Dairy products	58
7	Bread	122
8	Cereals	62
9	Pulses and nuts	27
10	Potatoes	90
11	Vegetables	159
12	Fruits	377
13	Sugar and preserves	34
14	Fats and oils	45
15	Nonalcoholic beverages	198
16	Alcoholic beverages	243

(α, β), and methoxychlor) and selected trace elements (iron and zinc) were determined in the 16 total diet food groups. Aflatoxin M_1 was also determined in the milk and dairy products groups, although aflatoxin M_1 exposure was not estimated owing to the very low levels detected. In subsequent revisions of the Basque TDS, food additives and new contaminants were included. Specifically, nitrates, nitrites, sulfites, ochratoxin A, dioxins, and PCBs were determined in selected food groups.

Dietary exposure estimates of organochlorine pesticide residues were very low and accounted for less than 7 % of the appropriate health-based guidance values, such as acceptable daily intakes (ADIs) and tolerable daily intakes (TDIs). These residues were determined during the period 1990–1995 and due to the very low number of detections, their determination was discontinued after 1995. Nutrient elements, namely iron and zinc, were determined in all total diet groups in the period 1990–1991. Average intakes of zinc were adequate but dietary intake of iron was deficient in females [3]. Sulfite was determined in the TDS food groups where its addition was permitted, and nitrates and nitrites were determined in relevant TDS food groups, including potatoes, vegetables, and meat products. The estimated intakes of these substances were well below their appropriate ADIs.

Lead and cadmium have been determined in all food groups since 1990. In 1994, lead dietary exposure was as high as 6.7 μg/kg body weight per week or 27 % of Provisional Tolerable Weekly Intake (PTWI), but a steady decrease has since been observed and in 2008, the estimated exposure was down to 3.2 μg/kg bw/week (13 % of PTWI). Cadmium dietary exposure has been relatively steady over the course of the Basque TDSs, and has ranged between 0.90 and 1.30 μg/kg bw per week (13–19 % of the PTWI).

Mercury and arsenic were both initially determined in all food groups. However, as measurable amounts were essentially only detected in the fish group, analyses were restricted to just this group and included 12 samples per year. Total mercury and total arsenic dietary exposures have always been very high in comparison to those estimated in other countries. This has been attributed to the very high fish consumption in this region of 89 g/day. Since 1996, inorganic arsenic, which is the most toxic form, has been determined and the weekly estimated exposures have always been very low (0.15–0.25 μg/kg body weight), being less than 1 % of the lower limit of the benchmark dose for a 0.5 % increase in lung cancer (MBDL$_{0.5}$) determined from epidemiological studies to be 21 μg/kg bw/week [4]. Since 2007, methylmercury (MeHg) has also been determined and estimated dietary exposures in 2007 and 2008 were 1.09 and 1.05 μg/kg bw/week, respectively, equivalent to almost 70 % of the JECFA-revised PTWI (1.6 μg/kg bw/week). As these exposures relate to average consumers, it is probable that extreme fish consumers could have dietary exposures that are well above the PTWI. Pregnant women are a particular risk group, since MeHg can cross the placenta. Hake and mackerel, which are consumed in higher amounts, accounted for the majority of the dietary mercury exposure, even though tuna and swordfish actually had the highest concentrations. One follow up investigation of the mercury and arsenic results was the determination of arsenic species in the different fish types that are included in the fish group of the Basque TDS [5–8].

The exposure to dioxins and dioxin-like PCBs has been assessed through their determination in five TDS food groups: eggs, meat and meat products, fish, milk and milk products, and oils and fats. These groups were analyzed in two different periods: 1994–1995 and 1999–2000 [9]. The highest concentrations of dioxins and dioxin-like PCBs in WHO-Toxic Equivalents (WHO-TEQ) were found, as expected, in the fish group where PCBs contributed 87 % of WHO-TEQ. This is in sharp contrast to the other food categories where dioxins actually made the largest contribution to the total WHO-TEQ. For total dietary exposure to dioxins, the fish group also was the highest contributor. The average estimated upper bound dietary exposure to dioxins and dioxin-like PCBs from the five TDS food groups was 175.5 pg WHO-TEQ/person/day (equivalent to 2.6 pg WHO-TEQ/kg bw/day or 18.2 pg/kg bw/week or 78 pg/kg bw/month) in 1999–2000. This value is slightly over the tolerable weekly intake (TWI) of 14 pg WHO-TEQ/kg bw/week proposed by the EU Scientific Committee for Food and the Provisional Tolerable Monthly Intake (PTMI) of 70 pg WHO-TEQ/kg bw/month proposed by the JECFA. The estimated exposure is in the range of the average exposures reported for the population of the European Union of 1.2–3 WHO-TEQ pg kg bw/day [10]. Comparing dietary exposures estimated in the 1999–2000 TDS to those obtained in 1994–1995 for samples of the same five food categories, a decrease of approximately 60 % in the total TEQs exposures was observed.

Ochratoxin A was determined in 14 of the 16 total diet food groups in 1999–2000. Estimated weekly exposures were very low (12.8 and 13 ng/kg bw, respectively), and accounted for only 11 % of the TWI of 120 ng/kg bw/week established by the European Food Safety Authority.

Conclusion

The results of the Basque TDS have enabled some priority areas to be identified. In particular, the high mercury and dioxin and PCB exposures associated with high fish consumption. However, it is of utmost importance to make a risk-benefit analysis, since fish is the main source of polyunsaturated fatty acids (PUFAs) and it also provides other important nutrients, such as high quality proteins, vitamin D, iodine, and selenium. The recommendations derived from this study should be applied to at-risk population groups, for instance, advising women to reduce consumption of certain fish species during pregnancy.

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Chapter 38
Total Diet Studies in Catalonia, Spain

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Introduction

The total diet study (TDS) in Catalonia began in 2000 with the objective to estimate the mean dietary exposures for different population groups segmented by age and sex, to the main environmental contaminants in Catalonia and assess the potential health risk these may represent. As the TDS is an ongoing study, it also enables the monitoring of trends in these diet-related exposures and the effectiveness of risk management and risk communication measures undertaken to reduce them.

Methodology

The Catalan TDS design is based on the World Health Organization (WHO) guidelines [1]. The consumption data on the different foodstuffs were obtained from a food consumption survey. Samples were taken for 51 widely consumed foodstuffs distributed into 12 groups (see Table 38.1). The TDS food samples were purchased in different types of food stores in various towns in Catalonia, with populations over 150,000 inhabitants. This geographical distribution of sampling is highly representative of the population, close to 70 %.

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Table 38.1 Food groups and specific foods in the Catalan total diet study

Group (number of foods) and specific foods
1. Meat and meat products (9) – beefsteak, hamburger; pork loin, pork sausage; chicken breast; lamb leg/chops; cooked ham; Frankfurt-type sausages; chorizo-type sausages
2. Fish and seafood (14) – sardines; tuna; fresh anchovies; horse mackerel; swordfish; salmon; hake; red mullet; sole, cuttlefish, squid, clams, prawns, mussels
3. Vegetables (4) – lettuce, tomatoes, green beans, cauliflower
4. Tuber (1) – potatoes
5. Fruit (4) – apples, oranges, pears, bananas
6. Eggs (1) – hen eggs
7. Milk (2) – Full cream milk, semi-skimmed milk
8. Dairy products (2) – natural yogurt, cheese
9. Bread and cereals (4) – traditional white bread, industrial bread, rice, pasta
10. Legumes (2) – lentils, beans
11. Fats (4) – olive oil, sunflower oil, margarine, butter
12. Biscuits and bakery products (3) – biscuits, croissants, buns

Inedible parts of samples were removed and the samples analyzed in the form of a composite sample. Each composite or analytical sample comprised a mixture of 24 separate samples of each individual foodstuff, which were all equivalent in terms of weight, fat content and other important characteristics.

The first TDS in Catalonia determined the levels of mercury, cadmium, lead, arsenic, dioxins (polychlorinated dibenzodioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs)), polychlorinated biphenyls (PCBs), hexachlorobenzene and polycyclic aromatic hydrocarbons (PAHs) [2]. A series of emerging persistent organic pollutants (POPs) were also investigated, such as polybrominated diphenyl ethers, polychlorinated diphenyl ethers, and polychlorinated naphthalenes. Due to their chemical structure, these may have toxicological similarities with other POPs and behave similarly in the environment.

The design and scope of the TDS have varied over time in terms of the foodstuffs analyzed, the food consumption surveys applied, the groups of contaminants included and the introduction of probabilistic methods to take into account various population-based factors in the assessment of the results.

The exposure assessment of the first TDS in Catalonia (2000–2002) showed that fish and shellfish made a significant contribution to the exposure of contaminants from the diet. These results led to a more thorough investigative study of fish in 2005, including the 14 most consumed species of fish and shellfish in Catalonia, in order to assess the dietary exposure derived from seafood consumption with better accuracy [3].

In 2006, the second Catalan TDS was carried out with an updated list of food-stuffs based on the most recent data from the Diet and Nutrition Survey of Catalonia [4]. This survey included a representative sample of the Catalan population comprised of 2,310 individuals of ages 10 to 80 years. The data was compiled

by a combination of two survey methods, namely, 24-h recall and quantitative questionnaires on the frequency of consumption of foodstuffs. Two new analytical groups were also added to the Catalan TDS, specifically, POP pesticides, including alachlor, aldrin, DDT and its derivatives, dieldrin, endosulfan, endrin, hexachlorocyclohexanes, heptachlor, and the mycotoxins aflatoxins and patulin.

Main Results and Trends

The 2006 Catalan TDS has demonstrated that estimated dietary exposures of most heavy metals are far below their health-based reference values, such as the Provisional Tolerable Weekly Intakes (PTWI) established by WHO (see Table 38.2). However, for methylmercury, the levels found are close to the maximum in women and are exceeded in children. Therefore specific recommendations have been given for pregnant women and children. The daily exposure of mercury from seafood was mostly due to tuna (38 %), followed by hake (23 %).

The estimated daily exposure of dioxins and dioxin-like PCBs in the 2000 study was 3.5 pg WHO-TEQ/person/kg/day. The largest contributions were from fish and shellfish (45 %), dairy products (21 %), cereals (10 %) and meat (8 %) (see Table 38.2).

Comparison of results of the 2006 Catalan TDS with those of the 2000 TDS enable some preliminary trends to be observed (see Table 38.3). Most noteworthy is the dramatic 70 % reduction in the dietary exposure of dioxins and dioxin-like PCBs, from 246.5 pg WHO-TEQ/day for a 70 kg male in 2000 down to 78.07 pg WHO-TEQ/day in 2000.

The results of the 2000–2002 Catalan TDS and the 2005 follow-up study of contaminants in fish and shellfish consumed in Catalonia have been published and are available from the web page of the Catalan Food Safety Agency (ACSA) [5]. The results of the second Catalan TDS are currently being prepared.

Table 38.2 Exposure to contaminants from 2006 Catalan total diet study

Contaminant	Estimated exposure for adult male	WHO toxicological reference value	% WHO reference value
Inorganic arsenic (As)	4.2 µg/kg bw/week	21 µg/kg bw/week	20 %
Cadmium (Cd)	1.56 µg/kg bw/week	7 µg/kg bw/week	22 %
Total mercury (Hg)	2.1 µg/kg bw/week	5 µg/kg bw/week	42 %
Methylmercury (CH_3Hg)	0.8 µg/kg bw/week	1.6 µg/kg bw/week	50 %
Lead (Pb)	3.9 µg/kg bw/week	25 µg/kg bw/week	15 %
Dioxins and dioxin-like polychlorinated biphenyls	3.5 pg WHO-TEQ/ kg bw/day	1–4 pg WHO-TEQ/ kg bw/day	87 %
Hexachlorobenzene (HCB)	0.0024 µg/kg bw/day	0.16 µg/kg bw/day	1.5 %

Table 38.3 Trends in dietary exposure to chemical contaminants in 2000 and 2006 Catalan total diet studies

Contaminant	2000 TDS (estimated exposure for a 70 kg male)	2006 TDS (estimated exposure for a 70 kg male)	Trend
Arsenic (As)	42.4 ng/day	39.6 ng/day	~
Cadmium (Cd)	15.6 µg/day	17.2 µg/day	~
Total mercury (Hg)	21.21 µg/day	18.58 µg/day	~
Lead (Pb)	27.5 µg/day	20.63 µg/day	↓
Polybrominated diphenyl ethers (PBDEs)	81.9–112.7 ng/day	75.45 ng/day	~
Polychlorinated naphthalenes (PCNs)	45.78 ng/day	7.25 ng/day	↓↓
Polychlorinated diphenyl ethers (PCDEs)	41.04 ng/day	51.68 ng/day	↑
Dioxins and furans (PCDDs/PCDFs)	95.41 pg WHO-TEQ/day	25.67 pg WHO-TEQ/day	↓↓
Dioxin-like polychlorinated biphenyls (dl-PCBs)	150.1 pg WHO-TEQ/day	52.40 pg WHO-TEQ/day	↓↓
PCDDs/PCDFs + dlPCBs	246.5 pg WHO-TEQ/day	78.07 pg WHO-TEQ/day	↓↓
Polycyclic aromatic hydrocarbons (PAHs)	8.42 µg/day	12.04 µg/day	↑
Hexachlorobenzene (HCB)	166.2 ng/day	71.62 ng/day	↓↓

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Chapter 39
Total Diet Studies in Sweden: Monitoring Dietary Exposure to Persistent Organic Pollutants by a Market Basket Approach

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Introduction

The concerns about and interest in environmental health issues have a long tradition in Sweden [1]. Already in the late 1950s, problems with mercury poisoning of birds eating mercury-treated seed were observed. From the mid-1960s, the levels of methyl mercury were analyzed in fish from a number of Swedish lakes, the waters with unacceptably high levels were put on a "black list" and fish from these lakes were banned on the open market. Also in the 1960s, the Swedish chemist Sören Jensen discovered very high levels of polychlorinated biphenyls (PCBs) in white-tailed eagle from the Baltic region [2] and soon thereafter, the problem with chlorinated organic pollutants in biota from the Baltic Sea was revealed. Among other pollutants, the high levels of PCBs, DDT and dioxins (polychlorinated diben-zodioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs)) were observed and discussed and their use, in case of PCB and DDT, prohibited or restricted. For these groups of organic pollutants, the levels in Baltic biota have decreased considerably since the 1970s [1], but the decrease in dioxin levels in biota, e.g. Baltic herring, has ceased and roughly unchanged levels have been found during the last 10 years and more. The levels of organic pollutants in Baltic herring are still much higher than in fish from open seas (such as the Norwegian Sea and North Sea), and very much so compared to other food groups.

Consumers within European Union (EU) are protected against high levels of selected persistent organic pollutants (POPs) by maximum levels (MLs) in animal products, for instance those concerning dioxins and dioxin-like PCBs [3]. Today Sweden and Finland have derogations for the EU-MLs for dioxins in fish, meaning

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that fish from the Baltic region, even with dioxin levels above the regulated MLs, can be sold nationally but not be exported to markets in other countries. One prerequisite for obtaining this derogation was the fact that both Sweden and Finland since long have issued dietary recommendations to restrict the consumption of fatty Baltic fish. In Sweden, children and women of childbearing ages are recommended to limit their consumption of certain fatty Baltic fish to not more than 2–3 servings per year [4]. The recommendations to other consumer groups are less strict (not more than one serving per week).

Because of the relatively high POP levels in fatty fish from the Baltic Sea and the fact that consumers in Sweden, as well as in the other Nordic countries, are keen fish eaters, the dietary exposure to POPs, and the contribution of fish consumption to the total exposure, are questions of concern [5]. In order to produce food intake data, the Swedish National Food Agency (NFA) has performed food consumption surveys in which food intake was assessed in adults and children. Food consumption data were subsequently linked with food occurrence data for the compounds of interest, based on analyses on specific food items, and intake estimations could be performed. NFA has performed food consumption studies on the adult population (i.e. 18–74 years old) in 1989 [6], 1997–1998 [7] and 2010–2011 [8]. In addition, a food consumption study in 2003 [9] focused on intake in children in three age groups, 4–5, 8–9 (grade 2) and 11–12 (grade 5) years old.

An alternate method to assess exposure of various compounds is by using a total diet study (TDS) method. This method has been recommended by the World Health Organization (WHO) as a cost-effective and robust way of obtaining data on chemical hazards in our diet [10]. By collecting such data, future health threats could be foreseen and be taken care of. Swedish Market Basket studies (MBS) are similar to TDS but differ from the WHO-recommended TDS design in that the food items to be analyzed are not prepared as for consumption (i.e. the items are analyzed as purchased), and that the Swedish studies have not included drinking water in the exposure estimations. As the Swedish MBS are based on national food production and trade statistics, no separation into different food consumer groups (based on age, sex, region, etc.) could be made, and only a national mean population exposure could be estimated in this way. Swedish MBS have been performed by NFA in 1999 [11, 12], 2005 [13] and 2010 [14], using similar methods and with the ambition to follow a 5-year scheme. Also earlier MBSs have been performed [15], but at that time both sampling and analytical standards were much different from today (with focus on radioactive cesium) and the result from that study is not directly comparable. By use of MBS methods, the Swedish mean exposure of both nutrients and potentially hazardous substances has been followed. Among other substances, POPs, such as PCBs, DDT, dioxins and brominated flame retardant PBDEs (polybrominated diphenyl ethers), have been analyzed. The following sections will present methods and estimations of POP exposure using Swedish MBS data. For some of these POPs, MBS exposure data may be evaluated in comparison with data obtained by food consumption survey methods.

Market Basket Study Methods

The basis for sampling is the per capita consumption data, derived from Swedish production and trade statistics (obtained from the Swedish Board of Agriculture). Using these data, selected food products were purchased, representing food categories consumed at a level of least 0.5 kg per person and year and thus covering approximately 90 % of the food supply available for consumption. In the 1999 MBS [11, 12], 123 food products were sampled and distributed into 15 food composites (e.g. meat, fish and dairy products), whereas the later studies [13, 14] omitted wine and spirits and aggregated some groups, resulting in 12–13 food composites (see Table 39.1). In 2010 study, the composites contained from 1 (eggs) to 19 (vegetables) separate food items. Because of questions regarding possible regional variation, the food items in both 1999 and 2005 were purchased in grocery stores in four different cities in Sweden, namely Sundsvall, Uppsala, Gothenburg and Malmö. However, as an evaluation of the data for several of the investigated compounds could not observe any important differences in levels of monitored compounds between these places of purchase, the MBS of 2010 sampled the food only at one place, namely Uppsala.

From each food unit/package, a fixed ratio (normally 1 % by weight) of the yearly per capita consumption was taken out for homogenate preparation and subsequent analysis. In case of food items where wastage could be supposed, inedible

Table 39.1 Food composites from market baskets sampled in the 2010 Swedish Market Basket Study

Food group[a]	Number of food items	Description
Cereal products	11	Flour, rice, grain, corn flakes, bread, pasta
Pastries	5	Cakes, biscuits including pizza
Meat products	16	Beef, pork, lamb, chicken, game, processed meats except pizza
Fish	16	Fresh and frozen, canned products, shellfish
Dairy products	18	Milk, sour milk, yogurt, cream, cheese, cottage cheese
Eggs	1	Whole eggs
Fats	13	Butter, margarine, oil, mayonnaise
Vegetables, including root vegetables	19	Fresh, frozen and canned products
Fruit	18	Fresh, frozen and canned products, juice, nuts
Potatoes	4	Fresh, French fries, chips
Sugar and sweets	11	Sugar, chocolate, sugar sweets, ice cream, sauces, dressings, ketchup
Soft drinks, lemonade, beer (≤3.5 % alcohol)	5	Soft drinks, mineral water, light- and medium-strong beer

[a]Note that the five composites in italics were used in estimating exposure to POP compounds, i.e. PCDDs/Fs, PCBs, PBDEs, HBCD, DDT, HCB, HCHs and chlordanes

parts (e.g. bone, skin, etc.) were removed prior to weighing. The edible parts of the food samples within a food composite were mixed together and carefully blended, using a household mixer. All together these homogenates (12 in the 2010 study), representing composites of specific food groups, were the general base for subsequent analyses.

After chemical analyses had been performed and analytical data were compiled the yearly per capita exposure was derived by a simple calculation, in which the amount of the actual compound in the homogenate was multiplied by a factor (in our case ×100, as we weighed in 1 % of the yearly consumption of each food item into the respective food homogenates). If the consumption on a daily basis is requested, the yearly consumption is divided by 365.

MBS can be used for exposure assessments of various compounds, but not all food groups were analyzed for all the different compounds of interest. As regards POP analyses (e.g. dioxins, PCBs and DDT), the analyses have focused on foods of animal origin, and in the three Swedish MBSs, the following food composites were analyzed: meat products, fish, dairy products, egg, fats (mixed vegetable/animal); sweet bakery products or pastries (supposed to contain marine fats) were included only in the 1999 study. In the MBS from 2005, also phenolic compounds (e.g. nonylphenol and bisphenol A) were investigated, and the exposure to these phenols was based on levels found both in the aforementioned animal food composites, and in addition also in vegetable food groups supposedly containing these compounds, i.e. cereal products, vegetables, fruit and potatoes. These data were presented in a report to the Swedish Environmental Protection Agency [16]. In the 2010 MBS study, both pesticides and polycyclic aromatic hydrocarbons (PAHs) were additionally included. Apart from toxic compounds, the Swedish MBSs have been used for obtaining nutrient data, used e.g. for validation of other exposure methods.

The analyses of the POP substances have been made both at the NFA and at external laboratories. Details on analytical methods are given in original articles [11–13] and a report [14]. In calculations of exposure, concentrations below the limit of detection/quantification (LOQ) were generally set to half the LOQ, but in the 2010 study actual levels below LOQ were used for intake calculations of PBDEs and HBCD. In this chapter we will mainly address data based on analyses of the following compounds that were analyzed in all three market basket studies: PCDDs, PCDFs, dioxin-like and non-dioxin-like PCBs, PBDEs, DDTs, hexachlorobenzene (HCB), hexachlorocyclohexanes (HCHs) and chlordanes.

POP Levels in Food

Levels of POPs were studied only in the food homogenates that were assumed to contain appreciable amounts of these compounds, i.e. food of mainly animal origin – fish, meat products, dairy products, eggs, and fats. This assumption was based on earlier studies on dioxins in which food from vegetable sources were found to add

Table 39.2 Persistent organic pollutant (POP) levels in fish from 1999 to 2010 Swedish Market Basket studies[a]

POP compound/group	1999 TDS	2010 TDS	2010 levels, as % of 1999
Total TEQ[b]	0.85	0.51	60
CB-153[c]	2.18	1.14	52
BDE-47	0.48	0.14	29
p,p'-DDE	4.51	2.13	47
HCB	0.98	0.52	53
HCHs	0.96	0.17	18
Chlordanes	2.40	1.03	43

[a]Values given in ng/g fresh weight, except total TEQ, which is given in pg WHO (1998)-TEQ/g fresh weight
[b]PCDD/Fs + dl-PCBs, presented as 1998 WHO-TEFs
[c]Major PCB congener found in food

very little to the total dioxin exposure [17–19]. On a fresh weight basis, the POP levels were generally considerably higher in the fish homogenate than in all the other food homogenates studied (other animal food groups, plus fats and oils, individually being second highest), a consequence of the much more effective biomagnification of POP compounds in the aquatic environment compared to the terrestrial compartment. The levels of various POPs in fish homogenates from the 2010 MBS are given in Table 39.2. High POP levels could be found in fatty fish from the Baltic Sea, a probable combined effect of earlier industrial pollution episodes and a limited water turnover rate. Consequently, the concentrations of POPs in these fatty fish could reach levels that make a high consumption a possible health risk, and Swedish dietary advice recommends a restricted consumption of these fish. In the MBS fish composite, approximately one third of the homogenate weight consists of fatty fishes (mainly herring, salmon, and mackerel) but of these only Baltic herring were caught in the Baltic Sea.

Among the studied groups of POPs, sumPCBs (represented in the table by CB-153) and sumDDTs are found at the highest levels in fish (Table 39.2), and our data show that these two compound groups are dominating among the POP compounds also in other food groups. Similar results have been reported by other international exposure studies [20, 21].

Estimation of POP Exposure

Based on the occurrence levels in the food homogenates, exposure to the studied POP compounds from each of the studied food groups could be estimated. These estimated exposures are based on the per capita consumption values, which will give a mean exposure but not the range of estimated exposures within the Swedish
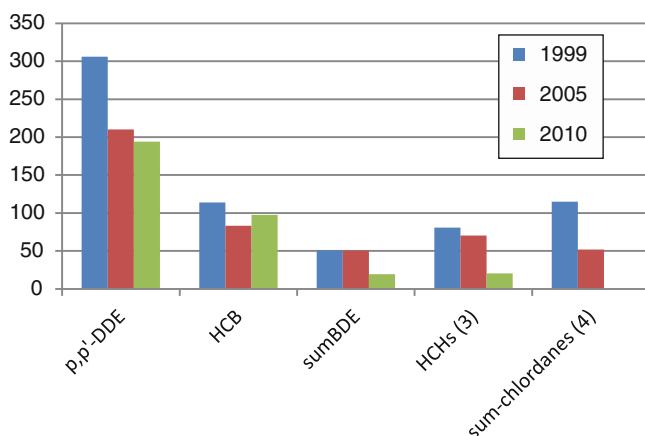
Fig. 39.1 Estimated exposure to selected persistent organic pollutants from the 1999, 2005 and 2010 Swedish Market Basket studies (in ng/day) (Sum-chlordanes exposure data from 2010 are absent due to lack of occurrence data for other food homogenates than fish. 2010 HCH data are sums of alpha- and beta-HCH, whereas 1999 and 2005 studies also include the gamma-isomer. SumBDE data are sums of nine congeners in 2005, otherwise five congeners)

population. The estimated exposures of p,p'-DDE, HCB, sumBDE (sum of brominated diphenol ethers), HCHs, and sum-chlordanes are shown in Fig. 39.1, which presents results of the 1999, 2005 and 2010 studies. By weight, the exposure is dominated by p,p'-DDE and (in Fig. 39.2) sumPCB, two groups of "classical" pollutants whose uses have been banned in Sweden but which are still found in high levels in the environment, and in food, because of their persistence and possible emission from unidentified sources. A lower exposure was found in the case of HCB, sumBDE, HCHs and sum-chlordanes. An even lower exposure level was estimated for dioxin-like compounds (94 pg WHO (1998)-TEQ (Toxic Equivalents)/ day) in the 1999 TDS, not shown in Fig. 39.1. However, the toxic potencies of the studied substances differ and the possible risks posed by the per capita intake of these compounds can be assessed by comparisons with health-based reference values (see below).

Based on the 2005 MBS, the contributions of different food composites to the total exposure of dioxins and dioxin-like PCBs and the sum of PCBs are shown in Fig. 39.2. The figure shows the important contribution from fish to the dioxin and dioxin-like PCB exposure of Swedish consumers, but that also meat, dairy products and fat/oils are important food groups that influence this exposure, and these groups are by far the predominant food exposure sources to all dioxin-like compounds. Similar distribution patterns were found for most POPs, although dairy products were relatively more important in case of HCB and HCH exposures. Although fish

Fig. 39.2 Relative contribution from different food sources to the total-TEQ (PCDD/DF+dioxin-like PCBs) and sumPCB (SumPCB: 15 congeners analyzed) intake (Data from 2005 Market Basket study)
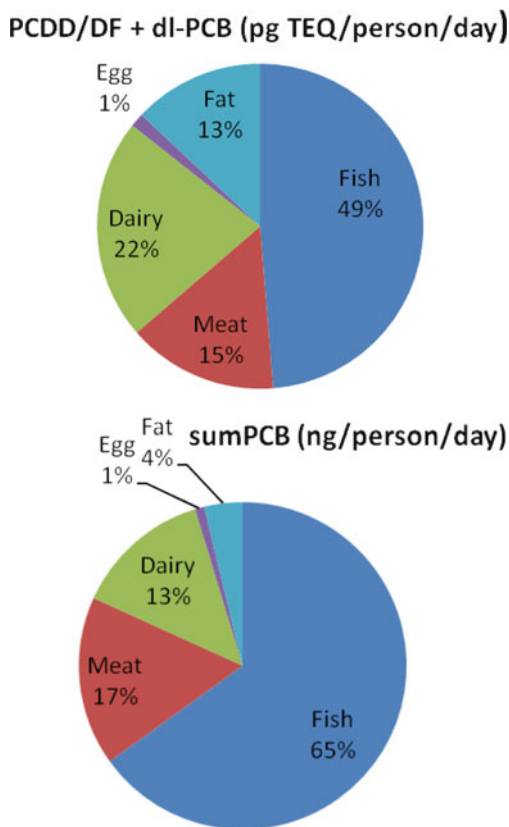
is a major contributor to the total POP exposure, the POP levels in fish are comparatively even more dominating, in comparison to other food groups. This reflects the fact that fish consumption, on a weight basis, is lower compared to the consumption of many other food groups.

Changes Over Time and Regions

The MBSs performed in 1999, 2005, and 2010 were designed to be comparable with each other, although some differences in study designs were introduced (e.g. inclusion of additional congeners in the sumBDE values). For most POP compounds
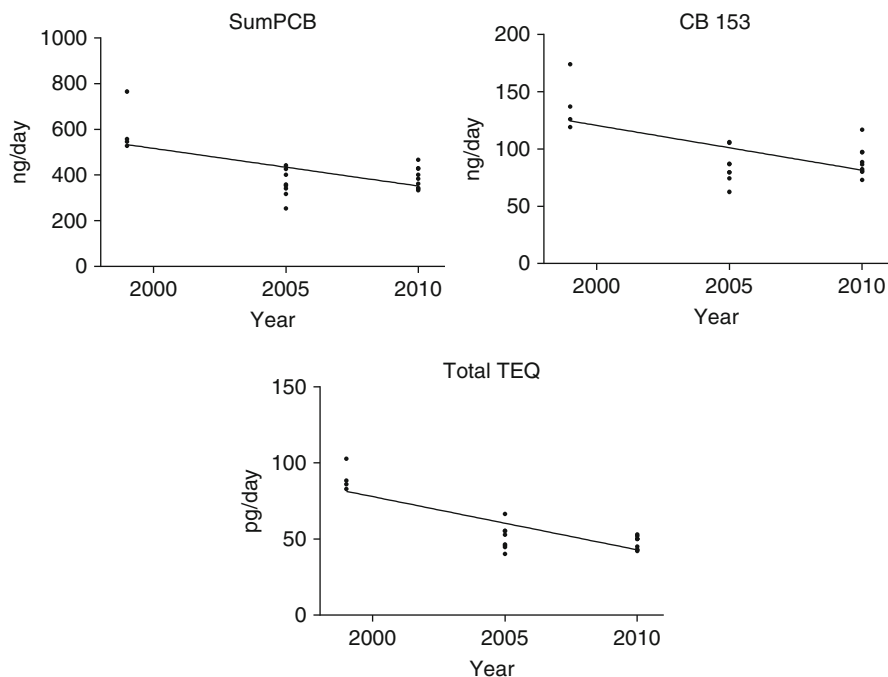
Fig. 39.3 Time trends of total exposure to sumPCB, the PCB congener CB-153 and total TEQ (PCDD/Fs + dl-PCBs), estimated from data obtained in the 2010 Swedish Market Basket study (All presented trends were significant (simple regression analysis, $p \leq 0.05$, $N = 4$–9; sample levels < LOQ were set to ½ LOQ))

a clear time-dependent decrease in exposure levels is suggested during this time period, and the 2010 MBS per capita exposure for several of the studied POPs had levels corresponding to 60 % or less of the levels observed in 1999 (see Fig. 39.3). However, decreasing levels are not always the case, and some brominated flame retardant congeners did not show any significant decrease during the studied time period.

The difference in exposure levels between the different MBS studies may be a result of a reduction of POP levels in many food items, changed food consumption patterns, and the fact that possible differences in chemical-analytical methods and approaches between the studies could have influenced the results (for methodological issues, see possible sources of error, below). As regards changes in food consumption patterns, the data from the MBSs 1999 to 2010 indicate clear increases in consumption of fish and meat, both with over 30 % (unpublished observation), which speaks against the suggestion that food pattern changes are causing the decrease in POP intake. Temporal decreases in POP exposure from food have been shown also in other studies, e.g. from Spain [22]. Moreover, in support of a decreasing temporal trend for POPs in food, decreasing POP levels in food-producing

animals from Sweden have been presented [23]. Between 1991 and 2004, the levels of CB-153, HCB and p,p'-DDE decreased by 6–7 % per year in fat from bovines taken at Swedish abattoirs, and the decrease in POP levels in fat from pigs decreased even somewhat faster (10–12 % per year). Also in biota from the Swedish coasts the PCB levels decreased by 5–10 % per year between 1978 and 2005 [24], such as in Baltic herring. However, the dioxin levels have not shown the same decreasing trend in Baltic herring during the last 10–12 years, which may indicate ongoing dioxin emissions into the Baltic Sea. Also in breast milk, decreasing levels of many of the studied POP compounds were observed with time. In milk from women from Uppsala County, Sweden, decreasing levels of dioxins, PCBs and DDT were observed between 1996 and 2006 [25]. The rate of decline of several PCB congeners was estimated to be 6–8 % per year.

The regional difference in occurrence levels in the MBSs was investigated by comparing results from food sampled in cities from four different Swedish regions [11, 13]. Although some minor differences were seen, they were not statistically confirmed. This is also expected, as there is an effective nationwide distribution of foods, resulting in a similar food assortments in most Swedish regions. In studies on POP levels in breast milk from different regions in Sweden, the spatial difference between regions was small although in some cases significant [26]. Also in the study of POP levels in fat from cows and pigs from different regions, some small regional differences were observed [23]. In the latter study, the levels of CB-153 and p,p'-DDE seemed to decrease somewhat from south to north of Sweden. To conclude, from the presented studies it is suggested that regional differences are small, if at all present, as far as POPs in foods are concerned.

Possible Sources of Error

The basis for the present estimation is the data on the Swedish per capita consumption of different food items and the occurrence data of POPs in homogenates of food composites. Both these data sets contain elements of uncertainty. In case of the consumption data, they are based on production and trade statistics, which represents a consumption level which is probably higher than what people actually eat (due to food wastes etc.). On the other hand, the food produced by local hunting, fishing and berry-picking, which in some Swedish regions can be a quite important addition to the total food consumption, is not included. It should also be noted that these data give only a mean value and do not give information on individual consumption patterns. In case of the analytical methods, the analyses showing levels less that the LOQ could introduce a considerable amount of uncertainty in the exposure calculations. Also, the number of analyzed congeners within a compound group (e.g. PBDEs) has in some cases been changed between the MBSs, a fact that could have some influence on the calculated summation levels and on the comparisons between time-points made on the basis of those data. In addition, the methods in

sampling, handling and grouping of food samples are important factors when comparing data from different studies. In the three mentioned MBSs, the POPs mentioned in Table 39.2 were analyzed at the same laboratory, i.e. at NFA, Uppsala, except for the dioxin/PCB analyses that were performed by two different external laboratories. Thus, except that the LOQ levels should preferably be low and remain unaltered, possible interlaboratory differences in analytical results should be checked if different labs are being used.

To conclude, if all potential types of uncertainties are taken together it is obvious that the exposure values calculated from total diet studies only with some approximation mirror a "correct" mean exposure of POPs by Swedish consumers. Nonetheless, the presented data indicates that an actual decrease in POP exposure has occurred between the three sampling time-points. The results imply that decrease in occurrence levels rather than changes consumption habits is the more probable reason for the observed decrease in POP exposure.

Validation of POP Exposure

Because of the mentioned uncertainties that may accompany MBSs, and indeed all types of exposure studies, an independent study of the exposure should ideally be performed using alternate methods, for the purpose of validation. In this case, data from the MBSs have been compared with data from Swedish POP exposure studies based on consumption data from population-based food consumption surveys. Using occurrence data mainly from 1998 to 1999, the exposure estimations for a number of POPs from a 2002 study [27] on adults were in fairly good agreement with the MBS from 1999 [11]. The best example of such agreement in results was seen in dioxins, where the mean exposure to PCDD/Fs and dioxin-like PCBs in the consumption survey was estimated to be 89–106 pg WHO-TEQ/day (adults) versus 96 pg WHO-TEQ/day using the MBS method. The comparison between exposure data produced by these different methods corresponds less well in the case of PCBs (CB 153: consumer questionnaire (mean) 182–207 ng/day vs. MBS 139 ng/day) and DDTs (p,p'-DDE: consumer questionnaire (mean) 345–348 ng/day vs. MBS 306 ng/day). As already stated, a number of factors could contribute to the observed differences between these methods, when comparing exposure levels of these POPs.

Comparison with POP Exposure in Other Countries

The presently reported POP exposures could be compared to respective data from other countries. In Norway, the Norkost survey from 1997 resulted in a dioxin (PCDDs/PCDFs and PCBs-TEQ) exposure of 139 pg I-TEQ (International Toxic Equivalents)/day [5] while a Finnish market basket study (food sampled 1997 and 1999) showed an exposure of 115 pg WHO-TEQ/day [21]. In the Finnish study, the

sumPCB exposure was 1,200 ng/day, and the sumBDE exposure 44 ng/day. The comparably high estimated Finnish PCB exposure could be noted, whereas in general the Nordic POP exposure estimates are rather similar. In examples from dioxin and dioxin-like PCB exposure studies in adult populations from non-Nordic countries (in pg WHO-TEQ/kg bw/day), 1.2 pg was estimated in Holland, [28] 1.36 pg in Spain [29], 2.2–2.4 pg in USA [20] and 3.2 in Japan [30]. These presented exposure data for dioxins and dioxin-like PCBs (based on food sampled in the later1990s) are similar, and in some cases clearly higher, to the value estimated for Swedish consumers in the Swedish study from 1999, i.e. 1.3 pg WHO-TEQ/kg bw/day (if<LOQ=½ LOQ) [11]. In the Swedish MBS from 2010 the total WHO-TEQ values were further decreased to 0.6 pg WHO-TEQ/kg bw/day [14]. Similarly low levels of dioxin exposure have been obtained in recent studies from other European countries, e.g. Belgium [31] and Spain [22] (both studies analyzing food sampled in 2008).

Risk Estimation Comments

The Swedish MBS from 1999 [11] estimated POP exposures to be below (total WHO-TEQ: 1.3 pg/kg bw/day) or well below (sumDDT: 8.9 ng/kg bw/day) internationally acceptable exposure limits (TDI for PCDD/DF+dl-PCBs: 2 pg total WHO-TEQ/kgbw/day [32], sumDDT: 10 µg/kg bw/day [33]) and in the subsequent MBSs of 2005 and 2010 the estimated POP exposure was further reduced. In the case of PBDEs a congener-based risk assessment document has been presented by EFSA [34] in which the BDE congener BDE-99 was shown to have a high relative toxic potency, resulting in a margin of exposure (MOE) of 60–108 in relation to the market basket exposure calculation from 2010. Also according to the 2010 MBS, the mean intake of dioxins and dioxin-like PCBs was about three times lower than the levels that are considered safe from a health-based perspective. However, the distribution in exposure levels of POPs has been found to be wide, and in the case of dioxins more than one-tenth of the Swedish population is estimated to have an exposure over the TDI of 2 pg total WHO-TEQ/kg bw/day [27, 35]. Therefore, the lack of individual exposure data in the MBSs conceals possible large variations in consumption habits, which must be kept in mind when discussing mean exposure values. However, as we could show an on-going decrease in exposure levels of most POPs, the potential risk from POP exposure in general should be reduced compared to the situation around year 1998–1999. However, in spite of decreasing levels of several of the "classical" POPs, new compounds with unknown, and different, properties may instead need to be studied more closely in order to prevent them from becoming potential health risks. Also in the area of cumulative toxicology, progress is being made, and interactive or additive effects may be important end-points in future risk assessments. Future confirmation on internationally agreed exposure limits for these "new" POP compounds may revise our view on possible risks of POPs in food and lead to new positions regarding risk management.

Conclusion

Swedish total diet studies have presented average exposure data of POPs, based on analyses of several food composites representing mainly foods of animal origin. Fish was normally the single food group with the highest levels on a fresh weight basis. Comparing POPs, sumPCBs and sumDDT were the two compound groups with the highest levels and the largest exposure by weight, but the dioxin exposure, although much lower on a weight basis, may be of similar or even greater relevance from a risk assessment perspective. When comparing MBSs performed in 1999, 2005, and 2010, a decrease in occurrence levels in food homogenates were seen for most POPs, resulting in a decreased per capita exposure in 2010, in several cases corresponding to 60 % or less of the 1999 levels. The POP exposure levels estimated in the 1999 TDS showed moderate to good agreement with data from a Swedish exposure study based on individual food analyses and a population-based consumption survey, performed at a similar time-point. The pollution situation in the Baltic region, and the relatively high Swedish fish consumption, are most likely important factors to explain the appreciable contribution from fish to the exposure to many POPs. At the same time, the total Swedish mean dioxin/PCB exposure from all relevant food groups was not found to be higher than for most comparable member states within the European Union.

To conclude, the Swedish MBS approach represents a robust and relatively simple and convenient type of total diet method for estimating the average exposure of various compounds, including POPs, present in food. By this method, changes in exposures over time, and differences between regions and countries may be studied, and emerging food hazard hopefully identified. However, as the Swedish MBS design only produces mean exposure values, this approach does not provide any information on actual individual exposures in a population, and extreme consumers with potentially high risk dietary patterns will not be identified. Moreover, although the TDS concept generally includes analyses of food as consumed, this was not done in the Swedish studies, and therefore the effects of food preparation could not be measured. Thus, complementary methods are recommended in monitoring exposure data in high risk groups.

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Chapter 40
Total Diet Studies—United Kingdom's Experience

Joseph Shavila

Introduction

The total diet study (TDS) is an important part of the United Kingdom Government's surveillance program for chemicals in food and has been carried out on a annual basis continuously since 1966. Results from the UK TDS are used, together with food consumption data from various surveys, to estimate dietary exposures of the general UK population to food chemicals, such as nutrients and contaminants. UK TDS data are also used to identify temporal changes in exposure and to make assessments of the safety and quality of the food supply. Such data can then be used as background information when considering issues, such as the possible health impact of incidents of high-level contamination and regulatory levels for contaminants in various foodstuffs. Results from the TDS also indicate where there is a need for more targeted surveys.

Analysis of TDS samples can provide an estimate of average intakes of particular nutrients at the population level. Where limited data are available on levels of particular nutrients this can provide a 'reality check' on nutrient intake values derived from food consumption data, and UK TDS samples from the mid 1990s were analyzed for selenium content [1] and fatty acid profiles [2] to provide such information.

UK TDS samples have in the past found uses in monitoring for pesticide residues. However this has been discontinued since 1996. The occurrence of some older pesticides, such as DDT, dieldrin and lindane in various UK TDS composite samples have been reported previously [3]. The pesticides analyzed were carefully selected to include those that had been regularly found in previous studies. However current approaches to monitoring pesticides in food have evolved considerably.

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In addition to its uses for monitoring food nutrients and ubiquitous chemical contaminants in food, UK TDSs have been used by the UK Food Standards Agency (FSA) to report levels of certain radionuclides (e.g. ^{90}Sr and ^{137}Cs) in general 'mixed diet' samples as part of its obligations under the Euratom Treaty for monitoring radioactivity in food.

Design of UK TDS

The design of the UK TDS has been described in detail elsewhere [4]. Essentially, the UK TDS consists of purchasing at retail level commonly consumed foods, processing them as for consumption, often combining the foods into food composites or aggregates, homogenizing them, and analyzing them for chemicals of interest. In the UK, it involves 119 categories of foods that are combined into 20 groups of similar foods for analysis. The relative proportion of each food category within a group reflects its importance in the average UK household diet and is largely based on an average of three previous years of food purchase data from the UK National Food Survey (now the Expenditure and Food Survey (EFS)) [5]. Foods are grouped so that commodities known to be susceptible to contamination (e.g. offal and fish) are kept separate, as are foods that are consumed in large quantities (e.g. bread, potatoes, milk).

UK TDS food samples are cooked in line with normal household practice, prior to analysis – for example, meat, rice and fish would be boiled, baked or grilled as appropriate. In cases where the food commodities are cooked prior to analysis and where the cooking process may lead to a reduction in residues, the reporting limits of the analytical methods for selected commodity combinations are lowered in order that lower level residues can be detected.

There have not been any significant changes in the way TDS samples are collected and grouped prior to analysis in the UK, apart from those now being collected from fewer locations. The fact that food groups are comprised of composite samples of individual foods means that the analytical data generated represent dietary averages. Thus, it is not possible to attribute the levels of a contaminant to specific foods in the group. It is possible to address this limitation by making adjustments to the sampling strategies by collection of sub-samples prior to compositing.

Although the TDS provides a means of obtaining average exposure data for a range of analytes, it may not adequately represent foods consumed by special sub-groups of the population, such as ethnic groups, younger children or those on special diets, nor foods that are not widely available on retail sale, such as some species of oily fish. A further limitation is that only retail foods are sampled. Exposures to chemicals from meals eaten in restaurants or other catering facilities are not covered. Therefore, if the consumption data used to derive exposure estimates are based on household consumption data only, foods eaten in larger quantities outside the home, could be underrepresented.

Use of UK TDS Data in Estimating Exposure

Data from the analysis of the UK TDS allow estimation of dietary exposure to chemical contaminants in food for the UK population as a whole. Such trends may reflect changes in food consumption patterns, changes in the concentrations of elements in foods, or both.

Population dietary exposures are estimated by multiplying the average amount of each food group consumed (based on consumption data from the EFS household survey) by the corresponding chemical concentration in the food group from the TDS study, then summing across all food groups. The EFS covers the total number of people in a household regardless of whether they consumed specific foods or not, and so the EFS consumption data are averaged for the whole population.

In addition to conducting exposure assessments at a population level, the FSA has an interest in assessing exposure at a 'consumer' level. Consumer exposure assessment, in its simplest form, involves combining data on the level of a chemical in a food (measured or predicted) with data on the consumption pattern of the food (usually derived from an individual dietary survey) in order to estimate the amount of the chemical ingested by an individual over a fixed period of time. The benefits of consumer-level exposure assessment include the ability to estimate high level (e.g. 97.5th percentile) consumption and the facility to remove 'non-consumers' of the food(s) of interest from the assessment. Considering consumers only is particularly important for foods that are consumed by a relatively small proportion of the population (e.g. different types of liver), allowing specific 'at risk' population sub-groups to be identified for targeted advice.

The FSA uses an in-house distributional model (Intakes II Program) for assessing dietary exposure to a range of contaminants in food. The software is a custom-made statistical program that combines individual dietary survey record with single values of a chemical concentration in food. Where a particular food is eaten, consumption is combined with the relevant chemical concentration for each participant in the survey from all the specified foods. The full distribution of participants' exposure is then calculated and from this distribution, the exposure summary statistics are extracted.

The main source of data used by the UK FSA to estimate food consumption for the purposes of conducting consumer exposure assessments, is the National Dietary and Nutrition Survey (NDNS). In the past, the NDNS was carried out as a series of cross-sectional surveys of diet and nutritional status. Data from each of four age groups were collected over the years 1992–1993 (preschool children aged 1.5–4.5 years, commonly referred to as toddlers [6]), 1994–1995 (older adults, aged 65+ years [7]), 1997 (young people aged 4–18 years [8]), and 2000–2001 (adults aged 19–64 years [9]). The respondents in the surveys were asked to complete diaries of foods and beverages consumed over a 4 or 7 day period (depending on the survey), inside and outside the home. This approach allows estimation of exposure at the consumer level.

A new NDNS is now in place, and since April 2008 has been collecting data from all age groups aged 1.5 years up, using a program of continuous fieldwork. The survey was changed to this 'rolling' approach in order to improve its ability to follow trends in food consumption and nutrient intakes. Headline results from the new program will be published annually. As well as food consumption, the NDNS also collects information on less frequently consumed foods to assist chemical exposure assessment, and also takes blood and urine samples to allow an assessment of longer term nutritional status.

Direct comparison of exposure estimates is not always a straightforward matter. Differences between exposure estimates can occur owing to different methods being used to calculate exposure (including data collection and estimate calculation) and because different statistical approaches are used (exposure can be calculated for entire populations, or for those parts of the population that actually consume the foods of interest). Such differences must be taken into account before considering how differences between national diets might relate to differences in actual exposures.

Advances in analytical methodology have been particularly useful for improving the dietary assessment of contaminants. For instance, the speciation of metals, such as arsenic in the analysis of the 1999 and 2006 TDS samples (Table 40.1), has allowed the tailoring of risk assessments to specific forms of these elements. Thus, exposure assessments based on the more toxic inorganic form of arsenic were conducted to refine the risk assessment of this metal. Improvements may also arise from the ability to detect lower concentrations of trace contaminants, such as dioxins and polychlorinated biphenyls (PCBs).

TDS Work in the UK Food Standards Agency

As shown in Table 40.1, studies conducted by the FSA using UK TDS samples span a range of contaminants that appear in food as a result of food processing or because of their presence in the environment. Links for the reports of these studies are given in the table.

The most recent study on measurement of the concentration of metals and other elements allowed the determination of the concentrations of 24 elements, including metals, to be reported. Composite samples for the 20 TDS food groups (including bread, fish and fruit) were collected from 24 randomly selected UK towns and analyzed for their levels of aluminum, antimony, arsenic, barium, bismuth, cadmium, chromium, copper, germanium, indium, lead, manganese, mercury, molybdenum, nickel, palladium, platinum, rhodium, ruthenium, selenium, strontium, thallium, tin and zinc. The results from this survey have been used to estimate dietary exposures to these elements for UK consumers and provide up to date information on their concentrations in foods. Through comparisons with previous TDSs, any trends in exposure to these elements in the typical UK diet have been established and the main dietary sources that contribute to these exposure levels have been identified.

Table 40.1 Analysis of TDS samples for chemical contaminants in food

Year	Link to website	Title of study
2009	http://www.food.gov.uk/science/surveillance/fsisbranch2009/survey0109	Survey on measurement of the concentration of metals and other elements from the 2006 UK Total Diet Study
2006	http://www.food.gov.uk/science/surveillance/fsisbranch2006/fsis1106	Fluorinated chemicals: UK dietary intakes: 2004 Total Diet Study samples
2005	http://www.food.gov.uk/science/surveillance/fsisbranch2006/fsis1006	Brominated chemicals: UK dietary intakes: 2003 and 2004 Total Diet Study samples
2005	http://www.food.gov.uk/science/surveillance/fsis2005/fsis7505	Analysis of 3-monochloropropane-1,2-diol (3-MPCD) in the UK diet: 2001 Total Diet Study
2005	http://www.food.gov.uk/science/surveillance/fsis2005/fsis7105	Analysis of Total Diet Study samples for acrylamide
2004	http://www.food.gov.uk/science/surveillance/fsis2004branch/fsis5604	Uranium-238 in the 2001 Total Diet Study
2004	http://www.food.gov.uk/science/surveillance/fsis2004branch/fsis5204	Brominated flame retardants in trout and eels from the Skerne-Tees river system and 2001 Total Diet Study samples
2004	http://www.food.gov.uk/science/surveillance/fsis2004branch/fsis5104arsenic	Arsenic in the diet: 1999 Total Diet Study samples
2004	http://www.food.gov.uk/science/surveillance/fsis2004branch/fsis4804metals	Survey of metals and other elements: 2000 UK Total Diet Study samples
2003	http://www.food.gov.uk/science/surveillance/fsis2003/fsis382003	Dioxins and dioxin-like PCBs in the UK diet: 2001 Total Diet Study samples
2002	http://www.food.gov.uk/science/surveillance/fsis2002/31pah	PAHs in the UK Diet: 2000 Total Diet Study samples
2000	http://www.food.gov.uk/science/surveillance/fsis2000/4diox	Dioxins and PCBs in the UK diet: 1997 UK Total Diet Study samples
2000	http://www.food.gov.uk/science/surveillance/fsis2000/5tds	1997 Total Diet Study-Fluorine, Bromine and Iodine

This latest TDS report was given consideration by the UK independent scientific advisory committee, the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) [10]. This report allowed the COT to comment on toxicological implications of dietary exposure to these elements and to make recommendations for future work.

Analysis of TDS samples for dioxins and dioxin-like chemicals has proved particularly useful since these persistent organic pollutants are resistant to metabolism and subject to bioaccumulation. Analysis of samples collected during the 2001 UK TDS for dioxins and dioxin-like polychlorinated biphenyls (PCBs) allowed the estimation of exposure trends over time. The study demonstrated that the estimated total dietary intakes of dioxins and dioxin-like PCBs by all age groups fell by around 50 % between 1997 and 2001.

Composite food group samples from the 2004 Total Diet Study (TDS) were used for the analysis of a range of fluorinated chemicals, including perfluorooctane sulphonate (PFOS) and perfluorooctanoic acid (PFOA). This work was carried out to allow an estimate of dietary exposures of fluorinated chemicals by UK consumers and to obtain an initial indication of whether any specific food groups are significant dietary sources. The COT considered that there was considerable uncertainty in exposures, since the majority of food groups did not contain PFOS and PFOA at concentrations above limits of detection. This finding could have been as a result of a dilution effect arising from the presence of foods in the composite sample that did not contain significant PFOS and PFOA levels.

Analysis of the 2003 and 2004 TDS for brominated fire retardants allowed estimates of dietary exposure to be derived for UK consumers. Based on the results, it was concluded that the estimated dietary exposure to brominated compounds did not have implications for health.

Total diet studies on contaminants that are generated as a result of processing and for storage, such as acrylamide and 3-monochloropropane-1,2-diol (3-MCPD) have been very illuminating. As the UK TDS on acrylamide is the subject of a separate chapter in this book, it will not be considered further here (see Chap. 50 – Using Total Diet Studies to Assess Acrylamide Exposure). A survey of the levels of 3-MCPD in samples from the 2001 TDS showed that no 3-MCPD was detected in 14 of the 20 food groups analyzed. It was shown that the highest level of 3-MCPD found at 33 µg/kg was in miscellaneous cereals, followed by fish at 19 µg/kg and bread at 11 µg/kg. Levels of 3-MCPD of between 4 and 6 µg/kg were found in meat products, poultry and oils and fats.

Conclusion

The World Health Organization (WHO) supports the TDS as the one of the most cost-effective means for assuring that people are not exposed to unsafe levels of toxic chemicals through food. TDSs continue to make an important contribution to the UK FSA's national and international commitments for the risk analysis of food chemical contaminants.

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Chapter 41
United States Food and Drug Administration's Total Diet Study Program

Katie Egan

The United States Food and Drug Administration (FDA) has conducted its Total Diet Study (TDS) continuously for nearly 50 years, albeit with many changes over that time. The US TDS grew out of concerns in the 1950s about the dietary exposure to two environmental contaminants: radionuclide fallout from nuclear weapons testing and the residues of chemical pesticides [1–3]. Details of the events that led to FDA's initiating its first TDS are given in Chap. 2 – The Origin of Total Diet Studies. A brief history of FDA's program and a description of the current US TDS are provided below; more detailed histories and information can be found in a number of publications [2, 4–8].

US FDA's Early Total Diet Study

The first US TDS was initiated in May 1961 in the metropolitan area of Washington, District of Columbia (DC) [2, 5]. The diet of teenage boys was chosen as the basis for the early studies since this population group consumes the greatest quantity of food and would consequently provide an estimate of the highest dietary exposure of contaminants on a per-person basis. A typical 14-day diet for teenage boys comprising 82 foods and beverages was developed from the United States Department of Agriculture (USDA) Food Plan at Moderate Cost. Four quarterly sample collections, or market baskets, were conducted between May and the following February 1962. For each market basket, samples of each food were purchased in retail stores in the DC area and prepared as consumed (table ready) by nearby institutional kitchens. The prepared samples were combined to form a single composite for each market

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basket, which was analyzed for strontium (Sr-90), cesium (Cs-137), organophosphate and organochlorine pesticide residues, and selected nutrients.

Through the 1960s, the geographic scope of the TDS was expanded to include more cities throughout the country, with between 18 and 44 market baskets collected per year. During that time, a total of 82 foods were collected for each market basket and then prepared as typically consumed in institutional kitchens in the FDA districts where the samples were collected. In 1971, the number of foods collected in each market basket increased from 82 to 120 and all sample preparation and analyses were centralized in the FDA Kansas City District Laboratory in Kansas City, Missouri to ensure more uniformity and efficiency in preparing and analyzing the samples. Samples collected throughout the country were shipped to the laboratory in Kansas City, where they were logged and labeled, cooked or otherwise prepared as consumed by a nearby contract kitchen, and then analyzed by the laboratory. In 1992, the Kansas City District Laboratory moved to its present location in Lenexa, Kansas.

In the 1970s, scientists began to recognize that infants and young children might be at increased risk from contaminants because of higher exposure on a per kg of body weight basis. In 1975, the US TDS was expanded to include the diets of infants and toddlers in addition to teenage boys.

In the first several years of the US TDS, all foods collected in a market basket were combined to form a single analytical composite. Beginning in 1965, the foods were divided among 11 or 12 food groups and combined to form food group composites. Separate composites were prepared to represent the diets of teenage boys and infant/toddlers. The food group composite approach provided valuable information about the contribution of each group to overall dietary exposure of the chemicals being investigated.

While the early US TDS focused on Cs-137, Sr-90, organochlorine and organophosphate pesticides and selected nutrients, over time the coverage increased to include more radionuclides and pesticide chemicals, as well as toxic elements. A number of industrial chemicals as well as nutrient elements were added during the 1970s.

Basis for the Current US TDS

FDA made several major changes to its TDS program in 1982: the number of foods increased from 120 to 234; the food list represented the diets of additional subgroups of children and adults; each food was analyzed individually; and four regional market baskets were conducted each year [5, 9].

The most significant of these changes was the decision to analyze each food individually rather than combining foods to form food group composites. This approach provided for the first time information about analyte concentrations in specific foods and the ability to determine contributions of each food to total dietary exposure. Analysis of individual foods also significantly lowered the analyte detection levels by eliminating the up to tenfold dilution of certain food items that occurred in the preparation of food group composite samples.

This methodology remains the basis for the US TDS today, although it is updated periodically to reflect new food consumption patterns as well as to incorporate new analytical methods. The current number of foods collected for each market basket is about 280. Each of the four regional market baskets conducted each year and different cities are selected within each region to provide greater geographic coverage in the program.

The preparation and analysis of individual foods in the US TDS has afforded additional benefits to other food safety monitoring activities within FDA. Since the TDS is conducted continuously, it provides a readily available source of samples of a wide range of foods that can be analyzed for contaminants or other components besides those routinely included in the TDS or other monitoring programs. Analytical results from the TDS have been used to establish background levels and dietary exposures, which can then help to target future monitoring efforts.

Responsibilities for Conducting the US TDS

From the beginning, the US TDS has been a collaborative effort among FDA offices in the Washington, DC area and FDA regional and district offices and laboratories. The main responsibilities for planning and carrying out the TDS lie with FDA's Center for Food Safety and Applied Nutrition (CFSAN) in Washington, DC, and the Kansas City District Laboratory in Lenexa, Kansas. The program relies on the FDA Office of Regional Operations (ORO), which oversees district offices and laboratories across the US, for providing the personnel to collect TDS samples from local grocery stores, malls, and takeaway restaurants and shipping them to the laboratory.

CFSAN directs the content of the program, such as the list of foods to be collected and instructions on preparing them, the locations and frequency of the sample collections, the analytes to be measured, and the analytical methods to be used. CFSAN also reviews and compiles the analytical results, maintains the US TDS website, and estimates dietary exposures based on TDS results. Since 1976 CFSAN has served as a WHO Collaborating Center for Food Contamination Monitoring and has worked closely with GEMS/Food in promoting the use of TDS globally, particularly among developing countries.

The Kansas City District Laboratory has been the hub of the US TDS since 1971. The laboratory personnel are responsible for coordinating the sample collections, arranging for foods to be prepared by a contract kitchen, preparing the analytical composites, and performing most of the analyses. They also ship portions of TDS samples to the other laboratories that are responsible for radionuclide and dioxin analyses.

The US TDS Food List

The TDS food list has been revised about every 10 years as new national food consumption surveys were conducted and new data on consumption patterns become available. Major revisions to the list were made in 1971, 1982, 1991, and

2003 [4, 5, 9, 10]. Of the approximately 280 foods in the current food list, about one-fifth are foods consumed primarily by infants and young children to 2 years of age. The other foods represent the major components of the average diets of older children and adults in the US.

The method for selecting foods for the US TDS, which was first developed in 1982, involves grouping or aggregating the large number of foods reported in the national consumption surveys (~3,000 items) into groups based on the similarity of their major ingredients. The average consumption amount of each food reported in the survey is also calculated. From each grouping of survey foods, the most representative food (i.e. consumed in the greatest quantity) is selected to be included in the TDS food list.

Many items in the TDS food list are staples in the American diet (e.g. grains, dairy products, fruits, vegetables, meat and poultry) and have been included in the program over many years. Analytical results from these staple foods provide valuable information regarding trends in levels of contaminant and nutrients and their relative contributions to dietary exposures. Other TDS foods reflect periodic changes in food patterns in the US. As an example, the most recent update of the food list, which was implemented in 2003, included more fast foods, reduced-fat items, and ethnic foods [4].

US TDS Analyses

As with other aspects of the program, the number and types of analytes have expanded and analytical methods have improved. Currently, TDS samples are analyzed routinely for approximately 350 different components, including more than 300 pesticide residues, elements (4 toxic and 12 nutrient), 13 radionuclides, and total PCBs [8]. More recently TDS samples have been analyzed for acrylamide, dioxins and perchlorate. The list of analytes changes periodically in response to FDA priorities and the need for information on background levels of emerging contaminants.

All foods are tested for residues of pesticides, including organohalogens, organophosphates, synthetic pyrethroids, herbicides, and fungicides. Selected foods are also analyzed for carbamates, phenylurea herbicides, chlorophenoxy acid herbicides, benzimidazole fungicides and ethylenethiourea (a toxic degradation product of the ethylenebisdithiocarbamates). Regarding elements, all US TDS foods are analyzed for arsenic, lead, cadmium, and all major nutrient elements; selected foods are analyzed for total mercury.

The analytical methods used in the US TDS are able to detect levels of analytes at much lower levels than those used for FDA's regulatory monitoring. Such sensitive methods are essential since the goal of the TDS is to determine realistic estimates of contaminant exposures from foods as consumed.

The Kansas City District Laboratory performs the majority of analyses (pesticides, elements, perchlorate). Radionuclide analyses are performed by FDA's

Winchester Engineering and Analytical Center in Massachusetts, and dioxin analyses are conducted by the FDA Arkansas Regional Laboratory.

The analyses include controls and checks to ensure the quality of the analytical results. All laboratory equipment is checked and calibrated on a regular basis. Samples are analyzed in batches of no more than 20 samples, and control samples are analyzed with each batch to ensure that there is no extraneous contamination. Test materials fortified with target compounds are analyzed to demonstrate the precision and accuracy of analyses. Results that are found to be outside the historical range or those not in compliance with regulatory standards are reanalyzed to confirm the initial finding before any follow-up action is initiated [11].

All analytical findings and documentation are reported by the laboratories into FDA's central database of results of its compliance and monitoring programs. CFSAN is responsible for the final step in the quality control process; the data are downloaded from the central database, reviewed, and compiled for posting on the US TDS website [8].

US TDS analytical results are reported on the website in two formats. Tables of summary statistics (e.g. number of samples, number of detects, mean, minimum, maximum) on all results from 1991 to the present. Individual results for each analyte and TDS food are available in downloadable text files that can be imported into spreadsheets or databases. Periodically, CFSAN provides such data to the GEMS/Food database in Geneva.

Dietary Exposure Estimates

Dietary exposure estimates based on US TDS analytical results can be calculated in two ways: (1) average exposure based on mean concentrations and mean consumption data, or (2) full distributions of exposure using individual data points for both analytes and consumption.

Since 1982, average dietary exposures to the US TDS analytes have been estimated by multiplying mean concentrations of analytes by average consumption amounts. Since 1991 dietary exposures have been routinely estimated for 14 age/sex groups including infants (6 months), toddlers (2 years), children (6 and 10 years), teenage boys and girls (14–16 years), and several groups of female and male adults (25–30 years, 40–45 years, 60–65 years, and 70 years and older).

When calculating the arithmetic mean concentrations of US TDS analytes, the treatment of samples for which no detected amount was found (non-detects) is an important consideration. The value assigned to the non-detected samples is generally determined by the nature of the analyte based on recommended international guidelines, which FDA follows when estimating exposure [12]. In the case of pesticides, which are intentionally used for specific crops, the concentration of a sample with no detectable residue is assumed to be zero. For other analytes that are naturally occurring (e.g. elements) or are unintentional contaminants (e.g. perchlorate), it is possible that the substance could be widely distributed in the food supply at very

low concentrations. In those instances, some value should be assigned to non-detects to avoid underestimating actual exposure. One of two approaches is generally taken: (1) assigning a value of one-half the LOD to all non-detects, or (2) calculating two means assuming zero and the LOD for non-detects, and reporting both concentrations and exposure estimates as a range from lower- to upper-bound values.

Average consumption amounts for each TDS food have been constructed for each of the 14 age/sex groups and are referred to collectively as the US TDS diets. The consumption amounts are derived from national food consumption surveys during the process of selecting the TDS foods, as described above. All foods reported in the national survey are aggregated based on the similarity of their major ingredients, and one food from each group of aggregated foods is selected to be included in the TDS food list [4, 9, 10]. Average consumption amounts are calculated for each food reported in the survey, and the sum of average consumption amounts for each group of aggregated survey foods equals the TDS diet consumption amount for that TDS food. To calculate dietary exposure, mean analytical results for each TDS food are multiplied by the US TDS diet amount for each food and then summed to obtain an estimate of total mean dietary exposure. This approach is based on the assumption that similar foods are likely to have similar concentration levels of TDS analytes and that each TDS food is a reasonable surrogate for all foods within the group of aggregated survey foods.

Estimating exposure based on the US TDS diets and mean analyte concentrations provides a quick and consistent way to calculate dietary exposures but it does not allow for estimating the full distribution of exposures. In 2009, FDA acquired the capability to link the individual analytical results for US TDS foods to the raw data from the national consumption survey to estimate a full distribution of dietary exposures [13]. Analytical results for a TDS food are linked to similar survey foods following the same aggregation scheme used for compiling the US TDS diets. Dietary exposures are calculated for each survey participant who reported consumption of a food using a randomly selected concentration value of the TDS food. Distributional exposure calculations can be based on all TDS foods (total dietary exposure) or selected foods, and for any population group of interest in addition to the 14 age/sex cohorts mentioned above.

US TDS Website

FDA maintains a website for the US TDS where more specific information about the program can be found [8]. Analytical results are available through the website in both summary tables and individual data files that can be imported into a database or spreadsheet. US TDS exposure estimates have been reported mainly in the scientific literature; a list of these publications is available on the TDS website [8]. The US TDS diets are also available on the website so that data users can calculate dietary exposures from the analytical results posted on the website. The data and information on the website are periodically updated to include new results and to reflect changes in the program.

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Part III
Special Topics in Total Diet Studies

Chapter 42
GEMS/Food and Total Diet Studies

Gerald G. Moy

Introduction

In 1948 the World Health Organization (WHO) was established as the United Nations' lead agency for public health. With some foresight, the WHO Constitution included a specific mandate for WHO to establish international safety standards for food [1]. Among some of its earliest work, WHO issued several monograph reports on food safety issues, including a 1953 monograph on the potential health risk of pesticide residues [2]. In 1956 WHO in collaboration with the Food and Agriculture Organization of the United Nations (FAO) began a series of meetings on the safety of food additives that continues to the present day. These meetings, which retain their original name of the Joint FAO/WHO Expert Committee on Food Additives (JECFA), are now also responsible for the safety evaluation of contaminants and residues of veterinary drugs [3]. In 1962 WHO, again in collaboration with FAO, began a similar series of meetings on the safety of pesticides residues on food, which are now known as the Joint FAO/WHO Meetings on Pesticide Residues (JMPR). Over the years JMPR has published an extensive series of evaluation reports and monographs covering over 200 active pesticide compounds [4].

Nowadays two meetings of JECFA and one meeting of JMPR are usually held each year, resources permitting. In addition, WHO and FAO convene expert consultations on topics of special urgency, such as the surprising discovery of acrylamide in many foods [5]. Members of these committees are international experts serving in their own capacities and who are subject to conflict of interest declarations. These unbiased, sound scientific assessments are particularly valuable to developing countries that do not have the capacity or capability to undertake such evaluations.

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When WHO and FAO established the Codex Alimentarius Commission (CAC) in 1963, these assessments were used as the basis for the development of risk management recommendations by CAC subsidiary bodies for many years.

However, as valuable as these assessments were, they did not provide very detailed assessments of exposure, in part because few countries were undertaking such studies. In the report of its 1967 meeting, JMPR briefly described the concept of total diet studies (TDSs) and emphasized that such studies of pesticide residues at the consumer level would be valuable in determining how the estimated dietary exposure of a pesticide compared with its corresponding Acceptable Daily Intake (ADI) [6]. Having been informed that several countries had initiated very useful TDSs, the 1968 JMPR report endorsed total diet studies as important tools for food safety monitoring [7]. As a result of this endorsement, a number of developed countries began to develop strategies and approaches for assessing the exposure of their populations to pesticide residues as well as other chemicals in their diet using TDSs.

Establishment of GEMS/Food

To better understand human exposure to chemicals, in 1976 the Global Environment Monitoring System – Food Contamination Monitoring and Assessment Programme (commonly referred to as GEMS/Food) was established by the United Nations Environment Programme (UNEP) as a joint project implemented by WHO in cooperation with FAO [8]. The main purpose of GEMS/Food is to inform governments, the CAC and other relevant stakeholders on levels and trends of chemical contaminants in food, their contribution to total diet, and their significance with regard to public health. Starting with 12 WHO Collaborating Centers for Food Contamination Monitoring, the GEMS/Food network now includes over 120 participating institutions located in over 70 countries around the world. GEMS/Food also maintains close linkages with other UN, multilateral and bilateral organizations.

GEMS/Food is an important part of national and international efforts to promote capacities for assuring the safety of the food supply from chemicals and providing the basis – where appropriate – for remedial actions, standards development, industry and public education and resource management. In 1979, GEMS/Food published advice for countries on establishing or strengthening their national programs for monitoring chemicals in food. In this regard, TDSs were mentioned as one approach to estimating dietary exposures of contaminants [9]. Six years later, GEMS/Food published a more detailed document that included practical advice for conducting TDSs [10]. To raise awareness of the need to better assess exposure to chemicals, GEMS/Food periodically prepared risk characterization documents to provide global overviews of the potential problems posed by chemicals in food [11] and the total diet [12, 13]. As another approach for assessing exposure, GEMS/Food was involved in human biomonitoring of human milk of certain chemicals that are

mainly found in food. Since its establishment, GEMS/Food has been collecting information on concentrations of DDT and other organochlorine pesticides in human milk and in 1998 issued a risk assessment on these chemicals [14]. This subsequently led to the establishment of the ongoing WHO Global Survey of Human Milk for Persistent Organic Pollutants (POPs), which is an integral part of international efforts to protect human health, ensure food safety and manage environmental risks. For further details, see Chap. 54 – Total Diet Studies for Infants— Example of Persistent Organic Pollutants in Human Milk.

GEMS/Food Databases

It is now widely recognized that food contamination monitoring is an essential tool for assuring the safety of food supplies and managing health risks at the international and national levels. In this regard, GEMS/Food has been collecting, collating and disseminating data on chemicals in food and the total diet as part of its mandate. One of the first tasks of GEMS/Food was to establish and maintain a database of information submitted by participating institutions on contaminant concentrations in foods. Later this work included a database on chemicals in the total diet. These databases represent one of the largest international collections of representative data on dietary exposure to chemicals. GEMS/Food provides relevant information on request.

Such data are often provided to FAO/WHO expert bodies, such as JMPR and JECFA, as well as to CAC and its subsidiary bodies, such as the Codex Committees on Food Additives (CCFA), Pesticide Residues (CCPR), Contaminants in Food (CCCF), and Residues of Veterinary Drugs in Food (CCRVDF). In some cases, CAC may specifically request information from GEMS/Food on concentration data and total dietary exposures in order to refine its risk management options.

Beginning in 1988, GEMS/Food routinely provided the CCPR with exposure assessments for pesticide residues in food based on calculations of the Theoretical Maximum Daily Intake, which was a screening tool to assess "worst case" dietary exposure. In 1995 at the request of the CCPR, GEMS/Food developed the International Estimated Daily Intake, which provided a more realistic estimate of total dietary exposure [15]. In 1997 GEMS/Food was instrumental in developing the first approach for assessing dietary exposure from a high percentile consumption of a single food commodity containing a high percentile residue concentration, which is now known as the International Estimated Short-term Intake [16].

GEMS/Food also cooperates with WHO member states in developing their capacities to estimate exposure of their populations to chemicals in their diets. In addition to supplies and equipment, GEMS/Food has provided assistance to participating institutions through a series of analytical quality assurance studies for heavy metals, aflatoxins and pesticide residues, which also served to promote the quality and comparability of data being submitted to GEMS/Food databases.

Support for Total Diet Studies

GEMS/Food has actively encouraged countries to conduct TDSs as the most cost-effective approach for assessing chemical contaminants in the diets of their populations. In this regard, GEMS/Food has collaborated with counterpart national agencies to sponsor a series of TDS workshops and training courses. The objectives of the workshops are to promote and support TDSs internationally and to provide a forum in which countries that had conducted such studies can share their experiences and expertise. As of 2009, international workshops have been held in Kansas City, USA (1999), Brisbane, Australia (2002), Paris, France (2004) and Beijing, China (2006), often in cooperation with FAO. Each of these workshops were preceded by a training course that offered lectures and opportunities for hands-on experience in the technical aspects of conducting TDSs as well as discussions regarding planning, implementing and assessing the outcome of the studies. Altogether ten training courses have been held over the past 10 years, which have trained more than 250 people from 60 countries.

Obviously the GEMS/Food databases on chemicals in food and in the total diet mentioned above can be useful to countries carrying out TDSs as a basis for assessing and comparing their results with those of other countries. In order to assist countries in managing the data, GEMS/Food has developed an Operating Program for Analytical Laboratories (OPAL), which has capabilities to handle individual and aggregate analytical results for chemicals in food (OPAL I) as well as dietary intake from chemicals in the total diet (OPAL II). These are discussed in more detail in Chap. 46 – OPAL—A Program to Manage Date on Chemicals in Food and the Diet. GEMS/Food also has other databases that may be useful in designing TDSs. For example, the GEMS/Food list of chemicals for a total diet study should be consulted in preparing their contaminants list (See Chap. 7 – Selecting Chemicals for a Total Diet Study). Similarly, the GEMS/Food Consumption Cluster Diets may be used by countries for planning their food lists, especially if national food consumption data are unavailable (see Chap. 43 – GEMS/Food Consumption Cluster Diets).

Within the WHO Region of Europe (EURO), the European Programme on Monitoring and Assessment to Potentially Hazardous Substances (commonly called GEMS/Food-EURO) was established in 1991 to provide specific assistance tailored to the priorities and needs of the region [17]. GEMS/Food-EURO has made a number of contributions to TDSs, including development of procedures for handling data below the limit of detection [18]. GEMS/Food-EURO also was an important contributor to European risk assessment publications that highlighted total diet assessments [19].

All six WHO Regional Offices have sponsored regional TDS training courses in cooperation with national counterparts in Brno and Prague (2000), Buenos Aires (2002), Cairo (2007), Jakarta (2007) Hong Kong (2008) and Yaoundé (2010). WHO Regions, particularly the WHO Western Pacific Region, have also been active in supporting national TDSs through provision of consultant services and supplies and equipment.

With the establishment of the World Trade Organization in 1995 and the coming into force of its Agreement on the Application of Sanitary and Phytosanitary

Measures (SPS Agreement), the standards, guidelines and other recommendations of CAC gained considerable weight. However, the most remarkable aspect of the SPS Agreement was that countries were obligated to use a sound scientific assessment of risk in establishing their health and safety regulations for food [21]. This requirement for risk assessment set in motion a critical review of international and national procedures for evaluation of food safety. While the hazard characterization of the toxic potential of chemicals had adequately been addressed, it became evident that the exposure assessment component had been neglected. Furthermore, unlike hazard characterization, which could be done at the international level, exposure assessment had to be conducted by each country in order to take into account local food consumption patterns and levels of contamination. In the developing world, little or no capabilities existed for monitoring of chemicals on and in food. Capacity building, if any, was directed toward supporting food exports. Consequently, the situation in many developing countries was that chemicals were being introduced and used without any protection for the environment or the consumer. Furthermore, without such data, these countries could not effectively participate in the work of CAC, which increasingly has limited its debate to risk assessment evidence. In order to assist such countries in developing their risk assessment capabilities, a consortium of five international agencies, including FAO and WHO, established a Standards and Trade Development Facility (STDF) [20]. Recently the STDF has seen it appropriate to allocate resources for TDSs in recognition of their importance to both health and trade.

Conclusion

Since the first TDS workshop and training course in 1999, over 30 countries have now implemented TDSs and many more are in the process of planning them. What has become clear is that all countries must conduct exposure assessments to protect their populations from chemical hazards in food and that a TDS is one of the most accurate and cost-effective methods for doing this. This recognition should result in TDSs receiving greater priority and resources than in the past. GEMS/Food has continued to support and promote TDSs as an essential tool for the sound scientific assessment and management of foodborne risks. However, the success of this approach will depend on the commitment of policy- and decision-makers to support TDSs and the dedication and talent of exposure assessors carrying out TDSs at the national level.

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Chapter 43
GEMS/Food Consumption Cluster Diets

Fanny Héraud, Leila M. Barraj, and Gerald G. Moy

Introduction

The World Health Organization (WHO) has developed the GEMS/Food [1] Consumption Cluster Diets, which provides an overview of the food consumption worldwide, through 13 dietary patterns covering 183 countries. Five regional diets were initially developed by GEMS/Food to respond to risk assessment needs at the international level following the Chernobyl disaster in May 1986. Estimates of food consumption were necessary to assess the potential exposure of populations to radionuclides that might contaminate food. Subsequently in 1988, the first GEMS/Food Regional Diets were developed from Food Balance Sheet (FBS) data collected by the Food and Agriculture Organization of the United Nations (FAO) for selected countries, representing five regional dietary patterns, namely Middle Eastern, Far Eastern, African, Latin American and European [2]. Beginning in 1989, these diets were used by the Joint FAO/WHO Meeting on Pesticide Residues (JMPR) and, subsequently, by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) to estimate long-term dietary exposure to pesticides residues, contaminants and toxins in food. They have also been used by the Codex Committee

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on Contaminants in Food as a screening tool in determining if a Codex Standard for a contaminant or toxin in a food or food group is warranted from a public health perspective [3].

In 1995, a Joint FAO/WHO Consultation on estimating dietary intake of pesticide residues recommended that the consumption data used at the international level for chronic dietary exposure assessments should take into account the differences in food consumption patterns, both within and among countries and that, "*An evaluation of national FBSs be conducted by WHO to determine appropriate groupings of countries into so called cultural diets*" [4]. This initiated a rather long and complex process, which would result 10 years later in the establishment of the GEMS/Food Consumption Cluster Diets (Cluster Diets). This chapter describes these diets and how they were derived and provides guidance for the use of these diets in the particular framework of a total diet study (TDS).

Derivation of Diets

Food Balance Sheet Data

As in the case of the previous GEMS/Food Regional Diets, the Cluster Diets are based on FBS data, which provide estimates of the per capita amount of food available for human consumption during a reference period (typically a year) at the national level. FBS data are currently the only production and usage estimates that are produced in a standardized manner in all countries and that are reported each year to the FAO [5]. This assures the comparability of data and allows for their aggregation at the regional level. However, FBS data have three main drawbacks. First, as a country estimate, they do not give any indication on food consumption variability among households or individuals. Secondly, they only provide estimates on consumption of raw and semi-processed commodities, such as polished rice, flour, fats and oils. They provide only limited information on the processes and do not cover home preparation and cooking methods prior to consumption. Finally, they do not take account of subsistence or home production habits at the national level. As a consequence, they may not be appropriate for all food risk assessment situations. While they can be used for assessing chronic exposure and risk for a population average, they are not applicable to specific subpopulations or consumer groups, e.g. subsistence fishermen, or for acute risk estimation. In general, they are less useful for assessing exposure to hazards that are introduced or occur during food processing. Because waste at the household or individual level is not taken into account, FBS data tend to slightly overestimate consumption [3]. Based on comparison with national food consumption surveys, the per capita food consumption estimates based on FBS data are generally about 15 % higher than actual average food consumption in the worst cases, e.g. fruits and other highly perishable products [6].

Clustering of Countries

In order to determine appropriate groupings of countries, a cluster analysis was first conducted on the 1990–1994 average FBS data. Nineteen marker foods chosen from 140 foods reported in 183 countries were used in the analysis. Countries were classified into groups based on the similarity in their consumption levels of these 19 marker foods and their geographical location. This method resulted in classifying the countries into 13 homogeneous groups, i.e. clusters, in term of consumption patterns (Fig. 43.1) [7]. The 1997 Joint FAO/WHO Consultation on Food Consumption and Exposure Assessment of Chemicals endorsed the development of new cluster diets [8].

Development of the Diets

The 13 cluster diets, including 383 different food items, were then constructed using the average FBS data from the 1997 to 2001 period. For each food item, the average consumption value based on the 1997–2001 data was first calculated for each country. Then, the consumption at the cluster level of each food commodity was determined as the average of the various countries where the average was weighted by their respective population size of each country. Consequently, the consumption pattern of clusters with large countries mainly reflects the consumption patterns within those countries. Where no data was reported for a particular food item in a country, the country was not used in the derivation of the weighted average for that food. In this way, a missing level of consumption was never assumed to imply zero consumption.

The FBS foods were then mapped to the foods in the GEMS/Food nomenclature system. However not all the GEMS/Food commodities specifically matched the FAO FBS data because the two food classifications systems are not totally compatible. In other cases, certain food commodities were not reported by all countries submitting FBS data. Thus, the initial mapping resulted in some gaps and mismatches, particularly for 58 of the 383 food commodities and groups included in the GEMS/Food system. Various methods were used to estimate missing foods. In some cases, these were estimated from a broader food group or as a sum of more detailed foods defined by the FAO FBS classification. In some other cases, they were estimated from other data sources, such as national food consumption surveys, obtained on request to the countries with the cooperation of the Codex Committee on Pesticide Residues. Finally, where the consumption was low, but could not be quantified, a default value of 0.1 g per person per day was used.

Some adjustments were conducted to ensure the consistency of the diets. In particular, the consumption value for a raw commodity was compared to the value for that commodity when back calculated from its processed products using the standard FAO processing factors [9], and if the back calculated value was higher, it was used instead of the original raw commodity value in order to give a higher, more conservative estimate.

GEMS/Food Consumption Cluster Diets

Letter codes for Consumption Cluster Diets

- A
- B
- C
- D
- E
- F
- G
- H
- I
- J
- K
- L
- M
- Data not available

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: World Health Organization
Map Production: Public Health Information and Geographic Information Systems (GIS)
World Health Organization

World Health Organization

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Fig. 43.1 Map of countries by GEMS/Food Consumption Cluster Diets

Use of the Diets

Description of the diets

The GEMS/Food Consumption Cluster Diets are available on the WHO website [10]. Figure 43.2 represents for each cluster, the contribution of the main food categories to the total diet.

Not surprisingly, the food categories with the highest amounts consumed are cereals and/or roots and tubers. They contribute between 25 % (Cluster M, America, Argentina, Australia, and New Zealand) and 60 % (Cluster J, Sahel Africa) of the total diet. For diets (H, B, C, D, L, and G) cereals is the highest contributor, and the main cereal component seems to vary according to a west/east gradient (from wheat to maize to rice). Roots and tubers are major contributors for the remaining diets (A, J, I, E, and F). Cassava is the main tuber component for the African clusters (A, I, and J), while potatoes are the main tuber component for the European clusters (E and F). Fruits and vegetables are the next highest consumed food group, representing between 23 % (Cluster I, southern Africa) and 38 % (Cluster B, southern Europe) of the total diet.

The next highest consumed food groups are products of animal origin. They contribute between 8 % (Cluster A, central Africa) and 30 % (Cluster M, North America, Argentina and Australia/New Zealand) of the total diet. Different profiles, representing the types of animal products are apparent. In two clusters (G and L corresponding to the Far-East region) fish products, meat products, eggs, and dairy
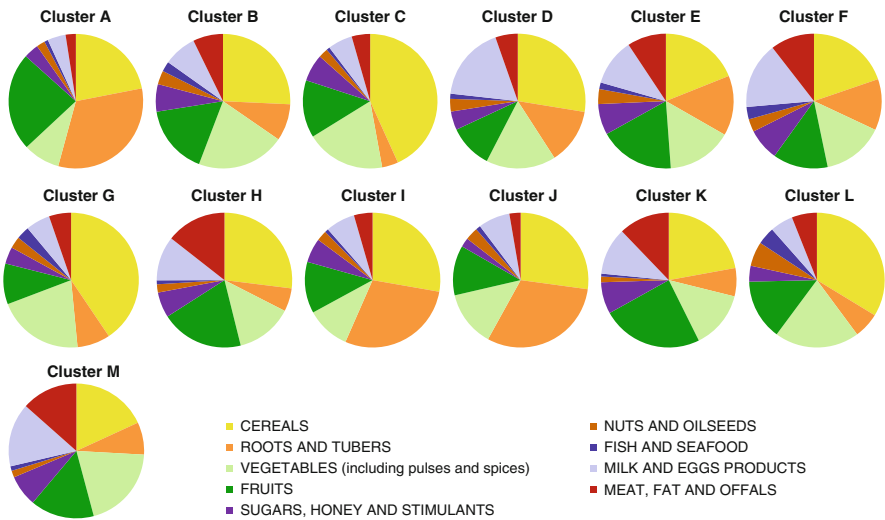
Fig. 43.2 Contribution of the main food categories to the total diet for the 13 GEMS/Food Consumption Cluster Diets

products, contribute equally (approximately 5 % each) to the total diet. In the remaining clusters, fish products have less importance as compared to the other products of animal origin. In Clusters B, C, E, K, and M, meat products and eggs and dairy products share contribute equally to the total diet, ranging from 5 % of the total diet for Cluster C (northern Africa) to 15 % of the total diet for Cluster M. In contrast, in Cluster H (west central Americas), meat products are one and half times more consumed than eggs and dairy products, whereas the reverse is observed for Cluster F (northern Europe). Finally, the consumption level of eggs and dairy products is between 2 and 3 times higher than meat products in Clusters A, D, I, and J (central Africa, Russia/former USSR, southern Africa, and Middle East, respectively).

Sampling Design of TDS

The Cluster Diets have two potential uses in the TDS framework. First, they can be used to plan the sampling design of a TDS. Second, they can be used to interpret TDS results in a dietary exposure assessment. Specifically the Cluster Diets provide consumption estimates of 383 food commodities. They can guide the selection of the commodities to be sampled during a TDS according to their importance in the total diet. They would be especially useful for TDSs, which are conducted at a regional level, e.g. at the European or the sub-Saharan African level. At such a level, the first issue is often to combine national consumption estimates, which are not easily comparable as they come from different study designs and because they may be described with incompatible food classification systems. The Cluster Diets compile comparable national consumption estimates weighting them according to the population size. Thus, they can be directly used to establish an initial food list for review at the regional level. Such a list can be further refined according to each country's characteristics, particularly in terms of food processing and home cooking habits before consumption. If the Cluster Diets are more accurate for a regional or international use, they could also be used at the national level as a substitution tool. This may occur for countries which consider their national FBS data to be of insufficient in quality or representativeness, for example in case of high subsistence production levels not covered by the FBS. In such a case, using the corresponding Cluster Diet assumes the consumption pattern observed at the regional level is the same as the national one.

Dietary Exposure Assessment

Once the food samples have been analyzed for the presence of chemicals, the Cluster Diets can be used as consumption estimates to assess the background level of total dietary exposure of the general population, which is the main purpose of a TDS.

As previously mentioned, the Cluster Diets will be more appropriate for a dietary exposure assessment conducted at the regional or international level than at the national level because of the weighting method that is used. If a country has a low population in relation to the other countries in the cluster, the interpretation at the national level may be difficult and need expert judgment.

It is usually considered that using Cluster Diets for exposure assessments will result in a slight overestimation of the risk. Nonetheless, in assessing exposure of potentially harmful chemicals, such overestimates err on the side of caution and are thus protective of public health. However, for assessing nutrient intakes, where adequacy of nutrition can be just as important as toxicity, this matter should also be taken into account, so as not to overestimate low nutrient intakes.

In general, the use of Cluster Diets fits better for environmental contaminants, natural toxins or pesticides residues than for chemicals that are applied or formed and/or transformed during food processing. In fact, the consumption values mainly relate to the whole raw agricultural commodity (RAC). For chemicals appearing or increasing during food processing, attributing the chemical concentration measured in food as consumed to an RAC consumption level will lead to a risk overestimation. This will be protective of public health for issues of toxicity, but sometimes a more refined estimate of actual exposure is required. For chemicals decreasing during process, attributing the chemical concentration measured in processed food to RAC consumption level may lead to an underestimation of risk, if the food is both consumed in processed and RAC forms. In the case of some commodities exclusively processed before consumption, the Cluster Diets do provide more detail. For example, for food oils, the Cluster Diets will not only provide consumption values for the RAC, i.e. oil seed, level but also for the semi-processed, i.e. crude oil, and processed levels, i.e. refined oil.

Expressed as average daily per capita food consumption, the Cluster Diets are typically a factor of three lower than the corresponding high percentile of consumption of food [11]. For foods consumed occasionally or seasonally, or by only a small subgroup of the population, this factor can be much higher. Therefore, these diets are not fit for assessing risks posed by hazards, which cause effects after short-term exposure, as it is sometimes the case for certain pesticides residues. However, such an issue is usually not within the scope of a TDS, which is focused on chronic exposure.

Conclusion

The GEMS/Food Consumption Cluster Diets may be used in the framework of a TDS, in order to set the food list to be investigated during the TDS or to estimate the dietary exposure levels of the population based on TDS results. If they are adapted from the regional or international level for use by a country, they should be completed by expert judgment at the national level. The current estimates of the GEMS/Food Consumption Cluster Diets are based on an average of the 5-year period

between 1997 and 2001. Following the recommendation of the 1997 FAO/WHO Consultation [9], the GEMS/Food Consumption Cluster Diets should be updated every 10 years or less if changes in dietary patterns are anticipated.

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Chapter 44
Food Mapping in a Total Diet Study

Julie L. Boorman, Janis Baines, Tracy L. Hambridge, and Janice L. Abbey

Introduction

Food mapping is the process of matching food consumption data, for foods that were consumed by individuals in national nutrition surveys, to the specific foods analyzed in a total diet study (TDS). The purpose of food mapping is to assign the limited number of food analytical concentrations to a wider number of foods consumed in the diet. Hence, one food may be assumed to 'represent' other foods of a similar type and the concentration for that one food is assigned to the food consumption amount for the wider group of foods. This is done because resources limit the number and types of foods that can be analyzed in a TDS.

Food mapping can also be used to derive model diets from national nutrition survey data, based on the foods sampled in the TDS. This is one option for countries developing their first TDS or where resources for complex data analysis are limited. Other options can include the use of food group composites in analysis rather than single foods (see Chap. 5 – Scope, Planning and Practicalities of a Total Diet Study, Chap. 6 – Preparing a Food List for a Total Diet Study, Chap. 8 – Preparing a Procedures Manual for a Total Diet Study, and Chap. 9 – Food Sampling and Preparation in a Total Diet Study).

Food mapping can be based on nutritional food groupings and/or expected presence of the food chemical in different food groups. The mapping procedure is not static and may change for each TDS. When mapping foods, it is important to consider how the samples were prepared and how this could influence the concentrations of the food chemicals of interest. When constructing food maps, there is a need to consider the ways in which foods are eaten and, where there is the

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intentional addition of a food chemical such as a food additive or pesticide, to what foods it is likely to be added or applied and where these foods may then be used in mixed foods.

There are three main levels in food mapping, namely direct mapping, mapping with the use of hydration and raw equivalence factors, and use of recipes. Each of these are discussed below and followed by examples and case studies.

Direct Mapping

Direct mapping is where the TDS foods can be directly matched to the same food and to similar foods from the nutrition survey, where one food can be assumed to represent a whole food group (See Example 1). When conducting direct mapping from foods in a national nutrition survey with composite samples analyzed in the TDS, it is important to consider whether the primary samples are a single food from a food group (e.g. oranges only) or a variety of similar foods from the same food group (e.g. oranges, lemons, limes and grapefruit). The nature of the composite samples will influence the assumptions that need to be made.

Example 1: Direct Mapping

Raw, peeled oranges were analyzed for a variety of pesticide residues in a TDS. No other citrus fruits or citrus fruit products were sampled. The food consumption data includes information on the consumption of raw oranges, grapefruit and mandarins and various citrus fruit juices.
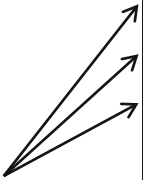
The first step is to allocate the concentrations of pesticide residues in the analyzed food (raw, peeled oranges) to the same or similar foods consumed in the nutrition survey. It could be assumed that the pesticide residue concentrations in all raw citrus fruits are the same as in raw oranges, however the way the food is consumed also needs to be considered. Raw grapefruit and raw mandarins are eaten in similar ways to raw oranges and all belong to the same Codex classification for raw commodities (Citrus Fruits). Lemons and limes are also in the same Codex classification group, but are not usually eaten raw and are only reported as being consumed as juice.

The analyzed food of raw, peeled oranges is mapped to raw, peeled oranges, grapefruit and mandarins. This is 'direct mapping' since the analyzed food is being mapped to the same food as analyzed and to similar foods (See Table 44.1).

The food map is then used to calculate the food consumption amount for the wider group of foods to which a single analyzed food is linked. This is illustrated in "Case Study 1: Step 1" later in this chapter.

In the case of citrus fruit juices, it is not reasonable to assume that the pesticide residue concentrations from raw oranges are the same as in citrus fruit juices since juice is an extract of the orange rather than being a whole peeled orange. Additionally, not all of the juices are reported in the nutrition survey in the same form; namely,

Table 44.1 Direct mapping

Analyzed food	Foods in the food consumption data
Oranges, raw, peeled	Oranges, raw, peeled
	Grapefruit, raw, peeled
	Mandarins, raw, peeled
	Juice, orange
	Juice, lemon
	Juice, lime
	Juice, mandarin
	Juice concentrate, orange

some are reported as consumed and some as the concentrate. The juice concentrate first needs to be converted to 'ready-to-drink' form so it is in the same form as other juices, before converting all juice to raw orange equivalents. To do this, hydration and raw equivalence factors need to be incorporated into the calculation (see the following section).

Mapping Using Hydration and Raw Equivalence Factors

The technique of mapping using hydration and raw equivalence factors is used where foods from the nutrition survey are in a different form to the sampled food. For example, the analyzed food is black coffee made up from instant coffee powder with water and the consumed food reported in the nutrition survey is instant coffee powder. Hydration factors are applied to foods that have water added when they are being prepared to a ready-to-eat form (e.g. dried pasta, rice, tea leaves, coffee powder, juice concentrate). Raw equivalence factors are applied to foods where processing has removed water (e.g. dried fruits, tomato paste) or the food has been extracted from a commodity (e.g. butter from milk, orange juice from oranges). Both hydration and raw equivalence factors are applied to some individual foods to convert the amount of food consumed in the nutrition survey to the equivalent amount of the food type that was analyzed. See Example 2 for further information on hydration factors and Example 3 for additional information on raw equivalence factors.

Other 'conversion' factors such as edible portion and processing factors are sometimes used in dietary exposure assessment calculations. However, since all foods analyzed in a TDS are the edible portion of a food that is prepared to a ready-to-consume state, conversions for edible portions of food are not required. Additionally, national nutrition surveys record food consumption amounts as edible

Table 44.2 Mapping using hydration factors

Analyzed food	Foods in the food consumption data
Oranges, raw, peeled	Oranges, raw, peeled
	Grapefruit, raw, peeled
	Mandarins, raw, peeled
	Juice, orange
	Juice, lemon
	Juice, lime
	Juice, mandarin
	Juice concentrate, orange **(hydration factor = 4)**

portions only. Processing factors are used where there is a concentration or reduction in the concentration of a chemical in a food following processing such as juicing, extraction or cooking (e.g. for agricultural chemical residues between olives and olive oil; oranges and orange juice, etc.). If changes in chemical concentrations are suspected following processing, consideration should be given to the form of food sampled and analyzed in the TDS. See Chap. 9 – Food Sampling and Preparation in a Total Diet Study.

Example 2: Using Hydration Factors

From Example 1, not all citrus fruit juices that were reported as consumed in the nutrition survey are in the same form – i.e. there are some ready-to-drink juices and one juice concentrate. To convert all of the juices to a 'ready-to-drink form', a hydration factor needs to be applied to the juice concentrate (since water is added to prepare the food to a 'ready-to-drink' form). For juice concentrate, 100 g of orange juice concentrate makes 400 g of orange juice, and therefore the hydration factor for fruit juice concentrate is 4 (See Table 44.2 above). The application of the hydration factor is as follows:

50 g orange juice concentrate consumed $\times 4 \rightarrow 200$ g 'ready-to-drink' orange juice as consumed

However the concentrate cannot yet be mapped to raw oranges. Example 3 provides details on the additional step to be performed.

Table 44.3 Mapping using hydration and raw equivalence factors

Analyzed food	Foods in the food consumption data
Oranges, raw, peeled	Oranges, raw, peeled
	Grapefruit, raw, peeled
	Mandarins, raw, peeled
	Juice, orange **(raw equivalence factor =2)**
	Juice, lemon **(raw equivalence factor =2)**
	Juice, lime **(raw equivalence factor =2)**
	Juice, mandarin **(raw equivalence factor =2)**
	Juice concentrate, orange **(raw equivalence factor = 2; hydration factor = 4)**

Example 3: Using Raw Equivalence Factors

From Example 1, citrus fruit juices were not able to be directly mapped to raw, peeled oranges since a juice is an extract of the orange rather than being a whole peeled orange. Consequently, the consumption of citrus fruit juices needs to be adjusted to account for the weight of raw oranges required to make the fruit juice. This is called a raw equivalence factor. It assumes that when the food (e.g. orange juice) is extracted from the original commodity (e.g. raw, peeled oranges) the food chemical is only distributed within the extract with no losses of the food chemical in the process. For example, if 200 g of peeled oranges are required to make 100 g of orange juice, then the raw equivalence factor for fruit juice is 2. The application of the raw equivalence factor is as follows:

200 g orange juice $\times$ 2 = 400 g raw peeled oranges

Both the hydration and raw equivalence factors are applied to the juice concentrate – first the hydration factor to calculate the amount of juice consumed; and second, the raw equivalence factor to convert the juice to an equivalent amount of raw peeled oranges (See Table 44.3 above).

The application of the both factors to the juice concentrate is as follows:

50 g of concentrate $\times$ 4 = 200 g orange juice
200 g of orange juice $\times$ 2 = 400 g raw peeled oranges

The food map is then used to calculate the food consumption amount for the wider group of foods to which a single analyzed food is linked to. This is illustrated in Case Study 1- Steps 2 and 3.

Case Study 1: Step 1

From the nutrition survey data, Person A ate the following foods during a one day period:

Food	Amount consumed (g)
Oranges, raw, peeled	200
Mandarins, raw, peeled	150
Juice, lemon	50
Juice concentrate, orange	50

As discussed in Example 1 of direct mapping, the first level is to map the analyzed food (raw, peeled oranges) to the same foods and similar foods consumed in the nutrition survey – for Person A, this is Oranges, raw, peeled and Mandarins, raw, peeled. No hydration factors or raw equivalence factors are needed for directly mapped foods. Therefore, the "revised" food consumption amounts for Person A for Oranges, raw, peeled and Mandarins, raw, peeled are as originally recorded in the nutrition survey (i.e. 200 and 150 g, respectively).

Food	Amount consumed (g)	Food from the TDS food map	Hydration factor	Raw equivalence factor	Revised food consumption amount (g)
Oranges, raw, peeled	200	Oranges, raw, peeled	n/a	n/a	200
Mandarins, raw, peeled	150	Oranges, raw, peeled	n/a	n/a	150
Juice, lemon	50				
Juice concentrate, orange	50				

Case Study 1: Step 2

As discussed in Example 2, hydration factors are used to convert the consumption amount for all of the juices to a 'ready-to-drink' form. In this case, a hydration factor needs to be applied to the juice concentrate. For Person A, the "revised" food consumption amounts for Juice, orange, concentrate is 50 g×hydration factor of 4 → 200 g of orange juice.

Food	Amount consumed (g)	Food from the TDS food map	Hydration factor	Raw equivalence factor	Revised food consumption amount (g)
Oranges, raw, peeled	200	Oranges, raw, peeled	n/a	n/a	200
Mandarins, raw, peeled	150	Oranges, raw, peeled	n/a	n/a	150
Juice, lemon	50		n/a		
Juice concentrate, orange	50	(Juice, orange)	*4*		*(200 juice)*

Case Study 1: Step 3

As discussed in Example 3, raw equivalence factors are used to convert all of the juices to equivalent amount of raw peeled oranges. For Person A, the "revised" food consumption amounts for Juice, orange, concentrate is 50 g×hydration factor of 4×raw equivalence of 2 → 400 g of raw peeled oranges. Similarly, the "revised" food consumption amount for Juice, lemon is 50 g×raw equivalence of 2 → 100 g of raw peeled oranges.

Food	Amount consumed (g)	Analyzed food from the TDS	Hydration factor	Raw equivalence factor	Revised food consumption amount (g)
Oranges, raw, peeled	200	Oranges, raw, peeled	n/a	n/a	200
Mandarins, raw, peeled	150	Oranges, raw, peeled	n/a	n/a	150
Juice, lemon	50	Oranges, raw, peeled	n/a	*2*	*100*
Juice concentrate, orange	50	Oranges, raw, peeled	4	*2*	*400*
Total citrus fruits (raw fruit equivalence)					*850*

   The total for citrus fruits (raw fruit equivalents) is now calculated (850 g per day). The "revised" food consumption amounts are now ready to use in the dietary exposure assessment calculations; the food chemical concentration from the analysis for raw peeled oranges will be assigned to 850 g citrus fruit, expressed as raw peeled fruit equivalents.

Recipes

Recipes are used in food mapping when foods from the nutrition survey are composed of more than one surveyed food i.e. is a 'mixed food' (e.g. fruit salad). This is to allow the food chemical concentrations for each component or ingredient in a 'mixed food' to be taken into account in the dietary exposure estimate as is shown in Case Study 2 below.

Case Study 2: Recipes

Fruit salad was reported as consumed in the nutrition survey. To be able to calculate the food chemical contributions from each of the fruit salad ingredients, a recipe needs to be developed. For the purpose of this case study, a typical recipe for fruit salad is provided below where all the foods in the fruit salad were analyzed in the TDS.

Food in the food consumption data	Analyzed foods from TDS	Recipe – proportion of the fruit in the fruit salad (%)
Fruit salad, fresh	Oranges, raw, peeled	8
	Apples, raw, unpeeled	10
	Bananas, raw, peeled	14
	Pineapple, raw, peeled	50
	Mango, raw, peeled	10
	Grapes, raw	8

Since fruit salad does not undergo cooking or other process where there is a weight loss between the raw ingredients in a recipe and the weight of the final food (e.g. as with roasting, frying, etc.), no weight loss needs to incorporated into this recipe. The weight loss factor differs from the hydration and raw equivalence factors.

Person A consumed 250 g of fruit salad on the day of a nutrition survey. The exposure to a food chemical from this quantity of food can be calculated using the recipe above as follows:

	Proportion (%)	Amount of ingredient in 250 g food (g/day)	Food chemical concentration to be assigned from TDS analyzed food[a] (mg/kg)	Food chemical dietary exposure from each ingredient[b] (mg/day)
Oranges, raw, peeled	8	20	100	2 (0.02 kg food/day × 100 mg/kg food)
Apples, raw, unpeeled	10	25	50	1.25

(continued)

	Proportion (%)	Amount of ingredient in 250 g food (g/day)	Food chemical concentration to be assigned from TDS analyzed food[a] (mg/kg)	Food chemical dietary exposure from each ingredient[b] (mg/day)
Bananas, raw, peeled	14	35	100	3.5
Pineapple, raw, peeled, cored	50	125	22	2.75
Mango, raw, peeled, de-stoned	10	25	70	1.75
Grapes, raw	8	20	50	1
Total	*100%*	*250*		*12.25*

[a]Determined by an analytical laboratory

[b]The weight of food consumed needs to be expressed in kilograms for this calculation as the unit for food chemical concentrations is mg/kg food. For example, 20 g orange should be expressed as 0.02 kg orange)

When developing representative recipes for 'mixed foods' from the nutrition survey, recipes should be chosen to reflect how the majority of people prepare the food/dish in the region/country being examined. Sources of recipe information can include cook books, magazines, the internet, research articles, food labels and talking with people from the population group/ sub-groups of interest in the TDS. The level of detail required for the recipe needs careful consideration since more detailed recipes require more resources for their development. However this level of detail may not be necessary for the purpose of the assessment. If minor ingredients, such as spices, are of particular interest because of possible high contamination or are widely used in foods, then they can be included in recipes. Other considerations for recipe development include:

- Form of the ingredient, e.g. dried, raw, cooked, etc.
- Moisture loss or gain
- Uptake of fats during cooking, e.g. deep frying
- Addition of salt

Consideration of Food Chemical Type

When determining whether a food reported as consumed in a nutrition survey can be directly mapped or needs to be mapped in conjunction with a hydration factor and/or a raw equivalence factor, it is important to consider the nature of the food chemical of interest as this can influence the decisions made, as illustrated in Example 4 below.

Example 4: Consideration of the Nature of the Food Chemical

Milk and margarine have been sampled in a TDS. Butter was reported as consumed in the nutrition survey and needs to be mapped to an appropriate TDS food, if one exists. If the TDS examined food additives, the analyzed food margarine could be directly mapped to butter if permissions for the use of the food additive in the national food standards apply to all fats and hence the food additives present in margarine are likely to be similar to those in butter (i.e.10 g butter is assumed to be 10 g margarine).

If the TDS examined contaminants or pesticide residues, the analyzed food milk should be mapped to butter with an appropriate raw equivalence factor applied to the amount of butter consumed since it is not reasonable to assume that the contaminant or pesticide residues in margarine and in butter are similar, as they are derived from different raw commodities (oilseeds and milk, respectively) and subject to different food processing methods.

If x grams of milk are required to make y grams of butter, the raw equivalence factor is w (derived from the fat content of each food). The application of the raw equivalence factor is as follows:

10 g butter × raw equivalence factor (w) = z grams milk

Conclusion

The possible implications (both positive and negative) of using the food mapping system need to be carefully considered prior to performing the dietary exposure calculations since they may contribute to uncertainty in the estimate (See Chap. 18 – Addressing Uncertainty and Variability in Total Diet Studies). The methodology, limitations and assumptions used in food mapping should be carefully documented and discussed in the final dietary exposure assessment report.

Chapter 45
Automated Programs for Calculating Dietary Exposure

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Introduction

The complexity of total diet studies increases significantly with increases in the number of chemicals and the number of samples analyzed. In some countries, individual food items are analyzed leading to thousands of results. This is especially challenging when combining this data with individual food consumption survey data, since the number of cohorts of interest can also be large. Even for deterministic methods, the logistical burden would preclude the manual calculation of exposure in all but the most simple total diet study design. In the case of semi-distributional methods of exposure assessment, manual calculations are not possible given the large number of operations involved.

It is, therefore, not surprising that automated programs for calculating dietary exposure have been developed to assist total diet study practitioners in this critical step of the study. These include both proprietary and nonproprietary programs. The latter have been developed as "in-house" programs by government and international agencies involved in exposure assessment. This chapter will describe four such programs, which are intended to illustrate the types and capabilities of programs that are available, but note that their inclusion here does not in any way constitute approval, endorsement or recommendation.

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DEEM

Exponent's Dietary Exposure and Evaluation Models (DEEM™ and DEEM-FCID™) [1] estimate chronic and acute dietary exposure for the US populations and for subgroups of the population. The latter uses the US Environmental Protection Agency (EPA) Food Commodity Ingredient Database (FCID). The two versions are collectively referred to as DEEM in this chapter. The DEEM dietary exposure assessment modules can be used to estimate the intake of toxicants, nutrients, pesticides, food additives, and natural constituents – in short for any chemical component of food or water. These substances can include inorganic and organic chemicals as well as microorganisms or toxins produced by microorganisms.

DEEM is designed to allow the user to tailor the analysis to provide the most appropriate estimates including acute and chronic exposures and to allow the user to understand the factors that have the most impact on those estimates by selecting from among several exposure assessment models. There are three general exposure assessment models available in DEEM: deterministic, semi-distributional and probabilistic (Monte Carlo). With appropriate adjustments these models can also be used for estimating cumulative exposures. In all cases the user can estimate typical exposure (e.g. mean, median) or percentiles (e.g. 5th, 10th, 90th, 95th, and 99th percentiles) for the entire population and for users of the foods of interest only.

Data used by the DEEM modules are of two types. The first types of data are those supplied by DEEM that cannot be changed by the user, although the user can use a subset of these data. These data are referred to as "hard" data and consist of the consumption and demographic profiles of the individuals in the selected food consumption surveys and the translation factors that convert foods as consumed (e.g. pizza) into the corresponding raw agricultural commodities and food forms (e.g. wheat, tomatoes, etc.). The current versions of DEEM contain data generated for the US population in the US National Health and Examination Survey (NHANES).

The second type of data are those that are supplied by DEEM but can be modified by the user. These data are referred to as "soft" data and include the default processing factors and the residue data. Residue data can be extracted from US Department of Agriculture's Pesticide Data Program via the DEEM RDFgen™ module, which automates single analyte and cumulative residue distribution adjustments and the creation of summary statistics. However, other residue data provided by the user can be used. The user can also provide other information, such as the proportion of the crop that will contain the designated levels and the chemical specific toxicity measures.

Single point estimates and/or distributions (whether empirical or parametric) may be used to describe the levels of the substance under evaluation as well as for the amount of the food that is consumed. Single point estimates are typically used to represent residues in foods that undergo a large degree of blending or when the number of samples is limited as in the case of total diet studies. Distributions are generally used in more complex dietary exposure assessments and in cases where

residue levels in foods may vary from unit to unit. In many exposure assessments a single point estimate is used for some values and distributions for others – depending on the goals of the assessment and the availability of the data. DEEM allows the user to modify residue estimates to reflect the percentage of a crop that is expected to contain the residue and to allow data from total diet studies to more closely match the food consumption data in DEEM.

Exposure estimates derived by DEEM can be compared to compound specific toxicity measures to derive risk estimates. Toxicity measures used by DEEM include the No-Observed-Effect Level (NOEL), the Reference Dose [whether acute (ARfD) or chronic (RfD)], and the Population Adjusted Reference Dose (PAD). However, the user may provide an alternative health reference value.

Sensitivity Analyses

For chronic exposure, DEEM allows the user to conduct sensitivity analyses via the Chronic Commodity Contribution Analysis to assess the relative contribution of all the foods and food forms included in a particular assessment to the total exposure or risk. It also allows the user to determine which foods and food forms contribute most to the total dietary exposures of each of the subpopulations considered. DEEM and DEEM-FCID are periodically updated in order to incorporate the most current food consumption data from NHANES. Additional information on DEEM is available from Exponent Inc. [2].

DIAMOND

The Dietary Modelling of Nutritional Data (DIAMOND) system was developed by Food Standards Australia New Zealand (FSANZ) in the 1990s. It is used by FSANZ for dietary exposure assessments associated with establishing standards for the composition of foods and for projects, such as the ongoing total diet studies. DIAMOND can be used to estimate dietary exposure to food chemicals, including nutrients, food additives, pesticides, contaminants and novel substances, as well as for reporting food consumption data.

DIAMOND uses SAS statistical software (SAS Institute Inc.) to process data. Results can be exported into Microsoft Excel for review and for reporting. DIAMOND does not have the in-built capability to undertake probabilistic exposure assessments but consumption data stored in DIAMOND can be exported to programs, such as Palisade Corporation's @Risk. Although DIAMOND is an in-house system developed specifically for FSANZ and not available commercially, it is available to selected Australian and New Zealand government agencies in countries via the Internet, with appropriate data security and access restrictions.

National nutrition survey (NNS) data for Australia and New Zealand are stored in DIAMOND and used for dietary exposure assessments. Individual food consumption amounts are available for each respondent from the 1995 and 2007 Australian NNSs and the 1997 Adult (15+years) and 2002 Children's (5–14 years) New Zealand NNSs. These data cannot be modified but can be reclassified as required.

Concentration data used will vary depending on the assessment being conducted but can include data from total diet study analyses, national food composition databases and information from the food industry. Concentration data are modifiable by the user.

DIAMOND also contains classification structures that mirror categories used for the regulation of food additives and agricultural and veterinary chemicals. Concentration data can be assigned to a group of foods with the same classification so that all foods in the same category will inherit the same concentration data (for example, the same permission to add a food additive). For total diet studies, customized categorizations can be used to group foods represented by a single analyzed food. Mixed foods are apportioned into their major ingredients using recipes, with different recipes used for consideration of processed foods and raw commodities. Factors to account for weight change, edible portion and hydration are built into DIAMOND as are health-based guidance values (e.g. Acceptable or Tolerable Daily Intake, Estimated Average Requirement). This information cannot be changed by users.

Data on market share, or proportions of crops treated, cannot be directly integrated into DIAMOND. Instead, this type of information is taken into account by modifying concentration data in proportion to share.

DIAMOND produces population dietary exposure estimates based on the distribution of food consumption reported in each NNS used, combined with single point chemical concentration data for different foods or food groups. Users can estimate typical exposure (e.g. mean, median) or percentiles (e.g. 10th, 90th, and 95th percentiles) for the entire population ('all respondents') and for users of the foods of interest only ('consumers only'). Results can be reported by age group and by gender. NNS sampling weights can be applied to the data to ensure the findings are nationally representative. Exposure estimates are able to be compared to the relevant health-based guidance value and reported as a percentage of this value or the percentage of the population exceeding (or not meeting) a value.

DIAMOND is generally used to undertake long-term dietary exposure assessments, although there is a module that conducts short-term exposure assessments. For long-term assessments, DIAMOND is able to estimate the proportion of the total dietary exposure to a food chemical that comes from different food groups. It is also possible to simply report food consumption rather than dietary exposure. DIAMOND also has the capability to undertake "budget-type" assessments using model diets. Detailed information about DIAMOND and about dietary modeling techniques used at FSANZ are available on the FSANZ Website [3].

The Future of DIAMOND

DIAMOND is to be replaced with another custom-built system known as Harvest. Harvest will integrate FSANZ'S existing food composition database and dietary modeling capabilities into a single system with greatly improved data storage, manipulation and reporting capabilities. Other planned features of Harvest include an easy to use graphical user interface, a greatly increased number of concurrent users and enhanced 'what if' modeling capabilities. For total diet studies, this should provide a much easier process for categorizing foods and a reduced time to produce reports.

Harvest is currently being developed but is likely to operate on a Microsoft SQL Server platform using SQL Server integration, analysis and reporting tools, Microsoft Sharepoint and a probabilistic modeling tool. External access to Harvest functions for FSANZ's partners will be part of the design. In addition, Harvest will deliver new ways to share information with professionals and the wider public.

MCRA

The Monte Carlo Risk Assessment (MCRA) is a computational tool to assess both the acute and chronic exposure to all kinds of chemicals present in food, both adverse (such as pesticides, environmental and processing contaminants, mycotoxins, etc.) and beneficial (such as micro- and macronutrients). The exposure to single compounds or a group of compounds (i.e. cumulative exposure) can be assessed, as well as the consumption of foods. MCRA has been used as the basis for many publications [4–7], including several opinions of the European Food Safety Authority (EFSA) [8–10].

In regard to total diet studies, chronic dietary exposure can be estimated using different statistical models present in MCRA. With these models all daily consumption patterns are multiplied with the average level of the compound per food, and summed over foods per day. This results in a set of daily mean exposure levels. This distribution is then corrected for the within-person variation. In MCRA three such models have been implemented, namely the beta-binomial-normal (BBN) model [11], the ISUF model [12, 13] and the logistic-normal-normal (LNN) model [14].

MCRA is a computational tool and can process all individual food consumption and concentration databases when formatted in the correct way. Users can use their own data to assess the dietary exposure and modify it in any way desired. MCRA offers many possibilities to tailor the input data to the needs of the user. For example, the exposure can be calculated for the whole population or on subsets based on, for example, age, gender, education, consumption patterns (e.g. only people that consume apple), etc. MCRA offers also the possibility to only include the part of the foods present in the concentration database in the assessment. Since it is often not possible to establish a direct link between the foods consumed and those analyzed

(e.g. raw agricultural commodities (RAC)), MCRA can link these data at different hierarchical levels, namely food, food group, ingredient and RAC level.

To assess the exposure to chemicals using MCRA, many features have been included to refine the assessments and to include all relevant variables. Examples of these features are the possibility to model co-factors (such as sex) and co-variables (such as age), relevant when the exposure differs between the gender and age groups. Furthermore, effects of processing can be included in the assessment as well as variability factors when assessing the acute exposure to pesticides using concentrations analyzed in composite samples. The recommendations of the EFSA regarding the handling of samples with concentrations analyzed below a certain analytical limit [15] have been incorporated in the tool. This also includes the possibility to include information on the proportion of the crop that will contain the designated concentrations in the model. MCRA also allows the user to perform uncertainty analyses to assess the accuracy of the estimated output by the use of the bootstrap methodology.

Exposure outcomes of MCRA include typical exposure measures (e.g. mean and median) as well as percentiles of interest (e.g. 5th, 10th, 90th, 95th, and 99th percentiles). These outcomes can be compared to compound (or group) specific toxicity measures, such as the Acceptable Daily Intake (ADI) for long-term exposures and the acute Reference Dose (acute RfD) for short-term exposures. Another output of MCRA is the contribution of foods to the total exposure distribution or an upper part (defined by the user) of this distribution. MCRA is regularly updated to include new developments regarding the modeling of dietary exposure and data handling. MCRA is freely available via the Internet for registered users at http://mcra.rivm.nl.

International Estimated Daily Intake

The International Estimate Daily Intake (IEDI) is a long-term (chronic) exposure assessment that was developed by GEMS/Food to provide guidance to the Codex Committee on Pesticides regarding the acceptability of recommendations for Codex Maximum Residue Levels for pesticides being considered for adoption by the Codex Alimentarius Commission. In 1997, GEMS/Food undertook the development of an automated Microsoft Excel spreadsheet application to facilitate the calculation of IEDI for pesticides being reviewed by the Joint FAO/WHO Meetings on Pesticide Residues for risk assessment. In the spreadsheet, the thirteen GEMS/Food Consumption Cluster Diets are used to provide the food consumption data (see Chap. 43 – GEMS/Food Consumption Cluster Diets). The chemical concentration data used is the median residue determined from field trials with the pesticide. While concentration data is based on the analysis of raw agricultural data, data on the fate of residues during processing, removal of inedible portion and cooking are used to improve the residue estimate. The intent is to estimate the concentration of residues in food as consumed. Consequently, the IEDI attempts to approximate the total diet approach, but with greater uncertainty. In addition, the IEDI spreadsheet

will also automatically calculate the risk characterization in terms of exposure as a percent of the relevant health-based guidance value. These international calculations yield deterministic estimates of mean exposure for the various regions of the world, which possess unique dietary patterns.

With some basic modifications, this automated spreadsheet for the IEDI can be used for total diet studies at the national level since the basic calculations are essentially the same. Instead of the pesticide residue concentrations from field trials, chemical concentration data obtained from a total diet study can be entered. Instead of the GEMS/Food Consumption Cluster Diets, national data on food consumption for the general population and, if available, food consumption data for cohorts of interest, such as age/sex groups, may be used. Entering the food consumption database would constitute the main effort, but this would only need to be done once. Modifications to the IEDI spreadsheet would be relatively simple and could be accomplished with only a basic knowledge of Excel. Once the diets have been revised, the calculations of the exposure for the cohorts would only require the entry of the chemical concentration values for the foods analyzed in the total diet study. The latest IEDI spreadsheet has been updated in cooperation with the Dutch National Institute for Public Health and the Environment (RIVM) and is downloadable from the WHO GEMS/Food Website [16].

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Chapter 46
OPAL—A Program to Manage Data on Chemicals in Food and the Diet

Gunter Sommerfeld and Gerald G. Moy

Introduction

The main purpose of the Global Environment Monitoring System/Food Contamination Monitoring and Assessment Programme [1], commonly known as GEMS/Food, is to compile data on food contamination and human exposure from different countries for synthesis, evaluation and presentation at the global and regional levels (see Chap. 42 – GEMS/Food and Total Diet Studies). In order to fulfill this mandate, one of the first tasks of GEMS/Food was the development of a data structure that would be used for collecting, storing and retrieving data on the levels of contaminants in food commodities. The original data structure was developed in cooperation with WHO Collaborating Centers for Food Contamination Monitoring located mainly in industrialized countries, which had extensive experience in handling such data. The data structure also includes a number of fields necessary to assess the reliability and comparability of the submitted data. Beginning around 1980, GEMS/Food began collecting aggregated contaminant/commodity data on standardized forms. Each one-page form constituted a single record representing the aggregated results of sometimes thousands of individual food samples. Once received by GEMS/Food, the information on the forms was transcribed using GEMS/Food codes and then uploaded onto a mainframe computer maintained at the World Health Organization (WHO) Headquarters in Geneva.

Using these databases, GEMS/Food prepared several global assessment reports and provided selected data in response to specific requests from data users, including the Codex Alimentarius Commission. Unfortunately the process of collecting, coding

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and entering such data was costly and tedious and most importantly, the process could not keep pace with the growing amount of data that was being generated. Similar problems in handling data were also being encountered by national laboratories, especially those that served as central repositories for data from satellite laboratories.

Electronic Reporting of GEMS/Food Data

As a result, in 1996 GEMS/Food started the development of a program for a microcomputer, which would replace the mainframe system. It was also envisioned that participating institutions would submit their data in electronic form, which could then be automatically integrated into the database. After the program was constructed, a manual for the electronic submission of data on contaminants in food and the total diet was developed [2]. The manual provides detailed information on encoding and formatting of data so that submitted data would be compatible with the GEMS/Food databases maintained at the WHO Headquarters. The manual outlines the protocols for submission of individual and aggregated data on concentrations of contaminants in specific food commodities as well as a protocol for data on levels of contaminants in the total diet. Thus, paperless reporting to GEMS/Food was possible and several countries, including the European Food Safety Authority, have written translation programs to convert their data structures into the GEMS/Food data format. In most cases this involves a rearrangement of fields, as most of the data fields are quite similar. However, two data fields are sometime difficult to harmonize. One such field is the contaminant identification code, which needs to be aligned by matching the code used by GEMS/Food with the code used by the submitting laboratory. While this rarely presents a problem, care must be taken to ensure that the method of analysis for the contaminant does not rely on a "residue definition" that differs from the GEMS/Food code. The "residue definition" is known to be a problem for certain nutrients and pesticides. This may also be a problem for identifying specific chemical species. For example, both mercury and arsenic have organic and inorganic forms that vary significantly in their toxic potentials.

The second data field that requires attention is the food identifier code. For primary agricultural commodities, GEMS/Food uses the commodities codes used by the Codex Alimentarius Commission (CAC) [3] and matching these with those of the laboratory is usually straightforward. For processed and mixed food, however, this has proven to be more difficult because of the diversity of foods as consumed. Alignment can be facilitated by using Langual [4], which is an international coding system based on multiple attributes. As many countries have developed a national Langual thesaurus for their foods, a consistent food code can be assigned for such foods. All Codex codes used by GEMS/Food have been converted to Langual, and have been incorporated into the databases.

Development of OPAL

During these developments, the need for more data from developing countries was being raised by the FAO/WHO expert bodies as well as by the CAC. In order to facilitate the submission of such data and to provide developing countries with a tool for collecting, storing and retrieving such data, GEMS/Food in cooperation with the WHO Collaborating Centers for Food Contamination Monitoring in Germany and New Zealand embarked on the development of what became known as the *Operating Program for Analytical Laboratories* (OPAL). OPAL was based on the program used by GEMS/Food microcomputer so that the data structure of OPAL is identical to that used by the GEMS/Food databases. The obvious advantage of this is that the data stored on OPAL by a national laboratory can be easily exported directly to global databases with little or no modification. OPAL consists of OPAL I, which is for individual and aggregated data on chemicals in food and OPAL II, which is for exposure to chemicals through the total diet. A brief description of functions and fields included in OPAL I and II are provided below.

OPAL I: Contaminant/Commodity Combinations

Analytical laboratories producing data on the concentrations of chemicals in food can use OPAL I to store, collate and report data on the results of individual samples. OPAL I also has the capability to automatically combined individual results into a single aggregate record with relevant parameters. Both individual and aggregated records can be searched, selected and exported using simple commands. Search elements include the country, contaminant, the food sampled and the sampling period. The exported file can be a spreadsheet or delimited text file. OPAL I uses the GEMS/Food data structures, in which individual and aggregated data are described using 17 and 22 fields, respectively. Readers are referred to the GEMS/Food Instructions for Electronic Submission of Data on Chemicals in Food and the Diet for further details [2].

Main Functions of OPAL I

OPAL I supports the management of individual and aggregated contamination data. For individual data, each record describes the contamination of one sample of a food item by one contaminant. This description contains the level of contamination in the sample and other information related to its measurement, such as limit of detection (LOD), limit of quantification (LOQ), etc. Sets of compatible individual measurements can be converted into one aggregate data entry using the aggregation function of OPAL I.

For aggregated data, each record of these data describes the contamination of multiple samples of one type of food item with one contaminant in one country in one sampling period. This description contains a number of individual parameters, which includes the minimum, mean, median, 90th percentile and maximum of these individual measurements.

The main functions for both types of data are similar, namely, data entry, data export and import, data retrieval, and data reporting. The entry of both aggregated and individual data on contaminants in food can, in principle, be accomplished in two ways in this system. Data may, through an input screen, be entered manually using the OPAL program. Alternatively, through the 'import function', data may be entered from other sources (regional or provincial authorities, GEMS/Food participating institutions, etc.), which may be received in electronic form e.g. compact disk (CD) or e-mailed for inclusion into the database. Note, however, that imported data must have the same data structure as OPAL I.

Data Entry

To enter data via OPAL I, templates for the individual and aggregated records are available for manual entry. After entering a record, a check of this record starts automatically. All data previously entered can be displayed. One may choose reduced sets of data records by using several predefined filters.

Data Import

Data from other sources, such as, regional laboratories or collaborating agencies, can be transferred electronically and automatically incorporated into the OPAL I database. This is enabled through the import function. If a data file was prepared using the export function of the OPAL I system, then importing such data is straightforward because the data structures are identical. However, for importing data that has been exported from other systems or software products, care must be taken that the structure and order of the data items of the imported file corresponds to the file definitions of OPAL I. If the transfer of such data occurs frequently, automated translation routines can be written to transcribe the data structure into the OPAL I structure provided that all of the fields are represented. For example, a translation program for converting OPAL I data into the format used by the European Food Safety Authority (EFSA) has been successfully developed. The main difficulty was the preparation of a table to interconvert GEMS/Food food identification codes with those used by EFSA. Another difficulty is that OPAL I reports the 50th, 90th percentiles, the minimum and the maximum for aggregated data, while every 10th percentile is reported in the EFSA data structure. Therefore, while EFSA data can be fully converted to the OPAL data structure, OPAL I data are missing the 10th, 20th, 30th,

40th, 60th, 70th, and 80th percentiles that are necessary to complete the EFSA data structure. However, OPAL I could still be included in the EFSA database, but with these fields would be left blank.

Data Export

Regarding data stored in the OPAL I database, these data, through the export function, can be retrieved and sent to other systems or authorities (e.g. WHO GEMS/Food) through e-mail or CD. One selects data (see Data Retrieval) to obtain data on specific time periods, contaminants and food items for the export dataset.

Data Aggregation

The aggregation procedure produces an aggregated record from compatible individual results; it is a bridge from the OPAL I management system for individual measurement data to aggregated data. This procedure calculates the statistical parameters for aggregated data, such as mean, median, standard deviation, and various percentiles. In doing this, "non-detect" results are used in the calculations according the recommendations of the GEMS/Food consultation held in Kulmbach, Germany in 1995 (see Chap. 16 – Reporting and Modeling of Results Below the Limit of Detection). These aggregated records can be seamlessly incorporated into the OPAL II database.

Data Retrieval

The use of the data retrieval function of OPAL I allows for the selection and retrieval of certain records of the database that can be used in the production of various reports. There are four selection possibilities available, namely country, contaminant, food item and sampling period. These are connected with the logic function "*and*", which means that only data records that fulfill all four selection criteria will be chosen for the reports.

Report Generation

After the desired subset of data has been selected (as described above), different reports using this data can be produced. Reports can be tailored to list the results by country, contaminant, food item and sampling period. Before report production, it

may be desirable to view the data selected for its verification. For this purpose the function "View" is implemented. If the selected records are deemed suitable, then the reports can be printed.

OPAL II: Exposure to Chemicals in the Total Diet

Based on the data in OPAL I, dietary exposure to a contaminant can be calculated by matching the concentration in a food or food composite with the corresponding food consumption for the cohorts of interest. Various methods are used to perform the calculation (See Chap. 17 – Dietary Exposure Assessment in a Total Diet Study). Many countries use computer software for this purpose, especially when the number of foods, contaminants and cohorts becomes large (See Chap. 45 – Automated Programs for Calculating Dietary Exposure). Dietary exposure information is encoded by OPAL II using 26 fields [2].

Main Function of OPAL II

OPAL II is a software system to manage data on dietary exposure. The main functions to manage these data are data entry, data export and import, data retrieval and data reporting.

Data Entry

The collection of data of exposure of the population to contaminants in food can, in principal, be accomplished in two ways in this system. Through an input mask, data may be entered manually, or alternatively, data may be imported from other sources as described below. To enter data via OPAL II, templates for the several levels of the data are available. After entering a record, a check of this record starts automatically. Previously entered data can be displayed. By using predefined filters, reduced sets of data records may be chosen.

Data Import

Data from other sources, such as provincial authorities and GEMS/Food participating institutions, can be transferred to OPAL II by CD or e-mail by using the import function. If the imported data was prepared by the export function of the OPAL II system, the imported data can be directly incorporated into the

database. Noncompatible data will need to be transformed into the OPAL data structure either manually or with a translation program tailored for the purpose.

Data Export

After data has been entered in OPAL II, this data can be sent to other systems or authorities, such as WHO GEMS/Food, through CD or e-mail using the export function. Data in the export file can be selected for specific contaminants, time periods, countries, studies, cohorts, or habitats.

Data Retrieval

The function of data retrieval supports the selection of certain records of the database that will be of interest in the production of different reports. There are six selection possibilities available, namely county, study, cohort, habitat, contaminant, and sampling period. These may all be connected with the logic function "and". A screen is available for each retrieval criteria showing the possible choices. For example, the current choices for cohorts in OPAL II include general population, adults (all, females or males), children (all, females or males), infants, pregnant women, vegetarians, and other. The selection switch and the number of all records and the number of the selected records are displayed for each item on these screens.

Report Generation

After the desired subset of data has been selected as described above, different reports using this data can be produced. Before report production, the function "View" allows for the selected data to be viewed and verified. If the selected records are deemed suitable, then the reports can be prepared according to various formats, including listing by one of the six selection criteria.

Summary and Conclusions

OPAL can provide laboratories and food safety authorities with a convenient means to collect, store and retrieve data on contaminants in food and the total diet. The internationally harmonized data structure contains the essential information usually needed to characterize and assess such data. Data stored in OPAL may be sorted and retrieved in several ways to respond to queries and to prepare reports. Selected

entries may be exported as Excel files or comma delimited files, which are compatible with other databases using OPAL or similar data systems. OPAL is available in English, French, and Spanish and currently operates on Microsoft Access for Windows XP. A new version of OPAL (OPAL-Web) is currently under development and will allow the direct submission through the web of XML and Excel files. This new system will keep all the functions of OPAL but without the need to update versions on local computers.

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4. For details on Langual. http://www.langual.org/

Chapter 47
Involving and Influencing Key Stakeholders and Interest Groups in a Total Diet Study

Cherie A. Flynn

Introduction

Building support for a total diet study (TDS), whether it is being undertaken for the first time or as part of an ongoing program of work, needs to be done in such a way as to take account of the wide and varied stakeholders and interest groups in the country. Undertaking a TDS is a significant piece of work for any country and involves a range of organizations, institutions and people, from both the public and private sectors, in its planning, implementation and funding. The results of such studies are of interest to government, researchers, public health officials, health practitioners and industry, as well as to the public at large. Food is a very intimate part of people's lives and consumers in many countries want to know more about what is in the food they are eating.

Being able to clearly identify the objectives and benefits of the TDS is an important first step in building support. A TDS is the primary source of information on the levels of various chemical contaminants and nutrients in the diet. A TDS can provide general assurances that the food supply is safe from certain chemical hazards. In addition, TDS results can be an indicator of environmental contamination by chemicals and can help in the development of priorities for possible risk management interventions by identifying what foods or food groups are the main sources of dietary exposure.

A TDS can also be used to assess the effectiveness of the measures previously put in place to reduce the exposure of the population to a chemical hazard or to address a nutrient deficiency. This can include measures taken that were not directly

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related to the food supply (e.g. reducing lead in petrol, which reduces emissions from vehicles leading to reduced opportunity for uptake by crops). Finally, a series of TDSs also allow trends over time to be followed.

As world trade in food and food commodities increases, countries need to be able to assure their consumers that the foods they are being offered for purchase, whether domestically produced or imported, are safe. For some countries, the rise in trade has also brought an increase in concern about the potential for foods to be tampered with and for food not acceptable in one country to be moved to another, where controls may be less strict or not exist. In this context, knowing what is in the food people are eating can be a key piece of information in being able to provide assurances to both domestic and international consumers. Undertaking a TDS can contribute such information and facilitates comparisons with other countries. WHO recognizes a TDS as one of the most cost-effective ways to assure people they are not exposed to unsafe levels of chemicals through food (refer also to Chap. 1 – Total Diet Studies—What They Are and Why They Are Important).

Identifying Key Stakeholders and Interested Parties

When considering that a TDS be undertaken, one of the first steps is to identify which government agencies or institutions (remembering there will be more than one) will be interested in the results of a TDS and, just as importantly, whether they have access to the necessary funding. Undertaking a TDS is a significant project for any country and it is important to be able to show what the benefits for the particular country are. This will require gaining an understanding of the goals and objectives of the particular government agency or institution that is to be approached to participate in or fund the TDS. It will also be helpful to find out what formal procedures or processes may need to be followed to propose such a project, to gain agreement to do it and to ensure access to the necessary resources – both funding and expertise. Knowing what these procedures are and what information is required at what stages of the process, so that such information can be prepared and ready when needed, can help avoid delays if there are specific deadlines involved. For example, requests for funding of projects may be limited to only a particular time in a financial year.

Moving through funding and approval processes can also be greatly assisted if there is a range of interested parties that can show their support for the proposal to undertake a TDS. Therefore identifying and approaching such parties so that a coalition of supporters is established should be one of the first tasks undertaken given the pre-eminent importance of securing government or government instructional support. The range of potentially interested parties can include:

- Government agencies responsible for control and/or monitoring of the food supply (including food ingredients and packaging) from production or importation through processing, manufacturing and distribution to the sale of foods and food ingredients either domestically or for export, as well as those agencies responsible for the wider public health and those involved in environmental management

- Growers, producers, manufacturers or sellers of the foods, as well as any industry organizations or associations representing those businesses
- Consumer representative organizations
- Various industries whose chemicals may be used in the production, processing or manufacture of foods, e.g. agrochemicals, food additives, and dietary supplements
- Academic researchers and scientists engaged in a wide range of areas, including public health, nutrition, food technology, animal husbandry, and horticulture

Once the key government agencies and other interest groups have been identified it is important to be well prepared when making the initial contact or commencing discussions. How initial contact or discussion about undertaking a TDS is done will depend on the conventions of the country concerned. Regardless of how this is done, it will be important to be able to convey what a TDS is and why it is important. Each of the parties listed above will have its own interests and stakeholders. Understanding what these interests are and how support for a TDS could advance such interests is an important part of building a support base.

For government agencies – be they responsible for control and/or monitoring of the food supply either domestically or for export, or for the wider public health, or environmental management – the results and/or the data generated by a TDS can provide key information, albeit of a general nature, about the safety and nutritional adequacy of the food supply or the effectiveness of controls in place for the country. A TDS can also identify matters that require further investigation, and can help in preparing advice as to where resources need to be focused to address a concern. For example, the results can be an indicator of environmental contamination by chemicals and can help in the development of possible risk management interventions by identifying what foods or food groups are the main sources of dietary exposure.

When risk management actions have been taken previously, a TDS can show what impact such actions have achieved. Another factor of particular relevance to developing and less developed countries as to the benefit of undertaking a TDS is that as economies develop, there may be increasing risks from chemical exposure – e.g. factories discharging waste into waterways where the water is subsequently used for irrigation of crops or an increased use of chemicals in food production systems as growers and producers strive for higher yields and have the resources available to purchase expensive chemical inputs. A TDS is a cost effective way for a government to gather information on such risks and where to focus limited resources to achieve the greatest benefit in terms of public health.

For growers, producers, manufacturers or sellers of the foods, as well as any industry organizations or associations representing those businesses, the results and/or data from a TDS can be a means of showing they are following good agricultural, animal husbandry or good manufacturing practices that support a safe food supply (for domestic consumers and consumers in other countries). Alternatively a TDS can help identify any areas that do require further investigation so that the safety or nutritional adequacy of the food supply can be improved.

For the industries whose chemicals may be used in the production, processing or manufacture of foods (e.g. agrochemicals and food additives), the results from a

TDS can be a means of showing that their products, when used according to labeled instructions, are not contributing to consumer health risks from exposure to a toxic hazard or a deficiency in an essential nutrient.

For academic researchers and scientists engaged in a wide range of areas, including public health, nutrition, food technology, animal husbandry, and horticulture, a TDS can provide information relevant to their various areas of work. Depending on the particular design of the TDS, food-chemical concentration data can be used with other databases, such as environmental monitoring and food composition.

For consumers and consumer representative organizations, a TDS is a means of providing general assurance that the food supply is safe and nutritionally adequate. Consumer confidence in the safety of the food supply is extremely important and a TDS offers risk communication advantages because it is relatively easy to understand.

Involvement of Key Stakeholder and Interest Groups: When and What

Once an initial level of support for undertaking a TDS has been established and work commences on the planning and design stages, maintaining the interest and involvement of the various stakeholders can help in ensuring that the proposal continues to implementation. Different components of a TDS can be of interest to various stakeholder groups. Involving these groups in the planning and design stages can also help build an understanding about the choices that will need to be made. Most governments do not have unlimited funds available to investigate all the issues that may be of interest to all the various interest groups in a country. It will be necessary, therefore, to make choices about foods to be sampled, number of samples to be taken, chemicals to be analyzed, and population groups to be estimated for dietary exposures. Some of these aspects will also be guided by the availability of other relevant information. For example, what foods are being eaten by whom and in what amounts.

Involving the various groups in the planning and design stages can provide an opportunity to set out the options, to explain what is possible within the budget and time available and to show that choices made in one area will mean that options in another area will be limited or become out of reach. For example, undertaking a multi-residue screen for agricultural compounds, such as pesticide residues can allow a significant number of chemicals (up to 300) to be analyzed at the same time, whereas analysis for some other chemicals, such as dioxin and dioxin-like compounds, require a separate and much more expensive analysis for much smaller numbers of chemicals. A choice to undertake an expensive analysis may mean that a smaller number of samples can be analyzed – this also can involve a choice about whether to composite foods or food groups to keep the number of analyses, and the costs, down. In turn, compositing foods will reduce the opportunity to get individual food data.

Establishing a level of understanding about these types of choices across the various interest groups can help build a level of consensus about what are the priorities for the country – what is most important to investigate. Setting out the options in either a written proposal or through meetings and discussion also increases the transparency of, and the reasons for, the decisions that have to be made. It is unlikely that all parties will necessarily agree completely with the final decisions on all aspects of the proposed TDS. However, undertaking a process that will allow the various stakeholders and interest groups to exchange views, either through meetings or in written form, can help to increase knowledge of the various perspectives and insights into the concerns of a particular group. It also provides the opportunity to be clear about what it is possible to do given the financial and other resource constraints within which most public sectors must operate.

After the planning and design is completed and the TDS has commenced, making the results available to the various interest groups in a timely manner is the next step in maintaining their interest and involvement (refer also to Chap. 19 – Communicating Results in a Total Diet Study). It is, however, important to remember that even when interest groups have been involved in the design and content of a TDS, they still have their own issues and concerns, which may highlight real or perceived deficiencies in the results. The simple fact is you cannot please all stakeholders and interested parties, especially those with opposing views. Even so, involving a range of interest groups in a TDS can be expected to have more positive than negative results.

Engaging Interest Groups: The New Zealand Example

The New Zealand Food Safety Authority (NZFSA) was established in 2002 (bring together responsibility for all aspects of food safety and regulation – domestic, import and export – that had previously been undertaken by the New Zealand Ministry of Health and the Ministry of Agriculture and Forestry).[1] Two of the key objectives set by the New Zealand government for NZFSA when it was established, were to *ensure efficient use of government and interest group resources* and to *be effective in coordinating and communicating with interest groups*. As a new organization, NZFSA also wanted to ensure that the decisions it made and the decision-making process were transparent and that there was consensus support from the various interest groups in New Zealand for those decisions.

Included in the responsibilities for NZFSA was the New Zealand Total Diet Study (NZTDS). There had previously been five such studies in New Zealand. Planning for the sixth NZTDS started in mid-2002 and involved various stakeholders as part of the NZFSA commitment to transparency and involvement with interest groups. This process was initiated by letters addressed to a wide range of

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[1] From 1 July 2010 NZFSA was amalgamated with the New Zealand Ministry of Agriculture and Forestry (MAF), and on 1 July 2011, the Ministry of Fisheries was also merged into MAF. On the 30 April 2012, the new ministry became the Ministry for Primary Industries (MPI).

consumer groups, industry associations, producer boards, public heath interest groups and associations, universities and research units, which advised that NZFSA was commencing planning for the sixth NZTDS, and asking if they wished to be involved. Thirty-five of those contacted responded positively and from these NZFSA built its contact list.

At the end of 2002, a written TDS proposal was circulated to the contact list asking for comments by the end of January 2003. The proposal and invitation for comment was also published on the NZFSA website. The document provided brief background information on what a TDS is and the history of such studies in New Zealand. The paper also set out:

- The proposed structure for the sixth NZTDS
- The proposed main components of the NZTDS, such as the chemical and food combinations to be analyzed, including an explanation of why each was suggested and options for consideration
- The proposed population age/sex groups for whom dietary exposures would be calculated

Following consideration of the comments, views and suggestions received, both in the written comments and at a meeting, NZFSA made the final decisions about the sixth NZTDS in April 2003. These were set out in a paper that included an explanation for each of the decisions. A copy was provide to all the interest groups and published on the NZFSA website. The 2003/04 NZTDS commenced in July 2003. All the documents relating to this process can be found on the New Zealand government food safety website [1]. As results from the 2003/04 NZTDS became available, the various interest groups on the contact list were sent an email advising of the planned release and providing them with the link to the relevant page on the website. A similar process was undertaken in respect of the 2009 NZTDS and the relevant documents can also be found on the New Zealand government food safety website.

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Chapter 48
Linking Nutrition Surveys with Total Diet Studies

Junshi Chen

Introduction

The conventional way of estimating dietary nutrient intakes in nutrition surveys is to use food consumption data from dietary surveys and combine these with the nutrient contents of the food from published food composition tables. Because a significant number of food items in the food composition tables are uncooked or unprepared, the loss of nutrients during cooking and preparation may not be taken into account, especially in the case of vegetables. Therefore, the use of a total diet study (TDS) can better reflect the actual intake of nutrients as compared with conventional nutrition surveys. In this chapter, estimated intakes of certain nutrients in Chinese TDSs, which were conducted between 1990 and 2000, are reported and compared to results from conventional nutrition surveys. See Chap. 23 – The Chinese Experience in Total Diet Studies for a complete list of nutrients that were analyzed in Chinese TDSs.

Comparison of Nutrient Intakes from Total Diet Study and Conventional Methods

In 1992, a comparison between TDS and national nutrition survey was conducted; both datasets are nationally representative. The results in Table 48.1 show that the macronutrient intakes from the two methods are very close. Furthermore, most mineral and lipid-soluble vitamin intakes from the two methods are reasonably consistent. However, some water-soluble vitamin intakes are lower in the TDS than in the

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Table 48.1 Nutrient intakes from total diets studies and conventional dietary surveys

Variables	TDSs	Dietary surveys	Variables	TDSs	Dietary surveys
Energy (kcal)	2,203	2,383	Thiamin (mg)	0.9	1.27
Protein (g)	64.0	66.1	Riboflavin (mg)	0.8	0.78
Fat (g)	51.2	59.9	Vitamin C (mg)	15.7	86.6
Carbohydrates (g)	366	389	Calcium (mg)	582	373
Carotene (μg)	1,621	1,270	Magnesium (mg)	285	332
Vitamin A (μg RE)	67.1	89.6	Iron (mg)	22.7	18.5
Retinol (μg RE)	337	260	Cholesterol (mg)	179	–

Fig. 48.1 Dietary intake of copper in 2–7-year-old children
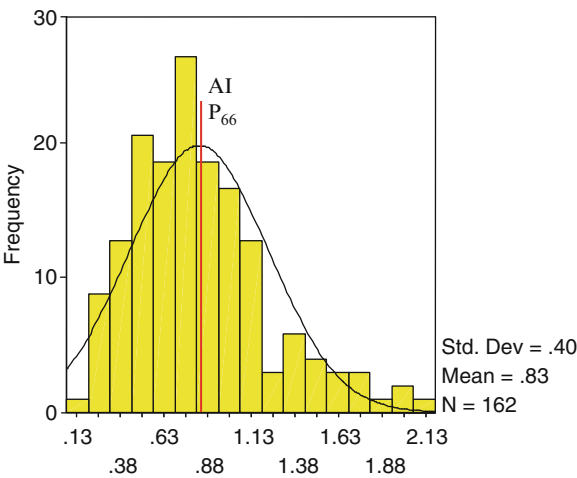
conventional nutrition survey, in particular, ascorbic acid. This is due to losses during cooking and preparation of the TDS samples.

Dietary Copper Intakes in Children

In order to find out whether dietary intake of copper (Cu) in Chinese preschool children (2–7 years old) is adequate, individual Cu intakes were estimated in the 2000 Chinese TDS based on the analysis of Cu content in 416 individual food samples (comprising 12 food groups) from 8 provinces [1]. The results (see Fig. 48.1) show that the 66th percentile of Cu intakes for these children was equal to or below the Dietary Recommended Intake of 0.9 mg established by the Chinese Nutrition Society [2]. This implies that a significant proportion of Chinese children (2–7 years old) had insufficient dietary Cu intake.

Table 48.2 Iron (Fe) intake by male adults in northern and southern regions of China (1990)

	Total Fe intake (mg/person/day)	Soluble Fe intake (mg/person/day) [% of total Fe intake]
Northern region	27.78	2.13 {7.7}
Southern region	18.67	2.09 {11.2}

Dietary Intakes of Different Forms of Iron

Iron (Fe) deficiency and related anemia are major nutrition problems in China. However, results from nutrition surveys consistently showed that dietary intakes of Fe were adequate. One explanation commonly agreed is that the Fe in the diet is of low bioavailability because the typical Chinese dietary pattern is based on plant foods. In order to verify this hypothesis, the contents of different chemical forms of Fe were analyzed in composite TDS food samples from northern regions and southern regions and the respective intakes of these forms of Fe were estimated [3]. The results in Table 48.2 show that soluble (bioavailable) Fe, which includes chelated iron, Fe^{2+} and Fe^{3+}, only accounted for a very small percentage of the total dietary Fe intake, both in northern and southern regions. Although the total Fe intake is higher in the northern regions than that in the southern regions, the absolute intake of soluble Fe in the two regions was quite similar (about 2.1 mg/person), which reconfirms the very low bioavailability of Fe in the Chinese diet.

Dietary Cholesterol Intake

Because the Chinese food composition tables have only limited data on cholesterol content, there was no dietary cholesterol intake information in most nutrition surveys. Therefore, cholesterol intakes were estimated in several Chinese TDSs [4]. Figure 48.2 shows that there were significant variations in cholesterol intakes among male adults in the four regions studied and there was a general trend of increasing cholesterol intakes in three of the regions between 1990 and 2000. The cholesterol intakes in the relatively poor North 2 region did not change, which is consistent with the lack of any increase of animal-derived food consumption during the period. In 2000, the average cholesterol intakes of male Chinese adults in all the regions except North 2 region exceeded the individual upper level (300 mg/person/day) recommended by the WHO. Further analysis of the food sources of cholesterol in the 2000 show that eggs were the major source (44–68 % of total intake), followed by meats (about 20–40 % of total intake), while seafood only accounted for about 6–22 % of the total cholesterol intake.
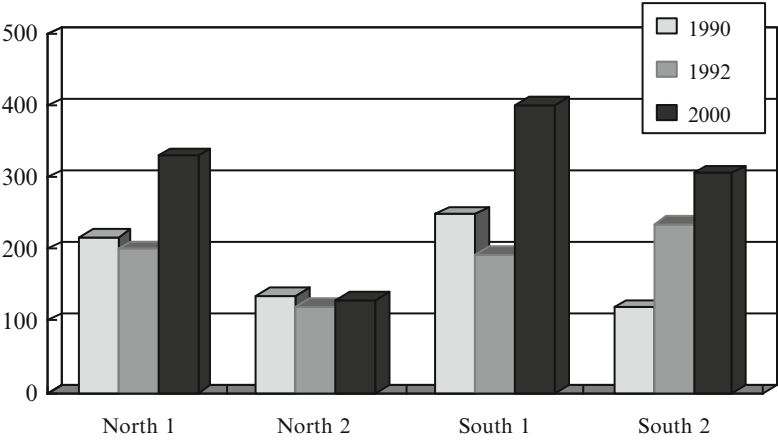
Fig. 48.2 Dietary intake of cholesterol in male adults by region (mg/person/day)

Table 48.3 Intake of dietary fatty acids in four Chinese regions (g/person/day)[a]

Fatty acids	North 1	North 2	South 1	South 2
8:0	0.1	0.0	0.0	0.0
10:0	0.1	0.1	0.1	0.1
12:0	0.2	0.1	0.1	0.1
14:0	0.5	0.4	0.4	0.7
16:0	16.9	6.9	10.8	13.0
18:0	6.0	3.1	2.9	4.6
20:0	0.2	0.1	0.2	0.1
22:0	0.6	0.9	0.3	1.3
16:1	0.9	0.5	1.0	1.2
18:1	24.6	17.3	21.2	28.3
20:1	0.4	0.3	0.4	0.6
22:1	0.7	1.1	0.9	0.3
18:2	24.7	10.5	17.2	17.1
18:3	3.4	5.5	2.3	2.8
20:5	0.0	0.1	0.1	0.0
22:3	0.1	0.0	0.1	0.0

[a]The values were calculated by multiplying the amount of fat intake by the percentage of the fatty acid

Fatty Acid Profiles and Intake

Fatty acids profiles were studied in all the three TDSs [4]. The results from the 2000 TDS are presented in Table 48.3, which shows that palmitic acid (16:0) and stearic acid (18:0) were the major saturated fatty acids (SFA) accounting for around 90 % of total fatty acids consumed in the Chinese diet; oleic acid (18:1) was the major mono-unsaturated fatty acids (MUFA) (more than 90 %); while linoleic acid (18:2) and linolenic acid (18:3) were the major poly-unsaturated fatty acids (PUFA) (17–28 %).

In comparison with the results of the 1990 and 1992 TDS, the intakes of erucic acid (22:1) were significantly reduced from 4–6 % to 1 %, due to the quality improvement of rapeseed oil, which is used widely in southern China. On the other hand, docosahexaenoic acid (DHA) (22:6 n-3) and eicosapentaenoic acid (EPA) (20:5 n-3) were not detected in the aquatic food composite samples, with only small amounts of 22:3 n-3 found in the food samples. Therefore, linolenic acid (18:3) was the major n-3 fatty acid in the Chinese diet. The ratio of SFA, MUFA and PUFA in the dietary intake of fatty acids in the Chinese diet was reasonable, i.e. 1:1.1:1.1 in North 1 region, 1:1.6:1.3 in North 2, 1:1.6:1.3 in South 1, and 1:1.5:1 in South 2. SFA was less than MUFA and PUFA, with MUFA as the major group of fatty acids.

Conclusions

Nutritional assessment of diets by TDSs could be an additional use of the TDS food samples and provide valuable information on nutrient intakes that are not available or incomplete in food composition tables. It could also provide better information on micronutrients, which have wide geographical variations in concentrations and on some unstable nutrients (e.g. water-soluble vitamins) and certain micronutrients than the conventional dietary survey method.

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Chapter 49
Emerging Chemical Contaminants in Total Diet Studies in China

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Introduction

A total diet study (TDS) enables the estimation and monitoring of dietary exposures to chemical residues, contaminants and nutrient elements. A TDS involves purchasing at the retail level foods commonly consumed by the population, preparing them as for normal consumption, homogenizing and compositing them, and finally, analyzing the foods for the chemicals of interest [1]. Starting in 1990, the Chinese TDS has become an important tool for monitoring dietary exposures to chemicals and their associated

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risk to public health and such studies have been undertaken five times in China at irregular intervals. Recently, some emerging chemical contaminants have become of great concern to the public and food control agencies in China. To assess the current status of these emerging contaminants in the Chinese food supply and indicate any potential exposure concern, the dietary exposures to dioxin-like compounds, chloropropanols, and acrylamide are now included in the TDS protocol.

The dioxin-like compounds (DLCs), including polychlorinated dibenzo-*p*-dioxins and dibenzofurans (PCDD/Fs) and polychlorinated biphenyls (PCBs), are ubiquitous, persistent, lipophilic pollutants in the environment. Ingestion of contaminated food, especially of animal origin with a high fat content is the principal exposure route for the general population [2]. Although DLCs had been monitored in the environment and food for several years in some developed countries, the concerns about these contaminants got public attention in China only after the crisis in Belgium in 1999. In China, due to its rapid industrialization, pollution has increased considerably, which may have resulted in increasing DLC levels in the environment and food.

Chloropropanols are a group of chemical contaminants formed in foods and include 3-monochloro-1,2-propanediol (3-MCPD), 2-monochloro-1,2-propanediol (2-MCPD), 1,3-dichloro-2-propanol (1,3-DCP), and 2,3-dichloro-2-propanol (2,3-DCP) as well as their fatty acid esters [3]. 3-MCPD is a processing contaminant formed in acid-hydrolyzed vegetable protein (acid HVP), a savory ingredient in stock cubes, soups, prepared meals, and snack foods. Other chloropropanols can occur, albeit usually in smaller amounts, in food. The presence of chloropropanols in food is of concern owing to their toxicological properties. In the 31st session (July 2008), the Codex Alimentarius Commission (CAC) adopted a maximum levels of 0.4 mg/kg for 3-MCPD in liquid condiments containing acid HVP (excluding naturally fermented soy sauce). In a recent survey of chloropropanols in foods in China, 3-MCPD is present in soy sauce and a wide range of foods and food ingredients [3]. In addition to acid HVP, high levels of 3-MCPD were also detected in instant noodle spices, oyster sauce, certain "health" foods, and beef products.

In 2002, scientists in Sweden announced the discovery of the chemical acrylamide in a variety of baked foods [4]. Further research subsequently determined that acrylamide can form in some foods during certain types of high-temperature cooking [5]. Acrylamide in food is a concern because it has been found to be carcinogenic in rodents and is therefore considered a potential carcinogen for humans [6]. In 2005, an international evaluation of acrylamide by JECFA identified margins of exposure (MOEs) for acrylamide of 300 for general consumers and 75 for high consumers. JECFA considers the MOE of 300 calculated for acrylamide to be low for a compound that is genotoxic and carcinogenic and concluded that the levels of acrylamide in food were of concern. Because of the identification of acrylamide in food, researchers around the world have centered on measuring acrylamide levels in the diet and studying the toxicology and epidemiology of acrylamide exposure.

TDS Methods

Study Design, Sampling, and Sample Preparation

The study design and experimental methods of Chinese TDS were similar to those used to carry out the TDS in 1990 [7]. The food composite approach was used to study the total diet in four regions representing the average dietary patterns of different geographical areas on the mainland and covering about 50 % of the Chinese population [8]. Each region comprised three provinces: North 1 (N1) comprised Heilongjiang, Liaoning, and Hebei; North 2 (N2) comprised Henan, Shanxi, and Ningxia; South 1 (S1) comprised Jiangxi, Fujian, and Shanghai; South 2 (S2) comprised Hubei, Sichuan, and Guangxi. Average food consumption of a "standard" Chinese man (18–45 years old with average body weight of 60 kg) from 90 households (30 households per survey site) was used as the standard food consumption model for the province and the value of three provincial pooled composites was used as the food basket consumption pattern for each region. All food consumed by the standard man was aggregated into 13 food groups, namely eggs, meats, fishes, milk, grains, vegetables, fruits, potatoes, beans, beverages and water, alcohol, sugars, and condiments. The samples were collected from local markets, grocery stores, and rural households, then cooked and prepared according to local food habits of each province. The prepared foods were then blended to form the respective group composites with weights proportional to the average daily consumption for the province. These provincial composites were shipped to the National Institute of Nutrition and Food Safety in Beijing, where the composites were further mixed to form four regional basket composites according to their corresponding weight proportion in food consumption. The samples were then frozen and stored at −30°C until analysis.

Analyses

The DLCs were analyzed by high-resolution gas chromatography–high-resolution mass spectrometry based on the Chinese National Standard Method GB/T5009.205–2007 modified from USEPA-1613 and -1668 [9]. Extraction of chloropropanols was carried out by a matrix solid-phase dispersion (MSPD) method and the concentrated extract was derivatized with heptafluorobutyrylimidazole. Identification and quantification of chloropropanols were carried out by using a benchtop gas chromatograph-mass spectrometer with a DB-5MS column. Acrylamide in food was also extracted by MSPD. Identification and quantification of acrylamide in samples were performed by liquid chromatography with mass spectrometry-mass spectrometry detection. All of the target contaminants were quantified with isotopic internal standards. The determination methods were

validated by participation in the interlaboratory program on dioxins in food organized by the Norwegian Institute of Public Health and in the Food Analysis Proficiency Assessment Scheme (FAPAS) for chloropropanols and acrylamide organized by Central Science Laboratory, UK. As animal-derived foods are the predominant intake sources of PCDD/Fs and PCBs in humans, only four animal-derived food groups were subjected to PCDD/F and dioxin-like PCB analysis. For chloropropanols and acrylamide, all food groups were involved in analysis.

Analytical Results of TDS Food Groups

The concentrations of DLCs, chloropropanols, and acrylamide in TDS samples are listed in Tables 49.1, 49.2, and 49.3, respectively. Generally, high contamination levels of DLCs were found in the fish groups followed by the meat groups. Lowest concentrations occurred in the milk groups. The results also showed major differences in PCDD/Fs contamination levels among the four regions. Regions S1 and N1 had the highest levels of PCDD/Fs in animal-derived foods. The concentration of PCDD/Fs in each food group from the North 2 region was the lowest of all the regions. Almost all congeners of dioxin-like PCBs were found in the samples.

As shown in Table 49.2, 3-MCPD and 2-MCPD were found above the detection limit with varying frequency of detection in all food groups except sugar, alcohol, and beverage groups. 1,3-DCP and 2,3-DCP were not detected in any samples. 3-MCPD was found at high frequency and high levels in fish, meat, bean, and vegetable groups.

In the present study only the potato, vegetable, bean, and sugar groups were found to contain acrylamide with levels above the limit of determination (LOD). In addition, trace acrylamide levels were detected in cereal products, but only in the S2 and N1 regions. Acrylamide was not detected in meat, egg, dairy, fruit, and alcoholic beverage groups.

Estimated Dietary Exposure

Calculation of Dietary Exposure

Daily dietary intakes of these emerging contaminants were estimated for the standard Chinese man by multiplying the measured concentrations in foods by the average daily consumption data from the surveys mentioned above. When the target compound was not detected in the sample, the concentration of contaminant in that sample was assigned a value of the limit of detection to give an upper-bound estimate of the exposure.

Dioxin and Dioxin-like PCBs

Table 49.4 presents the estimated daily intake of PCDD/Fs and dioxin-like PCBs expressed in Toxic Equivalents (TEQ) from the four food groups individually and in total for each region. Maximum daily exposure was in S1 (57.1 pg TEQ/day) followed by N1 (38.19 pg TEQ/day), S2 (21.56 pg TEQ/day), and N2 (9.06 pg TEQ/ day).

Figure 49.1 shows the large difference in exposure among regions that was thought to result from variations in both food consumption and contamination levels in the regions. For example, both contamination levels and consumption of animal-derived foods were the lowest in N2, so the exposure was the lowest among the four regions. Contributions from the four food groups varied between regions. Far higher than other food groups, the meat group made the greatest contribution to daily exposures in N1 (44.3 %), N2 (43.6 %), and S2 (48.4 %). With the highest contamination level and high consumption, the contribution (48.7 %) from the fish group was greatest in S1. In N2, although the contamination level in fish was higher, the contribution (18 %) from fish was less than that from milk/milk products (23.5 %) as more milk/milk products than fish are consumed in this region. Generally, in China, meat and fish account for a major fraction of daily exposure, which is similar to studies from other countries.

Owing to the bioaccumulation characteristics of PCDD/Fs and dioxin-like PCBs, the Joint FAO/WHO Expert Committee on Food Additives (JECFA) proposed a provisional tolerable monthly intake (PTMI) of 70 pg TEQ/kg body weight (bw) as being protective of human health [10]. Monthly intakes for the population in each region in this study ranged from 4.5 to 28.8 pg TEQ/kg bw, only accounting for 6.4–41 % of the PTMI.

Chloropropanols

Generally, the plant foods including grains, beans, potato, vegetables, and fruits are the major contributors, accounting for 57–85 % of the total exposure of 3-MCPD, while animal-derived food including meat, eggs, milk, and fish account for 10–35 %. Additional exposure was contributed mainly from beverages accounting for 5–13 %. As shown in Table 49.5 and Fig. 49.2, however, the profiles of contributions from food groups were different among four regions. The contributions from grains were the highest in S1 (27 %) and N2 (51 %), while the contributions from vegetables were the highest in S2 (36 %) and N1 (41 %). The contribution from the bean group ranking second was almost the same as grain in S1, which was not found in other regions. In N1, the proportion of meat was 21 % that ranked second in the region.

The total dietary exposure of 3-MCPD ranged from 15.5 to 25.3 μg/day for the population in the four regions in China (see Table 49.6). The maximum dietary exposure of 3-MCPD was found in S2 followed by N1, N2, and S1. The PMTDI for

Table 49.1 Concentration of PCDD/Fs and dioxin-like PCBs in animal-derived foods (ng/kg fresh weight)

Compound	Egg				Fish				Milk				Meat			
	N1	N2	S1	S2	N1	N2	S1	S2	N1	N2	S1	S2	N1	N2	S1	S2
2378-TCDD	0.01	ND	0.008	0.01	0.029	ND	0.077	0.019	ND	ND	0.005	ND	0.077	ND	0.01	ND
12378-PeCDD	0.019	ND	0.008	0.038	ND	ND	0.066	0.038	ND	ND	0.008	ND	0.008	ND	0.019	0.028
123478-HxCDD	0.019	ND	0.017	0.077	0.048	ND	0.505	0.058	ND	ND	0.011	0.009	0.033	ND	0.154	ND
123678-HxCDD	0.038	ND	0.025	0.038	0.029	0.029	0.033	0.048	0.006	ND	ND	0.015	0.011	ND	0.029	ND
123789-HxCDD	ND	ND	0.008	0.019	0.038	0.01	ND	ND	0.002	ND	0.003	0.004	0.003	ND	0.01	ND
1234678-HpCDD	0.125	0.077	0.111	0.269	0.135	0.096	0.352	0.077	0.029	0.014	0.019	0.021	0.088	0.044	0.154	0.154
OCDD	0.577	0.374	1.778	1.865	0.308	0.452	1.538	0.692	0.154	0.126	0.127	0.11	0.253	0.275	3.318	1.231
2378-TCDF	0.145	0.044	0.052	0.106	0.346	0.202	0.088	0.135	0.006	0.011	0.021	0.073	0.132	0.077	0.096	0.044
123-PeCDF	0.068	0.033	0.025	0.058	0.125	0.058	0.055	0.058	0.004	0.01	0.012	0.009	0.033	0.005	0.058	0.008
23478-PeCDF	0.048	0.022	0.034	0.058	0.145	0.068	0.11	0.077	0.029	0.018	0.035	0.034	0.143	0.055	0.096	0.011
123478-HxCDF	0.058	0.022	0.025	0.048	0.048	ND	0.055	0.029	0.023	0.031	0.022	0.031	0.165	0.077	0.048	0.033
123678-HxCDF	0.029	0.011	0.017	0.038	ND	ND	ND	0.019	0.018	0.017	0.014	0.021	0.077	0.033	0.019	0.044
2345678-HxCDF	0.019	ND	0.025	0.01	0.068	ND	ND	0.077	0.015	0.016	0.018	0.029	0.055	0.022	0.048	0.066
123789-HxCDF	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	0.011	ND	ND	0.01
1234678-HpCDF	0.029	0.022	0.017	0.029	0.077	0.058	0.077	0.038	0.01	0.018	ND	0.017	0.242	0.044	0.048	0.022
1234789-HpCDF	ND	ND	ND	ND	ND	ND	ND	ND	ND	0.005	ND	ND	0.044	ND	ND	ND
OCDF	0.029	0.022	0.025	ND	0.068	0.077	0.055	0.038	ND	0.013	0.023	0.005	0.143	0.022	0.019	0.011
PCB77	2.86	2.67	2.78	4.64	14.39	8.94	7.1	3.59	0.14	0.15	0.18	0.49	1.9	0.83	3.5	1
PCB81	0.29	0.24	0.24	0.61	0.63	ND	0.56	1	0.03	ND	0.004	ND	0.19	0.31	0.26	ND
PCB105	11.11	10.14	16.77	20.78	46.68	58.41	39.11	15.81	1.59	1.2	2.55	2.24	10.8	7.34	12.56	4.99

PCB114	0.78	0.69	1.36	1.64	3.98	3.71	3.59	1.81	0.18	0.15	0.26	0.28	1.31	1.39	1.16	0.53
PCB118	28.24	24.74	49.42	53.53	118.81	143.83	113.33	39.34	6.29	4.18	10.04	8.61	31.93	25.11	40.04	14.34
PCB123	0.68	0.54	0.98	1.26	2.85	5.35	2.27	0.71	0.12	0.09	0.2	0.09	0.4	0.4	0.59	0.31
PCB126	0.39	0.33	0.54	0.56	2	1.36	0.29	0.73	0.1	0.07	0.12	0.14	0.36	0.31	0.56	0.3
PCB156	3.4	2.63	7.89	8.54	14.75	15.41	15.73	4.04	0.61	0.4	1.14	0.87	4.07	4.14	5.39	1.93
PCB157	0.8	0.56	1.87	1.61	4.18	3.64	4.27	1.15	0.15	0.1	0.23	0.2	0.93	1	1.45	0.83
PCB167	1.58	1.2	4.18	3.76	7.65	7.89	8.34	2.39	0.26	0.19	0.54	0.44	1.39	1.43	2.04	1.06
PCB169	0.11	<0.05	0.27	0.19	0.78	0.29	0.49	0.29	0.02	0.05	0.05	0.06	0.24	0.26	0.26	0.14
PCB189	0.38	0.3	1.12	0.81	1.38	1.03	1.4	0.41	0.05	0.03	0.08	0.09	0.34	0.53	0.6	0.16

Table 49.2 Concentration of chloropropanols in various foods in the Chinese TDS regions (μg/kg fresh weight)

		Grains	Beans	Potatoes	Meats	Eggs	Fish	Milk	Vegetables	Fruits	Sugars	Alcohols	Beverages
1,3-DCP	S1	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	S2	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	N1	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	N2	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
2,3-DCP	S1	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	S2	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	N1	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	N2	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
3-MCPD	S1	3.67	66.4	ND	8.32	ND	10.6	3.55	8.71	ND	ND	ND	ND
	S2	ND	18	42	34.5	24.7	128	ND	23.7	ND	ND	ND	ND
	N1	3.3	8.6	5.2	74.5	42.3	38.4	ND	22.9	ND	ND	ND	ND
	N2	6.56	40.4	3.96	30	ND	16.7	5.7	10.1	4.51	ND	ND	ND
2-MCPD	S1	ND	20.4	ND	ND	ND	ND	ND	2.7	ND	ND	ND	ND
	S2	ND	6.94	14.9	5.6	7.7	25.2	ND	5.3	12.8	ND	ND	ND
	N1	7.5	16.2	ND	8.3	79.8	14.6	ND	7.3	ND	ND	ND	ND
	N2	ND	42.1	ND	ND	ND	ND	ND	4.22	ND	ND	ND	ND

Table 49.3 Concentration of acrylamide in samples of various commodities (µg/kg fresh weight)

	Grains	Beans	Potatoes	Meats	Eggs	Fish	Milk	Vegetables	Fruits	Sugars	Alcohols	Beverages
S1	ND	3.5	9.1	ND	ND	ND	ND	6.9	ND	5.8	0.52	ND
S2	6.3	4.7	27.5	ND	ND	ND	ND	10.1	ND	7.0	1.28	ND
N1	3.4	16.9	34.3	ND	ND	1.8	ND	21.5	ND	4.5	0.5	ND
N2	ND	8.3	18.1	ND	ND	4.0	ND	29.4	ND	5.1	0.6	ND

Table 49.4 The daily dietary exposure to PCDD/Fs and dioxin-like PCBs in Chinese TDS regions (pg TEQ/day)

	N1	N2	S1	S2
Eggs	6.91	1.35	6.99	5.47
Fishes	12.06	1.63	27.82	4.86
Meat	16.91	3.95	19.01	10.43
Milk	2.31	2.13	3.28	0.80
Total	38.19	9.06	57.10	21.56

Contribution (%) of different food to daily intake in parentheses
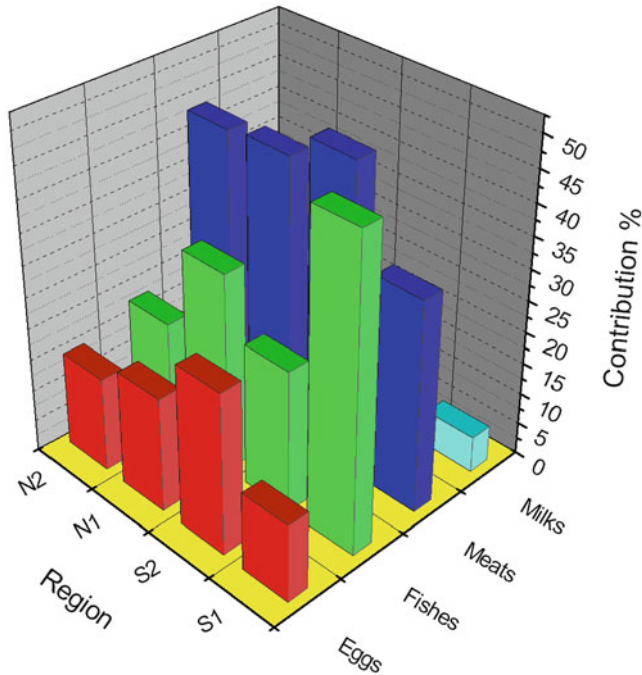
Fig. 49.1 The contribution of food groups to daily intake of dioxin-like compounds in Chinese TDS regions

3-MCPD is 2 µg/kg bw/day established by JECFA (10). The daily dietary intakes of 3-MCPD based on body weight in each region accounted for 12–20 % of the PMTDI. The current dietary exposure to 3-MCPD was relatively low for the population and it is concluded that there is little health risk from 3-MCPD for the population in China.

Table 49.5 Daily exposure to 3-MCPD from various food group in Chinese TDS regions (µg/day)

	Grains	Beans	Potatoes	Meats	Eggs	Fish	Milk	Vegetables	Fruits	Sugars	Alcohols	Beverages
S1	4.16	3.94	0.06	0.82	0.17	0.68	0.21	3.02	0.41	0.01	0.09	1.97
S2	3.7	1.4	1.6	3.4	0.7	2.7	0	9.2	0.2	0.01	0	2.4
N1	2.11	0.66	0.3	4.83	2.1	1.1	0.18	9.63	0.46	0.01	0.07	1.75
N2	8.67	1.76	0.29	1.16	0.06	0.1	0.39	3.3	0.37	0	0.01	0.86
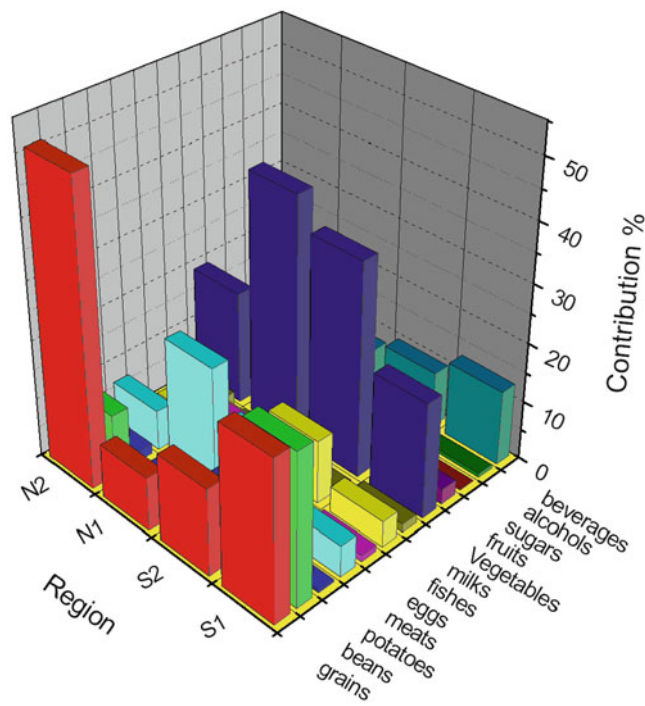
Fig. 49.2 The contribution of food groups to daily intake of 3-MCPD in Chinese TDS regions

Table 49.6 Total daily dietary exposure to 3-MCPD in Chinese TDS regions

	Dietary intake		PMTDI%
	μg/d	μg/kg bw/d	
S1	15.54	0.26	12.3
S2	25.31	0.42	20.1
N1	23.2	0.39	18.4
N2	16.97	0.28	13.5

Acrylamide

The daily exposures to acrylamide from each food group in the four TDS regions are presented in Table 49.7. Figure 49.3 shows the comparison of contribution of food groups in different regions. The vegetable group was the predominant contributor in each region with the percentage proportion ranging from 28 % to 76 %.

Table 49.7 Daily exposure to acrylamide from each food group in Chinese TDS (µg/day)

	Grains	Beans	Potatoes	Meats	Eggs	Fish	Milk	Vegetables	Fruits	Sugars	Alcohols	Beverages
S1	0.58	0.25	0.19	0.06	0.03	0.04	0.01	2.48	0.09	0.02	0.02	0.11
S2	8.31	0.37	1.11	0.05	0.02	0.02	0.01	3.84	0.04	0.01	0.03	0.12
N1	2.49	2.20	2.78	0.03	0.03	0.04	0.01	9.19	0.15	0.01	0.01	0.06
N2	0.82	0.45	1.65	0.02	0.01	0.03	0.00	9.94	0.08	0.00	0.00	0.04
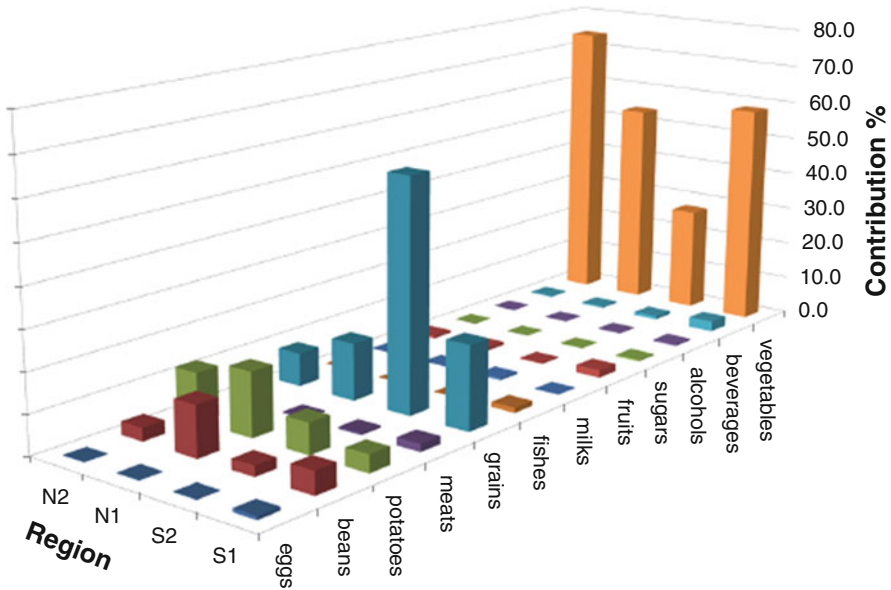
Fig. 49.3 The contribution of food groups to daily intake of acrylamide in Chinese TDS regions

Table 49.8 Total daily dietary exposure to acrylamide in Chinese TDS regions

	Dietary intake		MOE1	MOE2
	μg/d	μg/kg bw/d		
S1	4.25	0.07	2857	4286
S2	14.05	0.22	909	1364
N1	17.04	0.27	741	1111
N2	13.39	0.21	952	1429

The rest of dietary exposures were mainly from the grain, potato, and bean groups with varying contributions from 3 % to 60 %. Exposures estimated for the four regions were from 0.06 to 0.27 μg/kg bw/day, with overall average of 0.19 μg/kg bw/day, median of 0.17 μg/kg bw/day, and P97.5 value of 0.34 μg/kg bw/day. The main food group contributors to exposure were vegetables products (55 %), potato (11 %), cereals (26 %), and beans (6 %).

The total dietary exposure of acrylamide ranged from 4.2 to 17.0 μg/day for the populations in the four regions in China (see Table 49.8). The maximum of dietary intake of acrylamide was found in N1 followed by N2 with a marginally lower value. The MOEs of acrylamide in each region were calculated for neurotoxicity (based on the NOEL of 0.2 mg/kg bw/day) and carcinogenicity (based on the benchmark dose lower confidence bound of 0.3 ug/kg bw/day) respectively (see Table 49.8). The MOEs for carcinogenicity in four regions were all higher than 300 identified by JECFA.

Conclusion

The Chinese TDS has been successfully used to address concerns raised by emerging chemical hazards in the food supply. Using established TDS methods, useful information on the exposure of Chinese populations has been obtained that will contribute to informed risk management measures.

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Chapter 50
Using Total Diet Studies to Assess Acrylamide Exposure

Kevin D. Hargin

Introduction

Acrylamide has been used as an industrial chemical since the mid-1950s, but its presence in food was only discovered in May 2002. Since then there has been extensive international effort to investigate how acrylamide forms in food and how formation could be reduced. In addition, efforts have been made to develop and refine risk assessment for dietary exposure to acrylamide. Acrylamide is known to be neurotoxic in humans as a result of occupational and accidental exposure. Studies in animals have shown that acrylamide can have reproductive effects, cause cancer and also damage DNA (i.e. it is genotoxic). It is not known whether dietary exposure to acrylamide could cause cancer in humans, but based upon the evidence from the animal studies, it is considered probable [1].

Following the Swedish announcement of the presence of acrylamide in foods in April 2002, an expert consultation was quickly convened by the Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO) in June 2002 to review and evaluate existing data on acrylamide, and to provide interim advice to governments, industry and consumers. The European Scientific Committee on Food also assessed the implications for food safety posed by acrylamide. The Committee considered research conducted across Europe and endorsed the recommendations of the FAO/WHO expert consultation, including the recommendation that amounts of acrylamide in food should be reduced to as low as reasonably achievable (ALARA).

In 2005, the Joint FAO/WHO Expert Committee on Food Additives (JECFA) carried out a risk assessment showing that current estimated exposure levels may

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indicate a human health concern [2]. The International Agency for Research on Cancer had previously classified acrylamide as "probably carcinogenic in humans" [3]. The European Food Safety Authority's (EFSA) Scientific Panel on Contaminants in the Food Chain concluded in May 2008 that more data on the carcinogenicity of acrylamide in humans are required before it could fully re-evaluate its toxicity [4]. EFSA has plans to conduct a risk assessment by 2015.

Occurrence in Food

Acrylamide has been detected in a wide range of heat-treated foods especially dietary staples such as potatoes, cereals and cereal products. It is found in both foods processed by manufacturers and foods that are cooked in the home. Generally, acrylamide is formed when foods containing the natural amino acid asparagine and sugars, either present naturally or added, are heated at temperatures greater than 120 °C. It has been found in a wide range of home-cooked and processed foods, including potato chips (in the UK, potato crisps), French fries (in the UK, potato chips), bread, crackers (in Europe, crisp breads) and coffee. However, research has indicated that acrylamide does not occur in such foods subjected to lower temperatures and relatively short process times [5]. It is interesting to note that studies have shown acrylamide not to be formed in foods that have been boiled or microwaved [6]. Table 50.1 lists some of the foods that have been found to contain acrylamide.

Ingestion of excessive amounts of contaminants such as acrylamide through the food supply may potentially lead to detrimental effects on the health of consumers. Thus, it is essential to analyze the foods we eat for contaminants and other chemicals through regular monitoring and surveillance programs to assure that chemical levels found in foods remain safely within acceptable national and international reference values. As part of its mandate to ensure that chemicals are not present in foods at levels that would pose an unacceptable risk to health, the UK Food Standards Agency (FSA) carries out total diet studies (TDSs) to provide estimates of exposure for the UK population to chemicals through the food supply. TDSs involve the analyses of groups of foods that reflect the average food consumption patterns of a given population [7]. Results of the analyses can then be used in conjunction with national food consumption data to estimate the average exposure of the general population and certain subgroups to chemicals in foods. The data can also be used to identify changes or trends in exposure and to make assessments on the quality and safety of the food supply. The World Health Organization (WHO) supports TDSs as one of the most cost-effective means for assuring that people are not exposed to unsafe levels of toxic chemicals through food, while also recognizing the importance of TDSs to the development of Codex Alimentarius Commission standards and international trade [8].

The main purpose of a TDS is to protect consumers from chemical contaminants by monitoring exposure levels of the general population over time [9]. TDS programs can be set with varying levels of complexity and sophistication but usually have some degree of sampling to take account of geographic regions and seasonality.

Table 50.1 Foods found to contain acrylamide [16]

Food group	Food subgroup	Number of samples	Acrylamide (µg/kg) Mean	Minimum	Maximum
Bakery wares	White bread	7	84	60	117
	Wholemeal bread	6	17	15	33
	Rye bread	38	140	10	397
	Other bread	9	24	15	60
	Crackers excluding sweet crackers	43	301	10	830
	Other ordinary bakery products	32	137	10	1,987
	Crispbread and crisp rolls	212	411	10	2,380
	Bread type products	29	140	10	514
	Cakes, cookies and pies	135	202	10	1,080
	Other fine bakery products	5	557	169	1,491
Beverages (coffee and beer)	Coffee (as reported)	273	600	80	2,932
	Beer and lager	37	5	10	10
	Cider	1	5	10	10
	Malt drinks	3	107	90	130
Biscuits	Miscellaneous biscuits	189	303	10	1,950
	Gingerbread	680	569	10	7,834
	Ginger biscuits	139	585	15	2,220
	Almond based	79	310	10	1,234
	Shortbread	151	409	10	6,798
Cereals and cereal products	Whole, broken or flaked grain	4	15	10	30
	Flours and starch	3	42	13	112
	Muesli	51	64	10	258
	Maize-based cereals	110	98	10	545
	Rice-based cereals	11	251	20	1,649
	Wheat-based cereals	22	132	30	532
	Mixed grain cereals	15	137	50	260
	Oat-based cereals	6	95	10	274
	Bran based	15	304	20	640
	Rice cakes	8	137	15	250
Confectionery	Chocolate confectionary	47	138	10	826
	Sugar-based confectionary	23	151	10	548
Fruits, vegetables and nuts	Dried fruit	73	42	10	258
	Fruit in vinegar, oil or brine	32	169	3	1,548
	Fresh vegetables	5	13	15	20
	Dried vegetables	3	303	220	439
	Canned vegetables	27	10	10	68
	Nuts and seeds	1	200	200	200
Potatoes and potato products	Potato chips	349	626	10	4,215
	Reformed potato snack products	22	818	50	1,680
	French fries	723	299	10	3,428
	Fried potato products and roast potatoes	35	320	5	1,428
	Miscellaneous potatoes	1	66	66	66
Infant foods	Rusks	215	143	10	1,060
Snack products	Maize-based snacks	42	201	40	820
	Pretzels	10	165	60	273
Sugar syrup	Sugar-based syrups	3	156	15	438

The extent to which ethnic groups are taken into account may depend on the resources available and the diversity of the population and its diet. It is also important to include in a TDS provision to differentiate age and sex groups to be able to give a full picture of the exposure of different categories of consumers to the substances of concern.

TDS data differ from other chemical surveillance programs because they focus on chemicals in the diet and not on individual foods. Additionally, the foods are processed as for consumption in the home, thus they take into account the impact of cooking on the decomposition of less stable chemicals and the formation of new ones, e.g. acrylamide. As such, it is background levels of chemicals that are sought, not regulatory compliance.

This type of study is recommended by the WHO as an important activity for its member nations to undertake, as it provides reliable estimates of dietary intakes of contaminants.

Methods of Calculating Exposure to Acrylamide

The FAO/WHO expert consultation in June 2002 reviewed and evaluated available data on acrylamide, and provided interim advice to governments, industry and consumers [10]. Several preliminary exposure estimates were consolidated allowing the consultation to estimate that long-term acrylamide exposures would be in the range of 0.3–0.8 µg/kg bw/day [5]. The consultation stressed that the data available were sparse and that further work should be undertaken to produce more robust exposure estimates taking into account other dietary sources of acrylamide. JECFA, in their assessment in 2005 [11], estimated the average acrylamide exposure for the general population (1 µg/kg bw per day) and the exposure for consumers with high dietary exposure (4 µg/kg bw per day). JECFA, in their re-evaluation of acrylamide in 2010, concluded that new data on the levels of acrylamide in food did not significantly change the 2005 exposure estimates either for the general population or for consumers with high dietary exposure. The MOE values, too, were similar and thus the extensive new data from a variety of sources and studies supported their previous 2005 evaluation. Exposure assessments carried out in the UK estimated the mean adult UK consumer dietary exposure at 0.61 µg/kg bw/day and the high level adult consumer exposure at 1.29 µg/kg bw/day; both being well within the reported JECFA ranges [12].

The UK Total Diet Study

The UK Food Standards Agency, following the discovery of acrylamide in foods in 2002 and the health concerns raised by the toxicity of acrylamide, conducted a TDS in 2003 to estimate dietary exposure of the general UK population to acrylamide in

food [13]. A TDS representing the average UK diet has been carried out on an annual basis since the 1960s to estimate dietary exposure and possible trends in exposure to a wide range of contaminants in food. The results of the UK TDS on acrylamide were considered as part of the wider international body of evidence that contributed to the 2005 JECFA safety evaluation of acrylamide in food.

Methodology

Details concerning the design and conduct of the UK TDS is described in an earlier chapter (see Chap. 40 – Total Diet Studies—United Kingdom's Experience) and therefore will not be repeated here. Foods relevant for the exposure assessment of acrylamide include the miscellaneous cereals group with products such as biscuits and breakfast cereals. The majority of carcase meats were baked. Meat products which were all prepared as for consumption included sausages and pies. Poultry was mostly baked or grilled. Sugars and preserves included chocolate and confectionery and potatoes contained a range of cooked fresh and processed potatoes.

Homogeneity

The entire portion of each 2003 TDS sample was homogenized and divided into four parts for analysis. To ensure sufficient homogeneity, samples were tested by measuring the content of water-soluble metals. The method of homogenization varied according to sample type: oils and fats were stirred; milk and beverages were shaken; cereals and sugars were ground using a coffee grinder; and the remaining groups were homogenized in a blender. Each homogenized sample was then tested for sodium, magnesium, potassium, calcium and manganese using acid digestion followed by inductively coupled plasma mass spectrometry as a marker for homogeneity.

Acrylamide Analysis

In order to minimize degradation of acrylamide, samples were kept at room temperature and in the light for the minimum amount of time during preparation and analysis. Prepared samples were returned to storage in the dark at −20 °C. The TDS samples were analyzed for acrylamide in duplicate using a United Kingdom Accreditation Service accredited gas chromatography–mass spectrometry (GC-MS) method, by the Central Science Laboratory (now the Food and Environment Research Agency). A third sub-sample was spiked with a known amount of acrylamide, to determine the recovery of acrylamide by the method of determination. The full method is given in the laboratory report [14].

A portion of the food sample was extracted with hot water and then brominated to form 2,3-dibromopropionamide. The brominated derivative was extracted using ethyl acetate and the organic layer concentrated before analysis by GC-MS [13]. C_{13}-acrylamide was used as the internal standard. For analysis of the TDS samples, two modifications were made from the standard operating procedure [14]. In addition, calibration standards were added to cover the range 1, 5, 10, 20, 30, 40 and 50 µg/kg.

Four of the food groups analyzed i.e. bread, eggs, sugars and preserves and beverages, required additional clean-up by solid phase extraction before bromination, in order to remove extraneous compounds which are known to reduce sensitivity in these matrix types. Details of the analytical methods can be obtained from the laboratory report [14].

Quality Control

The quality control criteria used were as follows: Results of duplicate analysis were accepted if they had a relative standard deviation of less than or equal to 20 %. Acrylamide data were accepted only if the recovery of spiked samples were in the range 60–140 % with at least 75 % of the spiked samples within the range 80–120 %. The laboratory participated in Food Analysis Proficiency Assessment Schemes (FAPAS), namely, Series 30 (acrylamide) Round 1 (crisp bread) and Round 3 (breakfast cereal), as part of its quality control check. The FAPAS acceptance criterion was that the results should be within the range that would give a z-score of ±2. The measurement of uncertainty was determined from the analysis of the FAPAS test materials on a batch-by-batch basis. The limit of quantification (LOQ) was established for each food group and varied from 1 to 5 µg/kg, depending on the food group. Samples containing levels of acrylamide that could not be quantified were reported as having less than the LOQ.

Results

All results were corrected for recovery. Levels ranged from <1 to 112 µg/kg with the lowest detectable levels occurring in poultry (6 µg/kg) and the highest levels occurring in the 2001 potato group (112 µg/kg). Acrylamide was not quantified in 13 of the 20 food groups, namely, offal, fish, oil and fats, eggs, green vegetables, other vegetables, canned vegetables, fresh fruit, fruit products, beverages, milk, dairy products and nuts. These results are generally consistent with occurrence and formation of acrylamide and are consistent with results of other international research such as those recorded in the European Commission's Joint Research Centre-Institute of Reference Materials and Measurements database [15].

Table 50.2 gives the mean concentrations of acrylamide quantified in each of the 20 food group samples of the 2003 UK TDS and also includes the 2001 TDS potato group

Table 50.2 Mean concentrations of acrylamide in the UK total diet study 2003 samples, including 2001 potato group sample [13]

Food group	Acrylamide[a] (µg/kg)	Acrylamide levels used in exposure assessment (µg/kg) and rationale	
1. Bread	12	12	
2. Miscellaneous cereals	57	57	
3. Carcass meat	10	10	
4. Offal	<3	3	Acrylamide quantified in poultry and carcass meat therefore potential to form in offal [1]
5. Meat products	13	13	
6. Poultry	6	6	
7. Fish	<5	5	Food group may contain breaded and battered products which may contain acrylamide [18]
8. Oils and fats	<3	0	
9. Eggs	<1	0	
10. Sugars and preserves	23	23	
11. Green vegetables	<2	0	
12. Potato 2003 Group	53[b]		
12. Potato 2001 Group	112[c]	112	
13. Other vegetables	<5	5	Food group may contain roasted vegetables, which may contain acrylamide
14. Canned vegetables	<5	0	
15. Fresh fruit	<1	0	
16. Fruit products	<1	1	Food group may contain cooked components, which may contain acrylamide [16, 18]
17. Beverages	<1	1	Food group may contain coffee which may contain acrylamide [16]
18. Milk	<1	0	
19. Dairy products	<1	0	
20. Nuts	<3	3	Food group may contain peanut butter and roasted nuts, which may contain acrylamide [16]

[a] Mean of duplicate analyses and corrected for the analytical recovery. Analytical recoveries lay in the range 60–140 %
[b] Measurement uncertainty = ±28 %
[c] Measurement uncertainty = ±32 %

sample. The measurement uncertainties for these analyses are ±28 % and ±32 %, respectively. The 2001 TDS potato sample was used to estimate dietary exposure to acrylamide in this product group; this gave a more conservative, i.e. worse case, estimate of exposure, given it was made up of products more likely to contain acrylamide.

Discussion

The level of acrylamide quantified in the 2003 TDS potato group sample was lower than expected and lower than in the 2001 TDS potato group sample. No crisps or fried potato products were included in the 2003 potato products category and only a third of the potato and potato products included were baked, grilled or microwaved. The rest of the sample was boiled, steamed or prepared from instant mash potato. Since 2002, various initiatives to reduce acrylamide levels in food have been explored by the food industry and other researchers. Any impact of such initiatives will not be reflected in the acrylamide levels found in the 2001 TDS potato group sample, which did include crisps as well as baked and grilled potatoes/potato products.

Levels of acrylamide reported in toasted bread are generally higher than in fresh bread [16]. However toast was not included in the 2003 TDS. High levels of acrylamide were quantified in the sugar and preserves group; with the likely source of this acrylamide being chocolate, which was shown to contain significant levels of acrylamide. The current understanding of the formation of acrylamide suggests that acrylamide is mainly formed in starch-rich foods; however, acrylamide was also found in the carcass meat and poultry groups albeit at very low levels. Of the food groups tested, none was found to contain significant levels of acrylamide.

The dietary exposure estimates were derived from the TDS and are given in Table 50.3. Data show that cereal-based products and potatoes are the main sources of acrylamide in the UK diet. UK consumers' estimated exposure to dietary acrylamide, based on the TDS results, was similar to exposure estimates in other countries.

However, it should be noted that these dietary exposures are not directly comparable because of the different methods used (for example: different age groups; whole populations or consumers of particular products; using limited food groups rather than the whole diet). There have been many other estimates of acrylamide intake, some of which are detailed in Table 50.4.

When comparing dietary exposure estimates it is important to acknowledge their limitations. One of the intriguing characteristics of acrylamide contamination of foods is the variability in acrylamide levels; it is not unusual to find a large variation in the levels of acrylamide found in samples of the same products, and even between samples originating from the same batch. Table 50.5 gives the ranges for a variety of products sampled in the UK during November 2010 and April 2011 [17], while Fig. 50.1 shows the variability in acrylamide levels in more detail for different samples of French fries [18]. This variability is important when considering dietary exposure to acrylamide.

Table 50.3 Exposure[a] to acrylamide from food groups of the UK total diet study (all food groups combined) [13]

Dietary survey	Age range	Exposure estimate[b] (µg/kg bw/day)[c]	
		Average consumer[d]	High level consumer[d]
Adults		0.3	0.6
Female	19–64	0.3	0.6
Male		0.4	0.6
Young people	15–18	0.5	0.9
	11–14	0.6	1.1
	7–10	0.8	1.4
	4–6	1.0	1.6
Toddlers		1.0	1.8
Elderly (free living)		0.3	0.6
Elderly (institutional)		0.4	0.7
Vegetarians		0.3	0.7

[a]To calculate dietary exposure to acrylamide, the occurrence data from the analysis of the TDS samples was used together with consumption data from the following dietary surveys; the National Diet and Nutrition Survey of British adults, young people aged 4–18 years, toddlers aged 1.5–4.5 years and people aged 65 years and over and the British Marketing Research Bureau's dietary survey of vegetarians
[b]To estimate these dietary exposures the following acrylamide levels were used: For food groups where acrylamide was quantified, the quantified level was used. For food groups where acrylamide was not quantified but where it is known to be present in components of that group or has the potential to form in that group, an acrylamide level of the LOQ was presumed. Food groups where acrylamide was not quantified and where the group does not have the potential for acrylamide formation; it has been assumed that acrylamide is present at 0 µg/kg
[c]Body weight consumption is calculated using each dietary survey participant's body weight
[d]Consumer estimates are based only on those people who ate the food in question. The term "average consumer" refers to UK consumers who eat an average amount of food (for the UK). "High level consumers", also referred to as 97.5th percentile consumers, are UK consumers who eat in excess of the average amount of food

Conclusions

The estimated dietary exposure to acrylamide was 0.34 g/kg bw/day for the average adult consumer and 0.62 g/kg bw/day for high level (97.5th percentile) adult consumers. The highest estimate of exposure on a body weight basis was 1.84 µg/kg bw/day at the 97.5th percentile for toddlers aged 1.5–4.5 years. These are within the range reported in the JECFA evaluation of 2005 and confirmed in 2010 by the same committee as still valid.

The FSA has issued advice to UK consumers that people should eat a healthy balanced diet, including plenty of fruits and vegetables, bread, rice, potatoes, pasta and other starchy foods, some meat, fish, eggs, beans, milk and dairy foods, and just a small amount of foods and drinks high in salt, fat and/or sugar (including chips and crisps). The advice remains unchanged as a result of this TDS investigation for acrylamide and following subsequent surveillance results, up to and including the results from the 2012 published data [17].

Table 50.4 Summary of some exposure estimates for acrylamide

Organization, country	Population/sex (age)	Estimated dietary intake (µg/kg bw/day)	
		Mean	95th percentile; [a]90th percentile; [b]97.5th percentile
BfR, Germany	All, 15–18	1.1	3.2
SNT, Norway	Males	0.49	1.04[a]
	Females	0.46	0.86[a]
	Males (13)	0.52	1.35[a]
	Females (13)	0.49	1.2[a]
AFSSA, France	All	0.5	1.1
	All	1.4	2.9
SNFA, Sweden	All (18–74)	0.45	1.03
NFCS, Netherlands	All (1–97)	0.48	0.60
	All (1–6)	1.04	1.1
	All (7–18)	0.71	0.9
FSA, UK	Males (19–64)	0.4	0.6[b]
	Females (19–64)	0.3	0.6[b]
	All (1.5–4.5)	1.0	1.8[b]
FDA, USA	All (2+)	0.44	0.95[a]
	All (2–5)	1.06	2.33[a]

The UK estimate is for people who consumed particular foods; other estimates are mostly for the entire population

BfR Federal Institute for Risk Assessment, *SNT* Norwegian Food Control Authority, *AFSSA* French Food Safety Agency, *SNFA* Swedish National Food Authority, *NFCS* Netherlands Food and Consumer Products Safety Authority, *FSA* Food Standards Agency, *FDA* Food and Drug Administration

Fig. 50.1 Histogram of acrylamide levels found in French fries sampled as part of a 2009 Food Standards Agency Survey (Data based on 99 samples of French Fries collected from outlets as ready-to-eat between March 2008 and March 2009 [18])
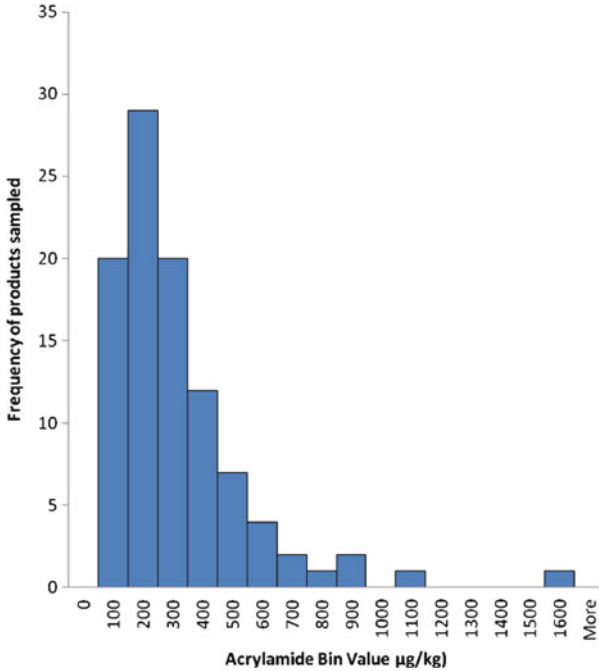
Table 50.5 Summary of acrylamide concentrations in the UK (mean and range) [17]

Product category	n	Mean (μg/kg)	Min (μg/kg)	Max (μg/kg)
Group 1 – French fries sold as ready to eat	**42**	**239**	**41**	**1,285**
Nov-'10 delivery	21	255	41	660
Mar-'11 delivery	21	223	53	1,285
Group 2 – Potato crisps	**20**	**835**	**220**	**2,061**
Nov-'10 delivery	10	738	220	1,859
Mar-'11 delivery	10	933	444	2,061
Group 3 – Pre-cooked French fries for home-cooking	**16**	**194**	**21**	**1,155**
Nov-'10 delivery	8	206	21	1,155
Mar-'11 delivery	8	183	39	491
Group 4 – Soft bread	**20**	**16**	**3**	**51**
White	8	15	7	37
Wholemeal	4	24	15	33
Others (e.g. in-store bakery, rye, linseed, rolls, etc.)	8	14	3	51
Group 5 – Breakfast cereals	**20**	**149**	**35**	**325**
Group 6 – Biscuits & crackers	**20**	**380**	**27**	**1,573**
Crackers	9	275	48	473
Crispbread	3	197	120	326
Wafers	1	154	154	154
Other (sweet)	7	625	27	1,573
Group 7 – Coffee	**20**	**501**	**49**	**1,009**
Roast coffee	8	212	172	243
Instant coffee	6	865	724	997
Coffee substitutes	6	521	49	1,009
Group 8 – Baby food other than processed cereal based	**20**	**13**	**3**	**27**
Group 9 – Processed cereal baby food	**20**	**65**	**3**	**598**
Biscuits and rusks for infants and young children	10	110	3	598
Other processed cereal-based foods for infants and young children	10	18	6	68
Group 10 – Others	**50**	**311**	**5**	**3,972**
Vegetable crisps	2	2,651	1,330	3,972
Canned black olives	1	884	884	884
Other potato products for home-cooking	6	579	44	1,604
Cocoa	2	442	176	707
Prefabricated crisps	2	364	285	443
Popcorn	2	328	205	451
Microwave French fries	2	327	327	328
Canned prunes	2	305	247	362
Novelty gingerbread	2	247	51	443
Cereal bars & granola	4	135	82	259
Tortilla/corn chips	2	103	79	127
Prefabricated potato products for home-cooking	4	68	18	108
Ethnic foods	6	64	25	120
Dried fruit	2	59	49	68
Cakes	5	33	12	86
Pastries	5	29	5	57
Chocolate	1	24	24	24

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Chapter 51
Polybrominated Diphenyl Ethers in Food in Australia—An Additional Use of the Australian Total Diet Study

Gillian Duffy and Janice L. Abbey

Introduction

One of the ways in which the total diet study methodology and data is utilized in Australia is in the investigation of emerging issues. For example, soon after the completion of the 22nd Australian Total Diet Study (ATDS) (see Chap. 20 – The Australian Experience in Total Diet Studies), concerns were raised internationally about the chemicals used as fire retardants, in particular, polybrominated diphenyl ethers (PBDEs). The structural similarity of PBDEs to dioxins and polychlorinated biphenyls (PCBs), combined with their bioaccumulative and persistent nature in the environment and human tissues, resulted in concerns about their potential health effects and possible adverse impact on the environment [1].

To investigate possible human health and safety risks posed by these chemicals from exposure through food, Food Standards Australia New Zealand (FSANZ) undertook a comprehensive dietary exposure assessment for PBDEs. At the time, there was little information on the extent of exposure of Australians to PBDEs from the diet or other sources. However, from the 22nd ATDS, nationally representative food samples already collected and stored were available for PBDE analysis.

The PBDE survey included a limited range of foods and could not be considered a total diet study per se; however, it provided a cost-effective opportunity to investigate the dietary exposure of PBDEs in Australia and characterize the potential human health risk associated with exposure through food.

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Background

What Are PBDEs?

PBDEs are man-made chemicals that are added to a wide variety of consumer and commercial products to improve their fire resistance. They are used in electronic goods such as: computer and television housings, toasters, hair dryers, irons, foam bedding and furniture, carpets and textiles, car interiors, electrical wire and cable insulation, and electrical connectors and sockets. The addition of PBDEs to consumer products is believed to have significantly contributed to a reduction in the loss of human life and property through fire. Commercial production of PBDEs began in the 1970s and their use has increased over time due to stricter fire control measures in many countries and greater use of plastic materials and synthetic fibers [2].

PBDEs are 'additive' flame retardants, meaning they are mixed with the polymer material being treated, but are not chemically bonded to the polymer matrix (as is the case with reactive flame retardants). Therefore, there is potential for the chemical to slowly leach out of the treated plastic product over its functional lifetime. The environmental release of PBDEs can occur during their production, as well as through the use and/or disposal of products that contain PBDEs [3]. The similarity in the chemical structure of PBDEs to dioxins and PCBs suggested a concern regarding PBDEs and human health effects. Although data on the toxicology and human health effects of PBDEs are limited, the available animal toxicity data indicate PBDEs have the potential to affect thyroid hormones and neurodevelopment [3, 4]. Extrapolation of results from various animal studies, suggests a potential risk for developmental effects in the unborn child. Thus, women of child bearing age and very young children are considered potentially vulnerable population groups in relation to PBDE health risks.

PBDEs as an Emerging Issue

PBDEs were being detected worldwide, in a range of foods including: dairy products, meat, fish, fish oils, shellfish, eggs, vegetables, and vegetable oils [4, 5]. An assessment of the human body burden levels in Australia, provided evidence that the population was being exposed to PBDEs, although the routes of exposure and metabolism of PBDEs were unknown [4, 6, 7]. Despite the limited information available at the time, the human body burden levels for Australia were somewhat higher than those observed in Europe. This finding was surprising as PBDEs were not manufactured in Australia. Enquiries about Australian PBDE data identified an information gap. There was little Australia data available on environmental levels and no data on levels in Australian food and raw agricultural commodities.

Investigating Dietary Exposure to PBDEs for the Australian Population and Potential Human Health Risk

To undertake a risk assessment for PBDEs, FSANZ considered how best to gather data on levels of PBDEs in food. Analytical methods to detect PBDEs in a variety of food matrices were available in Australia but analyses were quite costly. To minimize the costs associated with sampling, food preparation, and analysis as well as the need to seek assistance from the State and Territory agencies to collect food samples, FSANZ investigated the possibility of utilizing samples collected from other recent surveys. This investigation determined that:

- A number of suitable food samples were available from the 96 different foods already collected and stored from the recent 22nd ATDS
- The method of storage and types of containers used for storage would not affect the analysis of PBDEs or result in any unintended contamination
- There was a sufficient amount of each sample to conduct the additional analysis for PBDEs

Given this, additional PBDE analysis was conducted for a subset of samples.

The Analytical Survey

A total of 35 foods from the 22nd ATDS samples were analyzed for PBDEs from the following food groups: meat, dairy, oils and spreads, bread and bakery products, and vegetables. Figure 51.1 shows the 35 foods included in the survey.

These foods were selected to cover as broad a spectrum of the diet as possible. A review of the international research was used to identify foods that would potentially contain concentrations of PBDEs [4, 5, 8, 9]. Foods were also included in the analysis if they were likely to contribute significantly to PBDE exposure from the diet due to frequent consumption, or if they were consumed in large quantities by specific population sub-groups (such as infant foods). Tap water was also included in the analysis. In preparing food as 'ready-to-eat', local tap water is used rather than distilled water to account for substances that may be present in tap water in the overall estimate of dietary exposure [10].

The PBDE analysis measured 26 of the 209 individual PBDE congeners (including tri-, tetra-, penta-, hexa-, hepta-, octa-, nona-, and deca-brominated diphenyl ethers). These congeners were chosen as they were commonly found in the environment, had been reported to be found in foods internationally and, importantly, had accredited validated methods of analysis.

In the analysis of PBDEs used in this study, the limit of quantification (LOQ) was equal to the limit of detection (LOD); the limit varied for each congener in each sample analyzed. There was a lower degree of certainty where the results were reported as being less than the LOQ; this uncertainty increases when the LOQ is high [11].

Notes:
Food samples shown in **blue** indicate the five samples that had NO detectable PBDEs
†35 foods (39 samples) tested from samples collected for the 22nd ATDS. All States & Territory's assisted with sample collection. Foods were prepared in 'table ready' state. Limit of Detection/Limit of Quantification varied for each congener & food
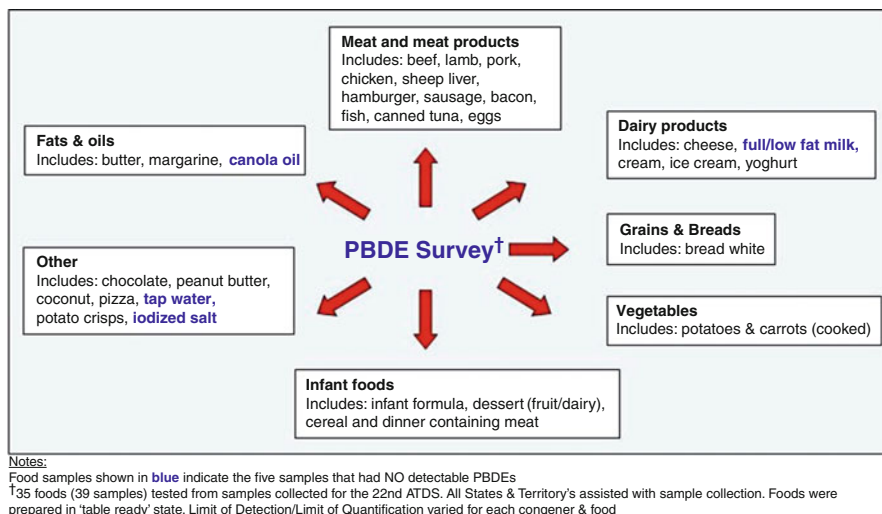
Fig. 51.1 An overview of FSANZ analytical survey examining PBDEs in foods

PBDE Concentrations in Foods

Thirty of the 35 foods tested contained PBDEs. A total of 39 samples were analyzed including duplicate samples of full fat milk, low fat milk, pork chops and beef sausage. Of the 1,014 congener measurements, non-detect results were reported for the majority (69 %). A total of 310 congener data points (31 %) reported with quantified values or 'detections' with values greater than or equal to the LOQ. The highest levels of PBDEs were detected in boiled eggs, grilled pork chops, bacon and cream, with infant foods containing relatively low levels. Tap water, full fat milk, low fat milk, canola oil and iodized table salt had no detectable PBDEs.

There are various approaches to dealing with non-detect values (Chap. 15 – Managing Concentration Data—Validation, Security, and Interpretation, Chap. 16 – Reporting and Modeling of Results Below the Limit of Detection and Chap. 18 – Addressing Uncertainty and Variability in Total Diet Studies). In this case, three PBDE concentration levels were derived for each food that reported a concentration at the LOQ: a lower bound value (non-detects assigned a zero value); a middle bound value (non-detects assigned ½ LOQ); and an upper bound value (non-detects assigned the LOQ). Figure 51.2 shows lower, middle and upper bound mean concentration levels of PBDEs in selected foods.

Dietary Exposure Estimates

As part of the risk assessment, PBDE dietary exposure was estimated for different population groups using food consumption data from the 1995 Australian National Nutrition Survey (NNS), following the usual ATDS dietary modeling processes

Explanatory notes:
Concentrations for water are given in ng/g.
Upper bound concentration for water was 3.12 pg/g
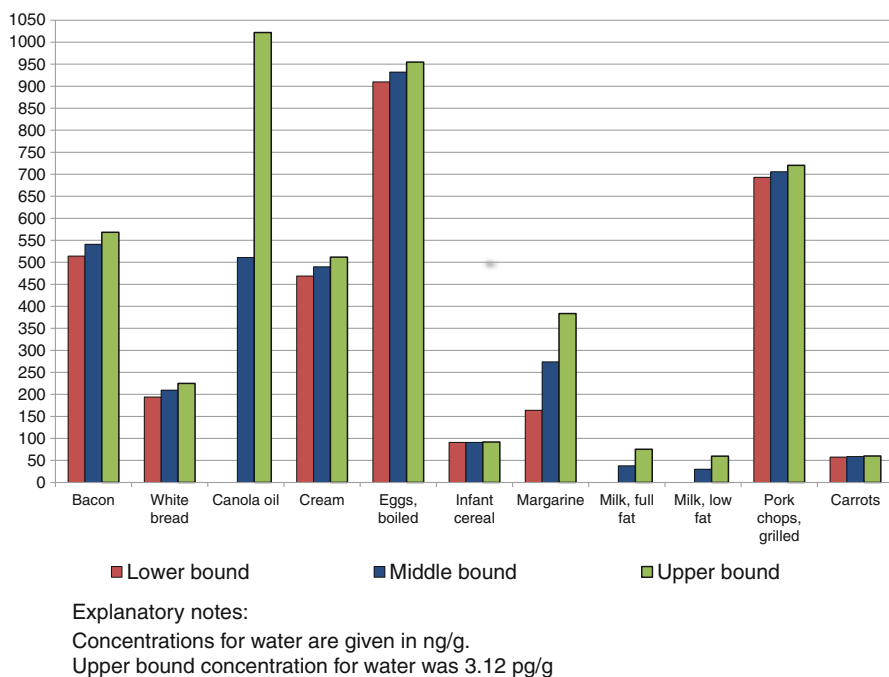
Fig. 51.2 Concentrations of PBDEs (pg/g fresh weight) in selected foods

(without water). Age groups were selected to represent specific life stages: infants (at 3 and 9 months), toddlers and young children (2–5 years), schoolchildren (6–12 years), teenagers (13–18 years) and adults (19 years and above). Males and females were assessed separately for all age groups except for infants aged 3 months and 9 months.

Uncertainties in the Exposure Estimates

There was uncertainty with the analytical data and the approach used for the exposure estimates that could not be quantified. One source of uncertainty related to the assignment of numerical values to PBDE congeners that were 'not detects' or not quantified (refer to the section on PBDE concentration in foods). A limitation of this PBDE analysis was that it was not possible to determine whether 'non-detect' values indicated that the chemical was not actually present in the sample or whether the particular assay method used was not sufficiently sensitive to detect/quantify it.

In the exposure estimates, the limited number of foods analyzed meant that analytical values for each food were mapped to much wider food groups, e.g. carrot PBDE concentration was assigned to all vegetables. Thus conservative

assumptions were used to ensure that the assessment did not underestimate the dietary exposure. Examples of assumptions used in the dietary exposure assessment of PBDEs are as follows:

- Where an individual NNS food was not mapped to an analyzed food, it was assigned a zero PBDE concentration, e.g. fruit.
- Where a food has a specified PBDE concentration, this concentration was carried over to mixed foods where the food has been used as an ingredient, e.g. milk in a sauce or custard.
- All vegetables were assigned the value found in either potatoes or carrots. The higher concentration determined for carrots was used to represent all vegetables, other than potatoes, as this better reflected levels found in vegetables in other studies [3] and yielded a more conservative estimate of exposure.

Estimated Dietary Exposures for Population Groups Aged 2 Years and Above

Dietary exposure estimates (calculated without water) showed that the exposures of the general Australian population to PBDEs from food were low (Table 51.1). Depending on gender and concentration used (lower, middle or upper bound), the estimated mean dietary exposures to PBDEs for 2–5-year-olds ranged between 3 and 68 ng/kg bw/day and 95th percentile exposures ranged between 7 and 232 ng/kg bw/day. For 6–12-year-olds estimated mean exposures ranged between 3 and 48 ng/kg bw/day and the 95th percentile exposures from 5 to 129 ng/kg bw/day. For 13–18-year-olds, estimated mean exposure ranged between 2 and 40 ng/kg bw/day and at the 95th percentile between 3 and 120 ng/kg bw/day. For the 19 years and above age group, estimated mean dietary exposures ranged between 1 and 15 ng/kg bw/day and at the 95th percentile between 3 and 57 ng/kg bw/day.

Estimated Dietary Exposures for Infants

At the time of the analysis, the National Research Center for Environmental Toxicology and the Department of Environment and Heritage had just completed an Australian study on the concentrations of PBDEs in breast milk [1]. Given this, FSANZ decided to use the available breast milk PBDE concentrations to estimate dietary exposure to PBDEs for infants. Theoretical infant diets were constructed for two different ages: for infants aged 3 months, who are solely breast-fed; and for infants 9 months of age, who consume a mixed diet consisting of milk (either breast milk or infant formula) and solid foods [11]. It was estimated that 3-month-old, fully breast-fed infants would have a mean dietary exposure of 51 ng/kg bw/day to PBDEs

Table 51.1 Margin of exposures (MOEs) for PBDE consumers in various population groups aged 2 years and over [11]

Age/gender	Concentration type[a]	Mean dietary exposure (ng/kg bw/day)[b]	95th percentile dietary exposure (ng/kg bw/day)	MOE[c] (mean exposure)	MOE[3] (95th percentile exposure)
2–5 years male	Upper bound	68	232	1400	400
	Middle bound	36	118	2,800	800
	Lower bound	4	7	28,000	1,400
2–5 years female	Upper bound	59	189	1600	500
	Middle bound	31	118	2,800	800
	Lower bound	3	7	29,000	1,400
6–12 years male	Upper bound	48	129	2,100	800
	Middle bound	25	67	3,900	1,500
	Lower bound	3	7	32,000	15,000
6–12 years female	Upper bound	41	113	2,500	900
	Middle bound	22	58	4,600	2,000
	Lower bound	3	5	39,000	20,000
13–18 years male	Upper bound	40	120	2,500	800
	Middle bound	21	62	4,800	1,600
	Lower bound	2	5	44,000	21,000
13–18 years female	Upper bound	25	75	4,000	1,300
	Middle bound	14	39	7,400	2,500
	Lower bound	2	3	60,000	29,000
19+ years male	Upper bound	15	57	6,800	1,700
	Middle bound	8	29	12,000	3,300
	Lower bound	2	4	59,000	27,000
19+ years female	Upper bound	11	45	9,200	2,200
	Middle bound	6	23	16,000	4,300
	Lower bound	1	3	73,000	34,000

Explanatory notes:

[a]Explanation of concentration types: Lower bound – zero value assigned to all results below the LOQ (non-detections). Middle Bound – 50 % LOQ value assigned to all results below the LOQ (non-detections). Upper bound – the LOQ assigned to all results below the LOQ (non-detections). The middle and upper bound estimates include values where congeners were not detected and are therefore conservative

[b]Estimated dietary exposures in ng/kg bw/day are calculated from the mean dietary exposure in ng/day and mean bodyweights. Mean body weights for each age and gender group were from 1995 Australian National Nutrition Survey data. Figures are rounded to the nearest whole number

[c]MOE calculated from threshold dose (0.1 mg/kg bw/day) divided by mean dietary exposure (ng/kg bw/day). MOE figures are rounded to one significant figure for MOEs up to 1,000 and to two significant figures where MOEs were above 1,000

(no 95th percentile estimate was made for 3-month-old infants). The 9-month-old breast-fed infant mean dietary exposure ranged between 29 and 35 ng/kg bw/day; and between 72 and 87 ng/kg bw/day at the 95th percentile. For the formula-fed 9-month-old, the estimated mean dietary exposure ranged between 7 and 14 ng/kg bw/day, and between 18 and 35 ng/kg bw/day at the 95th percentile (Table 51.2).

Table 51.2 Margin of exposures for PBDE for 3- and 9-month-old infants [11]

Population group	Mean body weight (kg)[a]	Concentration type[b]	Mean dietary exposure[c] (ng/kg bw/day)	95th percentile dietary exposure (ng/kg bw/day)	MOE[d] (mean exposure)	MOE (95th percentile exposure)
3 month breast-fed infant	6.4	Lower bound	51	NA	2,000	NA
9 month breast-fed infant	9.2	Upper bound	35	87	3,000	1,200
		Middle bound	32	80	3,400	1,300
		Lower bound	29	72	3,700	1,500
9 month formula-fed infant	9.2	Upper bound	14	35	7,000	2,800
		Middle bound	10	27	9,300	3,700
		Lower bound	7	18	14,000	5,500

Explanatory notes:

NA not assessed

[a]Three-month-old and nine-month-old mean body weights were based on male infant weights referenced from WHO (1983)

[b]Explanation of concentration types: Lower bound – zero value assigned to all results below the LOQ (non-detections). Middle bound – 50 % LOQ value assigned to all results below the LOQ (non-detections). Upper bound – The LOQ assigned to all results below the LOQ (non-detections). The middle and upper bound estimates include values where congeners were not detected and are therefore conservative

[c]Estimated dietary exposures in ng/kg bw/day are rounded to the nearest whole number. Calculated from the mean dietary exposure in ng/day and mean bodyweights

[d]MOE calculated from threshold dose (0.1 mg/kg bw/day) divided by mean dietary exposure (ng/kg bw/day). MOE figures are rounded to one significant figure for MOEs up to 1,000 and to two significant figures where MOEs were above 1,000

Food Groups Contributing to Total PBDE Dietary Exposure

The percentage contribution that each food group makes to the total estimated dietary exposure was calculated. This is done by dividing the sum of all consumers' exposures from one food group by the sum of all consumers' exposures from all foods containing PBDEs assessed, and multiplying this by 100. Lower bound results were used to calculate the percentage contribution each food group makes to total estimated dietary exposures as this provides the best indication and only includes foods containing levels of PBDEs at or above the LOQ. Figure 51.3 shows that the main contributors to across all population groups assessed (excluding 3-month-old infants), were bread, eggs, vegetables and meat.

Dietary Exposure and Potential Health Risk

In 2005, the Joint FAO/WHO Expert Committee on Food Additives (JECFA) reviewed the available toxicity data for PBDEs and concluded there was insufficient data to establish a tolerable weekly or monthly intake for PBDEs. A margin of
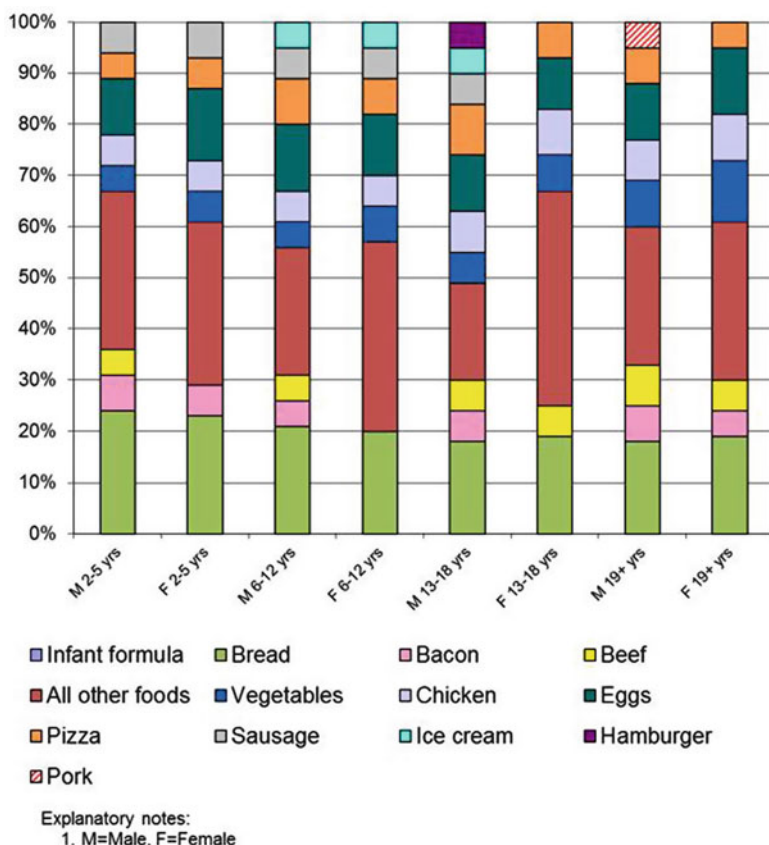
Fig. 51.3 Major contributing foods to total estimated PBDE dietary exposure

exposure (MOE) was then used to provide an estimation of the health risk of dietary PBDE exposure in different population groups [12]. JECFA also concluded

"the available data are inadequate to establish a common mechanism of action that would allow a single congener to be used as a surrogate for total exposure or, alternatively, as the basis for establishing toxic equivalency factors [13]."

It was noted by JECFA that for related bioaccumulative persistent contaminants such as polychlorinated biphenyls and dioxins [14, 15], the appropriate dose-metric for interspecies comparison of risk was a measure of the accumulating potency of PBDEs ('body burden' approach). For the majority of PBDEs studied, however, the data from experimental animals or concentrations in human tissues were considered insufficient to allow a comparison with an external dose. While it would be normal practice to establish a provisional tolerable weekly or monthly intake for bioaccumulative contaminants, such as the PBDEs, the incompleteness of the available database for each congener led JECFA to conclude that

"the limited toxicity data suggests that for the more toxic PBDE congeners with lower bromines, such as those contained in the commercial mixture called pentabromodiphenyl ether, adverse effects would be unlikely to occur at doses of less than approximately 100 μg/kg bw/day [13]."

Following an independent review of the available toxicological data, FSANZ concurred with the JECFA conclusions. Based on toxicity studies, a threshold dose (100 μg/kg bw/day) was used by FSANZ as the basis for determining the magnitude of the MOE for all PBDEs. The MOE is calculated by dividing the dose at which adverse effects were observed in laboratory animal studies by the estimated exposure to PBDEs from food. The lower the MOE, the greater is the potential public health risk [16]. Interpreting MOEs in the context of risk assessment and risk management requires consideration of a number of factors such as: as mode of action, nature and extent of uncertainties and human variation in susceptibility to the response of concern [16, 17].

It is noted that reference health standards for PBDEs have also been established by the European Food Safety Authority (EFSA) and the US Environmental Protection Agency (EPA). A guideline value of 0.1 μg/kg bw/day was set by EFSA based on JECFA's threshold dose of 100 μg/kg bw/day and using a 1,000-fold uncertainty factor [18]. This value is equivalent to a MOE of 1,000 over the threshold dose, and is therefore comparable to the FSANZ risk assessment approach. US exposure limits for several PBDEs (ranging from 0.1 to 7 μg/kg bw/day) are based on no observed adverse effect levels (NOAELs) much higher than the threshold dose of 100 μg/kg bw/day and to which relatively large uncertainty factors (up to 3,000) were applied to address data gaps [19]. On this basis, neither the European nor US reference health standards were considered to impact on the FSANZ risk characterization of PBDEs.

The mean and 95th percentile exposures of consumers only in each age/gender group were used to determine the MOE (Tables 51.1 and 51.2). As it can be seen, the selection of the lower, middle or upper bound estimate of dietary exposure had a profound effect on the magnitude of the MOE. If there are many food types in which PBDEs are not detected then the effect of assigning numerical values to non-detect results on the apparent MOE, and therefore the level of concern, will be exaggerated. In this study, only 31 % of all congener data points reported a quantifiable concentration in food.

The subgroup with the highest exposure was 2–5-year-old males, with MOEs of 1,400, 800 and 400 for 95th percentile exposures at the lower, middle and upper bounds, respectively. Results for female aged 2–5 years were similar. The difference in the MOE between the lower bound, which includes only measured values, and the middle or upper bounds, which include assigned values for foods that were below the LOQ, warrants some comment. It seems reasonable therefore to conclude that the likely true MOE for all groups will be somewhere between the middle and lower bound. For example, given the over-representation of non-detects in this survey, the MOE for males aged 2–5 years is more likely to be closer to the lower bound estimate of 1,400 than the middle bound estimate of 800.

The MOEs for 9-month-old breast-fed and non-breast-fed infants were also estimated. For formula-fed 9-month-old infants, the MOEs were approaching or exceeding 10,000 for lower and middle bound dietary exposure estimates.

Even at the 95th percentile dietary exposure the MOEs were 5,500 and 3,700 at the lower and middle bound respectively, and are sufficiently high to be of no concern. The level of exposure to PBDEs in 3- and 9-month-old breast-fed infants were approximately 4-fold higher than formula-fed infants, but still lower than the upper bound exposure of 2–5-year-old males. Nine-month-old infants would be expected to have higher dietary exposure to PBDEs on a body weight basis compared to children aged 2–5 years, due to their high food consumption relative to body weight. However, in this study, the estimated dietary exposure (ng/kg bw/day) for 2–5-year-olds was higher than for infants at the middle and upper bounds. This finding may be attribut-able to methodological differences in estimating dietary exposure of 9-month-olds compared with other population groups. In particular, the theoretical diet constructed for infants does not use individual dietary records to calculate consumption and dietary exposure estimates. Given the conclusion that the true likely MOEs for 2–5-year-old males will be close to 2,800, the exposure estimates for 3- and 9-month-old breast-fed infants are unlikely to be of concern, particularly as they are three orders of magnitude above the estimated threshold dose.

Conclusion

This study provided the most comprehensive analysis of PBDE levels in Australian foods yet undertaken and formed the basis of an analysis of exposure risk assess-ment of the Australian population for PBDEs. The dietary exposure estimate was used in conjunction with the available information on the hazard characterization of PBDEs to assess the human health risk associated with exposure to PBDEs in food. These calculations indicated that dietary exposure of the general Australian popula-tion, to PBDEs from food is low and there is an acceptable margin of exposure for all population groups. Based on the available evidence, food is unlikely to be a significant source of PBDE exposure.

This study also demonstrates the usefulness of nationally representative foods samples collected for a TDS, in assessing emerging food issues or for other moni-toring and surveillance activities. Although when considering the use of existing samples, it is important to ensure samples have been stored appropriately following the completion of the TDS analysis.

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Chapter 52
Risk Assessment and Management Interface—Example of Methylmercury in Fish

Jiri Ruprich and Irena Rehurkova

Introduction and Background

Fish and other seafood have worldwide nutritional importance. For approximately one billion people, it provides more than 30 % of their animal protein [1]. The world supply of fish and seafood in 2005 was about 105.3 millions metric tons [2]. Fish and seafood are an important source of animal protein, fat-soluble vitamins. e.g. A and D, minerals, e.g. iodine, selenium, and calcium, and omega-3 and -6 long-chain polyunsaturated fatty acids (PUFA), e.g. eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA). Average fish availability is 50 grams or more per person per day for over than half of the world's population with some countries exceeding 70 grams per person per day [3]. However, fish can be also a source of dietary exposure for environmental pollutants, e.g. persistent organic pollutants (POPs), including polychlorinated biphenyls (PCBs), DDT, dioxins (PCDD/Fs), organometallic compounds (e.g. organotin compounds), natural toxins, e.g. algal metabolites, and heavy metals, most notably lead and mercury. Sources of exposure can be via consumption of fish muscle and fat, but usually not both for the same contaminant.

Mercury (Hg) and its organic metabolite methylmercury (MeHg), which is one of the most toxic natural contaminants of fish, are widely distributed in the environment [4]. The average concentration of mercury in the earth's crust is about 0.5 mg/kg. The main sources of contamination for the environment are natural degassing from the earth's crust and oceans, which release about 150,000 tons per year. Mercury is released naturally also via volcanic activity. Man-made pollution occurs via mining, combustion of coal, usage in fungicides, and other minor uses, such as temperature- and pressure-measuring equipment. Of the man-made emissions,

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mining releases in the Mediterranean and South and East Asia are estimated to be about 10,000 tons per year, while other human activities are estimated to release about another 10,000 tons per year [4].

The chemical properties of mercury and its ions are diverse. Elemental mercury (Hg^0) is the only metal that is liquid at room temperatures and it is only slightly soluble in water and lipids. These properties have resulted in many practical applications. Mercury can also exist in inorganic mercurous (Hg^{1+}) compounds and mercuric (Hg^{2+}) compounds. Many stable complexes can be formed with biological systems, especially those containing the sulfhydryl group (−SH). Among organic compounds, alkyl mercury compounds are more toxic than aryl compounds. MeHg, which is the most toxic for higher organisms, including humans, is formed from elemental or inorganic mercuric compounds by various microorganisms. For microorganisms, this process is an effective path way of detoxification.

Available analytical options for mercury and/or MeHg depend on the objective. Total mercury can be quantified by neutron activation analysis, which requires expensive and highly specialized equipment, or more often by atomic absorption spectrophotometry (AAS). The sample is digested and oxidized with a mixture of sulfuric and nitric acids, converting all the mercury present into inorganic form (with possible losses by volatilization). After oxidation, the mercury is reduced to the metallic state and the amount present estimated in the form of vapor released from the solution in a stream of nitrogen by flameless AAS, using the 253.7-nm spectral line. Another advanced method, the advanced single-purpose AAS analyzer for direct mercury determination of both solid and liquid samples, is widely used in the Czech Republic. Preliminary chemical treatment of samples is not necessary. It uses vapor generation of mercury with post-capture and enrichment on the gold amalgamator. It achieves a very low limit of quantification (LOQ) of 0.1 ug/kg without matrix dependence. MeHg is normally analyzed by gas chromatography (GC). MeHg is extracted with organic solvents (usually benzene), re-extracted into aqueous cysteine solution and extracted back into organic solvents after acidification. MeHg is then analyzed by GC often with Inductively Coupled Plasma Mass Spectrometry (ICPMS) detection.

Assessment of Methylmercury Risks

MeHg is readily absorbed (up to 95 %) following ingestion. MeHg effectively crosses both the blood–brain barrier and the placenta. It results in higher levels of mercury in fetal rather than maternal brain. The major route of elimination is through the bile and feces. The developing nervous system is a very sensitive target for MeHg. The acute neurotoxic effects observed in humans poisoned with MeHg via the consumption of contaminated seafood is known as Minamata Disease [5]. Acute MeHg poisoning can result in mental retardation, cerebral paralysis, deafness and blindness, and cardiotoxicity, including high blood pressure.

Toxicity of MeHg has been recently evaluated by various international, regional and national risk assessment bodies. An evaluation done by the U.S. National Research Council (NRC) in 2000 established an intake limit of 0.7 µg/kg bw/week [6]. In June 2003 the Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO) Joint Expert Committee on Food Additives (JECFA) revised its Provisional Tolerable Weekly Intake (PTWI) for MeHg to 1.6 µg/kg bw/week from 3.2 µg/kg bw/week [7]. An opinion of the European Food Safety Authority (EFSA) related to mercury and MeHg in food was published in 2004. This opinion does not declare any new toxicological reference dose for risk characterization but used the JECFA established PTWI for MeHg [8]. Recently, EFSA revised its decision and established Tolerable Weekly Intake (TWI) of 1.3 µg/kg bw/week, expressed as mercury, because new studies indicated that beneficial effects related to omega-3 long chain fatty acids may have lead to an underestimation of the potential adverse effects of MeHg in fish [9]. Practical implications of these revisions can be quite serious as some fish and seafood consumers may possibly exceed these health-based guidance values.

Foods can contain different mercury compounds [5]. Mercury can be present as organic mercury compounds, e.g. MeHg, as inorganic mercury compounds, e.g. $HgCl_2$, and also as metallic mercury (elemental Hg^0). The chemical form of mercury in foods is influenced by absorption, distribution, metabolism and elimination from the body. The chemical form of mercury in fish generally averages more than 85 % of the most toxic MeHg in muscle, but can range as low as 18 % and all the way up to 100 % [10]. Factors identified for contributing to the variability of MeHg and total mercury ratios are age, fish size, sex, growth rate, feeding habits, marine/ freshwater/geothermal habitat, trophic depth, species, and food chain [11]. The variable range of MeHg/total mercury ratio data reported by international studies strongly suggest that the use of a fixed conversion factor to estimate methylmercury levels from total mercury concentrations are unlikely to provide accurate exposure estimates for health risk assessments and that actual measured MeHg levels should be used wherever possible. To this end, it would be highly desirable to measure both MeHg and total mercury in fish and seafood consumed, especially when the total mercury dose is close or over the toxicological reference dose, i.e. PTWI, for MeHg.

Due to its recognized toxicity, many countries have set legal limits for total mercury and/or methylmercury in foods. In European Community Regulation 1881/2006, a maximum level of 0.5 mg of total mercury/kg is prescribed for fishery products, with the exception of certain listed fish species for which 1 mg/kg applies. However, the Codex Alimentarius Commission has similar limits, but specifies that these apply to residues of methylmercury. Beside fishery products, mercury can be found in other foods but mainly as inorganic compounds. Expected average concentrations of total mercury in foods differs from 5 µg/kg for milk, dairy products and fruit, 10 µg/kg for vegetables, cereals and meats, to about 200 µg/kg for fish/seafood. Recently, JECFA established a PTWI for inorganic mercury of 4 µg/kg bw [12]. The previous PTWI of 5 µg/kg bw for total mercury was withdrawn. The

PTWI for inorganic mercury was considered applicable to dietary exposure to mercury from foods other than fish and shellfish. In agreement with JECFA, EFSA set the TWI for inorganic mercury at 4 μg/kg bw, expressed as mercury [9].

Public health protection requires ongoing monitoring programs focused on MeHg exposure. The main rationale for monitoring programs is as follows. The principal contribution of MeHg comes from fish and seafood; other foods contribute usually less than 10 % to exposure. Fish/seafood consumption is probably not distributed normally and hence some population groups can be significantly more exposed. Between population groups, pregnant women are in the highest risk category because of the very high sensitivity of the fetal brain and the ability of MeHg to easily cross the mother/placental blood barrier. As a practical matter, total mercury content in fish/seafood is generally used for estimating exposure to methylmercury. The previously established PTWI/TWI for MeHg should be applied when health risk is characterized for the first time.

In European Union (EU), under these circumstances, the EFSA recommendation on MeHg [8] did not consider the evaluation to be adequate enough to provide pan-European advice on fish consumption. Therefore EFSA asked national food safety authorities for additional guidance. Specifically, EU Member States were requested to collect available data or generate new data by means of specific dietary exposure studies. In most cases, individual consumption figures for fish and seafood were required for more precise dietary guidance.

Management of Mercury/Methylmercury Risks Using the Czech Total Diet Study

There are some distinct factors influencing exposure to mercury/MeHg. As the Czech Republic is land-locked, most fish and seafood are imported from various parts of the world. Czech production of freshwater fish is about 21,000 tons per year but a lot of this is exported. Total fish/seafood consumption (edible part) is traditionally very low, equivalent to about 11 g /person /day, only 10 % of which is freshwater fish [13]. Some lakes/rivers are contaminated with mercury. Sport fishing is a traditional activity for about 120,000 inhabitants and their additional consumption is about 10 g/person/day, of which about 7 g is carp.

The range of food with mercury in the Czech total diet study (TDS) is relatively narrow. TDS data for 1999–2003 with 1852 results had 1,005 results below the LOQ (LOQ=0.01–0.2 μg/kg) [14]. Only the food groups marine fish, freshwater fish, smoked fish, marinated fish and canned fish (see Table 52.1) had significant levels of total mercury.

Spices and liver were other foods with detectable mercury. Based on these analytical results and average food consumption data, the point estimate exposure dose for total mercury was calculated. The average exposure dose for the Czech population has been estimated to be 0.08 μg of total mercury/kg bw/week, which is only about 5 % of revised JECFA PTWI for methylmercury (see Table 52.2).

Table 52.1 Fish foods analyzed in the Czech TDS for the period 1999–2003

Food group	Type of fish	Number of individual samples	Consumption (g/kg bw/week)	Total Hg in samples (µg/kg) Average	±Std
Freshwater fish	Carp	60	0.210	21	10
Marine fish	Cod/hake	60	0.581	28	19
Smoked fish	Mackerel	60	0.175	75	20
Marinated fish	Herring	60	0.098	38	12
Canned fish	Sardines 75 %	60	0.287	31	19
	Miscellaneous 25 %	60			

Table 52.2 Point estimate for exposure to total mercury in the Czech TDS

Food group	Food consumption[a] (g/kg bw/week)	Total Hg[b] (µg/g)	Estimate exposure (µg/kg bw/week)[c]
Fish and products	1.4	0.0400	0.0560
Meat and products	16	0.0004	0.0064
Milk and products	24	0.0002	0.0048
Fruit	15	0.0003	0.0045
Vegetables	22	0.0004	0.0088
Cereals	23	0.0003	0.0069
Total	*101*		*0.0805*

[a]Estimate for pregnant women with 64 kg body weight

[b]Average data for total mercury in Czech Republic

[c]FAO/WHO JECFA PTWI for methylmercury = 1.6 µg/kg bw/week [EFSA TWI = 1.3 µg/kg bw/week]

Besides this average value for the whole population, higher exposures for specific population groups can be expected. In particular, due to changing dietary habits, mainly in the younger generation, it was necessary to develop a more rigorous exposure assessment on which national consumption guidance could be based. It involved the generation of additional concentration data of total mercury/MeHg in marine fish, seafood and freshwater fish, which required ongoing analyses due to changing import regions. New data from the national food consumption survey on individuals for distributional/probabilistic estimates was also used. The monitoring of total mercury/MeHg exposure biomarkers in hair and blood was refocused and the exposure of sport anglers and their families was evaluated. It also involved preparation of simple guidance on marine fish/seafood/freshwater fish consumption for women during pregnancy and lactation. At the same time, fish and seafood consumption was promoted in the media because consumption of these food is still very low in the Czech Republic in order to increase the intake of omega-3 and -6 long-chain PUFAs and other nutritionally important substances.

Biomarkers of exposure for MeHg were used to evaluate exposure by analyzing hundreds of samples of human blood and hair. The relation between the steady-state

concentration of mercury in blood and the average daily exposure has been described using a one-compartment model [6] as follows:

$$D = (C * b * V)/(A * f * bw)$$

where

D = dose (µg/kg of bodyweight per day)
C = mercury concentration in blood (µg/l)
b = elimination rate constant (0.014 per day)
V = blood volume (9 % of bodyweight for a pregnant female)
A = fraction of the dose absorbed (0.95)
f = the absorbed fraction distributed to the blood (0.05)
bw = body weight (64 kg for a pregnant female)

The comparison of Czech TDS results and calculated exposures associated with blood levels of mercury has been undertaken for children and adults. The above-mentioned formula has been applied to children with an acceptable correlation. However, for adults, blood levels were four times higher than expected according to dietary exposure. However, to try to explain this better, it is probably important to first reduce uncertainties associated with exposure from dental amalgams and other possible exposure sources.

All potential resources of information were taken into account in designing the new Czech fish/seafood-based dietary guidelines, which cover a range of topics that may be of interest to consumers (see Table 52.3).

Table 52.3 Fish/seafood-based dietary guidelines tailored for the Czech Republic

Food safety facts on mercury and fish consumption	Fish list based on recent import data for the Czech Republic
1. What is mercury?	*Fish high in mercury*
2. Mercury in fish	Shark
3. The role of food control systems	Swordfish
4. Fish species and limits on consumption	Tuna (Vietnam)
5. Freshwater fish - angling	*Fish medium in mercury*
6. Benefits from fish consumption	Tuna (Mediterranean)
7. Where to get more information	Bass (Mediterranean)
	Halibut (Scandinavian)
	Mackerel
	Fish low in mercury
	Salmon (Norway)
	Sardines
	Anchovy
	Tuna (Thailand)
	Shrimp (Greenland)
	Carp
	Herring
	Oysters (Bretagne)
	Octopus (Mediterranean)
	Cod/hake (Scandinavian)

Conclusions

The risk assessment of MeHg will have serious implications for drafting fish/seafood-based dietary guidelines. Decreases in the PTWI can have economic implications for some parts of the fishing industry. However, there is still no simple and fully effective method to evaluate health benefits versus risks from fish/seafood consumption. A recent FAO/WHO consultation concluded that when considering benefits of PUFAs versus risks of MeHg among women of childbearing age, maternal fish consumption was shown to lower the risk of suboptimal neurodevelopment in their offspring compared to women not eating fish in most circumstances evaluated [15]. However, the consultation also concluded that among infants, young children, and adolescents, the available data are currently insufficient to derive a quantitative framework of health risks and benefits of eating fish. Recently, new data from the Seychelles Child Developmental Study Nutrition Cohort have indicated that omega-3 long-chain PUFA in fish may counteract negative effects from MeHg exposure. The beneficial nutrients in fish that may have confounded previous adverse outcomes in child cohort studies from the Faroe Islands, was the reason EFSA lowered the TWI for MeHg [9]. There are many attempts to use new approaches, including *inter alia* calculation of so-called disability-adjusted life years (DALYs) [16]. Ongoing data collection on fish/seafood consumption and concentrations of MeHg are needed for improve exposure assessments. Additional epidemiological data are also needed to improve setting toxicological reference points, such as the PTWI. MeHg can potentially raise serious problems in achieving safe and adequate nutrition for certain groups with high fish/seafood consumption. Therefore, at-risk groups must be clearly identified and risk communication messages tailored to their needs must be disseminated [17]. For example, information about age, gender, ethnicity, health and socioeconomic factors, as well as typical diets, particularly fish consumption (species, amount and source) is essential for the development of an effective risk communication plan. Finally, the acceptability of the appropriateness of risk management measures is closely related to the public perception of risk. Therefore, total diet studies can provide a sound scientific basis for public health policy-making, which minimizes the risk and maximizes the benefits of fish consumption.

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Chapter 53
The German Approach to Estimating Dietary Exposures Using Food Monitoring Data

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Introduction

Currently (since February 2012) Germany is conducting a pilot total diet study (TDS) as member of the TDS-Exposure Project [1], which is supported by the European Commission. Within the pilot project, infrastructure and expertise will be established for future implementation of a full German TDS. Presently, the existing data gap can be partly filled by the extensive national food monitoring program. Thus, national exposure assessments for food as done by the Federal Institute for Risk Assessment (BfR) mainly rely on matched data from the food monitoring program and national food consumption surveys. This chapter will give a short overview on the data available in Germany for dietary exposure assessment. The German approach using data from food monitoring instead of TDS will be demonstrated using the example of cadmium exposure via food. Advantages and disadvantages of both approaches will be elaborated.

German Food Monitoring Program

The German food monitoring program is a systematic approach for choosing food items from the German market to be analyzed for certain substances. The main focus is directed on residues of plant protection products but also environmental

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contaminants, such as dioxins, polychlorinated biphenyls, heavy metals, and other contaminants. The food monitoring program has been performed by the Federal States of Germany since 1995. The program is coordinated by the Federal Office of Consumer Protection and Food Safety (BVL) that compiles all of the data generated in Germany. Data are made available to the BfR for exposure assessments of the German population. In order to use the monitoring data to obtain a representative estimate for the dietary exposure of a substance in Germany, a sampling design that differs from other monitoring programs is needed. One main difference is that random instead of targeted sampling is applied. Another difference is that the foods to be examined are part of a representative food basket.

Between 1995 and 2002, a food basket based on the National Nutrition Survey I [2] has been analyzed, including a total of 31,000 samples from 130 food items. The food basket and methods used for this monitoring period are described in Schroeter et al. 1999 [3]. The results and risk assessments for selected contaminants were published by the BVL in 2003 [4]. In 2007, the BfR was assigned by the Federal Ministry of Food, Agriculture, and Consumer Protection (BMELV) to propose a refined concept for the national monitoring of pesticide residues in food. The aim of the new design was to update the food basket using more recent nutrition surveys and to discuss ways to improve representativeness of the data. Hence, a food basket was developed from consumption data for German children as documented in the VELS-Study, [5] which started to be used in 2010. To also obtain data for adults, some food items that are normally not eaten by children but by adults (like beer, wine, and coffee) have been added to the food list. The selected foods cover 90 % of the whole diet based on the long-term mean consumption. The food basket consists of 64 food items with high variability in residue levels and 36 food items with low variability expected. The latter group will be analyzed every 6 years in a sample size of 188 samples per food item, all other in a 3-year cycle and with half of the sample size. The sample sizes are a compromise for statistical accuracy in estimating mean and high percentiles, on one hand, and financial and practical feasibility, on the other hand. Overall, in the new pesticide monitoring scheme, about 3,600 samples are analyzed each year.

The food basket and detailed recommendations regarding the study design were published by Sieke et al. in 2008 [6]. There are several criteria for representativeness given, that might be desirable from a scientific point of view. It should be mentioned that even if data are derived by random sampling, not all of these criteria could be controlled because of practical reasons.

After establishing the updated pesticide monitoring program, the BfR was asked to broaden the approach and make it useable for other contaminants as well. The pesticide monitoring is focusing on raw agricultural commodities (RACs) due to regulations for pesticide residues that are generally for nonprocessed foods to ensure safety of both processed and nonprocessed food. Thus, in a first step, only contaminants could be considered that will not be affected by preparation of foods or where the processing factors are well known. For all other contaminants, e.g. processing contaminants, such as acrylamide, polycyclic aromatic hydrocarbons, 3-monochloropropanediol-esters, and phthalates, other approaches like TDS have to be discussed in future.

In contrast to the former food basket from 1995 to 2002, which was a single food list valid for all contaminants, now agent specific food baskets were defined.

This was because some contaminants occur only in a few food groups or very specific food items. Thus, food items that may contribute highly to the overall exposure of a particular contaminant, may be missed when using a general food list that is characterized by highly consumed foods containing only low levels of the respective contaminant. Therefore, to avoid the chances of underestimating exposure, contaminant specific food lists were implemented.

The food lists are derived from consumption data for adults in the German National Nutrition Survey II. Since the survey includes very detailed food descriptions, the number of food items consumed is high. Therefore, a strategy was needed to reduce the number of food items for chemical analyses. This was done by defining homogenous food groups and by selecting a surrogate per food group. The surrogates will be used to extrapolate to all other foods within the food group. For example, "Edam" or "Tilsit" cheese will not be analyzed but "Gouda" samples were used instead. The resulting contaminant specific food lists were merged and also compared with the food list of the pesticide monitoring program to benefit from synergistic effects. Finally the new monitoring program was established in 2011 with about 3,400 samples to be analyzed per year.

The German National Nutrition Survey II

Besides data concerning contamination of foods due to hazardous substances, details about food consumption are crucial for exposure assessment. The German National Nutrition Survey II (NVS II) is the most recent national food survey in Germany providing information with regard to nutritional behavior of the young and adult population from the ages of 14–80. This study was conducted in 2005/2006 by the Max Rubner Institute (MRI) on behalf of the BMELV. About 20,000 people were selected randomly for a representative sample of the German population. The NVS II combines three different survey methods, namely, a dietary history, repeated 24-h recalls on two nonconsecutive days and further, the weighing records for a subsample of 1,000 people. In the dietary history, people were interviewed in a standardized way about their food consumption over the last 4 weeks using the software *DISHES* (Diet Interview Software for Health Examination Studies) [7]. Since environmental contaminants are primarily associated with chronic risks, the study design using a dietary history approach is appropriate for generating valid estimates of usual consumption for assessing exposure to cadmium via food.

The LExUKon Project: Aims and Methods

LExUKon [8] is the acronym for a German project for data preparation and standardization of procedures for exposure assessment of food-related exposure of environmental contaminants based on the NVS II. With this updated food consumption data, current exposure and the contribution of single food items or food groups

to overall exposure can be calculated. LExUKon especially aims at establishing food categories that are compatible to food groups with maximum levels (MLs) as defined in the European legislation to check dietary exposure against contemporary health-based reference values.

To assess dietary cadmium exposure, food consumption data were matched with data from food monitoring at the level of categories for MLs. Since regulated categories consist primarily of unprocessed single foods, consumption data published by MRI could not be used directly [9]. However, food as eaten was broken down according to recipes. Besides the desired food level, this is also important to avoid underestimation of the consumption of some foods, such as herbs, oilseeds, and cocoa that are often part of composite foods. For the exposure assessment of cadmium, it was assumed that preparation of foods has no influence on the cadmium content apart from the drying process, which was considered by using concentration factors.

Although food monitoring provides considerable data for cadmium, some food items eaten in the survey remain without data. Therefore, data from the literature were added and homogenous food groups that had been defined were used to extrapolate from foods with measured cadmium values to similar foods.

Results on Cadmium from the LExUKon Project

Results of the LExUKon project allow the calculation of whether dietary exposure of the German population and some subgroups exceed the health-based reference value for cadmium. Figure 53.1 shows the level of dietary exposure to cadmium for the total German population, vegetarians and the highest exposed age group (14–18 year olds) compared to the Tolerable Weekly Intake (TWI) of
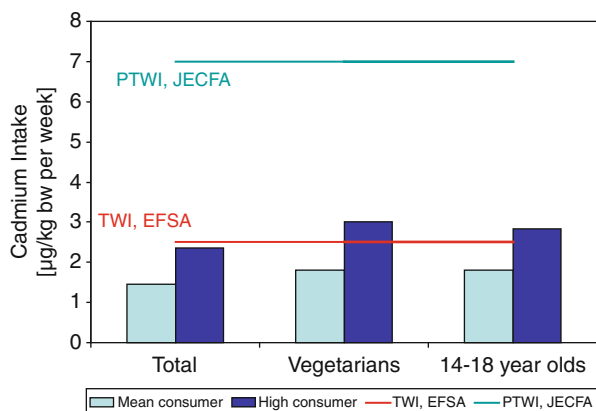
Fig. 53.1 Cadmium intake in Germany in different population groups compared to the TWI of EFSA and the PTWI of JECFA
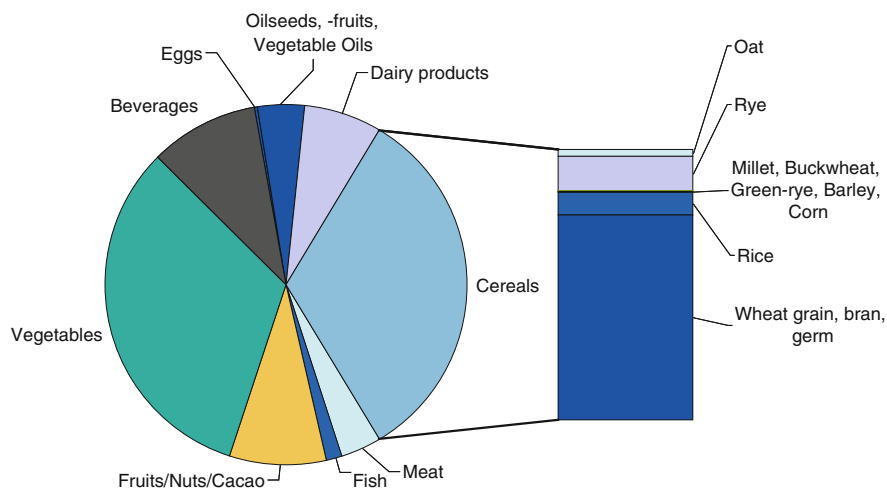
Fig. 53.2 Contribution of the main food groups to the intake of cadmium and disaggregation of the cereals group up to levels compatible with European regulation

2.5 μg/kg body weight per week established by European Food Safety Authority (EFSA) [10].

The upper reference line in Fig. 53.1 indicates the Provisional Tolerable Weekly Intake (PTWI) of 7 μg/kg body weight per week established by Joint FAO/WHO Expert Committee on Food Additives (JECFA) [11] in 1988. The figure demonstrates that consumers eating mean portions of all foods do neither exceed the PTWI nor the TWI. High consumers are defined according to EFSA [12] as high consumers of those two food groups contributing most to the overall mean exposure and average consumption for all other food groups. In the case of cadmium, the main contributors are the two food groups cereals and vegetables. Figure 53.1 reveals that high consumers nearly reach the TWI, while high consumers in the subpopulation of vegetarians as well as youths from 14 to 18 years exceed the TWI. Furthermore, it has to be kept in mind that the estimates only consider dietary exposure. Other sources contributing to cadmium exposure, such as inhalation of cigarette smoke must also be considered.

With respect to the fact that dietary cadmium exposure is relatively high, measures to reduce cadmium levels in food have to be discussed. Therefore, it is very useful to take a deeper look into the food groups established in the European Regulation (EC) No. 1881/2006 [13] amended by Regulation (EC) No. 629/2008 [14] and their contribution to cadmium exposure. Beyond this, the influence of regulated versus nonregulated food groups in relation to cadmium exposure can be compared in the LExUKon project. It has been calculated that 75 % of the mean dietary exposure is caused by regulated food items and 25 % by nonregulated food groups, like milk, oilseeds and cocoa. Figure 53.2 displays the contribution of the nine main
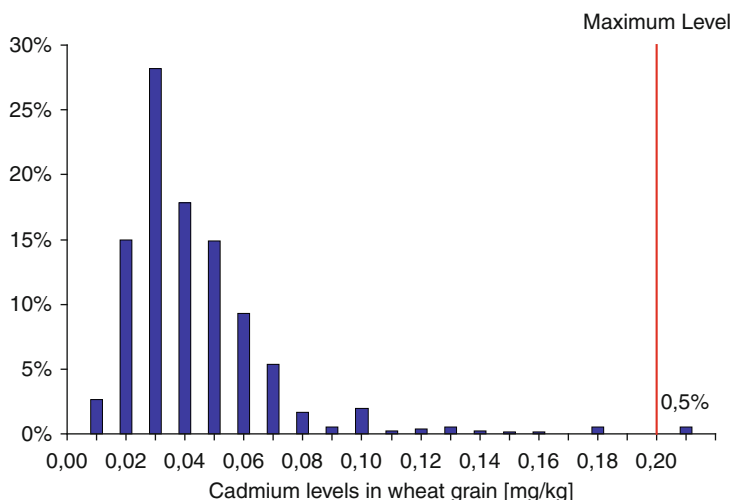
Fig. 53.3 Cadmium levels in wheat grain from the German food monitoring compared to the maximum level

food groups to cadmium exposure and illustrates the ability for further disaggregation of food categories using the example of cereals. On the basis of Fig. 53.2, it can be concluded that reducing MLs of cadmium in highly contaminated food groups, like seafood, offal or wild grown mushrooms, would hardly affect mean overall exposure. Instead it can be seen that due to high consumption levels, the main drivers of cadmium exposure are food groups like cereals or vegetables with mostly medium or low cadmium levels. Obviously, lower contaminated food groups can make a significant contribution to overall exposure when they are eaten in higher amounts.

Since wheat seems to be a main source for exposure to cadmium (see Fig. 53.2) the first thought to reduce cadmium intake would be to lower the ML of wheat. But as shown in Fig. 53.3, at least for the German market, it is obvious that most of the wheat samples have cadmium levels well below half of the MLs. Hence, even reducing the ML by half will probably have little effect on exposure.

Nevertheless, it has to be evaluated whether a reduction of MLs in food will be achievable under current conditions and how this would contribute to reducing cadmium exposure. The results of the LExUKon project are appropriate to be taken into account in such decisions.

Food Monitoring: An Alternative to TDS?

The aim of this section is to discuss whether the use of the German food monitoring program in the way described for the LExUKon project could be an alternative approach to TDS and to elaborate on common features and differences. A main objective of both approaches is to assess dietary exposure. The estimated weekly

exposure of cadmium as reported for the German population in the LExUKon project (1.45 µg/kg body weight) is higher than estimates from the UK TDS 2009 [15] (1.09 µg/kg body weight per week with occurrence data from 2006), the First French TDS 2005 [16] (0.32 µg/kg body weight per week with occurrence data from 2000 to 2001) and the Second French TDS 2011 (1.12 µg/kg body weight per week with occurrence data from 2006) [17]. The differences between both French TDS studies are higher than the difference between the UK or Second French TDS and LExUKon. Hence it cannot be determined whether differences between TDSs and LExUKon are due to different national eating habits, the methods or due to over- or underestimation of one of the approaches. In contrast to this, one rather outdated duplicate diet study in an industrial area of Germany shows considerably higher values [18] (3.3 µg/kg body weight per week with occurrence data form 1994/1995) than the LExUKon estimate. This is also valid for the results based on EFSA's Concise European Food Consumption Database, [19] where the mean dietary exposure across European countries was assessed to be 2.3 µg/kg body weight per week and ranged from 1.9 to 3.0 µg/kg body weight per week. Due to the broad food categories of the EFSA's database, it can be concluded that the approach used in LExUKon is more precise than the EFSA approach. Compared to the values obtained in the duplicate diet study, it can be seen that the estimate of the LExUKon project does not result in gross overestimation, even if the duplicate diet will probably overestimate current exposure due to rather outdated cadmium data and likely highly contaminated regions.

The TDS trend analyses are also applicable for the German approach. Based on food monitoring data from the period 1995–2002 and the German Nutrition Survey I, BVL already had performed a German exposure assessment for cadmium in 2003. The estimate of 1.2 µg/kg body weight per week cadmium dietary exposures is very similar to the recent assessment in spite of the different methodologies used in the nutrition surveys. With the new design of the food monitoring, an appropriate database is already established for future trend analyses. That is also true for the food consumption data that are regularly collected by the MRI in the German Nutrition Survey [20] since 2008.

A TDS approach might be applicable for all contaminants and is only limited by financial resources. Following the German approach, some requirements have to be fulfilled. It can be used for contaminants that are not heat sensitive and therefore, no processing factors are needed other than for mixing, dilution and drying. It can even be applied to all other contaminants under the condition that processing factors are available. Nevertheless it has to be stated that this is not the case for most of the contaminants. Pesticide residues are an exception because often processing factors are known from the authorization process and compiled by the BfR [21]. An advantage of the German approach is that individual recipes can be used to aggregate from RAC level to composite foods. On the other hand, due to financial resources, TDS usually covers only standard recipes. For both approaches, only standard household preparation procedures are considered because nutrition surveys normally do not provide information of cooking or baking times. For instance, the time of heating a product, like toast or fried potatoes, varies markedly between

households. This variability cannot be addressed within both approaches but will definitely have an influence on exposure assessments, e.g. for acrylamide.

Obviously, it will not be possible to have valid occurrence data for all contaminants in all foods of the diet. Hence, the exposure estimates both of TDS and German food monitoring program tend to underestimate the overall dietary exposure. However, the magnitude of underestimation can be reduced by choosing food surrogates within homogenous food groups as used in the German food monitoring program or other extrapolation strategies. Underestimation is also reduced by selecting food items that are frequently consumed and hence, representing a high percentage of the diet, as well as selecting foods which are known to have potentially very high concentrations (e.g. offal and shellfish for cadmium)[2]. As demonstrated for the LExUKon project, the underestimation is less in cases using RACs, recipes and processing factors. For contaminants with known processing factors, this is also a very cost-effective approach because there is a significantly smaller number of RACs compared to the high variety of processed and composite foods. Additionally the use of contaminant specific food lists as described for the new German food monitoring program will save resources and reduce the underestimation of exposure, because it also considers food items with low contribution to overall consumption, but high contribution to the exposure of a specific contaminant.

One of the advantages of the food monitoring program compared to most of the TDSs is the larger number of samples, which is also important for rarely consumed foods. Further, some TDS approaches face additional problems due to pooled samples. The analytical sensitivity has to be much higher for TDS otherwise it will result in many samples below the limit of detection that contribute to uncertainties in the exposure assessment. In case samples are not just composited within one food category, but also pooled with different food items, information regarding the contribution of several food items to the overall exposure will be lacking.

To discuss risk management measures, it is often necessary to calculate the contribution of single food items to overall exposure. Besides the above-mentioned problem of compositing, another difference of both approaches is that the calculation of the contribution of food items will be provided on different levels of disaggregation. For TDS, the information can be given on foods as consumed, which overcomes the need for processing factors. The German food monitoring approach is flexible regarding food categories and will be able to provide information on the level of food categories for several legislative scenarios, which is of most interest to risk management. That is also true for TDS given that the individual food approach is used in TDS where each food item is analyzed separately. Additionally there might be an advantage of the food monitoring approach in cases where costs can be shared with other food surveillance programs.

Considering the diversity of purposes of risk assessments and the high number of relevant contaminants as well as being aware of the advantages and disadvantages of both concepts, it can be concluded that both approaches should ideally complement each other. For some evaluations, like assessment of exposure of heavy metals, both approaches are adequate for exposure assessment. If the food monitoring approach identifies potential concerns, such as cadmium in cereals, then further refinement

may be necessary, such as a targeted TDS approach, where foods are analyzed after being prepared ready for consumption, which will better assess the potential risk to the consumer.

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Chapter 54
Total Diet Studies for Infants—Example of Persistent Organic Pollutants in Human Milk

Seongsoo Park, Rainer Malisch, and Gerald G. Moy

The Importance of Breastfeeding

Breastfeeding is an ideal way to feed infants; its benefits go far beyond sound nutrition, and children should not be deprived of being breastfed without clear and compelling reasons. Breast milk provides, in an easily digested form, all the nutrients an infant needs for the first 6 months of life. Breast milk actively protects infants against infection as it contains numerous anti-infective factors, including immunoglobulins and white blood cells, as well as growth factors that stimulate the development of the infant's gut. It is therefore not surprising that both the World Health Organization (WHO) and United Nations Children's Fund (UNICEF) have recommended that for the first 6 months of the infant's life, mothers should practice exclusive breastfeeding (i.e. no other food or drinks given, not even water) [1]. Breast milk should be the total diet of infants for this period, and also a significant part of the diet in the months and even years that follow. A total diet study for infants would then focus just on human milk and if the infants were older than 6 months, human milk and a limited number of other foods. In the US, these other foods most likely would include follow-on formula, cow's milk, and apple juice.

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Chemical Contaminants in Human Milk

While the broadest scientific consensus supports the benefits of breastfeeding, the widespread introduction of synthetic chemicals, particularly pesticides, has resulted in contamination of this pure and perfect food for the human species. In 1951, scientists at the US Food and Drug Administration first reported the presence of DDT in human milk [2]. Subsequently, a series of other organochlorine pesticides were also detected in human milk. These substances all share similar properties in terms of their high degree of fat solubility, their ability to biomagnify in the food chain, and their long half-lives in the body. Chemicals with these properties have since come to be known as "persistent organic pollutants" or POPs. In her seminal book *Silent Spring* in 1963, Rachel Carson described her concern for these chemicals by noting, "In experimental animals the chlorinated hydrocarbon insecticides freely cross the barrier of the placenta, the traditional protective shield between the embryo and harmful substances in the mother's body [3]." In addition to other toxic properties, she noted that these substances have the potential to disrupt the endocrine system, which had been documented in studies of wild animals, particularly birds. As a result, DDT was banned in most developed countries for agricultural use, although such use of DDT continued in developing countries for many years. Today many developing countries still permit the use of DDT for public health purposes for malaria control. However, the concern of public health authorities continued to grow as low-level exposure to POPs was shown to have adverse health effects and new and potentially more toxic POPs were identified. In particular, polychlorinated dibenzodioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs), which together are commonly known as "dioxins", and polychlorinated biphenyls (PCBs), are considered to pose significant public health risks based on a combination of their inherent toxicity and level of human exposure. In regard to dioxins, the cost of analysis, which can exceed US$1,700 per sample depending on the sensitivity required, precludes the widespread monitoring of foods. Consequently, such POPs are not often included in total diet studies. Furthermore, total diet studies cannot provide an accurate estimate of typical body burdens of POPs since these chemicals are known to bioaccumulate. For example, once stored in adipose tissues, DDT and particularly its metabolite DDE are stable unless they are mobilized during lactation or extreme weight loss when significant amounts of fat are burned [4]. Therefore, human milk surveys provide important complementary information on integrated long-term human exposure to POPs. In spite of the presence of chemical contaminants in human milk, the benefits of human milk have consistently outweighed any potential risks to the newborn except in the most extreme cases [5].

Biomonitoring of Human Milk

Since DDT was first detected in human milk, many studies of human milk have been carried out. Beginning in 1976, WHO through GEMS/Food [6] has collected and collated information on levels of POPs in human milk as well as in certain

animal-derived foods, such as butter (See Chap. 42 – GEMS/Food and Total Diet Studies). While the analysis of human milk, maternal blood and adipose tissue are all relevant matrices for assessment of body burdens of POPs, human milk is recognized as the preferred matrix for monitoring because it has important advantages, including:

- Non-invasive sampling
- High fat content
- Ease in collecting large volumes, e.g. 50 ml
- Low risk from infectious agents
- Individual samples can be pooled, thus offering significantly saving analytical costs
- Shipping through normal channels

Biomonitoring of human milk data can provide important information on the exposure of the fetus as the levels in human milk directly correlate to the mother's body burden. In addition, it provides information on the mother's diet since exposure to POPs is derived mostly through food. Such information provides guidance in the consideration of options for reducing levels of these substances in food and thus, in the human body. In this regard, one of the recommendations of a WHO risk assessment of organochlorine chemicals in human milk was that girls and women of childbearing age should try to limit their consumption of foods likely to contain these substances in order to protect their offspring [7].

The Stockholm Convention on Persistent Organic Pollutants

More recently, it has been recognized that human milk is an ideal matrix to generally monitor levels of POPs in the environment. In 2004, governments ratified the Stockholm Convention on Persistent Organic Pollutants, which is intended to eliminate or reduce environmental emissions and human exposure to twelve priority POPs [8]. The initial twelve POPs, the so-called dirty dozen, identified in the Stockholm Convention include nine older organochlorine pesticides, namely aldrin, DDT, chlordane, dieldrin, endrin, heptachlor, hexachlorobenzene, mirex, and toxaphene. For most of these substances, production and use have been banned or strictly regulated by most countries for some time. These POPs are now largely environmental contaminants, although DDT, as mentioned earlier, still has limited public health usage. The other three POPs under the Stockholm Convention include the industrial chemicals PCBs as well as two industrial and combustion by-products, the dioxins, polychlorinated dibenzodioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs). While the production of PCBs has been largely banned for many years, electrical transformers and other equipment containing these chemicals are still in use and pose potential disposal problems. In regard to PCDDs and PCDFs, better manufacturing controls and improved combustion processes, e.g. power generation and waste incineration plants, have led to significant reductions in emissions in Europe.

As the Secretariat to the Convention, the United Nations Environment Programme (UNEP) convened a Conference of Parties (COP) to discuss the details of

implementing the convention [9]. One of the issues discussed involved Article 16 of the Convention, which requires that the effectiveness of the Convention in reducing emissions of the twelve POPs be monitored. Based on the long experience of WHO in biomonitoring of human milk for dioxins, the COP agreed that human milk should be one of the core matrices to be monitored and requested that WHO and UNEP collaborate in a global survey of POPs in human milk. From WHO's public health perspective, human milk data can provide information on the exposure of fetuses as well as infants to these chemicals. Because human exposure to POPs is mainly through food, human milk data can also provide guidance on possible measures to reduce the exposure of the population through food. These measures directed at food are not the same as the source-directed measures targeted by the Stockholm Convention and may include regulatory limits for these chemicals in food and codes of practice to help avoid contamination, such as the control of animal feed.

Revision of the WHO Protocol Guidelines

Both PCBs and dioxins are occasionally detected in the food chain at high levels, sometimes the result of illegal disposal of waste oil. Over the period 1987–2001, WHO coordinated three international surveys of human milk for dioxins because of public health concerns. These surveys have revealed a downward trend in the levels of these chemicals in human milk, particularly in the Netherlands [10]. However, these surveys had a number of deficiencies, which made their reliability and comparability questionable. In response to the Stockholm Convention, WHO revised its guidelines for developing a national protocol for the biomonitoring such chemicals in human milk [11]. The new guidelines are intended to provide a scientifically sound basis for evaluating the levels of POPs in human milk over time, which would then be one component of assessing the effectiveness of the Stockholm Convention. The guidelines continue to support the monitoring of POPs for human health and food-chain contamination purposes. The protocol guidelines were revised based on the advice of the WHO Ad Hoc Human Milk Survey Advisor Group [12] and extensive field experience in undertaking surveys with human milk and other human samples.

A number of modifications were made to reduce variability in the results in order to more accurately assess changes in levels of POPs over time. For example, the new guidelines call for the recruitment of 50 individual donors per composite sample instead of 10 as previously recommended. Pooled samples are now analyzed for all twelve Stockholm POPs. Certain other POPs being considered for inclusion under the convention may also be analyzed on a case-by-case basis. In addition, the guidelines recommend that individual samples be analyzed for the nine pesticide POPs and marker PCBs in order to provide information on the distribution of individual

samples to enable the statistical assessment of time trends. Ethical issues, like informed consent and confidentiality, were also addressed and procedures strengthened. Given that breastfeeding reduces child mortality and has health benefits that extend into adulthood, greater efforts were made in the revised guidelines to further protect, promote and support breastfeeding in the context of these human milk studies. In order to promote comparability among countries, national protocols should closely follow the key elements of the guidelines, but sufficient flexibility is allowed to accommodate country-specific needs. For example, small countries may find it difficult to identify 50 donors in the age range specified. However, once a modified protocol has been accepted, all future surveys should use the same protocol to assure the comparability of results.

WHO Global Survey of Human Milk for POPs

Using the revised guidelines, WHO in collaboration with UNEP launched its global survey of human milk in September 2005. The new guidelines called for the local analysis of individual samples for the basic POPs, which may be determined using a simple gas chromatograph with an electron capture detector. To promote the analytical quality assurance of national laboratories, the WHO sponsored a proficiency testing scheme for pesticide POPs and marker PCBs. The exercise was organized by the WHO Reference Laboratory for POPs at the State Laboratory for Chemical and Veterinary Analysis (CVUA), Freiburg, Germany which also conducts the analysis of all pooled samples for the survey. Preliminary results were obtained from 13 countries, including laboratories in both developed and developing countries. While the results are confidential, they suggest that many laboratories have difficulty in the detection and reliable determination of many POPs of interest. This signals the need for more stringent quality assurance measures and, in some cases, capacity building before acceptable results can be achieved. For such laboratories, it has been recommended that individual samples be stored frozen until analytical proficiency can be demonstrated.

With the support of the Global Environment Facility, developing countries were invited to participate in the WHO Global Survey of Human Milk for POPs. Samples were collected in accordance with national study protocols, which were developed based on the WHO guidelines. Currently a total of 25 countries are participating in the survey. Pooled samples were analyzed at the CVUA in Germany. As of 30 November 2009, results were available from seven countries. Figure 54.1 presents the results of the WHO-coordinated international surveys for PCDDs and PCDFs in human milk, in which individual congeners are reported using WHO toxic equivalence factors (WHO TEFs) [13]. While only indicative, the data have generally shown a downward trend of these POPs in human milk.
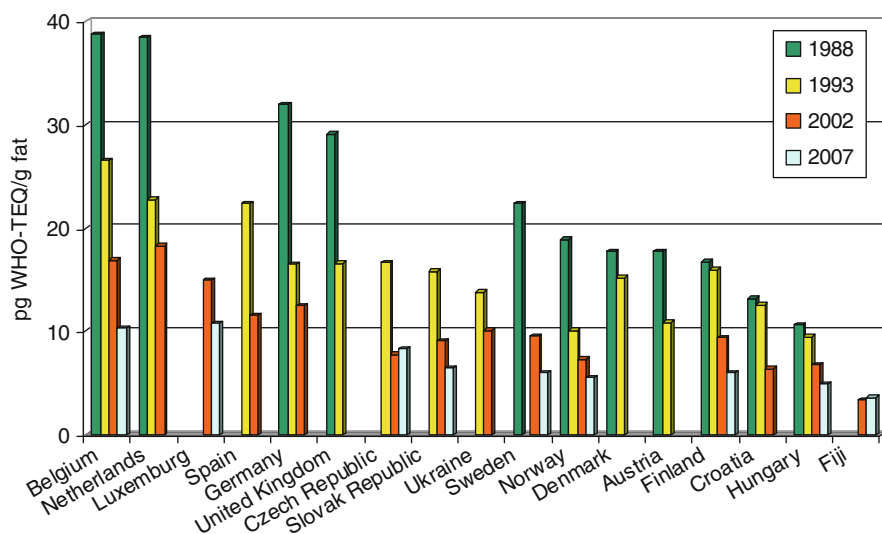
Fig. 54.1 Temporal trends of PCDDs/PCDFs in human milk in various countries (1988–2007)

Conclusions and Future Directions

Because of health, food safety, and environmental concerns raised by the presence of POPs in human milk, primary preventive measures to eliminate or reduce the introduction of POPs in the environment are the most effective long-term way to control exposure to these chemicals. Responsible authorities should examine their food monitoring and control programs to assess whether greater attention should be paid to foodstuffs potentially high in POPs. In this regard, total diet studies can be a cost-effective tool to examine current exposure levels and monitor trends over time.

This data should be augmented by biomonitoring of representative pooled human milk samples, which represent the total diet of infants for the first 6 months of life. Such data should correlate to total diet exposure estimates of POPs taking into account the respective half-lives of the various POPs. Such data are also essential for assessing prenatal exposure and for future epidemiological studies concerning developmental and other potential adverse effects. Finally, in the context of the Stockholm Convention, baseline and periodic surveys conducted every 4–5 years are essential for monitoring the effectiveness of the convention and should be reported to the Stockholm Secretariat.

It is also important that national governments identify geographical areas with potential for increased infant exposure either through maternal occupational exposure or ingestion of highly contaminated foodstuffs. In this regard, biomonitoring of human milk may be used as a screening tool to identify populations at risk.

Finally, any risk management decision should take into account the well-established benefits of breastfeeding as well as related socioeconomic factors. Except in the most extreme cases, mothers can and should be reassured that the significant benefits of breastfeeding outweigh any potential risk and that breast milk is by far the best food to give their babies.

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