National Dioxins Program

Technical Report No. 12
Human Health Risk Assessment of
Dioxins in Australia

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Foreword

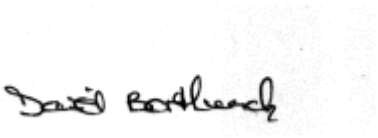
When the Australian Government established the four year National Dioxins Program in 2001, our knowledge about the incidence of dioxins in Australia was very limited.

The aim of the program was to improve this knowledge base so that governments were in a better position to consider appropriate management actions. Starting in mid 2001, a range of studies were undertaken which involved measuring emissions from sources such as bushfires, as well as dioxin levels in the environment, food and population. The findings of these studies were used to shed light on the risk dioxins pose to our health and the environment.

This work has been completed and the findings are now presented in a series of twelve technical reports.

Having good information is essential if there is to be timely and effective action by governments; these studies are a start. Our next step is to foster informed debate on how we should tackle dioxins in Australia, as this is an obligation under the Stockholm Convention on Persistent Organic Pollutants. The Department of the Environment and Heritage will be working closely with other Australian Government, State and Territory agencies to take this step.

Ultimately, the effective management of dioxins will be the shared responsibility of all government jurisdictions with the support of the community and industry.



David Borthwick
Secretary
Department of the Environment and Heritage

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- the project teams from the CSIRO, the National Research Centre for Environmental Toxicology and Pacific Air & Environment who undertook the studies assessing the levels of dioxins in the environment, the population and from emission sources, the overseas experts who provided advice to these organisations, and the many individuals across Australia who collected the samples in the field
- the Department of Agriculture, Fisheries and Forestry, who assessed the levels of dioxins in agricultural commodities
- Food Standards Australia New Zealand and the Department of Health and Ageing and who assessed the levels of dioxins in foods and assessed the health effects of dioxins
- officers of the Chemical Assessment Section in DEH who assessed the ecological effects of dioxins
- members of the National Dioxins Project Team which included representatives from the State and Territory environment protection agencies, the Australian Health Ministers Conference and the Primary Industries Ministers Council
- members of the National Dioxins Consultative Group which included representatives from industry and agricultural sectors, environment and public health groups and research institutions.

Project Team

This health risk assessment was conducted by the Office of Chemical Safety (OCS) within the TGA Group of Regulators, part of the Australian Department of Health and Ageing (DoHA). Preparation of the report was coordinated by Dr Les Davies. Chapter authors were Drs Les Davies, Graham Harvey, Kaylene Raynes, Michael Dornbusch and Deborah Willcocks. Ms Joanne Cuthbert was responsible for collation and indexing of the manuscript.

In-house review and editorial comments were provided by Dr Utz Mueller and Mr Mark Jenner of the OCS and Mr Jack Dempsey of the Population Health Division of DoHA. Comments and suggestions have been received from several State and Territory Government agencies, industry and community groups. External peer reviewers were Professor Helen Hakansson, Environmental Health Risk Assessment Unit, Institute of Environmental Medicine, Karolinska Institute, Stockholm, Sweden, and Steve Hrudey, Professor of Environmental Health Sciences, Department of Public Health Sciences, University of Alberta, Edmonton, Canada.

Preface

Dioxins are a group of fat-soluble chemicals which are highly persistent in the environment and which can accumulate in the body fat of animals. If exposure to dioxins is sufficiently extensive, they can cause a range of toxic effects in animals and humans, including skin lesions, reproductive disorders and cancer.

In Australia, relevant Australian Government agencies have been undertaking monitoring programs to determine whether dioxins and related compounds are present in humans, the environment, food, and in certain agricultural commodities. As part of these monitoring programs and their reporting, the Department of Environment and Heritage (DEH) and the Department of Agriculture, Fisheries and Forestry (DAFF) sought advice from the Department of Health and Ageing (DoHA) on establishing a tolerable intake for dioxins and related compounds.

Largely based on the deliberations of (1) the consultation between technical experts representing the World Health Organization European Centre for Environmental Health (WHO-ECEH) and the International Programme on Chemical Safety (IPCS) in May 1998; (2) the meeting of the European Community Scientific Committee on Food (EC-SCF) on the risk assessment of dioxins and dioxin-like polychlorinated biphenyls (PCBs) in food, in May 2001; and (3) the Joint Food and Agriculture Organization of the United Nations (FAO)/WHO Expert Committee on Food Additives (JECFA) evaluation of dioxins, at its 57th meeting in June 2001, Australia established a Tolerable Monthly Intake (TMI) for dioxins of 70 pg TEQ/kg bodyweight from all sources combined. This tolerable intake is equal to that set by JECFA, and includes polychlorinated dioxins, polychlorinated furans and dioxin-like PCBs, as specified under the WHO 1998 TEF scheme. This TMI was endorsed by the National Health and Medical Research Council (NHMRC) on 24th October 2002, as outlined in the booklet, Dioxins: Recommendation for a Tolerable Monthly Intake for Australians, published jointly by the NHMRC and the Therapeutic Goods Administration (TGA)[1], organisations within DoHA.

The tolerable intake value is a human health standard based on the toxicological effects of dioxins and related compounds in animals and humans, following known exposures. The tolerable intake value is not a measure of human exposure to dioxins and it is not an action level for dioxins in food or the environment. Rather, it is an intake standard, against which estimated human exposure from all sources combined should be compared.

This risk assessment document has estimated exposure of the Australian population to dioxins, based on levels measured in monitoring programs conducted by the DEH (air, soil, water sediments etc.), by DAFF (agricultural commodities) and Food Standards Australia New Zealand (food). Intake estimates have been compared with the tolerable

[1] Available through Government Info Bookshops. To purchase a hard copy, please contact AusInfo on their toll-free number 132 447, or via www.ausinfo.gov.au/general/gen_hottobuy.htm. The report is accessible electronically through the NHMRC homepage at http://www.nhmrc.gov.au.

monthly intake value in order to make an assessment as to whether there are likely to be any health risks to different segments of the Australian population. Furthermore, intake estimates and body burdens of dioxin-like compounds have been compared with equivalent values estimated in other countries, to see whether the population is more or less exposed than populations in other parts of the world.

It should be noted that occupational exposures are not specifically considered in this public health risk assessment, other than the inclusion of some relatively general comments about intakes from some specific exposure sources.

Executive Summary

This report has been prepared by the Australian Department of Health and Ageing (DoHA) as an appraisal of the health risks posed to the Australian population by polychlorinated dibenzo-p-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs) and the dioxin-like polychlorinated biphenyls (PCBs), known collectively as 'dioxins' or 'dioxin-like compounds'.

The Department of Environment and Heritage collected information on the levels of dioxin-like compounds in various environmental media in Australia, including air, soil, and sediments. It also collected data on concentrations of dioxins in the blood serum of different segments of the population. In related projects, Food Standards Australia New Zealand (FSANZ) measured the levels of these compounds in various foods and estimated dietary intakes in different population subgroups, the Australian Department of Health and Ageing (DoHA) measured dioxin-like compounds in breast milk, and the Australian Department of Agriculture, Fisheries and Forestry (DAFF) reported on levels in various agricultural commodities including meat, milk and fish. These, together with other data collected by the Department of Environment and Heritage, have been used in this population exposure assessment and health risk appraisal, conducted by the Office of Chemical Safety (OCS) within DoHA. This report also presents a summary overview of our current understanding of the health risks associated with exposure to dioxin-like compounds, and reviews health guidelines that have been established by Australia and other jurisdictions.

From a consideration of the Australian exposure data, and a review of the published scientific literature on dioxin-like compounds, the following observations and conclusions can be made.

Overview of exposure estimates for the Australian population

For the general population, over 95% of exposure to dioxin-like compounds is through the diet, with foods of animal origin such as meat, dairy products and fish being the main sources. Generally, Australian foods have levels of PCDD/Fs and PCBs that are similar to those reported in New Zealand and lower than those reported from other areas of the world. Thus, based on a dietary study for dioxin-like compounds conducted by FSANZ (FSANZ, 2004), the level of dietary intake of these chemicals for the Australian population appears to be lower than exposures reported for any other country where exposure studies have been undertaken. For all Australians aged 2 years or older, the mean upper bound estimated monthly intake of dioxins is 16 pg TEQ/kg bw/month, where the toxic equivalents (TEQ) are based on the toxic equivalent factors (TEFs) developed in 1997 for dioxin-like compounds by the World Health Organization (WHO) (Van den Berg et al, 1998). Monthly mean intakes per unit bodyweight are lower in females than males for the same age, and decline with age in both sexes, the most rapid decline apparently occurring after puberty. Unborn children are exposed to dioxin-like compounds *in utero*, and nursing infants are exposed to these contaminants present in breast milk. Because of their high dietary intake relative to bodyweight, highest mean intakes for all age groups occur in infants and toddlers.

Similarly, the results of the study of dioxin-like compounds present in serum (Harden et al, 2004) show that measured levels in the tissues of Australians are at the low end of the scale of levels reported internationally. The mean serum concentration across the population was determined as 11 ng WHO-TEQ/kg on a lipid-adjusted basis (range: 4.6-28 ng WHO-TEQ/kg lipid). From these serum data, body burdens and average lifetime daily exposures (ALDE) were calculated. The mean ALDE for all data was estimated as 1.32 pg WHO-TEQ/kg bw/day (minimum of 0.13 pg WH)-TEQ/kg bw/day for the population aged <16 years; maximum of 3.0 pg WHO-TEQ/kg bw/day for the population aged 60 years). The higher ALDE estimate compared to the estimated dietary intake is because the ALDE includes historical exposures, which are likely to have been higher than current exposures, as well as intakes from non-dietary exposure pathways.

A study (Müller et al, 2003a) measured concentrations of PCDD/Fs and dioxin-like PCBs in milk of Australian nursing mothers collected over late 2001 to 2003. Overall mean TEQ levels (upper bound) were 9.0 ng WHO-TEQ/kg of milk fat. The levels of dioxin-like chemicals in the breast milk of Australian women are similar across all regions of Australia but low by international standards. This reflects the conclusions about body burdens of dioxin-like compounds made from the serum level data. In Australia, concentrations of dioxin-like compounds in breast milk have fallen significantly (about 45%) within the past decade, an observation consistently noted in monitoring programs from a large number of other countries. This reflects a world-wide trend over recent decades of declining levels of dioxin-like compounds in the environment and in human tissues.

The generation of dioxins results predominantly from combustion processes and atmospheric transport represents the primary route for transport of dioxins into the environment.

Intake of dioxins by dermal absorption from, or ingestion of soil and by inhalation from air are only minor contributors to exposure of the general population to dioxins. Cigarette smokers are likely to have somewhat higher intakes of dioxins than non-smokers.

It has been estimated that bushfires may contribute at least 20-30% of the total release of dioxin-like compounds to the Australian environment. Bushfires, grass and scrub fires have been part of the Australian landscape for aeons. Thus, humans and the environment have been exposed to low levels of dioxin-like compounds and human metabolism has been coping with dioxin compounds for thousands of years.

The Australian National Pollutant Inventory (NPI) 2003 estimates the relative contribution of various sources to total dioxins emissions in Australia. Comparatively low levels of PCDD/F emissions have been reported relative to most other industrialized countries. It is possible that the sources with the largest estimated total emissions to the environment are not the major contributors of PCDD/F contamination of food (the largest contributor to intake of dioxin-like chemicals for the general population).

Nevertheless, protection of land and aquatic environments used for food production is very important, in order to reduce general population intakes of dioxin-like compounds.

Higher exposures, such as may occur in the workplace, have been restricted to smaller groups of people. Historical, occupational exposures to PCDD/Fs have largely been restricted to individuals involved in the handling and use of the pesticides such as pentachlorophenol (PCP) and 2,4,5-trichlorophenoxyacetic acid (2,4,5-T). These chemicals are no longer approved for use in Australia.

Toxic effects of dioxin-like compounds

The most widely studied of all the dioxin-like compounds is 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (2,3,7,8-TCDD, or TCDD). It has been shown to affect a wide range of organ systems in many animal species and can induce a wide range of adverse biological responses. The binding of TCDD to the so-called aryl hydrocarbon (*Ah*) receptor in cells appears to be the first step in a series of events that manifest themselves in biological responses, including changes at the biochemical, cellular and tissue level. Binding to the *Ah* receptor occurs in laboratory animals and humans. This being the case, the results of studies in animal have been used to predict health effects that may not yet have been demonstrated in human studies. Notwithstanding this common mechanism of action, it is noted that there are considerable species and strain differences in the acute toxicity of dioxins.

Adverse effects reported in animals following exposure to dioxins include immunotoxicity, endometriosis in Rhesus monkeys, developmental, behavioural effects in offspring of treated Rhesus monkeys, and developmental effects in rats (including reproductive toxicity in males and urogenital malformations in females).

Available epidemiological data indicate that dioxin-like compounds produce a variety of biochemical responses in humans, some of which occur at relatively low exposure levels. Induction of hepatic enzymes, changes in hormone levels and reduced glucose tolerance are examples of subtle changes that may occur at comparatively low exposures. However, these subtle effects are of unknown clinical significance, and may or may not indicate a toxic response or potential for a toxic response.

In humans, the most widely recognized and consistently observed effect following high dose exposure to TCDD is chloracne. The condition can disappear after termination of exposure or can persist for many years. Other effects on the skin include hyperpigmentation and hirsutism. TCDD can cause long-term alteration in glucose metabolism and there is some evidence of a weak correlation between the incidence of diabetes and occupational or accidental exposure to dioxins; however, background exposure to dioxins is not a significant risk factor for diabetes. Effects on the respiratory system, manifested mainly as upper respiratory tract irritation, have resulted from acute exposure to high concentrations of TCDD. Other irritant effects resulting from acute exposure include conjunctivitis with red and irritated eyes, and inflamed eyelids (blepharitis). TCDD exposure has been suggested to cause slight changes in thyroid function, but clinical illness associated with immune system disorders does not appear to have been associated with TCDD in any cohort studied. There is some suggestive

evidence of toxicity to the cardiovascular system. Some studies report that higher exposure to dioxins is associated with elevated blood lipids (hyperlipidemia) and increased frequency of ischaemic heart disease (damage due to poor blood circulation), valvular heart disease, and degeneration of the retina of the eye (retinopathy).

While dioxins can increase the incidence and severity of endometriosis in monkeys, epidemiology studies and small, hospital-based case-control studies have failed to provide compelling evidence for or against an association of environmental contaminants and endometriosis in humans. Results from human studies of developmental effects and exposure to TCDD have generally been inconclusive. Studies of the risk of spontaneous abortion involving occupational and environmental herbicide exposure have generally not found increased risks. Several studies indicate that paternal exposure to dioxins may be associated with the birth of more girls than boys; however, the median concentration of dioxin in fathers in one such study was about 20 times the estimated average concentration of TCDD currently found in human beings in industrialised countries.

The potential neurotoxicity of PCBs was first recognized when people in Japan (1968) and Taiwan (1978-1979) consumed rice oil highly contaminated with PCBs and PCDFs; offspring had poorer cognitive functioning as well as other behavioural problems. In the recent Dutch PCB/Dioxin Study, assessment of school-age children suggested that subtle cognitive and motor developmental delays arising from prenatal PCB and dioxin exposure were seen when parental and home characteristics were less optimal but such effects were not measurable in children raised in more optimal environments. A number of literature studies indicate that the beneficial effects of breast feeding on infant development far outweigh any possible negative effects arising from the somewhat higher intake of dioxins in breast-fed as cf. formula-fed infants.

Of the range of non-cancer health effects evaluated in exposed adult populations, some appear to be transient and not observed when exposure ceased, whereas other effects persist for some years. Overall, epidemiology studies on populations exposed occupationally or environmentally to TCDD have not demonstrated any significantly increased all-cause or non-cancer mortality.

Experimental studies demonstrate that TCDD is carcinogenic in all species and strains of laboratory animals tested. It has been characterised as a multi-site carcinogen. However, short-term studies have shown a lack of direct DNA-damaging effects, indicating that TCDD is not an initiator of carcinogenesis, but is a potent tumour promoter. Although the mechanisms of carcinogenicity are not fully known, the ability of TCDD to enhance proliferation and inhibit apoptotic processes in focal hepatic lesions supports an indirect mechanism of carcinogenicity. Nevertheless, in the whole-of-life rat cancer study which has driven cancer risk estimates made by a number of regulatory agencies, it should be borne in mind that there were also significant reductions in the incidence of a number of cancers including spontaneous benign tumours of the uterus, benign and malignant mammary tumours and pituitary adenocarcinomas (in female rats), and in adrenal gland phaeochromocytomas and pancreatic adenomas (in male rats). Although the mechanisms for such reductions in

tumour incidence are not well understood, reductions in body weight as a result of TCDD exposure and disruption of endocrine homeostasis are two possible explanations.

Epidemiological evidence from the most highly exposed occupational cohorts studied produces the strongest evidence in humans of an increased cancer risk from exposure to dioxins, when the data are considered for all cancers combined. There is weaker evidence of an increased cancer risk when the data for cancers at particular sites are considered. From the occupational studies, and an understanding of biological plausibility as shown by animal studies, the International Agency for Research on Cancer (IARC) has concluded that TCDD is carcinogenic to humans. It is difficult to find epidemiological data that have sufficient dose-response information to provide reliable risk estimates for cancer in exposed human populations. Modelling is complicated by uncertainties in extrapolating current body burdens of dioxins to past occupational exposure and by the choice of the dose-response model to fit the data. In specific cohorts, excess risks were observed for reproductive cancers (female breast, endometrium, male breast, testis) but, overall, the pattern is inconsistent. There is a small increase in relative risk for all cancer combined in the most highly exposed and longer-latency sub-cohorts. The possibility that this small increase in relative risk is due to confounding factors cannot be excluded.

A number of key studies documenting a variety of health effects of TCDD in laboratory animals have been used to establish human health guidelines for exposure to dioxin-like compounds. However, most data on the health effects of PCDD/Fs have been obtained using the most toxic congener, 2,3,7,8-TCDD. Despite only having limited data on the toxic effects of other dioxin-like PCDD/Fs and PCBs, it may be inferred that biochemical, cellular and tissue-level effects that are elicited by exposure to TCDD are also induced by other chemicals that have a similar structure and that bind to the *Ah* receptor. Thus there is general agreement that the use of Toxic Equivalence Factors (TEFs) to estimate the potency of dioxin-like compounds (relative to TCDD) is a useful procedure, applying the concept of additivity for the PCDDs, PCDFs and dioxin-like PCBs to provide total Toxic Equivalence Quotient (TEQ) estimates. The TEQ approach involves assessing the comparative effects of individual PCDD/F and PCB congeners on various biological end-points, and deriving TEFs based on the upper range of potency data for these effects. The concept of toxic equivalents in evaluating mixtures of PCDD/Fs and dioxin-like PCBs has been fundamental to the conduct of health risk assessments. Estimates of population exposures suggest that a significant proportion of the total intake of dioxin-like compounds (measured as TEQs) is from congeners other than 2,3,7,8-TCDD.

Tolerable Monthly Intake

Based on an analysis of various international hazard assessments and relevant literature published between 1999 and late 2003, it is considered that the Australian Tolerable Monthly Intake (TMI) of 70 pg/kg bw/month as recommended by the NHMRC and the TGA's Office of Chemical Safety in 2002 should be adequately protective of the general population with respect to effects of dioxin-like compounds. This value is the same as that set by the WHO/FAO Joint Expert Committee on Food Additives and Contaminants (JECFA) in 2002.

Health Risk Assessment

Intakes of dioxins from the various sources can be compared with the Tolerable Monthly Intake (TMI) health intake value established by the TGA and NHMRC (NHMRC/TGA, 2002). For the majority of the population, their average intake of dietary dioxins (per unit bodyweight) was significantly lower than this value, being between 10-54% of the TMI, somewhat higher in infants and toddlers, based on samples taken in 2000 and food consumption data from 1995. Estimates of intake based on serum concentrations suggests that during approximately the last 25 years the average intake was probably close to 1.3 pg WHO-TEQ/kg bw/day. On international comparisons with intakes estimated in other developed countries, these figures are not a significant cause of concern. Nevertheless, on the basis of scientific uncertainties in the establishment of the tolerable health intake value, sensible policy would dictate continuing efforts to reduce, where possible, the emissions of dioxin-like compounds to the environment.

A number of national agencies have endeavoured to provide quantitative estimates of cancer risk, based on low-dose extrapolation from both animal and human data. In view of the ongoing debate about the existence of a threshold level below which dioxins will not increase cancer risk, about the potency of the various dioxins, furans and PCBs in causing cancer, and the variability in various quantitative risk estimates, this assessment has not endeavoured to make a quantitative risk conclusion. The estimated intakes are below the TMI, which provides an adequate margin of safety for any possible increased risk of cancer. Furthermore, it is noted that the body burden of dioxins in the general population is significantly lower than the body burdens of the most highly exposed industrial cohorts where there is evidence of some increased cancer risk.

On the basis of the findings of this risk appraisal, the Australian population can be confident that current background exposures to dioxin-like compounds are generally low compared with other similar countries. Because of the ubiquitous presence of various dioxin-like compounds in human tissues, as well as in the milk of mothers worldwide, infants can be exposed to these compounds both prenatally and during breast feeding. A number of studies indicate that any neurological deficits associated with exposure to dioxins and other organochlorine contaminants appears to be associated with *in utero* exposure rather than breastfeeding. This finding adds to the reasons for taking a prudent and precautionary approach with respect to risk management steps to reduce population exposures to these chemicals. Nevertheless, all the available scientific and medical studies indicate that any subtle effects which might result from early exposure to extra dioxin-like compounds in breast milk are quickly outweighed by the multiplicity of beneficial effects from breast feeding.

This report, whilst not an occupational health and safety risk assessment, also briefly considers ‘special’ populations who may have be exposed to dioxin-like compounds above background levels eg. workers who were occupationally exposed to PCDD/F from the use of PCP in the timber industry and dioxin-contaminated 2,4,5-T in agricultural woody weed control. In view of the relatively small number of occupationally exposed cases known or studied in Australia, as well as the lack of data

on blood levels of TCDD/Fs and PCBs, it has not been possible to draw clear conclusions about health effects of such exposures.

Recommendations relating to risk management

Notwithstanding the observation that the Australian population is exposed to low levels of dioxins, it would be prudent, in the light of the environmental persistence and long biological half-lives for many of the congeners of these dioxin-like compounds, to take all reasonable steps to further reduce human exposure, by reducing and if possible eliminating, significant sources of PCDD/PCDF generation.

Although hundreds of epidemiology studies have looked at the human health effects of dioxin exposures, neither the full extent of dioxin contamination nor the magnitude of the associated human health risks are clearly understood (eg. Institute of Medicine; Schmidt 2004). However, in the light of increasing scientific information about the toxicity of dioxin-like compounds and data on body burdens present in the Australian population, the following recommendations with respect to reducing any potential risks to human health are made:

- A cautious and conservative approach should be adopted with respect to dioxin-like compounds. Thus, programs to reduce the release of dioxin-like compounds into the environment need to be ongoing.
- Ways to block the cycling of dioxins through the food supply need to be identified. Reducing the levels of dioxins in feed given to livestock, poultry and aquaculture fish will help to reduce the levels of dioxins in the food supply. This may be achieved by reducing the amount of animal fat used as a growth enhancer in stockfeed, and sourcing fish-based aquaculture feed (eg. pilchards, sardines) from non-polluted environments.
- Since foods high in animal fats are a source of exposure to these chemicals, current efforts to promote lower saturated fat intake in the population should continue[2].
- Current programs to discourage cigarette smoking should be maintained. In particular, any measures which reduce dioxin intake in young women are likely to help reduce their body burden of dioxins and ultimately, the amount of dioxins which may be transferred to their offspring, both prenatally (*via* trans-placental transfer) and postnatally *via* breast milk[3].
- The population burden of dioxin-like compounds should be monitored periodically, to see whether risk reduction strategies are effective.

Note that these recommendations are preliminary risk management recommendations made by the Office of Chemical Safety and they will be further developed following discussions with other government agencies and consideration of public input.

[2] Note that the relative specific heath risks of exposure to dioxins are low compared to those arising from a high intake of saturated fats

[3] As for dietary intake of saturated fats, the specific health risks associated with dioxin exposure are low compared to the known adverse effects of smoking

Contents

Figures

Tables

1. Introduction

Dioxins and related compounds are amongst the most studied of all chemicals. This interest arises because of the range of biological effects that they have been reported to cause in animal studies and in heavily exposed human cohorts, their potential to increase the incidence of cancers in people occupationally exposed to high levels of dioxins, their long half-lives in the environment and the human body, and the widespread and ubiquitous exposure of animals and humans to this class of compounds. Since dioxins are fat soluble, chemically stable and poorly metabolised, they can concentrate in body fat and build up under conditions of long-term exposure, both in animals and humans, and accumulate as they move through the food chain. These properties mean that even low levels of dioxins in the environment may eventually pose risks to animals and humans.

Although the exact impact of dioxins on people's health is not yet known, there are currently no clear indications that dioxins are causing increased disease in the general population.

International studies have concluded that around 95% of human exposure occurs through the consumption of food. People may also have some limited exposure through other routes such as breathing in air contaminated by dioxins in smoke (from bushfires, domestic wood heaters and cigarettes), factory or incinerator emissions, motor vehicle exhaust fumes, or from uncontrolled hazardous waste sites containing dioxins (eg. Furst et al 1992a; Liem et al 2000; US EPA 2000).

In Australia, available data suggest the levels of dioxins in the environment are generally low. In 1998 the Australian Government Department of Environment and Heritage produced an inventory of dioxins emissions to air. However, since only limited Australian data were available, this inventory had to use information from other countries to estimate dioxin emissions. In order to better understand how dioxins may be affecting human health and the environment in Australia, the Australian Government announced, in the 2001-02 Australian Government Budget, the decision to fund the conduct of a National Dioxins Program (NDP). It was agreed that the information gathered by the NDP would be used to estimate the extent to which people are exposed to dioxins, and determine the best actions Australia could take to reduce population exposure to dioxins.

The NDP has three phases. Phase One involved surveys of dioxin levels in the environment (air, soil, sediments, fauna) and people (plasma levels in people from various age groups and regions, and breast milk levels in first-time mothers) throughout Australia, in order to provide information to be used in the preparation of a new inventory of dioxins in Australia. Studies also assessed the contribution of bushfires, motor vehicles and domestic wood heaters to levels of dioxins in air. A survey of dioxin levels in foods was conducted by Food Standards Australia New Zealand (FSANZ). Phase Two used the findings of Phase One to provide the basis for assessing the potential risks of dioxins to the environment, as well as the potential risks for human health from exposure to dioxins either directly from the environment or from dioxin-contaminated food. Phase Three will use the Phase-Two risk assessments to develop

national management strategies to reduce, and where feasible, to eliminate the release of dioxins in Australia.

This document contains the results and conclusions of the Phase-Two human health risk assessment. It is structured into four main parts. The first part provides an overview of the known and possible effects of dioxins in animals and humans and considers a suitable intake level at which significant health effects are not expected to occur. The second part estimates likely dioxin intakes for the majority of the Australian population. The third part compares the estimated intakes with the health-based tolerable intake level and provides comment on likely health risks for the population. The final part of the report makes some suggestions for risk management measures aimed at reducing population exposures to dioxins and related compounds.

1.1 Overview

Much of the following overview text is taken from 'Dioxins: Recommendation for a Tolerable Monthly Intake for Australians' (NHMRC/TGA, 2002) and the references cited therein. Additional references used here are indicated. A number of published review volumes (eg. Schecter & Gasiewicz, 2003) provide useful reference information on the chemistry, toxicology and health effects of dioxins.

1.1.1 What are 'dioxins'?

The term 'dioxins' is used to describe a group of environmentally persistent halogenated aromatic hydrocarbon chemicals that includes polychlorinated dibenzodioxins (PCDDs), polychlorinated dibenzofurans (PCDFs), polybrominated dibenzodioxins (PBDDs), polybrominated dibenzofurans (PBDFs) and polychlorinated biphenyls (PCBs). The chlorinated compounds predominate and it is these which are the focus of this report. PCDDs, PBDDs, PBDFs and PCDFs are not manufactured intentionally but are by-products of combustion. They are formed naturally by volcanoes and forest fires, as well as by industrial processes such as waste incineration and the synthesis of certain chemicals. PCBs, on the other hand, were manufactured for approximately 50 years for use as components of insulating fluids in transformers and other electrical equipment.

The potential toxicity of dioxins began to be recognised over 40 years ago. Concern over the potential adverse effects of dioxins has been amplified by evidence that they are resistant to metabolism and tend to remain in the body fat of animals and humans for a long time. The different structurally related chemicals (referred to as congeners) that make up the dioxins have half-lives that vary from 3.7 years for the least persistent type to 50 years for the most persistent, with an average half-life of approximately 7 years.

1.1.2 Chemistry and physicochemical properties of PCDDs, PCDFs and PCBs

The PCDDs and PCDFs are chlorinated tricyclic aromatic hydrocarbons, made up of two benzene rings joined by either two oxygen atoms at adjacent carbons on each of the benzene rings (PCDDs) or by one oxygen atom and one carbon-carbon bond (PCDFs); their basic structures are given in Figure 1-1.

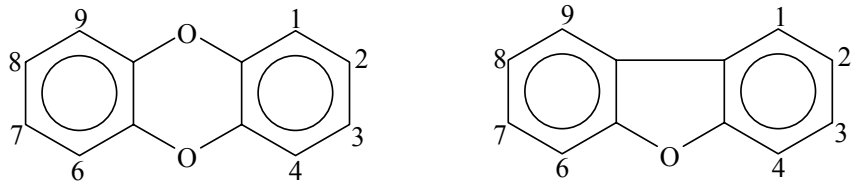

Figure 1-1 Structures of dibenzo-p-dioxin and dibenzofuran

Both groups of chemicals may have up to eight chlorine atoms attached at carbon atoms 1 to 4 and 6 to 9. Each individual compound resulting from this is referred to as a congener. Each specific congener is distinguished by the number and position of chlorine atoms around the aromatic nuclei. In total, there are 75 possible PCDD congeners and 135 possible PCDF congeners; groups of congeners with the same number of chlorine atoms are known as homologues. The number of congeners in each homologue group is shown in Table 1-1 (Müller et al, 2003a; Gilpin et al, 2003). The most widely studied of the PCDDs and PCDFs is 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). This congener is often generically referred to as 'dioxin', and represents the reference compound for this class of chemicals.

Table 1-1 Homologues and congeners of PCDDs and PCDFs

Homologue name	Abbreviation	No. of possible congeners	No. congeners with Cls at 2, 3, 7 & 8 positions
Monochlorodibenzo-*p*-dioxin	MCDD	2	0
Dichlorodibenzo-*p*-dioxin	DiCDD	10	0
Trichlorodibenzo-*p*-dioxin	TrCDD	14	0
Tetrachlorodibenzo-*p*-dioxin	TCDD	22	1
Pentachlorodibenzo-*p*-dioxin	PeCDD	14	1
Hexachlorodibenzo-*p*-dioxin	HxCDD	10	3
Heptachlorodibenzo-*p*-dioxin	HpCDD	2	1
Octachlorodibenzo-*p*-dioxin	OCDD	1	1
Monochlorodibenzofuran	MCDF	4	0
Dichlorodibenzofuran	DiCDF	16	0
Trichlorodibenzofuran	TrCDF	28	0
Tetrachlorodibenzofuran	TCDF	38	1
Pentachlorodibenzofuran	PeCDF	28	2
Hexachlorodibenzofuran	HxCDF	16	4
Heptachlorodibenzofuran	HpCDF	4	2
Octachlorodibenzofuran	OCDF	1	1

Congeners containing one, two or three chlorine atoms are thought to be of no toxicological significance. However, 17 congeners with chlorine atoms substituted in the 2, 3, 7 and 8 positions (i.e. in the lateral positions of the aromatic rings) are thought to pose a health and environmental risk. Increasing substitution from four to eight

chlorine atoms generally results in a marked decrease in their ability to cause biological effects of concern.

The PCBs are structurally similar to the PCDD/PCDFs and include 209 congeners, from the monochloro congener through to the fully chlorinated decachloro congener; the basic aromatic nucleus is shown in Figure 1-2. The distribution of PCB congeners arising from attachment of chlorine atoms to this nucleus is given in Table 1-2.

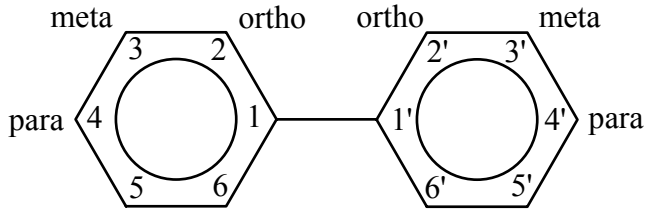

Figure 1-2 Structure of biphenyl

Table 1-2 Distribution of PCB congeners

No. of Cl substituents	1	2	3	4	5	6	7	8	9	10
No. of congeners	3	12	24	42	46	42	24	12	3	1

Like the PCDD/PCDFs, the biological effects of the PCBs are very dependent both on the degree of chlorination and on the position of the chlorine atoms around the aromatic nuclei (i.e. whether they are *ortho*-, *meta*- or *para*- to the phenyl-phenyl bridge at carbon-1). Certain PCBs, the non-ortho and mono-*ortho* congeners, can adopt a coplanar conformation that is structurally similar to the PCDD/PCDFs and appear to elicit dioxin-like responses through a similar mechanism of action. The non-*ortho* PCBs lack a chlorine substituent in any of the 2, 2', 6, or 6' positions while the mono-*ortho* PCBs have a single chlorine atom in any one of the 2, 2', 6, or 6' positions (see Table 1-3).

Table 1-3 Names of the 12 dioxin-like PCBs

PCB Name	**PCB No.**
Non-*ortho* PCBs	
3,3',4,4'-Tetrachlorobiphenyl	PCB 77
3,4,4',5-Tetrachlorobiphenyl	PCB 81
3,3',4,4',5-Pentachlorobiphenyl	PCB 126
3,3',4,4',5,5'-Hexachlorobiphenyl	PCB 169
Mono-*ortho* PCBs	
2,3,3',4,4'-Pentachlorobiphenyl	PCB 105
2,3,4,4',5-Pentachlorobiphenyl	PCB 114
2,3',4,4',5-Pentachlorobiphenyl	PCB 118
2,3',4,4',5'-Pentachlorobiphenyl	PCB 123
2,3,3',4,4',5-Hexachlorobiphenyl	PCB 156

2,3,3',4,4',5'-Hexachlorobiphenyl	PCB 157
2,3',4,4',5,5'-Hexachlorobiphenyl	PCB 167
2,3,3',4,4',5,5'-Heptachlorobiphenyl	PCB 189

PCDDs, PCDFs and dioxin-like PCBs are commonly referred to as 'dioxin-like compounds'.

In general, dioxin-like compounds have very low water solubility, high octanol-water partition coefficients, low vapour pressure and adsorb strongly to particles and surfaces (high K_{OC}) and are resistant to chemical degradation under normal environmental conditions. Thus, they are persistent in the environment and their high fat solubility results in their bioconcentration into biota and biomagnification up the food chain. Almost all 210 individual PCDD and PCDF congeners have been identified in emissions from thermal and industrial processes and consequently they are found as mixtures in environmental matrices such as soil, sediment, air, plants and lower animals, although their low aqueous solubility means they can hardly be detected in water and are largely immobile in soils.

The 'Illustrated Handbook of Physical Properties and Environmental Fate for Organic Chemicals', volumes 1 and 2 (Mackay et al, 1992a, 1992b) are useful references which provide data on the physical and chemical properties of dioxins and dioxin-like compounds, including water solubility, vapour pressure, Henry's Law constant, octanol-water partition coefficient and bio-accumulation factor. They include excellent illustrative examples about the partitioning behaviour of these contaminants in the environment.

1.1.3 Toxic equivalency factors

When found in the environment, biological tissues and industrial sources, dioxins are usually present as complex mixtures; this complicates hazard and risk assessment because the different congeners vary significantly in their toxicity. However, the potency of different dioxins can be ranked relative to TCDD, the most toxic member of the dioxin class. These rankings are known as toxic equivalency factors (TEFs). To be included in the TEF scheme, a compound must be structurally related to PCDDs and PCDFs, bind to the cellular aryl hydrocarbon (*Ah*) receptor, elicit *Ah* receptor-mediated biochemical and toxic responses, must be persistent, and accumulate in the food chain (WHO, 1998).

Several schemes for assigning TEFs to PCDD/Fs and PCBs have been used previously. However, the most recent review of TEFs was that of the WHO in 1998 (Van den Berg et al, 1998) (see Appendix XVIII for a comparison of TEF schemes). This review has subsequently been recognised by the United States Environmental Protection Agency (US EPA 2000) an many other countries (including Japan, Canada and the EU) as being the most appropriate scheme for estimating the toxicity of dioxin mixtures. Under the WHO TEF scheme shown in Table 1-4, TCDD is assigned a TEF of 1.0, and other PCDDs, PCDFs and PCBs have TEF values ranging from 1.0 down to 0.00001. To estimate the toxic potency of a given dioxin mixture, the mass concentration of each

individual component is multiplied by its respective TEF, and the products are summed to represent the TCDD toxic equivalence (TEQ) of the mixture. These TEFs will be periodically reviewed.

Throughout this document, the intake of dioxins will be expressed in units of TEQs, applying the 1998 WHO TEFs, unless they were derived using the previous international TEF scheme (US EPA, 1989), which is abbreviated as I-TEQ.

Table 1-4 WHO TEFs for human risk assessment

Congener	TEF value	Congener	TEF value
Dibenzo-p-dioxins		***Non-ortho PCBs***	
2,3,7,8-TCDD	1	PCB 77	0.0001
1,2,3,7,8-PnCDD	1	PCB 81	0.0001
1,2,3,4,7,8-HxCDD	0.1	PCB 126	0.1
1,2,3,6,7,8-HxCDD	0.1	PCB 169	0.01
1,2,3,7,8,9-HxCDD	0.1		
1,2,3,4,6,7,8-HpCDD	0.01		
OCDD	0.0001		
Dibenzofurans		***Mono-ortho PCBs***	
2,3,7,8-TCDF	0.1	PCB 105	0.0001
1,2,3,7,8-PnCDF	0.05	PCB 114	0.0005
2,3,4,7,8-PnCDF	0.5	PCB 118	0.0001
1,2,3,4,7,8-HxCDF	0.1	PCB 123	0.0001
1,2,3,6,7,8-HxCDF	0.1	PCB 156	0.0005
1,2,3,7,8,9-HxCDF	0.1	PCB 157	0.0005
2,3,4,6,7,8-HxCDF	0.1	PCB 167	0.00001
1,2,3,4,6,7,8-HpCDF	0.01	PCB 189	0.0001
1,2,3,4,7,8,9-HpCDF	0.01		
OCDF	0.0001		

Note: TEFs are based on the conclusions of the WHO meeting in Stockholm, Sweden, 15-18 June 1997 (Van den Berg *et al,* 1998).

The database on many of the polybrominated compounds has been less extensively evaluated, and these compounds have not been assigned TEFs by the WHO. Consequently, polybrominated compounds have not been explicitly considered in this assessment, which focuses on PCDDs, PCDFs and PCBs. Evaluation of the most common chlorinated congeners is generally considered to be sufficient to characterise environmental dioxins. PBDDs and PBDFs could be included in future assessments if sufficient information becomes available and inclusion is considered desirable on toxicological grounds (see eg. Birnbaum et al, 2003).

TEFs are based on the present state of our knowledge and it is likely that some values may be revised as new data becomes available. It should be noted that the widely-accepted approach of combining TEFs into a single exposure metric (TEQ) is not

without controversy, considered by some to be a simplistic approach to dealing with complex mixtures of dioxin-like compounds (eg. Starr, 2003). For example, some congeners may act as *Ah*-receptor antagonists, blocking or altering the effects of other congeners.

It is recognised that in addition to synthetic halogenated aromatic hydrocarbons, there are a number of quite potent natural compounds that can interact with the *Ah* receptor. These include indole-3-carbinol (IC3) and related compounds from cruciferous vegetables. Polycyclic aromatic hydrocarbons (PAHs) and other aromatic amines formed during cooking can also interact with the *Ah* receptor, and may further complicate risk assessment (Safe, 1998). However, it is still unknown whether these compounds exert a significant influence on the toxicity of dioxins, and their possible effects cannot be assessed at present.

1.1.4 Exposure

Dioxins are ubiquitous in the environment, being found throughout the industrialised world in air, soil and sediments, as well as in food. Human exposure to dioxins can occur through working in industries in which they are by-products, from industrial accidents, and through food (including breast milk). Intake *via* inhalation and dermal absorption is likely to represent a very small source of exposure to dioxins.

Exposure of the general public to dioxins is predominantly through the diet, with food of animal origin being the major source. Contamination of food is primarily caused by dioxin emissions to the atmosphere from various industrial or thermal processes (eg. bushfires, wood heaters, waste incineration, production of chemicals), with subsequent deposition onto farmland and water bodies, followed by bioaccumulation up terrestrial and aquatic food chains. Other sources of dioxin-like chemicals can include contaminated stockfeed (for cattle, chicken and farmed fish), improper application of sewage sludge to agricultural land, flooding of pastures, waste effluents and certain types of food processing.

Based on measured concentrations of dioxins, furans and PCBs in food, and data on national food consumption, the 2001 JECFA evaluation estimated that median long-term intakes of PCDDs and PCDFs are 33-42 pg TEQ/kg bw/month for adults living in the United States or Western Europe. Estimates for New Zealand and Japan derived from measured concentration and food supply data were significantly lower, at 18 and 7 pg TEQ/kg bw/month, respectively[4]. If dioxin-like PCBs are also included, the daily total TEQ intake increases by about 25 per cent in the United States and is approximately doubled in other regions. Recent studies from countries that started to implement measures to reduce dioxin emissions in the late 1980s, such as the Netherlands, UK and Germany, clearly show that dioxin levels in food have decreased since that time, with a consequent reduction in dietary intake of these compounds by a factor of almost 2 over a 7-year period (WHO, 1998). In Canada, regulatory and guideline initiatives have markedly reduced PCDD and PCDF emissions from waste incinerators and bleached kraft pulp mills, with consequent declines in the

[4] The New Zealand and Japanese estimates may be higher than the true intake, as food *supply* exceeds food *consumption* by at least 15 per cent.

concentrations of these chemicals in fish and shellfish (Larsen et al, 2000). Similar measures have been undertaken in other countries, including Australia.

On a bodyweight basis, the daily intake of dioxins for breastfed babies is reported to be significantly higher than that for adults. A WHO field study showed that mean levels of PCDD/PCDF and PCB in human milk were higher in industrialised areas (10-35 pg I-TEQ/g milk fat) than in developing countries (<10 pg I-TEQ/g milk fat) (WHO 1996). However, there is clear evidence of a decrease in PCDD/PCDF levels in human milk between 1988 and 1993, with the highest rates of decrease in areas with the highest initial concentrations (WHO, 1996).

Examples of accidental exposures of local populations to PCDDs, PCDFs and PCBs include the incident at Seveso, Italy, and fires in PCB-filled electrical transformers. High exposure may also be caused by accidental contamination of food eg. industrial contamination of edible food oil, such as occurred at Yusho (Japan) and Yu-Cheng (Taiwan). While many industrial sources of occupational exposure have been identified and worker exposures have been reduced or eliminated, historic median TCDD levels in blood of highly exposed workers have been 1-3 orders of magnitude higher than blood levels in the general population. Body burdens caused by accidental or occupational exposure are normally dominated by only a few congeners; congener patterns are different from background exposure arising primarily from indirect exposure through the food supply where bioaccumulation can modify congener patterns.

1.1.5 Mechanisms of toxicity

The *Ah* (for aryl hydrocarbon) receptor is important in mediating the biological and toxicological effects of TCDD and dioxin-like compounds. Although the precise chain of molecular events is not fully understood, alterations in key biochemical and cellular functions are likely to be responsible for dioxin toxicity. Activation of the *Ah* receptor has two major consequences: increased transcription of various genes (eg. those coding for drug-metabolising enzymes) and immediate activation of tyrosine kinases; tyrosine kinase enzymes catalyse the transfer of the phosphate of ATP to tyrosine residues on protein substrates including enzymes and receptors, thus affecting enzyme activity and receptor function. The *Ah* receptor can also regulate expression of other networks of genes, either directly or indirectly. Activation of the *Ah* receptor can result in endocrine and paracrine disturbances, and alterations in cell functions, including growth and differentiation. Some of these effects have been observed both in humans and animals, indicating the existence of common mechanisms of action in different species. Some of the ligands that bind the *Ah* receptor may block its activation by behaving as weak agonists, or antagonists (eg. Safe and McDougal 2002). This means that binding of the *Ah* receptor by some members of the dioxin class could conceivably block the action of other, more toxic congeners, complicating the risk assessment of dioxin mixtures.

1.1.6 Cellular targets for dioxins

A family of so-called ‘nuclear receptors’ (NRs) function to transduce chemical signals into transcriptional responses in the cell nucleus by controlling the activity of specific target genes.

These NRs can be activated (and repressed) by a range of endogenous chemicals including the steroid hormones, retinoids (active metabolites of vitamin A), vitamin D, thyroid hormone, glucocorticoids and mineralocorticoids, and various xenobiotics including aryl hydrocarbons.

As discussed above, the *Ah* (for aryl hydrocarbon) receptor, a ligand-activated transcription factor involved in the regulation of a large number of genes, is considered to be a key site in mediating the biological and toxicological effects of TCDD and dioxin-like compounds.

TCDD and other PAHs exert effects on retinoid, thyroid hormone and vitamin D metabolism at very low doses following TCDD exposure (Hoegberg et al, 2003; Lilienthal et al, 2000; Nilsson & Hakansson, 2002; Van Birgelen et al, 1995). Likewise, a recent study has demonstrated that the agonist-activated AhR/Arnt[5] heterodimer directly associates with estrogen receptors, suggesting a novel mechanism of estrogenic signalling modulation (Ohtake et al, 2003).

1.1.7 Kinetics of dioxins and the concept of body burden

The fate of dioxins in the body is unusual, primarily because most of the congeners are extremely fat soluble but are practically insoluble in water. Following ingestion and absorption from the small intestine, dioxins are readily distributed via the blood to all organs, but they are preferentially retained in adipose (fatty) tissue. The release of stored dioxins from adipose tissue into the circulation is extremely slow, limiting the rate of metabolism by the liver and subsequent excretion in the faeces via the bile. Hence, the time to excrete half of an ingested dose of dioxins (the half-life) is usually measured in years. As discussed above, dioxins are composed of a mixture of compounds and each has a different half-life, but the commonly quoted average in humans, based on data from Seveso, ranges between 7 and 10 years.

The long half-life of dioxins means that, over decades, even a low rate of exposure leads to accumulation of dioxins in the body. Continual exposure from contaminated food might lead in the long term to an extremely high body burden (i.e. the total amount of dioxins in the body). Therefore, it is important to minimise the levels of dioxins in food. The capacity of humans to store dioxins in fat is so great that it would be expected to take 40–50 years to reach a balance or steady state, where the rate of intake equals the rate of excretion. Thus, a few exposures that exceeded the accepted dietary limit by ten- or even a hundred-fold would not significantly change a body burden accumulated over several decades. A single dose of dioxins of 5000 pg or a lifelong intake of around 1 pg/day would result in a similar body burden.

The biochemical and toxicological effects of dioxins, furans and PCBs relate more closely to their concentration in the target tissue than to the daily dose. Dioxins accumulate in vital organs and therefore it is difficult to directly measure the concentration in particular tissues except at post-mortem. However, the body burden of dioxins correlates strongly with levels in adipose tissue and serum and can, therefore, be readily estimated by measuring dioxin levels in adipose tissue or serum, or estimated

[5] Arnt = aryl hydrocarbon receptor nuclear translocator

from the ingested dose. Also, it has been assumed that data on body burden overcomes interspecies differences in the absorption, distribution, metabolism and excretion of dioxins. Therefore, the consultations by the WHO, the EC-SCF and JECFA concluded that the body burden is the measurement of choice for comparing risks between humans and animals. JECFA concluded that the appropriate averaging period for evaluating intake of these compounds is one month or more, whereas the EC-SCF favoured an interval of one week.

2. Hazard Assessment

2.1 Introduction

This chapter contains summary information about the hazards (or intrinsic toxicity) of dioxins and related compounds. It is not a risk assessment, which estimates the likely exposure of the population to dioxins and compares that intake with estimated safe intake levels which are established from a knowledge of the toxic effects of the compounds and the doses at which these effects are likely to occur. It updates the information contained in the 2002 hazard assessment overview which recommended an Australian TMI for dioxins (NHMRC/TGA, 2002) by considering relevant research on dioxins conducted since the 2002 report, as well as recent assessments and reports prepared by other national and international organisations or agencies. Note that this document is not a *de novo* hazard assessment but a summary overview report. Furthermore, its focus is on findings from in vivo studies in animals and clinical and epidemiology studies in humans; therefore it does not consider mechanism-of-action or in vitro studies.

A considerable number of comprehensive reviews of the toxicology of dioxins and dioxin-like compounds have been written in recent years. The 1998 review of dioxins by the Agency for Toxic Substances and Disease Registry (ATSDR) of the Public Health Service of the US Department of Health and Human Services is one of the most comprehensive reviews of the subject to date. The information in the 'Overview' (Section 2.2) is largely taken from a number of reviews including that of the ATSDR (ATSDR, 1998), the reports of the meetings of the 1998 WHO-ECEH/IPCS consultation (WHO, 1998; Van Leeuwen et al, 2000a & b), the EC-SCF (EC Scientific Committee on Food, 2001) and JECFA (FAO/WHO, 2001). To update these reviews, a monograph on Dioxins and Health (Schecter & Gasiewicz, 2003) provided a useful information source. Information contained in Section 2.3 ('Summary of the Toxicity of Dioxins') includes results of a literature search (conducted in September 2003) on the human health effects of dioxins[6].

[6] The search, conducted by Ms Kristen Dyer, was based on retrieving articles dealing primarily with risk assessment, excluding articles on dioxin levels in food, soil, animals, people; bio-monitoring of dioxins in humans; and managing dioxins. Databases searched included: Medline; Medline-in-process; Embase; Biosis (Biological Abstracts); Elsevier Biobase (Current Awareness in Biological Sciences); Toxline; EnviroLine; AMI (Australasian Medical Index); plus the catalogue of the Australian Government Department of Health and Ageing library.

2.2 Summary of the Toxicity of Dioxins

2.2.1 Animal data

2.2.1.1 Key studies

Numerous published studies have documented a variety of adverse effects of TCDD in experimental animals. The following Table lists a number of studies which have been pivotal in establishing human health guidelines for exposure to dioxin-like compounds.

Table 2-1 Some key toxicity studies used in the derivation of human health criteria

Study	Species/Strain	Biological effect
Kociba et al, 1978	Rats, Sprague-Dawley	Cancer
Schantz & Bowman, 1989; Schantz et al, 1992	Monkeys, Rhesus	Neurobehavioural effects in offspring
Mably et al, 1992a, b	Rats, Holzman	Decreased sperm counts in offspring of treated dams; decreased weights of testis and accessory sex organs
Rier et al, 1993	Monkeys, Rhesus	Endometriosis
Gray et al, 1997a	Rats, Long Evans Hooded	Accelerated eye opening and decreased sperm counts in male offspring
Gray et al, 1997b	Rats, Long Evans Hooded	Increased genital malformations in female offspring
Gehrs et al, 1997; Gehrs & Smialowicz, 1999	Rats	Immune suppression in offspring
Faqi et al, 1998	Rats, Wistar	Decreased sperm production and altered sexual behaviour in male offspring
Ohsako et al, 2001	Rats, Holzman	Decreased anogenital distance in male offspring

Adverse effects reported in animals following exposure to dioxins include immunotoxicity, endometriosis in Rhesus monkeys, developmental behavioural developmental effects in offspring of treated Rhesus monkeys, and developmental effects in rats (including reproductive toxicity in males and urogenital malformations in females).

The results of a two-year carcinogenesis bioassay conducted by Kociba et al (1978) have been the most often utilized for cancer risk assessment of TCDD. Sprague Dawley rats of both genders were given 2,3,7,8-TCDD (99% pure) in the feed to achieve intakes of 0, 1, 10 and 100 ng/kg bw/day. Results indicated that at 100 ng/kg bw/day, TCDD

caused an increase in the incidence of hepatocellular hyperplastic nodules and carcinomas in female but not in male rats. At this dose, statistically significant increases in squamous cell carcinomas of the lungs (females) and tongue and nasal palate/nasal turbinates (males) were also reported. Conversely, at this dose there was a significant reduction in the incidence (in female rats) of spontaneous benign tumours of the uterus, benign and malignant mammary tumours and pituitary adenocarcinomas, and (in male rats) adrenal gland phaeochromocytomas and pancreatic adenomas. Although the mechanisms for such reductions in tumour incidence are not well understood, reductions in body weight[7] as a result of TCDD exposure and disruption of endocrine homeostasis have been suggested as two possible reasons for these findings.

There was also a reduction in the incidence and severity of chronic renal disease in aged male rats. At the mid dose (10 ng/kg bw/day) there was no evidence of TCDD effects on tumour incidence, although an increased incidence of hepatocellular nodules was observed. Lifetime ingestion of TCDD at the low dose (1 ng/kg bw/day) did not cause any effects considered to be of toxicological significance. A re-evaluation of liver specimen slides from the female animals was performed by a pathology panel (Keenan et al, 1991). They found about two-thirds fewer tumours present in the livers of female rats than in the original report. The panel established a NOEL for hepatocellular carcinomas of 10 ng/kg bw/day. A further review of the slides (Goodman & Sauer, 1992) substantially confirmed results showing a dose-related increase in tumour incidence (hepatocellular adenomas - 2/81 control; 1/50 low-dose; 9/50 mid-dose; and 14/45 high-dose: hepatocellular carcinomas - 0/86, 0/50; 0/50 and 4/45: hepatic eosinic foci - 31/86; 23/50; 37/50 and 40/45).

In a developmental toxicity in rhesus monkeys (Schantz et al, 1992), groups of 8 female rhesus monkeys were fed a diet containing 0, 5, or 25 ppt TCDD for a total of 16.2 months, throughout the mating period, gestation, and lactation. After 7 months of exposure, the monkeys were mated with unexposed males (to a maximum of 10 matings) until conception occurred, with dosing continuing during mating, gestation and lactation. Only 1 monkey in the 25 ppt group delivered a viable offspring; this offspring was not studied behaviourally. When the offspring (3 males and 3 females per exposure group) were 8.6 months of age, they were placed in 3 peer groups of 4 monkeys and allowed to play for 1.5 hours without interference. The peer groups consisted of two TCDD-exposed monkeys and two control monkeys. Behavioural patterns (social interactions and other behaviours such as vocalisation, locomotion, self-directed behaviour, and environmental exploration) were monitored 4 days/week for 9 weeks. No overt signs of toxicity were observed in the mothers or offspring and birth weights and growth were not adversely affected by TCDD exposure. Significant alterations were observed in play behaviour, displacement, and self-directed behaviour in the TCDD-exposed offspring; they tended to initiate more rough-tumble play bouts and retreated less from play bouts than controls, were less often displaced from preferred positions in the playroom than the controls, and engaged in more self-directed behaviour than controls. No other significant alterations in behaviour or alterations in reflex development, visual exploration, locomotor activity, or fine motor control were found (Bowman et al, 1989b). In tests of cognitive function, object learning was significantly

[7] Actual bodyweight changes not provided in the Kociba et al (1978) paper.

impaired, but no effect on spatial learning was observed (Schantz & Bowman, 1989). The dietary level of 5 ppt was stated to be equivalent to an intake of 120 pg/kg bw/day.

Ten years after termination of approximately 4 years of TCDD exposure in female Rhesus monkeys [maternal animals from the Shantz et al (1992) study summarised above], Rier et al (1993) reported a dose-related increase in the incidence and severity of endometriosis, and identified a lowest observed adverse effect level (LOAEL) of 5 ppt in the diet (120 pg/kg bw/day) for moderate endometriosis.

In studies in Holzman rats, Mably et al (1992a, b) found significant decreases in daily sperm production and the amount of mature sperm stored in the cauda epididymis of rats exposed prenatally to a single dose of 2,3,7,8-TCDD on gestational day (GD) 15; in rats, day 15 corresponds to the onset of the endocrine-sensitive phase of sexual differentiation. Decreases in weights of testis, cauda epididymis, ventral prostate and seminal vesicle were observed in juvenile, pubertal, post-pubertal, and sexually mature rats prenatally exposed to TCDD on GD 15. The lowest LOAEL for these effects (decreased testis weight) was 64 ng/kg bw, identified in the Mably et al (1992c) study. The effects do not appear to result from reduced plasma androgen concentrations during the perinatal period as originally proposed and do not completely correspond with the developmental effects of known anti-androgens (Theobald et al, 2003).

Gray et al (1997a) investigated the reproductive effects of TCDD administration on GD 15 in male Long Evans Hooded rat offspring. Pregnant dams were dosed by gavage with 0, 0.05, 0.20 or 0.80 µg/kg bw TCDD in corn oil. Male offspring (10-12/group) were monitored for viability, growth, and reproductive function. Accelerated eye opening was observed in all dose groups cf. controls (50% of the animals in the low and mid-dose groups and 79% in the high-dose group). Reduced pup survival and growth retardation were observed in offspring from the high-dose group. Percentage pup survival on days 3 to 22 ranged from 82% to 93% at the high dose whilst survival in all other dose groups (including controls) was 99-100%. The most sensitive adverse effect was a 25% reduction in ejaculated sperm numbers at the lowest dose tested (0.05 µg/kg bw). The number of animals affected was not reported.

Gray et al (1997b) also investigated the effects of a single dose of TCDD on GD 15 on female offspring of Long Evans Hooded rats (18-24 pups/dose group). Delayed vaginal opening was observed in progeny from dams exposed to 0.80 µg/kg bw. The mean distance from urethral to vaginal opening was 6.8 mm in the high-dose group *vs* 11.03 mm in controls. A dose-related increase in the percentage of females with a temporary or persistent vaginal thread was observed, from 15% in control animals to 97% in the highest exposure group. The threads were permanent in 2.5% of controls, as compared to 10%, 27%, and 92% of offspring from the 0.05, 0.20 and 0.80 µg/kg bw groups respectively; at the two highest doses, the increases were statistically significant. Partial to complete clefting of the phallus was displayed in offspring at 0.20 (20% of offspring) and 0.80 µg/kg bw (75%). Other morphological changes in animals from these dose groups were increased length of the urethral slit, increased distance from the urethral opening to the tip of the phallus, and decreased distance from the urethral opening to the vaginal orifice. Time to pregnancy was delayed in female offspring from the high-dose group, although fertility rate was not affected. Histopathological changes in the ovary,

cervix, and vagina were observed in animals necropsied at 20 months of age. The investigators noted that GD 15 might not have been the most sensitive for the detection of ovarian alterations, endometrial hyperplasia, and a shortened reproductive life span.

Gehrs et al (1997) and Gehrs and Smialowicz (1999) studied the persistence of delayed-type hypersensitivity (DTH) suppression in the offspring of Fischer 344 rats exposed to TCDD by gavage at 0, 0.1, 0.3 or 1.0 µg/kg bw on GD 14. DTH suppression was determined by measuring the DTH response to bovine serum albumin in the offspring at 4 to 19 months of age. TCDD significantly suppressed the DTH response in males at up to 19 months of age. While the females' DTH response was reduced at 8, 12 and 19 months, significant suppression was observed only at 4 months of age. The lowest maternal dose of TCDD that produced DTH suppression was determined by measuring the DTH response to BSA in 4- and 14-month-old offspring of dams dosed orally with 0, 0.1, 0.3 or 1.0 µg/kg kg bw on GD14. In males, suppression was observed at a maternal dose as low as 0.1 µg/kg bw at 14 months of age, while a maternal dose of 0.3 µg/kg bw was necessary to cause suppression in the 14-month-old females. It was concluded that suppression of the DTH response associated with perinatal TCDD exposure persists through late adulthood, occurs at low maternal doses (i.e. 0.1 µg/kg bw), and is more pronounced in male than in female rats. Whilst differences in subsets of thymocytes and lymph node cells were noted between control and TCDD exposed offspring, no clear correlation was established between altered subpopulations of thymic cells and suppressed DTH responses.

The animals most sensitive to dioxin-induced adverse effects were the male offspring of Wistar rats (Faqi et al, 1998). In this study, dams received an initial loading dose of 25, 60 or 300 ng ^{14}C-TCDD/kg bw two weeks prior to mating, followed by weekly maintenance doses of 5, 12 or 60 ng/kg bw throughout mating, pregnancy and lactation. These maintenance doses were intended to prevent the maternal body burdens from declining below 20, 48 and 240 ng/kg bw, respectively, assuming an elimination half-life of three weeks for TCDD in adult rats. The study failed to demonstrate a NOEL because decreased sperm production and feminised sexual behaviour were observed in male offspring of the lowest dose group at 70-170 days of age. By reference to toxicokinetic data in pregnant rats (Hurst et al, 2000a, b), the EC Scientific Committee on Food (EC-SCF) estimated a maternal steady-state TCDD body burden of 39 ng/kg bw in dams at lowest dose, which was taken as the LOEL. The Joint Expert Committee on Food Additives (JECFA) applied linear and nonlinear curve fitting to the same data, and arrived at maternal steady-state body burden estimates of 25 and 39 ng/kg bw, respectively.

The lowest NOEL was found in a reproduction study by Ohsako et al (2001) in which Holtzman rats received a single oral dose of 0, 12.5, 50, 200 or 800 ng TCDD/kg bw on the 15th day of pregnancy (GD 15). Male offspring displayed reduced anogenital distance and androgen receptor mRNA levels in the ventral prostate, with a LOEL of 50 ng/kg bw. The NOEL was 12.5 ng/kg bw. Assuming that 60 per cent of a single gavage dose was retained in the body at GD 16, the NOEL of 12.5 ng/kg bw and the LOEL of 50 ng/kg bw would result in maternal body burdens of 7.5 and 31 ng/kg bw, respectively. By reference to toxicokinetic data in pregnant rats (Hurst et al, 2000a, b),

JECFA estimated a maternal body burden of 13–19 ng/kg bw at the NOEL, with a corresponding estimate of 51–76 ng/kg bw at the LOEL.

The above NOEL should be protective with respect to another sensitive indicator of the effects of TCDD in animals, that of tooth development. Kattainen et al (2001) examined the effects of TCDD on tooth development in three rat lines that differ in their TCDD sensitivity and *Ah* receptor structure, derived from TCDD-resistant Han/Wistar (Kuopio) and TCDD-sensitive Long-Evans (Turku/AB) rats. The main target teeth were the third molars, since their development spans from the perinatal period to about 6 weeks after birth. Pregnant dams were exposed to 30 -1000 ng/kg bw TCDD on gestation day 15. Pups were euthanised at the age of 5 or 10 weeks and the jaws examined by stereomicroscopy and radiography. TCDD at 1000 ng/kg completely prevented the development of the third lower molars in 60% of males and 50% of females in the most sensitive rat line while <6% of pups in the more resistant lines lacked this target tooth. In the most resistant strain TCDD exposure also dose-dependently diminished the proportion of lower third molars which had erupted by the age of 5 weeks. In the other more sensitive strains, less than 30% of the lower third molars had partially or completely erupted by postnatal day 35. Molar size was dose-dependently reduced in the 3 lines; the third lower molars were most severely affected, with the reduction reported to be significant at 30 ng/kg bw in one of the less-sensitive lines and at 100 ng/kg bw in the other two lines (including the most sensitive one). The same investigators studied the effects of higher TCDD doses (single dose of 50 or 1000 µg/kg bw) given to dioxin-resistant Han/Wistar rat dams one day after delivery, so that pups had post-natal exposure during lactation (Lukinmaa et al, 2001). Pup heads were analysed radiographically or histologically at postnatal days 9 and/or 22. A greater proportion of pups at the higher dose lacked third molars (at the bud stage at the start of the experiment) than those at the lower dose (9/13 *vs* 1/6). The teeth of control pups developed normally. In contrast to controls, none of the 11 experimental pups examined radiographically (6 at the higher dose and 5 at the lower) showed mineralization of their third molar cusps. Results indicate that the effects of TCDD on rat tooth development depend not only on the dose but also on tooth type and developmental stage. It was suggested that the interference by TCDD with tooth morphogenesis with the consequent arrest of development is likely to involve epithelial-mesenchymal signalling.

Studies in rats have shown that TCDD can arrest molar tooth development after *in utero* and lactational exposure, and that the sensitive stage is temporally restricted. To define the stage at which TCDD is able to arrest tooth development and the cellular background of the effect, mouse embryonic molar tooth explants including early developmental stages from initiation to late cap stage were exposed to TCDD in organ culture. Results indicated that TCDD can arrest tooth development *in vitro* if the exposure starts at the initiation stage, whereas exposure at later stages leads to smaller tooth size and deformation of cuspal morphology. It appears that TCDD interferes with tooth development by stimulating apoptosis in those cells of the dental epithelium which are predetermined to undergo apoptosis during normal development (Partanen et al, 2004).

Pregnant rhesus monkeys aged 5-7 years were given TCDD subcutaneously on day 20 of gestation at an initial dose level of 0, 30 or 300 ng/kg bw (1 ml/kg vehicle). For

maintenance of body burden, 5% of the initial dose was administered every 30 days during pregnancy and lactation, until day 90 after birth. No abnormalities were detected in the control and 30 ng/kg groups whereas more than half of the young in the 300 ng/kg group had tooth abnormalities. The upper permanent lateral incisors were most frequently affected. Of the deciduous teeth, the central incisors seemed to be most sensitive to TCDD. The permanent premolars were also frequently affected, whilst the canines and the first molars were not. These results indicate that the LOAEL body burden for induction of tooth abnormalities in rhesus monkeys is greater than 30 ng/kg bw but less than 300 ng/kg bw. On the basis of this dose-response information, the authors (Yasuda et al, 2004) concluded that the current TDI for dioxins in Japan (4 pg/kg bw/d; equivalent to 120 pg/kg bw/month) "needs no immediate modification".

2.2.1.2 Cancer

Experimental studies demonstrate that TCDD is carcinogenic in all species and strains of laboratory animals tested. It has been characterised as a multi-site carcinogen. However, short-term studies have shown a lack of direct DNA-damaging effects, indicating that TCDD is not an initiator of carcinogenesis. It appears that that TCDD is not directly genotoxic but is a potent tumour promoter (see eg. Wyde et al, 2002) and as such, can give the appearance of being a complete carcinogen. Also, the ability of TCDD to enhance proliferation and inhibit apoptotic processes in focal hepatic lesions further supports an indirect mechanism of carcinogenicity. Of the organ systems positive for TCDD-mediated carcinogenesis in rodent bioassays, a complete mechanism of action has only been proposed for thyroid follicular cell carcinogenesis, and it is considered that humans would be less sensitive than rats to the induction of this tumour type by TCDD (Teeguarden & Walker, 2003). The WHO consultation (WHO, 1996) noted that the NOEL of TCDD for hepatic adenomas in a 2-year study in rats was 1 ng/kg bw/day at which dose the body burden was 60 ng/kg bw.

At this stage, the finding that TCDD reduces the incidence of some spontaneous tumours in rodents at some sites (see above discussion of the Kociba et al, 1978 results) and the mechanism(s) by which this occurs, is not well understood.

2.2.2 Human data

2.2.2.1 Non-cancer endpoints

The incidence of adverse health effects other than cancer has been, and is being evaluated in population groups exposed to dioxins, dioxin-like and non-dioxin-like polychlorinated aromatic compounds in a variety of exposure scenarios. Epidemiological data indicate that some conditions (eg alterations in metabolic parameters and mortality from cardiovascular and non-malignant liver disease) may be increased in exposed populations compared to the unexposed referent groups. However, of the range of non-cancer health effects evaluated in exposed adult populations, many were transient and not observed when exposure ceased. Populations exposed occupationally or environmentally to TCDD have not demonstrated any significantly increased all-cause or non-cancer mortality (Bertazzi et al, 1989; Cook et al, 1986, 1987; Fingerhut et al, 1991a, b; Ott et al, 1980, 1987; Wolfe et al, 1995; Zack & Suskind, 1980). Likewise, no overall excess mortality was reported in workers exposed

to TCDD as a result of an accident which occurred on 17 November 1953 at the BASF facility in Germany (Ott & Zober, 1996; Thiess et al, 1982; Zober et al, 1990).

The most widely recognised and consistently observed effect following high dose exposure to TCDD is chloracne (ATSDR, 1998; US EPA, 1994; Pesatori et al, 2003). The condition can disappear after termination of exposure or can persist for many years. Other effects on the skin include hyperpigmentation and hirsutism (Ashe & Suskind, 1950; Suskind & Hertzberg, 1984). In certain instances, effects persisted for several years. Increased levels of hepatic enzymes and slight alterations in lipid profile have been reported in humans exposed to high levels of TCDD (ATSDR, 1998), although the effects were mild and often transient. Temporary enlargement of the liver has also been observed (US EPA, 1994). TCDD can cause long-term alteration in glucose metabolism (Henriksen et al, 1997; Pesatori et al, 1998) and slight changes in thyroid function (Zober et al, 1994). Effects on the respiratory system, manifested mainly as upper respiratory tract irritation, have resulted from acute high exposure to TCDD (ATSDR, 1998). Other irritant effects resulting from acute exposure include conjunctivitis with red and irritated eyes, and blepharitis[8] (US EPA, 1994). There is some suggestive evidence of toxicity to the cardiovascular system (ATSDR, 1998; Steenland et al, 1999) and limited information regarding body weight effects in humans (ATSDR, 1998). Some of these effects are discussed in more detail below.

The most severe exposure of humans to TCDD is reported to have occurred in 1997 (Geusau et al, 2001a). Two office workers in a textile research institute in Vienna were exposed to massive TCDD intoxication from an unknown source (probably from prior synthesis of 2,4,5-trichlorophenol in the facility). Inadvertent exposure, probably by oral ingestion, most likely occurred in October 1997 with the most severely affected patient reporting to a dermatology clinic in March 1998. This 30-year-old female patient was shown to have the highest blood lipid level of TCDD ever recorded in a person, 144,000 pg/g blood lipid[9], corresponding to an estimated body burden of 1.6 mg of TCDD and a dosage of 25 µg/kg body weight. This patient suffered severe, persistent and disfiguring chloracne, but other than some gastrointestinal symptoms (nausea, vomiting, epigastric pain and loss of appetite, with gastritis confirmed by gastroscopy), only a few clinical and biochemical health effects were observed over the first 2 years of follow-up. There were moderate elevations of blood lipids, leukocytosis, and anaemia, but no evidence of a primary bone marrow disorder. The persistence of leukocytosis was most likely to be due to the inflammatory skin condition and the intermittent administration of corticosteroids rather than a direct effect of TCDD. Similarly, the persistence of anaemia was most likely to be due to the skin inflammation, although a direct effect of TCDD on erythropoiesis cannot be ruled out. Lymphocyte subset analysis showed a marginal decrease in the percentage of natural killer (NK) cells but several other immunological parameters were within normal limits. Detailed investigations ruled out any disturbance of the hypothalamic-pituitary axis. Pulmonary function, neurological, psychodynamic and electrophysiological examinations were unremarkable, as were

[8] A chronic or long-term inflammation of the eyelids and eyelashes. Among the most common causes are poor eyelid hygiene; excess oil produced by the glands in the eyelids; bacterial infection; and an allergic reaction.

[9] The highest previously reported human levels of TCDD were 10,400 pg/g blood fat in an adult and 56,000 pg/g in a child, arising from the Seveso incident.

chest X-rays and abdominal ultrasound. Menstruation ceased in late autumn 1997 (the presumed time of intoxication) and secondary amenorrhoea was still present in late 2000 after she stopped using contraceptives in summer 1999. This amenorrhoea may be due to TCDD inhibition of estradiol synthesis or its cytochrome P450-mediated metabolism, or to hyperprolactinaemia which coincided with the initiation of antidepressant therapy with 5HT antagonists which are known to increase prolactin levels. The second patient, a 27-year-old woman, was also highly intoxicated with TCDD, 26,000 pg/g of blood lipid, but apart from some mild facial chloracne (cleared within a year, following treatment with topical tretinoin) and gastrointestinal symptoms, she was apparently largely unaffected. Routine laboratory and immunological parameters were within the normal range, apart from marginally elevated cholesterol and lipase, an elevated number and percentage of B lymphocytes and a decreased percentage of NK cells. Three other workers with elevated blood levels of 856, 149 and 93 pg/g blood lipids were asymptomatic. The estimated intakes for the two highly-exposed patients significantly exceed the estimated median lethal dose of dioxin (0.6 - 2.0 μg/kg bw) in guinea pigs, the most sensitive species tested. However, long-term follow-up of these patients will be necessary to assess the occurrence of chronic sequelae, including cancer.

Additional references on these two clinical cases include Geusau et al (1999), Geusau et al (2001b), Geusau et al (2002), and Abraham et at (2002).

2.2.2.2 Chloracne

As noted above, the most consistent observation following human exposure to TCDD is chloracne. Mocarelli et al. (1991) described chloracne in people from Zone A in Seveso who had serum TCDD levels ranging from 828 to 56,000 ng/kg lipid. With the exception of one person who developed less severe chloracne, all people who had lipid-adjusted TCDD levels over 12,000 ng/kg (ppt) developed severe chloracne. Several people with levels below 12,000 ppt developed less severe chloracne; the lowest reported TCDD level associated with chloracne was 828 ppt at the time of the accident. In the group that developed chloracne, >95% were under 20 years old, including the person with the lowest reported serum lipid TCDD concentration. In fact, children appear to develop chloracne at lower serum TCDD concentrations than adults (Assennato, 1989; Mocarelli et al, 1991). One reason for the observed variability with respect to the blood concentration of TCDD associated with chloracne is that some people absorbed much of their dose *via* dermal contact while others ingested the dioxin. It appears that the blood level which can produce chloracne can be much smaller if it arises from dermal contact rather than from oral ingestion. Nevertheless, it appears likely that a dose threshold needs to be overcome in order for chloracne to occur (Greene, Hays & Paustenbach, 2003). In the case of the very highly-exposed office worker in Vienna (144,000 ng/kg blood lipid; Geusau et al, 2001a; see above), the chloracne cysts were subject to recurrent deep inflammation, requiring surgical removal of comedones and treatment with methyl-prednisolone, analgesics and antibiotics. In the second highly-exposed patient (26,000 ng/kg blood lipid) there were only mild manifestations of chloracne. This was attributed to the exposure most likely being by the oral rather than the dermal route, and supporting the suggestion that, in the absence of direct skin contamination, higher systemic threshold levels may be necessary for chloracne to develop.

2.2.2.3 Diabetes etc

Data from several epidemiological studies suggest that significant exposure to TCDD increases the risk of diabetes mellitus, resulting from decreased cellular glucose uptake. Follow-up assessment of the population exposed to dioxin after the 1976 accident in Seveso, Italy, was extended to 1996. An overall increase in diabetes was reported, notably among women (RR = 2.4, 95% CI: 1.2 - 4.6) (Bertazzi et al, 2001).

In 1997, the IARC considered results on four highly exposed industrial cohorts; Steenland et al (1999) extended the follow-up period for the largest of these cohorts (5132 chemical workers at 12 US plants) by 6 years. In cohort mortality analyses, diabetes (any mention on the death certificate) showed a negative exposure-response trend.

In an attempt to reconcile disparate results from two key studies on TCDD and diabetes, data from 990 US Air Force veterans (Ranch Hand) and 1275 referents were re-analysed, as were those on a NIOSH population of 267 chemical workers and 227 referents (Steenland et al, 2001b). An increasing trend was found in prevalence of diabetes with increased TCDD exposure in the Ranch Hand population, with excess risk largely confined to the highest 8% of the exposed group (>78 ppt serum TCDD), which had an OR of 3.21 (95% CI 1.81 - 5.72) vs those with <10 ppt TCDD. However, no such positive dose-response was found in the NIOSH chemical worker population i.e. there was little overall evidence that the exposed workers were at higher risk than non-exposed workers of diabetes or abnormal fasting glucose. The reason for the difference in diabetes dose-response trends between the two studies is unknown. Furthermore, Greene and Paustenbach (2002) and Greene et al (2003) argue that, since the estimated LOAEL for diabetes in the NIOSH cohort (6 people with diabetes in the highest exposure group) is over 30-fold greater than the estimated LOAEL in the Ranch Hand cohort, it is “highly unlikely” that TCDD is a significant risk factor for diabetes.

Calvert et al (1999) conducted a cross-sectional study on 281 workers employed more than 15 years earlier in the manufacture of 2,4,5-trichlorophenol or its derivatives at two US chemical plants. Mean current serum lipid adjusted TCDD was 220 pg/g lipid in workers and 7 pg/g lipid among 260 referents. The prevalence of diabetes mellitus was not significantly different between the workers and referents and did not significantly correlate with increasing TCDD concentration. However, diabetes was found in six of 10 (60%) workers with current serum TCDD concentrations >1500 pg/g lipid. Excluding subjects being treated for diabetes, workers in the group with the highest half-life extrapolated TCDD concentrations had a significantly increased adjusted mean serum glucose concentration compared with referents, as well as a significantly higher adjusted mean free thyroxine index. These findings provide modest evidence that TCDD exposure may affect glucose metabolism and thyroid function.

Blood serum lipid concentrations of TCDD in 69 persons living within 25 miles of a Superfund site in the USA (Vertac/Hercules site, Jacksonville, Arkansas) ranged between 2 and 94 ppt. When subjects with TCDD levels in the top 10% (TCDD > 15 ppt, n = 7) were compared to subjects with lower levels (2-15 ppt, n = 62), their plasma insulin concentrations at fasting and 30, 60 and 120 min following a 75 g glucose load were significantly higher. There were no group differences in age, obesity, gender

distribution, total lipids, or glucose levels. Excluding other known risk factors for hyperinsulinaemia, the study authors suggested that high blood TCDD levels might be a factor in insulin resistance (Cranmer et al, 2000).

Longnecker and Michalek (2000) examined the association of serum TCDD with prevalence of diabetes mellitus and with levels of serum insulin and glucose in 1,197 veterans in the US Air Force Health Study who never had contact with dioxin-contaminated herbicides; their serum dioxin levels were within the range of background exposure typically seen in the USA ($\leq$10 ng/kg lipid). Compared with those whose serum dioxin level was in the first quartile (<2.8 ng/kg lipid), the multivariate-adjusted odds of diabetes among those in the highest quartile ($\geq$5.2 ng/kg lipid) was 1.71 (95% CI = 1.00-2.91). The association of background-level dioxin exposure with the prevalence of diabetes in these data may be due to reasons other than causality but a causal contribution cannot be dismissed.

Longnecker and Daniels (2001) noted that rates of both type 1 and type 2 diabetes mellitus have been increasing, with genetic factors accounting for less than half of new cases. For type 1 diabetes, higher serum levels of PCBs have been associated with increased risk but overall, the data were limited or inconsistent. With respect to risk of type 2 diabetes, data were suggestive of an association with TCDD but were inconclusive. Other researchers (eg. Greene et al, 2003; Kogevinas, 2001; Koveginas et al, 2001) have similarly concluded that the evidence for increased risk for diabetes with TCDD exposure is inconsistent.

An analysis by Remillard and Bunce (2002) estimated that background exposure to dioxin-like compounds by the reference population in a number of published epidemiology studies contributed less than 1% of their diabetes risk.

In a survey of Australian Vietnam veterans (self-reporting questionnaire), the reported prevalence of diabetes was a little higher than expected for this population (DVA, 2000). Thus, 2,391 respondents (6%) reported ‘diabetes’, with the expected general population estimate from the National Health Survey (NHS) being in the range 1,558-2,003 (for the age profile and number of respondents). ‘Diabetes’ was not defined in the questionnaire and veterans may have included a single high sugar value as diabetes - these conditions are separated in the NHS. The report concluded that a relationship between exposure during service and the disease “is difficult to confirm”. This result is perhaps not particularly surprising since it appears that all Australian veterans from the Vietnam war were surveyed i.e. those who might have been more exposed to Agent Orange during Operation Ranch Hand do not appear to have been separately identified. [Current government policy allows for treatment and compensation responses to this condition following diagnosis.]

It may be concluded that there is suggestive evidence of a weak correlation between diabetes incidence and occupational or accidental exposure to dioxins[10]. However,

[10] The issue of whether there could be a reverse correlation does not appear to have been addressed in studies to date ie could diabetics haave different metabolic/physiological characteristics which might alter their capacity to metabolise and/or excrete dioxins or PCBs?

background exposure to dioxins is not a significant risk factor for individuals who have not been occupationally or accidentally exposed.

2.2.2.4 Cardiovascular effects

In 1997, the IARC considered results on four highly exposed industrial cohorts. Steenland et al (1999) extended the follow-up period for the largest of these cohorts (5132 chemical workers at 12 US plants) by 6 years. In cohort mortality analyses, Standardised Mortality ratios (SMRs) for heart disease showed a weak increasing trend with higher exposure.

Follow-up of the population exposed to dioxin after the 1976 accident in Seveso, Italy, was extended to 1996. Chronic circulatory and respiratory diseases were moderately increased, suggesting a link with accident-related stressors and chemical exposure (Bertazzi et al, 2001).

Between 1965-1968 in the former Czechoslovakia, ca. 80 persons became ill due to occupational exposure to TCDD. Pelclova et al (2002) investigated disorders in a group of 12 of the most highly exposed subjects (mean estimated concentration at the time of exposure approx. 5000 pg/g plasma lipid). The mean TCDD level in 1996 was 256 pg/g plasma lipid (range 14-760). Hyperlipidemia, atherosclerotic plaques, increased intima-media thickness of the carotid artery cf. controls, ischaemic heart disease and degenerative changes of the ocular fundus were very common in the group. TCDD levels correlated with the highest levels of triglycerides and cholesterol found during the 35-year follow-up.

In a study on 1,224 Korean veterans who served in Vietnam and 154 non-Vietnam veterans, Kim et al (2003) reported that "service in Vietnam" resulted in an increased frequency of eczema (odds ratio = 6.54), radiculopathy[11] (OR = 3.98), diabetes (OR = 2.69), peripheral neuropathy (OR = 2.39), and hypertension (OR = 2.29), compared to non-Vietnam veterans, adjusting for potential confounders. Higher exposure to Agent Orange among the Vietnam veterans was claimed to be associated with increased frequency of ischaemic heart disease, valvular heart disease, and retinopathy.

2.2.2.5 Immune system effects

Studies in animals indicate that the immune system is a sensitive target of TCDD toxicity, with inhibition of immunoglobulin secretion and decreased resistance to bacterial, viral, and parasitic infections. However, information regarding the toxicity of TCDD to the human immune system is scant and inconsistent (ATSDR, 1998; Baccarelli et al, 2002; US EPA, 1994). Natural killer cells were increased in a population of chemical workers exposed to TCDD examined 17 years after termination of exposure (Jennings et al, 1988). A 2-year assessment of two Viennese office workers who had massive exposure to TCDD in 1997, quantitative and functional analysis of the immune system was unrevealing, apart from a decreased percentage of NK cells (Geusau et al, 2001a). Nearly 20 years after the Seveso accident, immunoglobulin and

[11] Nerve root irritation which is caused by either compression of the nerve root where it emanates from the spinal cord area, or from a stretch injury or inflammation of the nerve; can cause a shooting pain sometimes described as an electrical feeling.

complement plasma levels were measured in a random sample of the population in the most highly exposed zones (n = 62) and from surrounding non-contaminated areas (n = 58). Plasma IgG levels decreased with increasing TCDD plasma concentration whereas IgM and IgA immunoglobulins and C3 and C4 complement proteins[12] did not exhibit any consistent association with TCDD levels (Baccarelli et al, 2002). Clinical illness associated with immune system disorders has not been associated with TCDD in any cohort studied (Greene et al, 2003).

2.2.2.6 Endometriosis

Evidence shows that dioxins can increase the incidence and severity of endometriosis in monkeys and can promote the growth or survival of endometrial tissue implanted into rodents in a surgically induced model of endometriosis. However, small, hospital-based case-control studies have failed to provide compelling evidence for or against an association of environmental contaminants and endometriosis (Rier & Foster, 2002, 2003).

A population-based historical cohort study was conducted 20 years after the 1976 factory explosion in Seveso, Italy, which resulted in the highest known population exposure to TCDD (Eskenazi et al, 2002). Participants were 601 female residents of the Seveso area who were less than 30 years old in 1976 and had adequate stored sera. 19 women with endometriosis and 277 non-diseased women were identified. The relative risk ratios for women with serum TCDD levels of 20-100 ppt and >100 ppt were 1.2 [90% CI = 0.3-4.5] and 2.1 (90% CI = 0.5-8.0), respectively, relative to women with TCDD levels <20 ppt. In conclusion, a doubled but non-significant risk for endometriosis among women with serum TCDD levels of >100 ppt was reported, with no clear dose response.

A case-control study to determine the possible association between endometriosis and chronic exposure to dioxins and PCBs included 42 infertile endometriosis cases and 27 mechanically infertile controls enrolled at one of the US collaborating Centres for Reproductive Medicine between 1996-1998. Results showed no statistically significant association between levels of dioxin-like compounds and the occurrence of endometriosis in infertile women (Pauwels et al, 2001). Tsutsumi et al (2000) have reported that breast-fed infants have an unexpectedly lower incidence of endometriosis in adult life than non breast-fed infants, noting that such females have a possible greater exposure to dioxins in milk.

2.2.2.7 Reproductive and developmental effects

The majority of studies on human reproductive and developmental effects concern paternal exposure to TCDD, and have evaluated its potential toxicity long after a high exposure had occurred (IARC, 1997). Studies of the risk of spontaneous abortion involving occupational and environmental herbicide exposure have generally not found increased risks (ATSDR, 1998; IARC, 1997; Institute of Medicine, 1994; Sweeney, 1994; US EPA, 1994). Findings from studies of US Vietnam veterans suggested an

[12] Serum complement comprises a group of proteins that facilitate immunological and inflammatory responses. There are 9 major components labelled C1 through C9. The so-called complement cascade involves a series of enzymatic reactions that take place in the blood.

effect with increasing self-reported or inferred Agent Orange exposure (Institute of Medicine, 1994). However, the inconsistency with results of the occupational and environmental exposure studies and the marginal magnitude of the increased risk make these results suspect (Institute of Medicine, 1994). A study of workers in US factories producing Agent Orange did not find an association between paternal serum TCDD levels and the incidence of spontaneous abortion (Schnorr et al, 2001). Most studies of spontaneous abortion have suffered from a high level of misclassification of exposures and outcomes, small sample sizes, lack of data on TCDD levels at the time of conception, and differences in case definition. Similarly, results from human studies of developmental effects and exposure to herbicides or TCDD have, in the main, been inconclusive (ATSDR, 1998; Institute of Medicine, 1994; Sweeney, 1994; US EPA, 1994). The studies have been limited due to small sample sizes (for specific birth defects), potential biases in the findings, and uncertainties regarding the assessment of exposure. Egeland et al (1994) demonstrated that current and half-life serum dioxin levels were positively and significantly related to luteinizing and follicle stimulating hormones and inversely related to testosterone levels in male workers from the NIOSH cohort. Vietnam veterans were found to have a significantly lower sperm concentration relative to non-Vietnam veterans (CDC, 1989). The ability to produce children was not affected, and with the exception of Ranch Hand veterans, the most highly exposed military personnel, Vietnam veterans did not have increased body burdens of TCDD. No associations between TCDD exposure and hormone levels or sperm characteristics were observed among Ranch Hand veterans (Henriksen et al, 1996); however, the investigators noted that the members of this cohort were exposed to lower levels of TCDD and for shorter duration than the workers followed by Egeland et al (1994).

Considerable attention has been paid to the sex ratio of children born to populations exposed to dioxins. Children (346 girls and 328 boys) born between 1977 and 1996 to potentially exposed parents from Seveso, Italy, showing an increased probability of female births with increasing TCDD concentrations in the serum of the fathers ($p = 0.008$). Fathers exposed when they were younger than 19 years of age sired significantly more girls than boys (sex ratio 0.38; 95% CI 0.30-0.47), an effect which may persist for years after exposure. The median concentration of dioxin in fathers in this study was similar to doses that induce epididymal impairments in rats and is about 20 times the estimated average concentration of TCDD currently found in human beings in industrialised countries (Mocarelli et al, 2000). The sex ratios of live births in Japan after accidental exposure to PCBs and PCDFs in 1968 were reviewed (Yoshimura et al, 2001). Data on all births (85 live) from parents exposed from 1968 to 1977 in Fukuoka and a region of Nagasaki, were examined. The sex ratio was not significantly different from normal (0.513). However, the authors noted that further investigation, especially of offspring of those who were younger than about 19 years of age at the time of the Yusho incident, is warranted. Men who worked in US factories which produced Agent Orange were exposed to TCDD at levels hundreds of times higher than TCDD levels in the general population. Wives of TCDD-exposed chemical workers and wives of non-exposed neighbourhood referents were interviewed to determine reproductive history while paternal serum TCDD level at time of conception was estimated for each pregnancy, using serum samples taken in 1987. Although estimated TCDD levels in the exposed worker population were much higher than in other studies, this study (Schnorr et al, 2001) did not find an association between paternal serum TCDD levels and the sex

ratio of offspring. The sex ratio of children of pesticide workers who produced trichlorophenol and 2,4,5-trichlorophenoxy acetic acid from 1961 to 1988 in the city of Ufa, Bashkortostan, Russia was investigated. TCDD and other dioxins were analysed in 84 blood samples, with median TCDD toxic equivalents blood lipid values of 240 ng/kg i.e. more than 30 times higher than background levels from the region. The sex ratio in the combined cohort of 227 children from exposed workers (150 males and 48 females) was 0.40 (M/M+F), significantly lower than those for the city of Ufa and elsewhere, while the sex ratio of offspring according to maternal or paternal exposure was 0.38 and 0.51 respectively. Thus, paternal exposure was associated with the birth of more girls in this study (Ryan et al, 2002).

A recent Russian paper reports on adverse reproductive outcomes in the town of Chapaevsk (Samara Region, Russia), home to the Middle Volga chemical plant which is one of the largest environmental polluters in region. From 1967 to 1987 it produced lindane (hexachlorocyclohexane) and its derivatives. The mean frequency of spontaneous abortions for a recent seven-year period was 24.4% higher in Chapaevsk than in other towns in the Samara region. The average rate of premature labour was also significantly higher, at 45.7 per 1000 women. The frequency of newborns with low birth weight was 7.4%, slightly (but not statistically) higher than the 5.1-6.2% for Russia and most other Samara region towns. The numbers of congenital morphogenetic conditions (CMGC) were determined in 369 children born between 1990 and 1995. The average number of CMGC per child was claimed to be significantly higher than in other parts of the region. These preliminary results indicate adverse reproductive outcomes which, although the town suffers from pollution with a range of different chemicals, the authors associate with high dioxin levels in human milk and blood (Revich et al, 2001).

NIOSH scientists studied pregnancy outcomes of wives of chemical workers exposed to chemicals contaminated with TCDD. Their findings did not support any relationship between paternal TCDD exposure and spontaneous abortion or sex ratio of offspring (Schnorr et al, 2001) or lowered birth weight or pre-term delivery (Lawson et al, 2004).

2.2.2.8 Neurological and developmental cognitive effects

Neurological symptoms observed in TCDD-exposed workers include lassitude, weakness of the lower limbs, muscular pains, increased perspiration, loss of appetite, headaches, nervousness, anxiety, irritability, and loss of libido (Ashe & Suskind, 1950; Jirasek et al, 1974, 1976; Moses et al, 1984; Oliver, 1975; Pazderova-Vejlupkova et al, 1981; Suskind, 1985). In Japanese Yusho patients who ingested rice oil containing PCBs and PCDFs in 1968, some still complain of numbness of extremities (Yoshimura, 2003). Clinical and neurophysiological examinations (motor conduction velocity of the peroneal nerve, sensory conduction velocities of the sural and ulnar nerves) on 156 dioxin exposed workers (42 with, 114 without chloracne) from a pesticide-producing plant found that exposure to 2,3,7,8-polychlorinated dioxins and furans led to mild sensory neuropathy of the legs in a minority of the most severely exposed persons (Thomke et al, 1999). In veterans of Operation Ranch Hand, the unit responsible for aerial herbicide spraying in Vietnam from 1962 to 1971, there was an increased risk of indices of peripheral neuropathy in the high-exposure group at assessment in 1992 and 1997; however, the authors urged caution in interpretation of these findings until the relationship between pre-clinical diabetes mellitus and peripheral neuropathy is further

evaluated (Michalek et al, 2001). Also in veterans of Operation Ranch Hand, an analysis of cognitive function (performed in 1982) found that veterans in the fifth quintile of dioxin levels (measured in 1987 and 1992) exhibited reduced verbal memory function; although statistically significant, these differences were relatively small and of uncertain clinical significance (Barrett et al, 2001).

For children exposed *in utero*, postulated adverse health effects include subtle developmental delays and thyroid hormone alterations. Much of the focus of recent research has been on the effect of prenatal PCB exposure on cognitive and neurological development. The potential neurotoxicity of PCBs was first recognized when people in Japan (1968) and Taiwan (1978-1979) consumed rice oil contaminated with PCBs and PCDFs; offspring had poorer cognitive functioning as well as other behavioural problems. Taiwanese 'Yu-Cheng' children born up to 6 years after their mother was exposed were as affected as children born within the first year, when compared at the same ages; effects on IQ persisted up to 16 years of age, but behavioural problems diminished with time (Lai et al, 2001; Liu et al, 2001). Further studies, including on children whose mothers consumed PCB-contaminated Great Lakes fish, have produced discrepant results. Recent Dutch research reported a negative relationship between prenatal PCB exposure and intellectual functioning at 3.5 years of age, without any relationship between intellectual functioning and exposure to dioxins and dibenzofurans. Additional studies are being conducted in Europe and North America (Schantz, 2001).

In the Netherlands a prospective study was started in 1989 to investigate the effects of background PCB and dioxin exposure on the development of healthy babies born at normal term. Prenatal PCB exposure was related to lower psychomotor scores at 7 months of age, and poorer neurological condition at birth and at 18 months. Postnatal PCB and dioxin exposure through lactation was related to lower psychomotor development at 7 months (Vreugdenhil & Weisglas-Kuperus, 2000). In a follow-up of the Dutch PCB/Dioxin study, cognitive abilities were assessed in 42-month-old children. *In utero* exposure to "background" PCB concentrations was reported to be associated with poorer cognitive functioning in preschool children. Children of mothers at the upper end of exposure were at greater risk (Patandin et al, 1999a). Whilst findings suggested that prenatal exposure to PCBs and dioxins might have subtle negative effects on early neurological and cognitive development of children, a consistently beneficial effect of breast-feeding on brain development from 18 months up to school age was reported, despite a higher PCB exposure from breast milk. However, by 6 years of age, preliminary results showed no evidence that cognitive and neurological development were affected by pre- and postnatal exposure to these pollutants (Boersma et al, 2001). In the Dutch PCB/dioxin study, the assessment of school-age children suggested that subtle cognitive and motor developmental delays arising from prenatal PCB and dioxin exposure was seen when parental and home characteristics were less optimal but such effects were not measurable in children raised in more optimal environments (Vreugdenhil et al, 2002a).

In the US Collaborative Perinatal Project (CPP), designed to identify determinants of neurological deficits in children, prenatal PCB exposure in relation to children's cognitive test scores was studied. Pregnant women were recruited from 12 US study

centres from 1959 to 1966, and the children were followed until age seven. Third-trimester serum from 806 women selected at random and from an additional 96 women whose children had either a low or high IQ score was analysed for 11 specific PCBs. The data provided no support for the hypothesis that *in utero* exposure to background levels of PCBs was associated with lower IQ scores at age seven (Gray et al, 2000). Silkworth et al (2002) applied causation analysis to 24 epidemiology studies (on 2,573 children in 6 international cohorts) that sought an association between maternal PCB exposure and neurodevelopmental effects. The authors concluded that although there is biological plausibility, a causal association between the ascribed cause (PCBs) and the purported effect (impaired neurodevelopment) was without empirical support. Performance of more highly PCB-exposed breast-fed children was not diminished, but was positively correlated with duration of breast-feeding. Some negative correlations reported between neurodevelopment and PCBs were equally attributable to lead or mercury.

2.2.2.9 Tooth Development

In vivo and *in vitro* studies show that rat and mouse teeth are sensitive to TCDD throughout their development (eg. Kattainen et al, 2001; Lukinmaa et al, 2001; Partanen et al, 2004). The sequence of morphogenetic events can be affected, leading to failure of tooth germs to develop as a result of accelerated and increased apoptosis in the dental lamina connecting the oral epithelium and the tooth germ. Later exposure can reduce tooth size or, in more advanced teeth, root development can be arrested (Lukinmaa et al, 2001). TCDD can also affect the function of secretory ameloblasts and odontoblasts, resulting in delayed or defective mineralization of the molar teeth and failure of enamel and dentin formation to be completed in the continuously erupting rat incisors (Lukinmaa et al, 2001 and references therein).

In two episodes of epidemic poisoning in Japan and Taiwan (so-called Yusho and Yu-Cheng incidents, respectively), developmental effects were observed in infants and children born to mothers who had been exposed to PCDFs and PCBs (see eg. Yoshimura, 2003; Rogan et al, 1988). These included a higher incidence of natal teeth[13] and later, missing permanent teeth, delayed eruption of permanent teeth, and disturbed root development (Ikeda, 1996; Rogan et al, 1988).

Twenty-five years after the dioxin accident in Seveso, Italy, 48 subjects exposed in their childhood in more (zones A and B) or less contaminated (zone R) areas were randomly recruited for examination of dental and oral aberrations (Alaluusua et al, 2004). Subjects were matched with 65 subjects from the surrounding non-ABR zone for age, sex, and education. The prevalence of developmental enamel defects in group less than 5 years of age at the time of exposure was 42% (15/36) in zone ABR subjects and 26% (10/39) in non-ABR subjects, correlating with serum TCDD levels ($p = 0.016$). Hypodontia[14] was seen in 12.5% (6/48) and 4.6% (3/65) of zone ABR and non-ABR subjects, respectively, also correlating with serum TCDD level ($p = 0.05$). In contrast, dental caries and periodontal disease (both due to infections), oral pigmentation and salivary

[13] Natal teeth are teeth present at birth and neonatal teeth erupt during the first 30 days. Normally the lower central incisors are the first teeth to erupt at approximately 6 months of age.
[14] Congenital absence of one or more teeth.

flow rate were unrelated to exposure. Whilst the authors commented that the results supported their hypothesis that dioxins can cause dental aberrations, they noted that (1) almost one hundred different factors can affect development of dental enamel (citing Small & Murray, 1978) and (2) the results on hypodontia should be treated with caution because of the small study population and the small number with hypodontia, and that a larger study on children under 3 at the time of the accident (the most critical age for tooth agenesis) should be conducted.

A Finnish study (Alaluusua et al, 1996) looked at 2 different populations of children; the first population comprised 40 children who had mineralization defects in the permanent 1st molars, and their age, living area, and sex-matched controls. The median duration of breast feeding was 9 months in the affected children compared to 6 months in the controls. The defects were more extensive after prolonged breast feeding. The second population consisted of 97 children whose mothers had been encouraged to extensive and prolonged breast feeding (>8 months). Of these children, 24 had mineralization defects. In both populations, mineralization defects were associated with the duration of breast feeding. The result led to the conclusion that long breast feeding may increase the risk of mineralization defects in children, possibly because of environmental contaminants (not identified in this study). In a later study, Alaluusua et al (1999) examined the dentition of 102 children aged 6-7 years for the presence of hypomineralisation enamel defects, in order to correlate any effects on the permanent first molars with concentrations of the most toxic PCDDs/PCDFs and 33 PCB congeners in breast milk samples collected when the children were aged 4 weeks. Exposure was evaluated from the duration of breastfeeding (mean 10.5 months) and the concentrations in milk (assuming a yearly 25% first-order decline during lactation). Intrauterine exposure was estimated to correspond to the exposure *via* milk for two months. Mineralisation defects occurred more often and were more severe in children who had been exposed to higher amounts of polychlorinated aromatic hydrocarbons than in those exposed to lower amounts.

Holtta et al (2001) examined the prevalence of demarcated hypomineralization lesions of teeth in 2 Finnish towns by the Kymijoki River which is severely contaminated by dioxins and furans. The 4,120 permanent first molars of 1,030 children were studied and the prevailing levels of dioxins and furans in human milk were measured. Neither the prevalence of dental lesions nor the levels of PCDD/Fs in human milk were increased in riverside residents compared with figures reported earlier from other areas of Finland. The prevalence of the defects in Kotka and Anjalankoski was 14.2% and 5.6% respectively, with corresponding PCDD/F levels in breast milk of 13.4 and 10.9 I-TEQ pg/g fat. Higher levels of fluoride in the second town may have lowered the prevalence of demarcated lesions ie. it is not valid to draw correlations between the prevalence of the defects and the difference (relatively minor) in exposures to PCDD/F levels. Only in Anjalankoski was the duration of breast-feeding associated with the prevalence of the defects.

A total of 34,457 infants born in 1997-2000 in four hospitals in southern Finland were examined for natal and neonatal teeth (Alaluusua et al, 2002). Exposures to PCBs and PCDD/Fs was evaluated by measuring the 17 most toxic PCDD/Fs and 36 PCB congeners in breast milk samples when the children were 4-8 wks old. A total of 34

infants had one or two natal (29 infants) or neonatal teeth (5 infants). The milk analyses showed that the median level of PCDD/Fs was 11.9 WHO-TEQ pg/g in fat, and that of PCBs was 7.24 WHO-TEQ pg/g in fat ie. levels corresponded to the prevailing levels in Norway at the time. No association was found between pollutant levels and occurrence of natal and neonatal teeth, indicating that the prevailing levels of PCDD/Fs and PCBs are likely to be below the threshold to cause perinatal eruption of teeth.

2.2.2.10 Cancer

In 1997, the IARC considered results on four highly exposed industrial cohorts; Steenland et al (1999) extended the follow-up period for the largest of these cohorts (5132 chemical workers at 12 US plants) by 6 years. The SMR for all cancers combined was 1.13 (95% CI = 1.02-1.25), with statistically-significant positive linear trends in SMRs with increasing exposure for all cancers combined and for lung cancer. The SMR for all cancers combined for the highest exposure group was 1.60 (95% CI = 1.15-1.82). Analyses suggest that high TCDD exposure resulted in an excess of all cancers combined, without any marked specificity. However, excess cancer was limited to the highest exposed workers, with exposures that were likely to have been 100-1000 times higher than those experienced by the general population. Based on the data from the US NIOSH cohort of workers exposed to dioxin, Steenland and co-workers (Steenland et al, 2001a; Steenland & Deddens, 2003) estimated that doubling background levels of exposure (eg. by eating a significant amount of dioxin-contaminated fish) could increase lifetime risk of cancer death by ca. 0.1 to 1.0%; since the background risk of cancer death by age 75 is 12% in the USA, doubling background levels of dioxin exposure would increase this lifetime risk to somewhere between 12.1 and 13.0%.

Salvan et al (2001) performed an analysis of all cancer and lung cancer mortality in relation to estimated absorbed dose of TCDD in the NIOSH cohort of chemical workers. At a dose level of 100 times the background, their estimates obtained with a 10-year lag translated into a relative risk of 2.03 (95% CI =1.19-3.45) for all cancer and of 2.66 (95% CI = 1.07-6.64) for lung cancer.

Follow-up of the population exposed to dioxin after the 1976 accident in Seveso, Italy, was extended to 1996. During the entire observation period, all-cause and all-cancer mortality did not increase. Fifteen years after the accident, mortality among men in high-exposure zones A (804 inhabitants) and B (5,941 inhabitants) increased from all cancers (RR = 1.3, 95% CI = 1.0-1.7), rectal cancer (RR = 2.4, 95% CI = 1.2-4.6), and lung cancer (RR = 1.3, 95% CI = 1.0-1.7), with no latency-related pattern for rectal or lung cancer. An excess of lympho-haemopoietic neoplasms was found in both genders (RR = 1.7, 95% CI = 1.2-2.5). Hodgkin's disease risk was elevated in the first 10-year observation period (RR = 4.9, 95% CI: 1.5, 16.4), whereas the highest increase for non-Hodgkin's lymphoma (RR = 2.8, 95% CI = 1.1-7.0) and myeloid leukemia (RR = 3.8, 95% CI = 1.2-12.5) occurred after 15 years. No soft tissue sarcoma cases were found in these zones (0.8 expected) (Bertazzi et al, 2001).

Using data from the Seveso Women's Health Study (SWHS), Warner et al (2002) examined the association between individual serum TCDD levels and breast cancer risk. The cohort comprised 981 women who were infants to 40 years old at the time of the factory explosion in 1976, who resided in the most contaminated areas, and had

archived sera that was collected soon after the explosion. Cox proportional hazards modelling showed that the hazard ratio for breast cancer associated with a 10-fold increase in serum TCDD levels was significantly increased to 2.1 (95% CI = 1.0-4.6), leading to the conclusion that individual serum TCDD is significantly related with breast cancer incidence among women in the SWHS cohort.

Epidemiological evidence from the most highly TCDD-exposed cohorts studied produces the strongest evidence of an increased cancer risk from exposure to dioxins, when the data are considered for all cancers combined. There is weaker evidence of an increased cancer risk when the data for cancers at particular sites are considered.

It is difficult to find epidemiological data that have sufficient dose-response information to provide reliable risk estimates in exposed human populations. Modelling is complicated by uncertainties in extrapolating current body burdens of dioxins to past occupational exposure and by the choice of the dose-response model to fit the data. Scientific debate about the potential human carcinogenicity of dioxin-like compounds has been ongoing for many years and recent meta-analyses (US EPA, 2000; Starr, 2001; Crump et al, 2003) from three occupationally-exposed cohorts have reached such different conclusions that the debate is certain to continue. While the potency estimate from the US EPA's analysis was stated to imply approximately 4,000 additional cancer deaths in the USA solely from background intake of dioxin-like compounds (about 1 pg TEQ/kg/day), Thomas Starr's own analysis implied zero extra cancers from all exposures to dioxin-like compounds, including those arising from dietary intake (Starr, 2003). Crump et al (2003) concluded that their analysis provided "some evidence that TEQ exposures near current background levels are carcinogenic". Further consideration of the issue by Starr (Starr, 2003) indicated that resolution of the debate would depend on detailed information about exposures to TCDD and direct-acting carcinogens in the workplace, as well as a model which adequately takes into account TCDD's characteristics as a tumour promoter. Starr was also strongly critical of extrapolations from TCDD analyses to ones based on TEQ, stating that "the evidence regarding the potential carcinogenicity of TEQ is simply inadequate".

Mackie et al (2003) have commented on the US EPA's standard low-dose linear extrapolation method for estimating dioxin cancer risk (US EPA, 2000) and the subsequent consideration by the EPA's Science Advisory Board (SAB) (US EPA, 2001a). As an alternative to the linear extrapolation model, the SAB considered a model which suggested that dioxin was a threshold carcinogen, with data suggesting that the threshold was an order of magnitude higher than exposure levels of the general population. A re-analysis of this model by Mackie et al indicates that without the inappropriate population weighting in the model considered by the SAB, the range of possible estimated thresholds is extremely wide and completely overlaps the level of general US background exposures, with the conclusion that there is no evidence for or against the proposition that dioxin is a threshold carcinogen. More standard statistical approaches (Steenland et al, 2001b; Becher et al, 1998) found no evidence of a threshold.

Yamaguchi (1999) has cautioned against relying on estimates of absolute risk from epidemiological studies in human populations, noting that estimates of cancer risk

arising from exposure to chemicals varied very significantly between eg. smokers and non-smokers.

As noted above under 'Animal data', the background incidence of certain tumours is reduced in rodents by TCDD. In this regard, Kayajanian (2002) has suggested that the NIOSH study on exposed chemical plant workers indicates a J-shaped response, with increased cancer incidence at higher exposures being preceded at lower doses by a significantly reduced incidence. Kayajanian (1999) used plant-worker mortality data which underlie the 1990 US National Institute for Occupational Safety and Health (NIOSH) report on dioxins to identify tissue/organ sites at which dioxin exposure is associated with, reductions in mortality. Observations in men included reductions in urinary organ cancers, including bladder cancers; multiple myeloma; respiratory diseases, including emphysema and pneumoconioses and other respiratory diseases; total disease other than cancer; and total disease.

Ketchum et al (1999) studied cancer prevalence and exposure to TCDD in veterans of Operation Ranch Hand, the Air Force unit responsible for the aerial spraying of herbicides in Vietnam from 1962 to 1971. The risk of cancer at sites other than the skin within 20 years of service was increased in the low (odds ratio [OR] = 3.4, 95% CI = 1.5-8.0) and high (OR 2.7, 95% CI = 0.9-8.0) TCDD exposure categories, but the pattern was inconsistent with another study, suggesting that the excess risk may not have been caused by dioxin exposure. Overall, there was no consistent evidence of a dose-response gradient and no significant increase in cancer risk in the high dioxin exposure category, the subgroup of greatest *a priori* interest.

Kayajanian's analysis of Operation Ranch Hand data (Kayajanian, 2000) suggested that significant increases in systemic, melanoma, and total skin cancers are observed in those veterans not significantly exposed to dioxin; however, amongst those Ranch Hand airmen who served in Southeast Asia, exposure to dioxins is associated with a significant reduction of elevated systemic cancers and total skin cancers. In the Operation Ranch Hand Study, a significant reduction in prostate cancers as a function of increasing dioxin body burden was reported in US veterans of African origin but not in Caucasians (Kayajanian, 2001). Zafar and Terris (2001) also evaluated the rate of prostate cancer in Vietnam veterans. Those referred for prostate biopsy who reported a history of Agent Orange exposure were compared to veterans who denied such exposure; there was no evidence of a relationship between prostate cancer incidence and Agent Orange exposure.

The Australian Government Department of Veterans' Affairs conducted a mortality study on Vietnam veterans (the "Vietnam Veterans Mortality Study") covering the period from the end of the Vietnam War until 31 December 1994 (Crane et al, 1997). The death rate from all causes for Vietnam veterans relative to other Australian males was estimated to be 0.68 (95% CI 0.63 to 0.74) for 1964-79 and 1.07 (95% CI 1.02 to 1.12) for 1980-94; these estimated SMRs take account of the known variation in death rates by age group and calendar year. The overall level of excess mortality was difficult to estimate because of the 'healthy worker effect' which would lower the death rates for some causes, and the bias in the estimation method due to the underestimation of deaths. Compared with deaths from other sites of cancer, death rates from soft tissue and other

sarcomas, non-Hodgkin's lymphoma, and Hodgkin's disease, which were suggested as being consistently associated with exposure to herbicides or dioxin, were not statistically significantly elevated. This study suggests there may be a slight excess risk of death from lung cancer and prostate cancer. The report authors noted that while this elevation may be related to some exposure that occurred during service in Vietnam, there are multiple other and more usual risk factors associated with both cancers that should also be considered. Although not hypothesised in the protocol for this study, Vietnam veterans may have been at increased risk of death from head and neck cancers between 1980-94.

2.3 Recent Assessments of Dioxins

Comprehensive risk assessments of dioxins have been performed by a number of organisations or groups in recent years including the International Agency for Research on Cancer (IARC), the US EPA, the EC Scientific Committee on Food (EC-SCF), the WHO European Centre for Environmental Health (WHO-ECEH) and the Joint Expert Committee on Food Additives (JECFA). These assessments incorporate knowledge from research on molecular biology, animal toxicity and epidemiology in exposed human populations.

2.3.1 Assessment by the International Agency for Research on Cancer

In 1997, the IARC classified TCDD as 'carcinogenic to humans' (Group 1). The IARC's decision was based primarily on evidence in four groups of highly-exposed industrial workers. IARC also took into consideration the following supporting evidence:

- there was 'sufficient evidence'[15] that TCDD was carcinogenic at several sites in experimental animals (acting *via* the cellular aryl hydrocarbon (*Ah*) receptor, which is present in and functions the same way in humans and laboratory species);
- there were studies showing that the concentrations of TCDD in tissues from rats exposed to carcinogenic dosage regimens in bioassays are similar to those found in the tissues of heavily-exposed human populations with an apparent increased risk of cancer (IARC, 1997).

Taking all of the evidence into consideration, the following overall evaluations were made by IARC (1997):

- 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin (TCDD) is carcinogenic to humans (Group 1).

[15] IARC usually applies the criterion of 'sufficient evidence of carcinogenicity' when a causal relationship has been established between the agent or mixture and an increased incidence of malignant neoplasms or an appropriate combination of benign and malignant neoplasms in (a) two or more species of animals or (b) in two or more independent studies in one species carried out at different times or in different laboratories or under different protocols.

- Other polychlorinated dibenzo-*p*-dioxins are not classifiable as to their carcinogenicity to humans (Group 3).
- Dibenzo-*p*-dioxin is not classifiable as to its carcinogenicity to humans (Group 3).
- Polychlorinated dibenzofurans are not classifiable as to their carcinogenicity to humans (Group 3).

The IARC noted that in these high-exposure industrial cohorts, the blood lipid levels estimated to the last time of exposure were 2000 ng/kg (mean, with levels up to 32,000 ng/kg; US cohort), 1434 ng/kg (geometric mean, range 301 - 3,683 ng/kg; Dutch cohort), 1008 ng/kg (geometric mean; German workers with severe chloracne), and up to 2252 ng/kg (Boehringer cohort, Germany). These calculated blood levels of TCDD at the time of exposure were in the same range as the estimated blood levels in the two-year rat carcinogenicity study (Kociba et al, 197; see assessment above). In rats exposed to 100 ng/kg bw/day in the diet (hepatocellular carcinomas (females) and squamous cell carcinomas of the lung (females), estimated blood lipid TCDD levels were 5,000 - 10,000 ng/kg TCDD. At 10 ng/kg bw/day (the NOEL for hepatocellular carcinomas, but with an increased incidence of hepatocellular nodules), estimated blood lipid TCDD levels were 1,500 -2,000 ng/kg TCDD. At the lowest dose (1 ng/kg bw/day) at which no toxicological effects were reported, the mean blood lipid TCDD level was 540 ng/kg. Thus, the workers in the industrial cohorts studied were likely to have been exposed to TCDD levels similar to those in the experimental animal studies, levels which were 100–1000 times higher than those experienced by the general population.

2.3.2 Assessment by the ATSDR

While the Agency for Toxic Substances and Disease Registry (ATSDR) of the Public Health Service of the US Department of Health and Human Services is not an 'international' organisation, its 1998 review of dioxins is one of the most comprehensive reviews of the subject produced to date.

The ATSDR (1998) estimated a Minimal Risk Level (MRL)[16] of 1 pg TEQ/kg bw/day for chronic oral exposure to TCDD, based on developmental toxicity in monkeys (Schantz et al, 1992). This study is presented in more detail under 'Animal data' (see above). Relative to controls, significant alterations in play behaviour, displacement, and self-directed behaviour were observed in offspring of dams exposed to 5 ppt TCDD in the diet, corresponding to a daily intake of 120 pg/kg bw. Offspring behaviour was studied from 8.6 months of age for a period of 9 weeks. An uncertainty factor of 90 was used (3 for the use of a marginal LOAEL, 3 for extrapolation from animals to humans, and 10 for human variability) to derive the MRL. (Note that body burden was not used

[16] Minimal Risk Level (MRL): An estimate of daily human exposure to a hazardous substance that is likely to be without an appreciable risk of adverse non-cancer health effects over a specified route and duration of exposure. MRLs are derived using the NOAEL/LOAEL plus safety factor approach. MRLs established by the ATSDR are generally based on the most sensitive endpoint considered to be of relevance to humans. This should not be confused with Maximum Residue Limit, a control level for pesticide residues in agricultural commodities.

to scale across species in the derivation of the MRL, as compared to eg. the WHO derivation of the TDI.)

The ATSDR also derived an MRL of 0.0002 µg/kg/day (200 pg/kg/day) for acute-duration oral exposure (14 days or less) to TCDD, based on a NOAEL of 5 ng/kg and a LOAEL of 10 ng/kg for immunological effects in female B6C3F1 mice (Burleson et al, 1996); statistically significant increases in mortality were observed in influenza A infected mice exposed to 10, 50 and 100 ng/kg TCDD. An uncertainty factor of 30 (3 for extrapolation from animals to humans and 10 for human variability) and modifying factor of 0.7 (to account for the higher bioavailability of TCDD from an oil gavage vehicle than from food) were used to derive the MRL from the NOAEL. Similarly, an MRL of 0.00002 µg/kg/day (20 pg/kg/day) was derived for intermediate-duration oral exposure (15–364 days) to TCDD, based on a NOAEL of 0.7 ng/kg/day for immunological effects (decreased thymus weights) in Hartley guinea pigs fed TCDD in the diet for 90 days (DeCaprio et al, 1986). The LOAEL for this effect was 5 ng/kg/day. An uncertainty factor of 30 (3 for interspecies extrapolation and 10 for human variability) was used.

The ATSDR concluded that the available epidemiology data suggest that 2,3,7,8-TCDD may be a human carcinogen. Statistically significant increases in risks for all cancers were found in highly exposed workers with longer latency periods. Although the estimated SMRs were low, they were consistent across studies with the highest exposures. The evidence for site-specific cancers is weaker, with some data suggesting a possible relationship between soft-tissue sarcoma, non-Hodgkin's lymphoma, or respiratory cancer with 2,3,7,8-TCDD exposure. The ATSDR emphasised that some of the human studies did not provide adequate exposure data and were confounded by concomitant exposure to other chemicals.

2.3.3 Re-assessment by the US EPA

In April 1991, the US EPA announced that it would conduct a scientific re-assessment of the potential risks posed by exposure to dioxins and related compounds, as a follow-up to their initial assessment, first released as a draft in 1984 (US EPA, 1984a).

The principal finding of their draft re-assessment (US EPA, 2000) was that although dioxins can initiate biochemical and biological events potentially leading to a range of cancer types and non-cancer effects in animals and humans, *'there is currently no clear indication of increased disease in the general population attributable to dioxin-like compounds*'. However, the US EPA stated that the lack of a clear indication of disease could not be taken as evidence that dioxins were having no effect. The report suggested that current data and scientific tools might not be able to detect effects. The EPA did not recommend a reference dose[17] (RfD) for dioxins, reasoning that any RfD estimated using the traditional approach for setting such values, would probably be 100–1000 times below current human intakes and body burdens. Hence, the EPA review did not

[17] An RfD is a health risk goal below which there is likely to be no appreciable risk of non-cancer effects over a lifetime of exposure. The RfD concept is ostensibly equivalent to an acceptable daily intake (ADI) or tolerable daily intake (TDI).

produce an exposure standard for humans that could be considered for adoption by Australia.

In 2000/2001 the Science Advisory Board panel reviewing the draft questioned the EPA's quantitative cancer risk estimates, stating that it was not appropriate for EPA to characterise the risks in such a quantitative manner without providing a similar quantitative estimate of the uncertainty in the risk estimates; the Board was not able to reach consensus on a single value for a dioxin cancer potency factor. The panel also considered that it would be useful to have estimates of non-cancer risk from low-dose exposures, but accepted that the database currently did not allow for such estimates to be reliably developed at present (Paustenbach, 2002). It is interesting to note that the majority of the SAB panel recommended that an RfD should be derived, stating that the non-cancer hazard appeared to be the most sensitive adverse effect, rather than the cancer hazard. [A summary of the 2001 Science Advisory Board report is given in Paustenbach (2002).]

As at the time of preparing this hazard assessment overview, the US EPA is yet to release its final risk assessment on dioxins. The US EPA's Science Advisory Board's (SAB) Dioxin Reassessment Review Subcommittee (DRRS) of the SAB Executive Committee met between November 2000 and April 2001 to review sections of the EPA draft EPA document. The DRRS considered that, notwithstanding the fact that it was critical for the EPA to carefully consider current data and modelling gaps and to develop a research plan to remedy them, additional research was unlikely to bridge many of these gaps in the foreseeable future. Therefore it recommended that the EPA proceed expeditiously to complete and release its risk assessment, taking appropriate note of the findings and recommendations of the DRRS report and other public comments. Further, recognising the very long biological and environmental persistence of dioxins, the DRRS stated that it was important that EPA continue to try to limit emissions (and human exposure) to this class of chemicals. On 31 May 2001 the SAB forwarded its final review report to the EPA. A revised draft dioxin reassessment was then transmitted to the Interagency Working Group on Dioxin (IWG) on 17 January 2003; the IWG is made up of American government agencies responsible for human health, food, and the environment and which are working together under the auspices of the National Science and Technology Council to ensure a coordinated government approach to dioxin related issues. On 29 October 2003 the IWG officially requested that the National Academy of Sciences (NAS) re-review the draft dioxin reassessment. This NAS review is expected to take approximately 15 months[18].

2.3.4 Assessment by the WHO-ECEH Consultation (1998)

The WHO European Centre for Environmental Health (WHO-ECEH) has been coordinating a program on dioxins, in collaboration with the IPCS. The program is aimed at evaluating the possible health risks, and prevention and control of environmental exposure of the general population to these chemicals. WHO-ECEH and IPCS jointly organised a consultation entitled *Assessment of the health risk of dioxins: re-evaluation of the Tolerable Daily Intake (TDI)*. The meeting was held in May 1998

[18] The EPA plans to make available on its website the version of the dioxin reassessment that is undergoing NAS review.

in Geneva, and was attended by 40 experts from Australia[19], Belgium, Canada, Denmark, Finland, Germany, Italy, Japan, The Netherlands, New Zealand, Spain, Sweden, the United Kingdom and the United States (WHO, 1998; Van Leeuwen et al, 2000).

2.3.4.1 Conclusions from the WHO Consultation

In assessing the risk from dioxin-like compounds, the consultation focused on the most sensitive adverse effects (hormonal, reproductive and developmental effects) that are observed at low doses in animal studies. These effects occur at body burdens in rats and monkeys in the range of 10–50 ng/kg bw.

Human daily intakes that would lead to body burdens similar to those associated with adverse effects in animals were estimated to be in the range of 10-40 pg/kg bw/day. Since body burdens were used to scale doses across species, the consultation concluded that it was not necessary to use an uncertainty factor to account for toxicokinetic differences between species. However, the estimated human intake was based on LOELs and not on NOELs. In addition, uncertainty remains regarding potential differences in susceptibilities within the human population, the comparative susceptibility of humans and animals, and the half-lives of elimination for the different components of a mixture of dioxins and PCBs vary significantly. To account for these uncertainties, the consultation recommended a composite uncertainty factor of 10.

Based on the range of estimated daily human intakes (10-40 pg/kg bw) that would lead to body burdens similar to those associated with the most sensitive adverse effects in animal studies, and applying an uncertainty factor of 10, a TDI range of 1-4 pg TEQs/kg body weight was established.

The consultation recognised that subtle adverse effects might already be occurring in the general population in some countries at current background levels of exposure to dioxins and dioxin-like compounds. Therefore, it recommended that every effort should be made to reduce exposure to the lower end of this range.

2.3.5 Assessment by the EC-SCF meeting (2001)

The EC-SCF is responsible for advising the EC on scientific and technical questions concerning the safety of food, and its advice is used as a basis for EC rules on consumer health and food safety, toxicology and hygiene in the food production chain. In 2000 and 2001, the EC Scientific Committee on Food (EC-SCF) also assessed the risk of dioxins (EC Scientific Committee on Food, 2000; 2001). It used as its starting point the WHO 1998 evaluation (see Section 2.3.4).

2.3.5.1 Conclusions from the EC-SCF

The EC-SCF based their updated risk assessment on the LOEL for reproductive toxicity in male offspring of pregnant rats from the study by Faqi et al (1998), rather than the rat and monkey studies used by the WHO. An estimated human daily intake (EHDI) of 20

[19] The Australian participant was Professor Michael Moore, National Research Centre for Environmental Toxicology (NRCET), Brisbane.

pg/kg bw/d was calculated from the estimated steady state TCDD body burden in the rat dams at the LOEL of 25 ng/kg bw. When choosing an appropriate safety factor for deriving a TDI, an uncertainty factor accounting for interspecies variation was not considered necessary because the NOEL and LOEL were expressed in terms of body burden, thereby scaling doses from animals to humans. The committee also concluded that no uncertainty factor was required to account for differences within or between species in toxicodynamics (eg. *Ah* receptor binding affinity and enzyme induction). The ultimate safety factor consisted of an uncertainty factor of 3.2 to account for variation between individuals in human toxicokinetics (i.e. differences in absorption, accumulation, metabolism and excretion), and an additional factor of 3 because a LOEL rather than a NOEL was used. Thus, the safety factor was 9.6 (i.e. 3×3.2). Application of this 9.6-fold safety factor to the EHDI of 20 pg/kg bw yielded a TDI of 2 pg/kg bw/day. Due to the long half-lives of TCDD and related compounds in the human body, this figure was converted to a TWI of 14 pg/kg bw. In order to extend this TWI to include all 2,3,7,8-substituted PCDDs and PCDFs and the dioxin-like PCBs, the EC-SCF established a group TWI of 14 pg WHO TEQs/kg bw for these compounds.

The EC-SCF stressed that:

> *'given the average dietary intakes of dioxins and dioxin-like PCBs in the European countries of 1.2–3.0 pg/kg bw/d, a considerable proportion of the European population would still exceed the TWI derived by the Committee.'*

The EC-SCF noted that the most sensitive endpoints in animal studies were developmental and reproductive effects in rats and monkeys and endometriosis in monkeys and that the TWI they established would adequately protect against the carcinogenic effects of TCDD which require substantially higher body burdens and for which a threshold approach is applicable due to its non-genotoxic nature.

In the rat carcinogenicity study (Kociba et al, 1978) the LOAEL for liver tumours was taken as 10 ng/kg bw/day, corresponding to a body burden of 294 ng TCDD/kg bw. In order for humans to obtain a similar steady-state body burden, a daily intake of 150 pg/kg bw would be needed. The EC-SCF also concluded that rats were more sensitive than humans to the carcinogenic effects of TCDD (based on a body-burden comparison), albeit within less than one order of magnitude.

The Committee emphasised that it did not perform a quantitative risk assessment of the health risk associated with exposure to dioxins and dioxin-like PCBs because "the available data on high dose animal studies and studies of human occupational and accidental exposures cannot be extrapolated quantitatively with any confidence down to values corresponding to the background exposures of the general population". It further noted that the TWI is not a lower bound of toxicity, it is an estimate of a safe level of intake and is derived conservatively using uncertainty factors applied to NOAELs or LOAELs. Thus, slight exceedance of the TWI does not mean that there is an appreciable risk to health of individuals, but that exposure above this level leads to an erosion of the protection embedded in the TWI.

2.3.6 Assessment by the FAO/WHO 57th JECFA meeting (2001)

The Joint FAO/WHO Expert Committee on Food Additives (JECFA) evaluated dioxins at its 57th meeting in Rome, in June 2001 (FAO/WHO, 2001)[20]. JEFCA serves as the scientific advisory body to the Codex Alimentarius Commission (CAC) on matters relating to food additives, contaminants, and residues of veterinary drugs in food. The CAC sets international food standards aimed at protecting the health of consumers and facilitating international trade in foods.

2.3.6.1 Conclusions from the JECFA

The JECFA meeting concluded that a tolerable intake for TCDD could be established, based on reproductive effects in the male offspring of TCDD-treated rat dams. For assessment of tolerable intake, JECFA chose the LOEL established in the study of Faqi et al (1998) and the NOEL provided by the study of Ohsako et al (2001). Two different models were used to estimate the equivalent maternal body burden with long-term dosing: a model that assumed a linear relationship between maternal and foetal body burden, and a nonlinear model (see Table 2-6). After compensating for the background body burden of PCDDs and PCDFs found in untreated rats, JECFA derived estimated human monthly intakes (EHMIs) of 237 and 330 pg TEF/kg bw, using the linear and nonlinear models, respectively, from the study by Ohsako et al (2001). The corresponding EHMI values derived from the study by Faqi et al (1998) were 423 and 630 pg TEF/kg bw.

The committee then derived safety factors to apply to the EHMI values. In common with the 1998 WHO consultation, JECFA considered that the use of body burdens to scale doses from animals to humans removed the need to account for interspecies differences. To account for differences between individuals in human toxicokinetics, a safety factor of 3.2 was applied to the EHMIs associated with the NOEL identified by Ohsako et al (2001). No additional safety factor was applied to account for differences in human toxicodynamics. A larger safety factor was applied to the EHMI associated with the LOEL identified by Faqi and co-workers. JECFA considered that use of a LOEL warranted an additional safety factor of 3, leading to an overall safety factor of (3 x 3.2) = 9.6. The four resulting provisional tolerable monthly intake (PTMI) values ranged from 44 to 103 pg/kg bw/month.

Table 2-2 JECFA derivation of provisional tolerable monthly intake values from reproductive toxicity in rats

Study	Linear model		Nonlinear model	
	Ohsako et al (2001)	Faqi et al (1998)	Ohsako et al (2001)	Faqi et al (1998)
End point (in male offspring of treated dams)	NOEL (decreased anogenital distance at higher doses)	LOEL (decreased sperm production, sexual feminisation)	NOEL (decreased anogenital distance at higher doses)	LOEL (decreased sperm production, sexual feminisation)

[20] The Australian delegate to the 57th meeting of the JECFA was Dr Peter Abbott, Food Standards Australia New Zealand (FSANZ), Canberra, ACT

Study	Linear model		Nonlinear model	
	Ohsako et al (2001)	Faqi et al (1998)	Ohsako et al (2001)	Faqi et al (1998)
Maternal TCDD body burden (ng/kg bw)	7.6	25	7.6	25
Equivalent maternal body burden with long-term dosing (ng/kg bw)	13	25	19	39
Background body burden (ng/kg bw)	3	3	3	3
Total body burden (ng/kg bw)	16	28	22	42
Equivalent EHMI (pg/kg bw/mo)	237	423	330	630
Safety factor	3.2	9.6	3.2	9.6
Derived PTMI value (pg/kg bw/mo)	74	44	103	66

Taking the mid-point of the range, JECFA chose a PTMI for PCDDs, PCDFs and coplanar compounds of 70 pg TEF/kg bw/month. JECFA was satisfied that establishment of a tolerable intake based on non-cancer effects would also address any carcinogenic risk. The committee noted that in a long-term study in rats in which the incidence of liver tumours was increased over that in controls, the LOEL of 10 ng/kg bw/day corresponded to a steady-state body burden of 290 ng/kg bw/day; in order for humans to attain a similar steady-state body burden, they would have to have a daily intake of 150 pg/kg bw. Although the excess cancer risk at the highest exposures in human epidemiology studies was statistically significant, the JECFA commented that these results needed to be evaluated with caution as the overall risks were not high and the strongest evidence was for industrial populations with exposures two to three orders of magnitude greater than that of the general population, and also with heavy exposure to other chemicals. Furthermore, lifestyle factors such as smoking were not evaluated. It was noted, *inter alia*, that there were few precedents of carcinogens that increase the risk for cancer at all sites combined, with no excess risk for any specific tumour predominating. A "benchmark dose" was calculated from the effective dose estimated to result in a 1% increase in cancer mortality (ED01), on the basis of a meta-analysis of data for three industrial cohorts with well-documented exposure. However, the ED01 differed quite widely and depended strongly on the assumptions made. Furthermore, a number of uncertainties would influence the predicted ED01, including the exact exposure of the occupational cohorts and, to a lesser extent, the effects of factors not considered.

The Committee concluded that a tolerable intake could be established for TCDD on the basis of the assumption that there is a threshold for all effects, including cancer. Carcinogenicity due to TCDD was not linked to mutagenicity or DNA binding, and it occurred at higher body burdens in animals than other toxic effects. Thus the Committee concluded that the establishment of a tolerable intake based on effects other than cancer would also address any carcinogenic risk.

The JECFA report stated that:

'*the PTMI is not a limit of toxicity and does not represent a boundary between safe intake and intake associated with a significant increase in body burden or risk. Long-term intakes slightly above the PTMI would not necessarily result in adverse health effects but would erode the safety factor built into calculations of the PTMI. It is not possible given our current knowledge to define the magnitude and duration of excess intake that would be associated with adverse health effects.'*

The report also indicated that '*despite the uncertainties, the results suggest that a considerable fraction of the population will have a long-term mean intake above the PTMI'*.
In view of the long half-lives of PCDDs, PCDFs and PCBs, the committee concluded that it would not be appropriate to establish an acute reference dose for these compounds.

2.3.7 Other Published Assessments

2.3.7.1 Exponent, USA

A published study by Exponent, a major independent US consulting firm (Greene et al, 2003; Greene & Paustenbach, 2002) reviewed published studies involving laboratory animals and humans which addressed non-cancer effects. The analysis confirmed that developmental toxicity was the most sensitive effect of TCDD consistently seen in mice and rats; a NOAEL of 13 ng/kg (maternal body burden) was identified as the most pertinent for deriving a reference dose (RfD) for humans. Using this NOAEL and assuming 50% bioavailability, the equivalent human body burden is achieved with a daily dose of approximately 7 pg/kg bw/day. The authors noted that the use of body burden rather than dose, and the fact that male rat foetuses were the most susceptible population, it was appropriate to use safety factors of 1 for both inter-individual variation and sensitive subpopulations.

In humans, the most consistent adverse effect is chloracne. From Seveso chloracne data (see above under 'Chloracne'), the peak body burden of an affected child with the lowest serum TCDD concentration was 828 ng/kg lipid adjusted, or 207 ng/kg body burden - assuming 25% lipid). Using a safety factor of 10 (for conversion from a LOAEL to a NOAEL), Greene and Paustenbach calculated an absorbed RfD of 5 pg/kg/day; assuming 50% bioavailability, this equates to 10 pg/kg bw/day as a dose safe for the development of chloracne, even in children. The true value of the dose which could cause chloracne is likely to be significantly higher because the chloracne may well have been caused by the localised concentrations of TCDD on the skin rather than the systemic body burden. Alternatively, the lower 95th percentile confidence level for the mean peak TCDD serum concentration for people with chloracne (9,729 ng/kg lipid or 2,432 ng/kg body weight – assuming 25% lipid) could be used to develop an RfD. With a safety factor of 10 to account for inter-individual variation and a further 10 to account for sensitive subpopulations, Greene and Paustenbach estimated that an RfD of 6 pg absorbed/kg/day would not cause chloracne. Assuming 50% bioavailability, this also equates to an RfD of approximately 10 pg/kg bw/day.

The authors concluded that an RfD of 5–10 pg/kg bw/day, based on chloracne in children and developmental effects in foetal rats, should be a conservative health intake value and would indicate that current consumption levels are unlikely to pose an adverse health risk in the general population. However, due to the uncertainty in our knowledge and the less-than-perfect nature of epidemiology studies, it is important to strongly support the continued reduction in emissions of TCDD and other dioxin-like compounds to the environment.

2.4 National Exposure Standards for Dioxins

A number of national regulatory agencies have established human exposure standards for dioxins, generally referred to as tolerable daily or weekly intakes.

2.4.1 Japan

Following the same principles as the WHO 1998 re-evaluation of TDI (WHO, 1998), a joint committee from the Japanese Environment Agency and the Ministry of Health and Welfare considered the establishment of a TDI for PCDD/Fs and dioxin-like PCBs (Environment Agency and Ministry of Health and Welfare, 1999; Ohno, 2001). From the data of Gehrs et al (1997) and Gray et al (1997b), they concluded that a level of approximately 86 ng/kg is the lowest maternal body burden value just below or above which effects are manifested, including female genital anomalies that were considered to be significant as a toxic endpoint. The committee noted that in some toxicity studies, effects had been observed at lower body burdens, but when dose-dependency, reliability, reproducibility and the toxicological significance of the tests were considered, they were thought to be inadequate to use as indices for human health effects; these included the studies on endometriosis (Rier et al, 1993), reduced learning ability in offspring of monkeys (Schantz & Bowman, 1989), and decreased sperm counts in offspring of rats (Gray et al, 1997a). (This latter study drove the lower limit of 1 pg TEQ/kg bw/day of the WHO TDI range of 1–4 pg TEQ/kg bw/day.) For a maternal body burden of 86 ng/kg, an estimated human daily intake of 43.6 pg TEQ/kg bw/day was derived, and, by using an uncertainty factor of 10 (as per WHO, 1998), a provisional TDI of 4 pg TEQ/kg bw/day was derived.

2.4.2 New Zealand

In the February 2001 report to the New Zealand Ministry for the Environment, *Evaluation of the toxicity of dioxins and dioxin-like PCBs: A health risk appraisal for the New Zealand population* (Smith & Lopipero, 2001), New Zealand intakes of dioxins and dioxin-like compounds were compared with the TDI target value established by the WHO (WHO, 1998) and the Minimal Risk Level (MRL) set by the ATSDR (ATSDR, 1998) of 1 pg TEQ/kg bw/day. However, one of the recommendations of this report was that "identifying a tolerable daily intake [for New Zealanders] is not recommended".

2.4.3 The Netherlands

The exposure limit derived by the Health Council of the Netherlands (1996) is the same as the lower end of the TDI range derived by the WHO (1998) of 1–4 pg WHO-TEQ/kg bw/day. The Council's Committee on the Risk Evaluation of Substances considered that studies on Rhesus monkeys that reported objective recognition effects (Bowman et al,

1989a), endometriosis (Rier et al, 1993), and prenatal death (Bowman et al, 1989b), and a study in Marmoset monkeys that reported a change in lymphocytes (Neubert et al, 1992) were the most relevant for the derivation of a health-based criterion. From these, a LOAEL of 0.1 ng/kg bw/day was determined, and considered to be equivalent to a NOAEL of 0.05 ng/kg bw/day. Safety factors of 5 (for interspecies variation between monkeys and humans) and 10 (for differences in sensitivities between humans) were applied to give an exposure limit of 1 pg/kg bw/day; the Committee considered that this limit should be applicable to the intake of mixtures of PCDD/Fs and dioxin-like PCBs, expressed as total TEQ. The Netherlands supports the objective of the European Commission's Strategy for Dioxins to reduce human intake levels to below 14 pg WHO-TEQ/kg bw per week (ie. the TWI recommended by the EC-SCF); this strategy was agreed by the European Council of Ministers in December 2001 (COM, 2001).

2.4.4 United Kingdom

The TDI of 10 pg TCDD/kg bw/day recommended by the WHO Expert Group in 1990 (WHO, 1991) was endorsed by the UK Department of Health's Committee on the Toxicity of Chemicals in Food, Consumer Products, and the Environment (COT) (MAFF, 1992) on the basis of carcinogenicity, and reproductive and development effects. Subsequently, the COT recommended that the TDI could be regarded as 10 pg TEQ/kg bw/day based on the combined intakes of PCDD/Fs and dioxin-like PCBs (COT, 1997). In 2001 the COT produced a detailed review on dioxins and dioxin-like PCBs (COT, 2001). The Committee concluded that the available human data did not provide a sufficiently rigorous basis for establishment of a tolerable intake, so it was necessary to base its evaluation on data from studies conducted in experimental animals. It concluded that the most sensitive end-point was the effects on the developing reproductive systems of male rat foetuses exposed *in utero*. Based on this, the COT recommended that the TDI for dioxins and dioxin-like PCBs be reduced from 10 to 2 pg WHO-TEQ per kg bodyweight. This is in line with the recommendations of other bodies such as the European Commission's Scientific Committee on Food and the Joint FAO/WHO Expert Committee on Food Additives.

2.5 Hazard Summary and Discussion

This hazard assessment has reviewed some of the large amount of data on the toxicology and epidemiology of dioxin-like compounds, and summarises recent hazard assessments made by international organisations and several national agencies. Reviews of experimental data by a range of national and international agencies indicate that endocrine and reproductive effects should be among the most sensitive effects in both animals and humans.

Adverse effects reported in animals following exposure to dioxins include immunotoxicity, endometriosis in Rhesus monkeys, developmental behavioural effects in offspring of treated Rhesus monkeys, and developmental effects in rats (including reproductive toxicity in males and urogenital malformations in females). The animals most sensitive to dioxin-induced adverse effects were the male offspring of treated rats. In a study by Faqi et al (1998), dams received a loading dose of 25, 60 or 300 ng 14C-TCDD/kg bw two weeks prior to mating, followed by weekly doses of 5, 12 or 60 ng/kg bw throughout mating, pregnancy and lactation. Decreased sperm production and feminised sexual behaviour were observed in male offspring at the lowest dose, which was taken as the LOEL. The Joint Expert Committee on Food Additives (JECFA) applied linear and nonlinear curve fitting techniques to derive maternal steady-state body burden estimates of 25 and 39 ng/kg bw, respectively, at this LOEL. The lowest NOEL was found in a reproduction study by Ohsako et al (2001) in which Holtzman rats received a single oral dose of 0, 12.5, 50, 200 or 800 ng TCDD/kg bw on the 15th day of pregnancy. Male offspring displayed reduced anogenital distance and androgen receptor mRNA levels in the ventral prostate, with a LOEL of 50 ng/kg bw and a NOEL of 12.5 ng/kg bw. By reference to toxicokinetic data, JECFA estimated a maternal body burden of 13–19 ng/kg bw at the NOEL and 51–76 ng/kg bw at the LOEL.

In humans, the most widely recognised and consistently observed effect following high dose exposure to TCDD is chloracne. The condition can disappear after termination of exposure or can persist for many years. Other effects on the skin include hyperpigmentation and hirsutism. Increased levels of hepatic enzymes and slight alterations in lipid profile have been reported in humans exposed to high levels of TCDD, although the effects were mild and often transient. Temporary enlargement of the liver has also been observed.

TCDD can cause long-term alteration in glucose metabolism and slight changes in thyroid function. Evidence is suggestive of a weak correlation between diabetes incidence and occupational or accidental exposure to dioxins; however, background exposure to dioxins is not a significant risk factor for individuals who have not been occupationally or accidentally exposed.

Effects on the respiratory system, manifested mainly as upper respiratory tract irritation, have resulted from acute high exposure to TCDD. Other irritant effects resulting from acute exposure include conjunctivitis with red and irritated eyes, and blepharitis.

Clinical illness associated with immune system disorders does not appear to have been associated with TCDD in any cohort studied.

There is some suggestive evidence of toxicity to the cardiovascular system. Some studies report that higher exposure to dioxins is associated with hyperlipidemia and increased frequency of ischaemic heart disease, valvular heart disease, and retinopathy.

While dioxins can increase the incidence and severity of endometriosis in monkeys, epidemiology studies and small, hospital-based case-control studies have failed to provide compelling evidence for or against an association of environmental contaminants and endometriosis in humans.

Results from human studies of developmental effects and exposure to TCDD have generally been inconclusive. Studies of the risk of spontaneous abortion involving occupational and environmental herbicide exposure have generally not found increased risks. Several studies indicate that paternal exposure to dioxins may be associated with the birth of more girls than boys; however, the median concentration of dioxin in fathers in a study on a Seveso cohort was about 20 times the estimated average concentration of TCDD currently found in human beings in industrialised countries.

The potential neurotoxicity of PCBs was first recognised when people in Japan (1968) and Taiwan (1978-1979) consumed rice oil contaminated with PCBs and PCDFs; offspring had poorer cognitive functioning as well as other behavioural problems. In the recent Dutch PCB/dioxin study, assessment of school-age children suggested that subtle cognitive and motor developmental delays arising from prenatal PCB and dioxin exposure were seen when parental and home characteristics were less optimal but such effects were not measurable in children raised in more optimal environments. Nevertheless, findings on studies on children exposed to near background levels of PCBs and dioxins are controversial; the application of causation analysis to 24 epidemiology studies that sought an association between maternal PCB exposure and neurodevelopmental effects led to the conclusion that although there is biological plausibility, a causal association was without empirical support. A US study indicated that performance of more highly PCB-exposed breast-fed children was not diminished but was positively correlated with duration of breast-feeding.

Recently data has been collected from animal and human studies which raise concerns that teeth development may be a sensitive target for dioxin toxicity. Dental hard tissues (ie. enamel and the dentin) are not remodelled once they have been formed and hence disturbances in the function of the enamel-forming ameloblasts and the dentin-forming odontoblasts are permanent in nature and thus amenable to investigation. Whilst there is evidence of effects on tooth development arising from significant exposures to dioxin-like compounds in animal studies and humans (Yusho, Yu-Cheng and Seveso incidents), recent results from Finnish studies are not so clear cut with respect to population exposures to general ‘background’ levels. Certainly, prevailing levels of PCDD/Fs and PCBs in Finland appear to be below the threshold to cause perinatal eruption of teeth. A firm conclusion on whether hypodontia and mineralisation defects are associated with pre- and/or perinatal exposure to dioxin-like compounds would appear to require further studies involving larger numbers of children.

Of the range of non-cancer health effects evaluated in exposed adult populations, some appear to be transient and not observed when exposure ceased, whereas other effects persist for some years. Overall, epidemiology studies on populations exposed occupationally or environmentally to TCDD have not demonstrated any significantly increased all-cause or non-cancer mortality.

Epidemiological evidence from the most highly TCDD-exposed cohorts studied produces the strongest evidence of an increased cancer risk from exposure to dioxins, when the data are considered for all cancers combined. There is weaker evidence of an increased cancer risk when the data for cancers at particular sites are considered. In specific cohorts, excess risks were observed for reproductive cancers (female breast, endometrium, male breast, testis) but, overall, the pattern is inconsistent. The relative risk estimates are generally low, they are relatively consistent across studies with the highest exposures. While they are not likely to be explained by confounding, this possibility cannot be excluded.

It is difficult to find epidemiological data that have sufficient dose-response information to provide reliable risk estimates for cancer in exposed human populations. Modelling is complicated by uncertainties in extrapolating current body burdens of dioxins to past occupational exposure and by the choice of the dose-response model to fit the data. Scientific debate about the potential human carcinogenicity of dioxin-like compounds has been ongoing for many years and recent meta-analyses from three occupationally-exposed cohorts have reached such different conclusions that the debate on the carcinogenic potency of dioxins will continue for quite some time.

Three recent key international evaluations have established that hormonal, reproductive and/or developmental effects are the most sensitive indicators of dioxin-related toxicity in experimental animals. Despite some differences in the most significant studies and in the methodology used to analyse the data, the WHO, the EC-SCF and JECFA reached similar conclusions and recommended a similar health intake standard. As shown in Table 2-3, when expressed in terms of daily dose, the human intake standards proposed by the EC-SCF and JECFA lie close to the mid-point of the TDI range of 1–4 pg TEQ/kg bw/day proposed by the WHO consultation.

Table 2-3 Comparison between the standards (as TEQ) for human intake of dioxins, furans and dioxin-like PCBs agreed by WHO (1998), EC-SCF (2001) and JECFA (2001)

Exposure standard	pg kg bw/day	pg/kg bw/week	pg/kg bw/mnth
WHO consultation (1998)	**1–4**	7–28	30–120
EC-SCF (2001)	2	**14**	60
JECFA (2001)	2.3	16.3	**70**

Note: The recommended exposure standards are shown in bold, with conversions to a daily, weekly or monthly basis in plain type.

In 2002 Australia recommended a Tolerable Monthly Intake (TMI) for Australians of 70 pg TEQ/kg bodyweight from all sources combined, and including polychlorinated dioxins, polychlorinated furans and dioxin-like PCBs (NHMRC/TGA, 2002), this value being equivalent to that set by the JECFA. It was suggested at that time that this TMI be

reviewed following any further hazard evaluation of dioxins by international agencies, or the publication of significant new findings.

This re-assessment notes that, although the cancer hazard posed by this chemical has probably received the bulk of attention over the past 20 years, non-cancer hazards are likely to be more important than the cancer hazard at current background levels to which the general public may be exposed. In studies in animals, developmental toxicity appears to be most sensitive effect of TCDD, consistently seen in mice and rats. A range of adverse effects following dioxin exposure have been reported in various epidemiology studies in humans over the past 25 years, of which the most consistently reported adverse effect is chloracne.

Based on our analysis of various international hazard assessments and relevant literature published between 1999 and late 2003, it is considered that the Australian TMI of 70 pg/kg bw/month as recommended by the NHMRC and the TGA's Office of Chemical Safety should be adequately protective of the general population with respect to effects of dioxin-like compounds. Nevertheless, in view of uncertainties in the data and of adverse trends or findings in populations with higher exposures than the general public, continuing efforts should be made to minimise releases of these compounds to the environment.

Whilst several agencies have recommended against the establishment a health reference dose (eg. the US EPA, the NZ Ministry for the Environment), it is noted that the majority of the panel members of the US EPA's Science Advisory Board (SAB) recommended to the EPA that an RfD should be set.

3. Exposure Assessment

Methodology and Terminology

In conducting a human exposure or intake assessment, use is made of analytical data on levels of dioxin-like compounds in foodstuffs and various environmental media. With respect to exposure to dioxin-like compounds, this exposure assessment focuses on 17 PCDDs and PCDFs and 12 co-planar PCBs which are included in the WHO TEQ. Issues to be considered include how representative of the foodstuff or environmental medium was the sampling and how accurate was the assay method. Furthermore, interpretation of reported data are complicated by different ways in which congeners that are not actually detected are represented in sums or averages. Such non-detects need to be considered since a non-detect can mean that the compound is not there, or that the assay method used was not sufficiently sensitive to detect it. In other cases, the methodology may detect a compound but not be sufficiently sensitive to accurately quantify it.

When dioxin-like PCDD/PCDF and/or PCB congeners are not detected in an assay, there are three ways of incorporating such non-detects into the estimate of total TEQ levels. The non-detected congeners can be taken to be present at zero concentration, in

which case the TEQ estimated is the *lower bound* estimate. If non-detects are taken as being present at the Limit of Detection (LOD)[21] of the assay, then the TEQ reported is the *upper bound* estimate. The lower-bound and upper-bound estimates correspond to the minimum concentration known to be present and to a larger concentration that might be present. In almost every case, the upper bound will be an overestimate of the true value, the degree of over-estimation decreasing with increasing assay sensitivity. If non-detects are assumed to be present at 1/2 the LOD, the TEQ parameter is referred to as the *medium bound* estimate. It should be noted that if the lower bound and upper bound totals are far apart (as is often the case, particularly when assay methodology is not particularly sensitive), the medium bound estimate is not necessarily any closer to the 'true' TEQ than is either of the other two estimates. In the light of the issues above, comparisons of data collected by different programs and measured by different laboratories has to be carried out with great caution (Startin & Rose, 2003).

In the following Chapter, TEQ values estimated in different studies are sometimes compared. It should be noted several ways of calculating TEQ values have been developed eg. the Nordic TEQ (N-TEQ), the International TEQ (I-TEQ) and the WHO-TEQ. The N-TEQ (no longer used) differs from the I-TEQ mainly in that in the N-TEQ the octa-dioxin/furan congeners are not counted, while in I-TEQ they are given a TEF of 0.001; this would result in N-TEQ calculations being slightly lower than the equivalent I-TEQ calculations. WHO-TEQ values are based on the most recent scientific consensus (Van den Berg et al, 1998), withdrawing TEFs for the di-ortho PCBs (PCB170 and 180) that were assigned earlier and revising TEFs for 1,2,3,7,8-pentaCDD, octaCDD, octaCDF and PCB77. Recalculating I-TEQs as WHO-TEQs would commonly result in an approximately 10% increase in TEQ levels (Van Leeuwen et al, 2000; Smith & Lopipero, 2001). The differences between the respective TEFs are not great. Although the most important dioxin-like PCBs have been given TEF values, it should be appreciated that PCBs may interact with cellular sites other than the *Ah* receptor and therefore have some other effects that cannot be expressed in terms of TCDD equivalence. For more information on the TEQ concept and its use, see Ahlborg et al (1994) and Van den Berg et al (1998) and Appendix XVIII for a comparison of TEFs.

3.1 Current Levels in the Australian Population

3.1.1 Blood serum analysis

The aim of the study by Harden et al (2004) was to measure the serum levels of polychlorinated dibenzo-p-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs) and polychlorinated biphenyls (PCBs) in pooled blood serum collected throughout Australia between 2002-2003. De-identified serum samples were selected from surplus pathology samples and stratified according to gender, age and region, as follows:

[21] LOD – the lowest concentration of a chemical that can be qualitatively detected using a specified laboratory method (ie. it can be detected but not quantified). This may be compared with the Limit of Quantitation (LOQ), the lowest concentration of a chemical that can be detected and quantified with an acceptable degree of certainty.

Age Stratification

- <16 years (0 – 15 years, born 1987-2002 inclusive)
- 16-30 years (16-30 years, born 1972-1986 inclusive)
- 31-45 years (31-45 years, born 1957-1971 inclusive)
- 46-60 years (46-60 years, born 1942-1956 inclusive)
- 60 years (> 60 years of age, born in 1941 or earlier)

Geographic Stratification

- Four urban regions:
  - Northeast (Brisbane, Tweed and Gold Coast and other major population centres in Queensland);
  - Southeast (Sydney, Canberra, Wollongong, Newcastle and other major population centres in New South Wales);
  - South (Melbourne, Adelaide, Hobart and other major population centres in Victoria);
  - West (Perth and other major population centres in Western Australia)
- One rural region:
  - Including rural areas from all States and the Northern Territory, according to the population distribution

Where there were sufficient numbers of samples collected for each of the 50 strata, each stratum was represented by duplicate pools, analysed independently. For individuals less than 16 years old from the South and West urban regions, there were insufficient numbers of samples available, hence samples in these strata were assayed as a single pool for each gender and region, rather than in duplicate. In total, 9090 samples from the 50 strata were collected and pooled to give 96 pools.

With the exception of the number of samples collected for either sex aged <16 years in the West and South urban regions, the number of samples in each stratum was between 122-202, with an average of 193 ± 18 samples. The number of samples collected for the strata <16 years in the South and West regions were between 67-68 and 24-28, respectively. The approximate percentage of the population represented by each age strata was between 5-10%. The approximate percentage of the total Australian population represented by the 5 regions; Northeast, Southeast, South, West urban regions and one rural area were 25, 20, 9, 7 and 19% respectively. Figure 3-1 shows the geographical distribution of the collection regions.

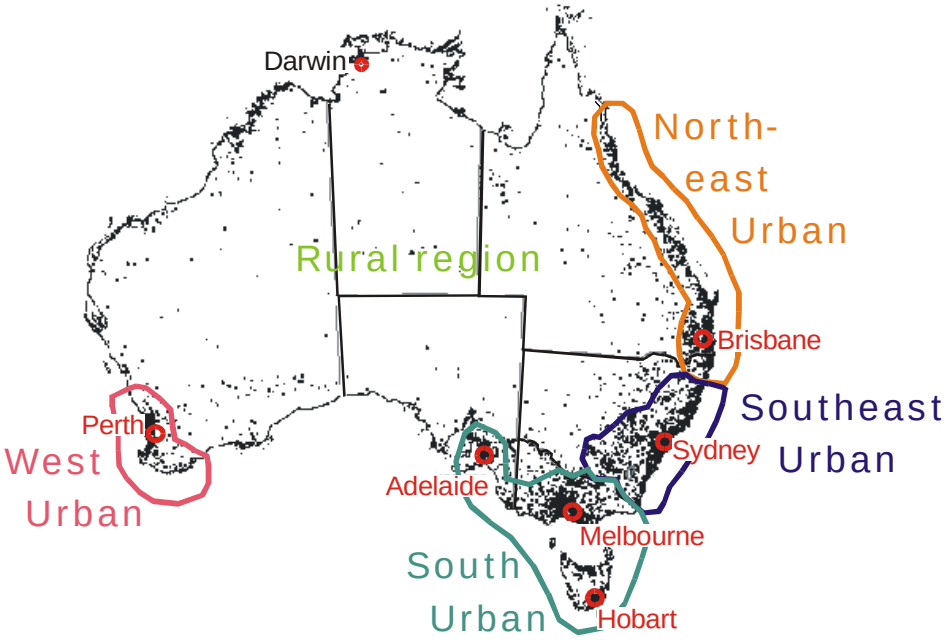

Figure 3-1 Map indicating the sampling regions of four major population areas of Australia.

The population density of each region is indicated in black (2002 data from the Australian Bureau of Statistics).

All pooled samples were sent to ERGO-Forschungsgesellschaft mbH, Hamburg, Germany for analysis, and 10 duplicate samples were sent to Health Canada, Ottawa, Canada for inter-laboratory comparison. Both laboratories are accredited for analytical dioxin analysis. Inter-laboratory and intra-laboratory variation between average values was approximately 10% and within acceptable ranges. The ERGO data were analytically reproducible, exhibiting normalised differences of between 10.3 to 21.7% for the 4 pools selected, when measured in duplicate.

The decision to use surplus pathology samples (and the possible attendant bias towards individuals who may have had some degree of physiological perturbation) *vs* a specific but totally random collection of samples across the population was made on the basis of (1) procedural complexity, including the need for more staff and material resources; (2) necessity to seek consent from each participant; and (3) much lower sample numbers for a given budget. A pilot study to compare results from pathology samples (males 30-45 years old) with samples taken for the purposes of medical examination for insurance cover (males 30-45 years old) was performed. For most of the congeners, the difference was less than 20% and thus may be explained by normal variations in analytical sensitivity. The findings indicated that there was the possibility of greater variation within the same group (ie. insurance pool 1 *vs* insurance pool 2) than between the different groups (insurance and pathology).

3.1.1.1 Levels of PCDD, PCDFs and PCBs in Blood Serum

Dioxin compounds accumulate in the fat stores of the human body. It is assumed that under steady-state conditions, the dioxin concentration in fat stores is equivalent to that present in the lipid fraction of the blood. Thus the dioxin concentration in blood is calculated on a lipid weight basis.

The concentrations of PCDD/Fs and PCBs, as TEQs calculated using WHO-TEFs (Van den berg et al, 1998) on lipid weight basis, are expressed as upper and lower bound TEQ. Only the upper bound TEQ values are reported in the text. Both lower and upper bound TEQ values stratified by age group, sex and region are recorded in Appendices (Appendix VII and VIII).

3.1.1.1(a) Total PCDDs, PCDFs plus PCBs

Table 3-1 gives the results for total WHO-TEQ (PCDD/Fs plus PCBs) for all analysed pools from the 5 age groups and regions for each sex.

Table 3-1 Australian serum levels of total dioxins (WHO-TEQ ng/kg lipid) measured in two pools (P1, P2) by age group, gender and region.

Sex	Age (years)	Northeast Urban		Southeast Urban		South Urban		West Urban		Rural Area	
		P 1	**P 2**	**P 1**	**P 2**	**P 1**	**P 2**	**P 1**	**P 2**	**P 1**	**P 2**
Male	<16	5.9	5.6	8.0	5.8	6.1	N/A	6.5	N/A	6.5	6
	16-30	5.8	5.0	5.9	7.6	6.0	5.4	4.7	4.9	5.3	6.6
	31-45	7.2	7.3	8.2	11	6.5	8.1	7.7	9.8	7.1	8.0
	46-60	12	15	13	14	14	12	11	10	12	12
	>60	17	19	22	18	19	20	18	19	16	19
Female	<16	5.5	5.3	6.3	7.3	**4.6**	N/A	5.9	N/A	8.3	6.8
	16-30	5.8	6.1	7.1	8.1	6.0	4.9	4.8	5.3	6.1	6.5
	31-45	9.0	7.7	14	11	7.3	7.6	7.2	7.2	8.6	9.8
	46-60	14	12	15	16	11	10	9.7	9.9	12	12
	>60	25	22	25	**28**	21	19	19	21	22	27

Data are given as upper bound values for PCDD/Fs plus PCBs
N/A = only one sample pool was analysed due insufficient number of samples.
Bold text = maximum and minimum values

The mean total WHO-TEQ (PCDD/Fs plus PCB) for all pooled samples was 10.90 ng WHO-TEQ/kg lipid. For males and females, the mean levels were 10.35 ng WHO-TEQ/kg lipid and 11.48 ng WHO-TEQ/kg lipid, respectively.

The serum levels of total dioxins expressed as TEQ varied by a factor of 6.1 from a minimum of 4.6 ng WHO-TEQ/kg lipid detected in South urban females <16 years (pool 1) to a maximum value of 28 ng WHO-TEQ/kg lipid in Southeast urban females >60 years (pool 2) (refer to bold type in Table 3-1).

3.1.1.1(b) Contribution from PCDDs and PCDFs

Total PCDDs and PCDFs across all regions were very similar (see graphs in Appendix II). The mean total PCDD/Fs by age group and sex, averaged across all regions is shown in Table 3-2. The levels of total PCDD/Fs increased with increasing age of the donor. The levels of total PCDD/Fs expressed as TEQ varied by a factor of 5.9 from a minimum value of 2.9 ng WHO-TEQ/kg lipid detected in Southeast females <16 years (pool 2) to 17 ng WHO-TEQ/kg lipid detected in Southeast females >60 (pool 2). There was a tendency for PCDD/Fs to be marginally higher in individuals from the Southeast and rural regions compared to Northeast, South and West regions (refer to appendix II). The contribution of PCDD/Fs to the total dioxin TEQ across all regions and age groups was between 59-67%.

3.1.1.1(c) Contribution from PCBs

As with PCDD/Fs, there is a general trend of increasing PCB concentrations with age (Table 3-2). This age trend was evident from individual congener data, the sum of PCB congeners and PCB WHO-TEQ. The levels of PCBs expressed as TEQ varied by a factor of 9.2 from a minimum value of 1.3 ng WHO-TEQ/kg lipid detected in a pool of South region females 16-30 years (pool 2) to a maximum value of 12 ng WHO-TEQ/kg lipid detected in >60 year old females living in the rural region (pool 2). The contribution of PCBs to the total dioxin WHO-TEQ was between 33-41% and was similar across all regions.

3.1.1.1(c)(i) PCB #126 and PCB #169 Loadings

The percent contribution of PCB #126 and PCB #169 to the total WHO-TEQ for PCBs is shown in Figure 3-2 (refer to as PCB loading). PCB #126 and PCB #169 were selected for analysis because they exhibit the highest TEF values, of 0.1 and 0.01 respectively, are the most toxic of all the PCB congeners and made the greatest contribution to the total PCB TEQ for any strata (Appendix III).

There was a decrease in the PCB #126 loading from the younger strata (<16 year old, Male 61.3%; Female 69.7%) compared to the older strata (>60 year olds, Male 38.7%; Females 43.0%), across the 5 regions, despite the increasing total PCB WHO-TEQ with age. Across all age groups, individuals located in the Southeast region had marginally higher PCB #126 loadings compared to other regions, with females and males exhibiting a 7-15% and 1-8% increase in PCB #126 loading, respectively. Generally females exhibited ~5% higher PCB #126 loading than males of similar age within the same region (Figure 3-2).

The mean percent contribution of PCB #169 to the total PCB WHO-TEQ was less than 5% across the 5 regions and age groups for both sexes. The PCB loading of #169 was significantly less than PCB #126 due to the 10-fold lower TEF value. Individuals in the West region exhibited marginally higher PCB #169 loadings compared to other regions, with males and females exhibiting <0.8% increase in PCB #169 loading. On average, males exhibited approximately 1% higher PCB #169 loading compared to females in the same age group (Figure 3-2).

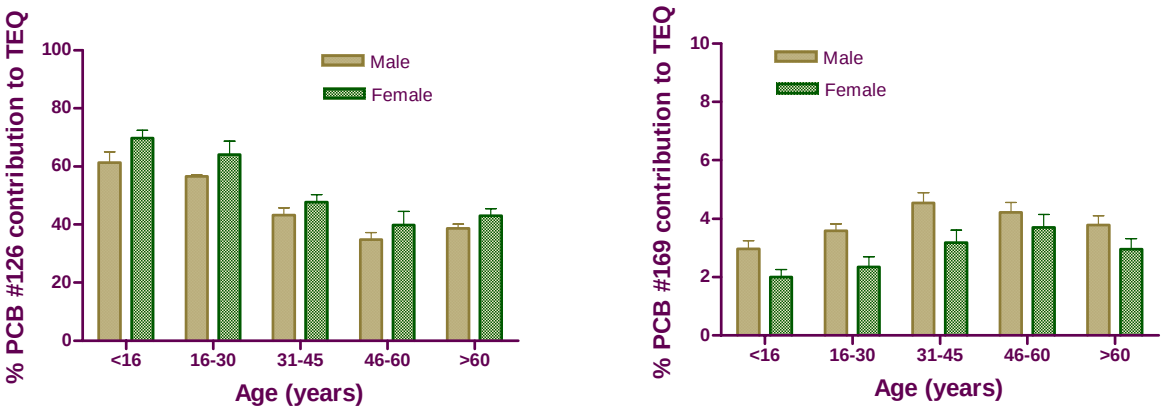

Figure 3-2 Percent contribution of PCB #126 and PCB #169 to the total PCB WHO-TEQ for a representative sample of the Australian population.

Data shown represents % contribution of PCB #126 and PCB #169 to the total WHO-TEQ for PCBs (upper bound).

Table 3-2 Serum concentrations of PCDD/Fs, PCBs and total dioxins (PCDD/Fs plus PCBs) of Australians by age group and gender averaged across regions.

Sex	Age (years)	Serum concentration across regions (ng WHO-TEQ/kg lipid)[#]		
		Minimum	Maximum	Mean[$] ± SD
PCDD/F TEQ				
Male	<16	3.90	5.30	4.21 ± 0.34
	16-30	3.40	4.60	3.69 ± 0.38
	31-45	4.50	7.10	5.34 ± 0.55
	46-60	6.40	9.30	7.76 ± 0.74
	>60	8.70	12.00	11.21 ± 1.12
Female	<16	**2.90**	4.30	3.54 ± 0.53
	16-30	3.40	4.10	3.68 ± 0.23
	31-45	4.90	6.70	5.67 ± 0.41
	46-60	6.60	9.20	7.76 ± 0.69
	>60	14.00	**17.00**	14.30 ± 0.76
PCB TEQ				
Male	<16	1.50	2.30	2.11 ± 0.75
	16-30	1.70	2.90	2.00 ± 0.37
	31-45	1.50	4.80	2.68 ± 0.74
	46-60	3.60	6.20	4.68 ± 0.84
	>60	6.30	9.60	7.28 ± 0.93
Female	<16	1.40	4.70	2.49 ± 1.15
	16-30	**1.30**	4.70	2.38 ± 1.13
	31-45	1.80	7.10	3.21 ± 1.84
	46-60	3.10	8.10	4.33 ± 0.69
	>60	5.90	**12.00**	9.99 ± 4.80
Total TEQ (PCDD/Fs plus PCB)				
Male	<16	5.60	8.00	6.32 ± 0.57
	16-30	5.00	7.60	5.69 ± 0.72

Sex	Age (years)	Serum concentration across regions (ng WHO-TEQ/kg lipid)[#]		
		Minimum	Maximum	Mean[$] ± SD
	31-45	6.50	11.00	8.02 ± 0.97
	46-60	7.30	14.00	12.44 ± 1.09
	>60	16.00	22.00	18.51 ± 0.99
Female	<16	**4.60**	8.30	6.05 ± 1.16
	16-30	4.80	8.10	6.06 ± 0.99
	31-45	7.20	14.00	8.88 ± 2.02
	46-60	9.70	16.00	12.09 ± 1.99
	>60	19.00	**28.00**	24.26 ± 5.16

TEQs calculated using the 1998 WHO-TEFs. Data reported as upper bound TEQs. Bold print indicates maxima, minima for PCDD/F, PCB or Total WHO-TEQ.

$ This does not correspond to a summation of the PCDD/F TEQ and PCB TEQ levels reported in the table, because the minimum PCDD/F TEQ and PCB TEQ occur in different samples, and similarly the maximum PCDD/F TEQ and PCB TEQ are for different samples.

* Minima, maxima and means were calculated using data from individual pools for males <16 and females <16 from the South Urban and West Urban regions.

3.1.1.2 Analysis of the factors that affect the concentration of dioxins in human blood sera

Exposure to persistent organic pollutants and subsequent body burden can be influenced by a range of factors including the age and sex of donor and the region in which the donor resides. Note that in this study, sample donors may have only resided in the area from which the sample was collected for a short period of time. Furthermore, the study design did not allow assessment of whether individuals within a particular pool had been excessively exposed to dioxin-like compounds through either diet or occupation.

3.1.1.2(a) Effect of age on serum levels of PCDD/Fs and PCBs

Figure 3-3 indicates the effects of age on the levels of total dioxins (PCDD/Fs plus PCBs) in males and females from each of the 5 regions. For all regions, the WHO-TEQ for total dioxins increased with age from the 16-30 years of age group onwards.

There was a clear trend of increasing levels of total dioxins (PCDD/Fs plus PCBs, expressed as WHO-TEQ) from the younger strata (16-30 years; 5.88 ± 0.42 ng WHO-TEQ/kg lipid) to the older strata (>60 years; 21.39 ± 0.91 ng WHO-TEQ/kg lipid) in samples from all regions. Notably, this increase in concentration only applies from the second youngest age group onward whereas no difference was observed between the concentrations in the 0-16 year old groups (6.19 ± 0.41 ng WHO-TEQ/kg lipid) and the 16–30 year old groups (5.88 ± 0.32 ng WHO-TEQ/kg lipid).

Because of the limited number of samples, pooling of samples, and limited stratification of subjects sampled, it is not possible to detect whether females who breast fed would have lower levels of dioxins than those who did not; this investigation would require a more detailed study.

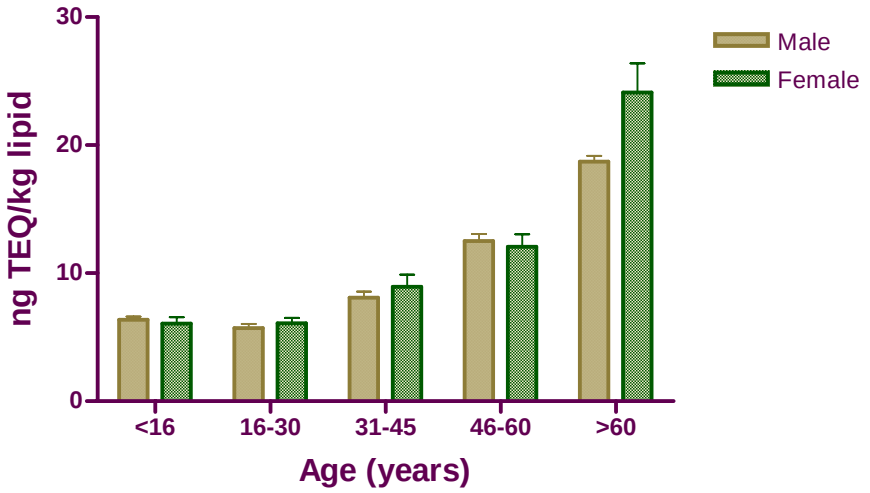

Figure 3-3 Mean total dioxin (PCDD/Fs plus PCBs) WHO-TEQ in the serum of a representative group of Australian population, by age and sex.

Data shown represent average upper bound WHO-TEQ values for pooled samples across 5 regions obtained for males and females from 5 age groups.

Many studies (Buckland et al, 2001; Wittsiepe et al, 2000; Schuhmacher et al, 1999; Jimenez et al, 1996) have shown that serum concentrations of dioxin compounds (PCDD/Fs and PCBs) increase with increasing age of the individual. One factor influencing this is the fact that older people were exposed to higher environmental levels of dioxins than those growing up now; this is discussed in further detail below.

3.1.1.2(b) Regional differences in the levels of PCDD/Fs and PCBs

Within age groups, the levels of PCDD/Fs, PCBs and total dioxins (PCDD/Fs plus PCBs) in serum appear to be very similar across all regions. With the exception of the <16 year old females, the serum concentrations from the Southeast region exhibit marginally higher levels of total dioxin WHO-TEQs compared to the West, South, Northeast urban and rural regions. For <16 year old females the highest levels of total dioxins were found in the rural region (Figure 3-4). With the exception of older rural females (>60 years), total dioxin WHO-TEQ values were similar between urban and rural areas. Rural women from the older strata (>60 years old; 25.4 ng WHO-TEQ/kg lipid) had a higher total dioxin WHO-TEQ compared urban females of the same age (22.0 ng WHO-TEQ/kg lipid averaged across the 4 urban regions).

Given that the major route of exposure for dioxins is via the diet and that the food that is consumed throughout Australia is derived from similar sources, the level of dietary exposure would be very similar across the country[22]. Thus it was not surprising that no significant regional differences in the levels of dioxins in blood serum were observed.

[22] Like the USA, nutritional exposure is subject to national food distribution systems (IOM, 2004).

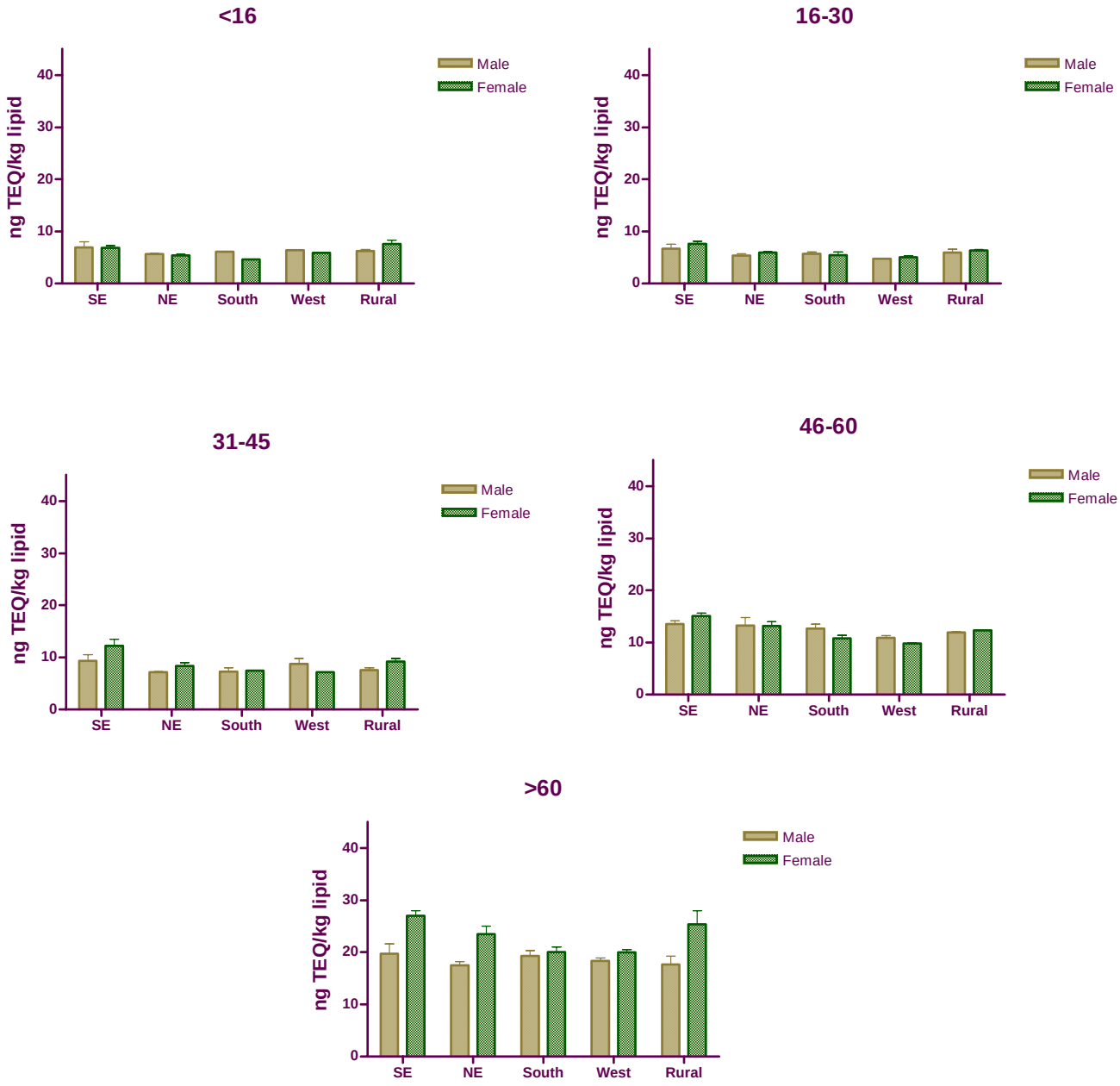

Figure 3-4 Mean total dioxin (PCDD/Fs plus PCBs) WHO-TEQ in the serum of a representative group of the Australian population by sex, age group and region.

Data shown represent average upper bound WHO-TEQ values for pooled samples across 5 regions obtained for males and females from the 5 age groups.

3.1.1.2(c) Effects of gender on the levels of PCDD/Fs and PCBs

With the exception of the >60 years age group, the total dioxin (PCDD/Fs plus PCBs) WHO-TEQ per unit lipid did not show any systematic difference between males and females. For the >60 years age group, the total dioxin WHO-TEQ for females appears to be slightly higher than males. This difference cannot be explained by differences in the average age as these were remarkably similar for males and females.

In females, the absolute amounts of total dioxin WHO-TEQs per unit body weight would be higher than in males are due to their increased percent body fat (refer to body burden section).

3.1.1.3 Comparison of serum levels with International Data

3.1.1.3(a) Comparison of Australian serum levels of PCDD/Fs with other countries

A comparison of the Australian levels of PCDD/Fs with those from other countries is depicted in Figure 3-5. Data can be found in tabular form in Appendix IV.

3.1.1.3(a)(i) North American studies

Tepper et al (1997) investigated PCDD/F levels in serum of males from community residents (control group), low-exposure-potential workers and high-exposure-potential workers from a pulp and paper mill in the USA. The median PCDD/F serum level in the control group viz.19.1 pg/g lipid was not appreciably different from that in the other two exposure groups. This value is approximately 3-fold higher than the mean of 6.4 pg/g serum lipid in Australian males, a value which was obtained by averaging across all 5 age groups (see Table 3-2).

Mean PCDD/F TEQs of pre-delivery blood and postpartum blood obtained from 5 females residing in upstate New York between 1995 and 1996 were 12.1 pg/g and 10.0 pg/g lipid respectively (Schecter et al, 1998). (The authors did not state which TEFs were used in this study and the age of the donors was not specified.) These results are somewhat higher than those found in the current Australian study in which the mean PCDD/F WHO-TEQ for reproductive-age females (averaged across 16-30 and 31-45 year age groups; See Table 3-2) was 4.7 pg/g of serum lipid.

3.1.1.3(a)(ii) European Studies

In a study of the PCDD and PCDF levels in serum from exposed and non-exposed workers from 3 sawmills in Finland, a mean I-TEQ level of 50.4 pg/g lipid was found in the non-exposed groups from all 3 sawmills (Kontsas et al, 1998). In comparison, the mean TEQ for Australian males aged 31- 60 years (averaged across 31-45 and 46-60 year age groups given in Table 3-2) is 6.6 pg WHO-TEQ/g of serum lipid.

A study in Mataro, Spain, by Gonzalez et al (2000) assessed the levels of PCDDs and PCDFs in 201 “non-occupationally” exposed subjects, of both genders, aged between 18-69 years. The serum concentration of PCDD/Fs increased with age in both sexes and, as in the current Australian study, was slightly higher in females than males.

Another Spanish study by Jimenez et al (1996) evaluated the background serum levels of PCDDs and PCDFs in 11 non-occupationally exposed people (aged between 19-55 years) living in Madrid in 1993. Calculated I-TEQ values were 8.78 pg/g and 6.96 pg/g lipid for PCDDs and PCDFs, respectively. Total PCDD/F I-TEQ was positively correlated with age (correlation coefficient = 0.79, $p<0.01$).

In a third Spanish study in Tarragona, Schuhmacher et al (1999) determined the concentrations of PCDDs and PCDFs in individual plasma samples of 20 non-occupationally exposed subjects (7 female, 13 male). Subjects were aged between 28-62 years and lived in the vicinity of a new hazardous waste incinerator or in an industrial region. The mean I-TEQ value given was 27.0 pg/g lipid (27.7 pg/g lipid for women and 25.2 pg /g lipid for men). A significant correlation ($r = 0.565$, $p < 0.01$) between the age of the subjects and the levels of PCDD/F in plasma could be observed but no significant differences were found in relation to the specific residential area (urban or industrial).

The 3 Spanish studies discussed above found TEQs for PCDD/Fs to be higher than those found in Australia. In the current Australian study, the mean WHO-TEQ for PCCD/Fs for both sexes, aged between 16-60 years (averaged across 16-30, 31-45 and 41-60 year age groups for both sexes; see Table 3-2) was 5.65 pg WHO-TEQ/g lipid.

Covaci et al (2001) analysed concentrations of PCDDs and PCDFs in 47 pooled human serum samples from 200 women aged between 50 and 65 years living in 2 areas of Flanders, Belgium in 1999. The WHO-TEQ values for PCDDs, PCDFs and PCDD/Fs from rural and suburban areas were 25.6, 23.2 and 48.7 pg/g fat respectively. No statistical differences in individual PCDD/F concentrations between the rural and suburban areas were found, nor was there any statistical difference found between WHO-TEQs for the 2 regions. PCDD/F levels in Flemish women (approx. 49 pg WHO-TEQ/g) were found to be higher than measurements in women living in other industrialized and neighbouring countries, and were considerably higher than current mean levels in Australian females of similar age who had a mean of 11.1 pg WHO-TEQ/g lipid (averaged across 46-60 and >60 years age groups; see Table 3-2).

In Norway, Johansen et al (1996) determined the concentrations of PCDDs and PCDFs in whole blood samples from 24 consumers of crabs, and 10 referents. Subjects were males aged 40-54 years of age. The Nordic-TEQs for PCDDs, PCDFs and PCDD/Fs were 9.7, 11.4 and 21.4 pg/g fat, respectively. The authors state that they found no correlation between the level of PCDD/Fs and age. In the Australian study, a Nordic-TEQ[23] would be approximately 2% lower than the WHO-TEQ, thus the mean total WHO-TEQ for males aged between 31-60 years (average across 31-45 and 45-60 year age groups given in Table 3-2) of 6.6 pg WHO-TEQ/g lipid is significantly lower than that found in the Norwegian study.

Wittsiepe et al (2000) analysed 744 individual whole blood samples collected from Germany in 1989-1998. The gender of the sample donors was not stated. The mean

[23] The Nordic-TEQ does not include OCDD/F compounds (WHO-TEF values of 0.0001) in the calculation of the TEQ, thus using the current Australian data, the Nordic-TEQ would be less than the WHO-TEQ by approximately 2%.

levels of PCDD/Fs found were 43.7 pg I-TEQ/g lipid in 1989, 20.7 pg I-TEQ/g lipid in 1997/98 and 35.6 pg/g I-TEQ/g lipid for 1989-1998 inclusive. The average ages for the periods 1989, 1997/98 and 1989-1998 were 43.6, 44.2 and 43.1 years respectively. The authors state that PCDD/F levels exhibit a positive correlation with age for most of the congeners, the sum values and the calculated toxicity equivalents. In comparison, the mean WHO-TEQ for PCDD/Fs for Australians aged between 31-45 (both sexes; sampled during 2003), was 5.5 pg WHO-TEQ/g lipid.

Menzel et al (1998) determined the dioxin blood level of exposed and 16 unexposed workers in Germany. The levels for exposed workers were greater than unexposed workers. The median PCDD/F level was 18.5 I-TEQ pg/g blood fat for unexposed workers. In another German study, Päpke et al (1996) collected blood samples in 1994 from 134 subjects. The I-TEQ for PCDD/Fs was 19.1 pg/g lipid. Even allowing for the minor differences between I-TEQ[24] and WHO-TEQ, this value is significantly higher than the mean PCCD/F WHO-TEQ of 6.72 pg/g lipid for the Australian population across all age groups. [Note that in view of declining environmental levels over recent decades, the time difference in sampling (1994 *vs* 2003) should be taken into account.]

In a third study from Germany, Wuthe et al (1996) measured blood fat concentrations of PCDDs and PCDFs in pooled samples from children (142 boys, 144 girls, <12 years) and in individual samples from adults. The overall mean PCDD/F I-TEQ was 18.4 pg/g lipid. The children were from 3 different areas in Southern Germany, an urban industrial area, an industrial area within a rural setting and a rural area. The PCDD/F I-TEQ was 8.2, 9.0 and 10.1 pg/g lipid for the 3 regions, respectively. In the current Australian study, the mean PCDD/F WHO-TEQ for children aged <16 years was 3.9 pg/g lipid.

3.1.1.3(a)(iii) Asian Studies

The studies from Asia suggest that levels of PCDD/Fs in human sera are higher in Japan and lower in China when compared to the Australian data.

Kumagai et al (2002) studied the concentrations of PCDDs and PCDFs in exposed and unexposed workers in Japan. The average age of controls was 42.1 years. The mean serum WHO-TEQ of PCDD/Fs in the controls was 20.3 pg/g lipid.

From a survey of the levels of dioxins in human blood (112 women and 131 men) conducted by the Environment Agency of Japan in fiscal year 1998, the mean WHO-TEQ for PCDDs and PCDFs was 11pg-TEQ/g fat with a range of 0.91-33 pg-TEQ/g fat. A total of 234 of the 253 subjects resided in "normal environmental regions" and 19 resided in the vicinity of waste incineration facilities. There were no significant differences detected between the regions.

The Australian mean PCDD/F TEQ across both sexes and all ages was 6.9 pg WHO-TEQ/g lipid, which is lower than mean PCDD/F values from both Japanese studies discussed above.

[24] I-TEQ is approximately 10% lower than the WHO-TEQ

Schecter et al (1996) reported on the concentrations of PCDD/Fs in the general population in a city in the Jiangxi province of China. Two pools of human blood were analysed, one from participants 15-19 years of age and the other one from participants 35-70 years of age. The total dioxin WHO-TEQ in pg/g lipid was 4.8 for the 15-19 year-old age group and 6.4 for the 35-70 year-old age group. These values are similar to 3.7 pg WHO-TEQ/g lipid for Australians aged 16-30 years, but lower than 8.7 pg WHO-TEQ/g lipid found for Australians aged over 31 years. The authors note that China, in comparison with more industrialised countries, has had low background levels of dioxins and furans and that this is most likely a result of lower levels of chemical use and environmental contamination.

3.1.1.3(a)(iv) New Zealand studies

In a study by Buckland et al (2001), 1,834 samples were analysed for levels of PCDDs and PCDFs. Samples were obtained from people of either sex aged >15 years, Maori and non-Maori. The samples were pooled according to age, ethnicity, sex and geographic location to obtain 60 pools. The mean PCDD/F concentration across the New Zealand population aged >15 years was 12.8 pg WHO-TEQ/g lipid. The levels of PCDD and PCDF congeners increased from 6.69 pg WHO-TEQ/g lipid for the 15-24 age group to 20.7 pg WHO-TEQ/g for the >65 age group. In comparison, the Australian mean WHO-TEQ PCDD/Fs for 16-30 year olds and >60 year old groups was 3.7 and 13 pg/g lipid, respectively.

In another New Zealand study, Hannah et al (1994) reported the mean levels of WHO-TEQ PCDD/Fs in blood from 28 unexposed subjects aged between 20-60 years of either sex to be 11.5 pg/g lipid. This corresponds with results from Buckland et al (2001). In comparison, the Australian mean WHO-TEQ PCDD/Fs for 16-60 year olds was 5.65 pg/g.

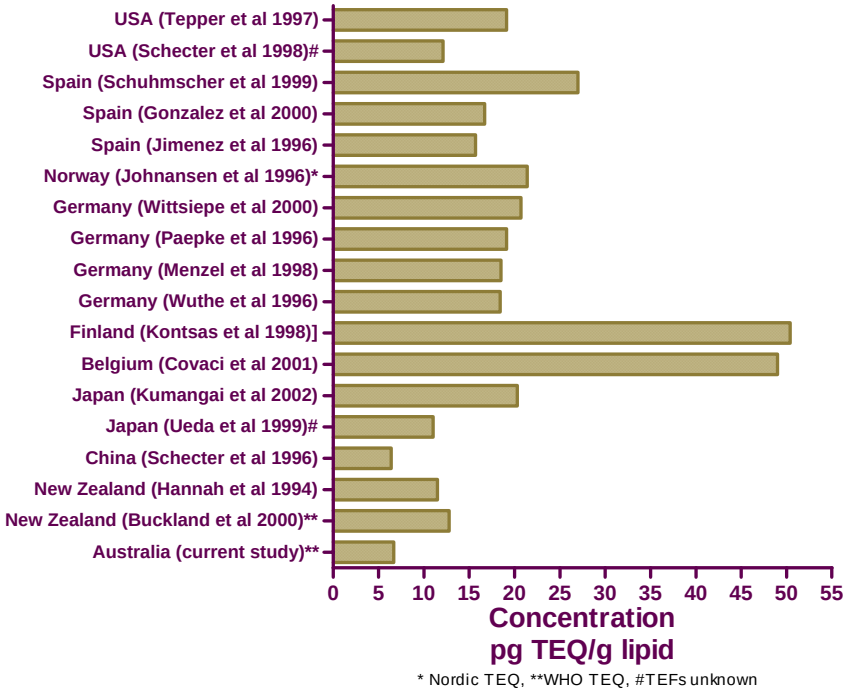

Figure 3-5 International comparison of blood serum levels of PCDD/Fs in non-occupationally exposed populations.

Data are reported as I-TEQs unless otherwise stated. The Nordic-TEQ does not include OCDD/F compounds (the WHO-TEF values for OCDD/F are 0.0001) in the calculation of TEQ, thus the Nordic-TEQ would underestimate the WHO-TEQ. The I-TEQ overestimates the WHO-TEQ by approximately 10%.

3.1.1.3b A comparison of Australian levels of PCBs with other countries

A comparison of the Australian levels of PCB #169 and PCB #126 with those from other countries is depicted in Figure 3-6. Data can be found in tabular form in Appendix IV or in the original blood serum monitoring report (Harden et al, 2004).

It was difficult to make comparisons between the current Australian data and international data for the levels of PCBs, due to the inclusion of varying PCB congeners chosen for analysis in international studies. Furthermore, many authors have not provided TEQ values or the raw data to make these calculations.

3.1.1.3(b)(i) North American studies

Kang et al (1997) investigated PCB levels in the serum of male community residents from the USA. The study group also included low exposure-potential workers and high exposure-potential workers from a pulp and paper mill. The mean serum concentrations of PCB #126 and #169 were 18 pg/g and 27 pg/g lipid, which was similar to previous results from pooled samples of the general population and in fishermen from Quebec (Kang et al, 1997). The TEQ for PCB #126 and PCB #169 was 1.8 pg WHO-TEQ/g

lipid and 0.27 pg WHO-TEQ/g lipid, respectively. This is similar to the levels in the current study for males in the Australian population where PCB #126 was 1.58 pg WHO-TEQ/g lipid and PCB #169 was 0.15 pg WHO-TEQ/g lipid. Age, body mass index, and consumption of locally caught fish were deemed to be significant predictors for non-ortho PCB levels in human serum.

Greizerstein et al (1999) determined the levels of PCB congeners in the serum of seven lactating women in New York State, USA. The mean age of the donors was 31 years old. The sum of the congeners present above the limit of detection was used to estimate the total PCB concentration which was in the range 2.6 to 5.8 ng/g of serum. The congener contributing the greatest to the total PCBs in serum was PCB #118, with a serum concentration of 28.5 ng/g. In Australian females aged 31-45 years, the average concentration of PCB #118 was 3.6 ng/g. The authors did not report the TEQ.

In a study by Schecter et al (1998) the pre-delivery and post delivery whole blood of five women living in upstate New York was analysed in the time interval between 1995 and 1996. The mean non-*ortho* PCB concentration was 35.4 pg/g lipid for pre-delivery blood and 27.6 pg/g lipid for post delivery blood. Mean TEQ (non-*ortho* PCBs only) levels were 2.26 pg/g for pre-delivery blood and 1.70 pg/g for postpartum blood. The authors did not state which TEF were used. The concentration for PCB #126 was 21.7 pg/g lipid for pre-delivery blood and 16.3 pg/g lipid for post delivery blood. For PCB #169 the concentration was 9 pg/g lipid for pre-delivery blood and 6.7 pg/g lipid for post delivery blood. The post-delivery blood values were similar to those for Australian women aged between 16-45 years, with PCB #126 and #169 WHO-TEQ values of 7.0 and 16.1 pg/g lipid.

Shadel et al (2001) determined the levels of four PCB congeners (# 77, #81, #126 and #169) in a group of 150 men and women in Missouri, USA. Subjects had no documented exposure to PCBs. The concentration of PCB #126 was 10.8 pg/g lipid and for PCB #169 was 15.7 pg/g lipid. The TEQs for PCB #126 and PCB #169 were 1.08 pg and 0.16 pg WHO-TEQ/g lipid, respectively. The corresponding WHO-TEQ values for the Australian population were 1.8 pg WHO-TEQ/g lipid and 0.13 pg WHO-TEQ/g lipid. (PCB #126 WHO TEQ calculated from current study using the non-detect value and the maximum value where applicable.)

3.1.1.3(b)(ii) European studies

In a Finnish study by Kontsas et al (1998), levels of PCBs in exposed and non-exposed workers from 3 sawmills were analysed. In this study all participants were males, aged 31-52 years. The total sample size for the unexposed group was 18 and the mean plasma level for PCB #126 was 69.4 pg/g lipid. The mean plasma value for PCB #169 at 3 different sawmills was 82.8 pg/g lipid. The mean I-TEQs for PCBs for non-exposed workers was 11.1 pg/g lipid and ranged from 8.3 to 14 pg/g lipid for 3 sawmills. The mean WHO-TEQs for PCB #126 and PCB #169 for the Australian study were 1.42 and 0.16 pg/g lipid, respectively for males aged 31-60 years.

A study in Madrid, Spain, by Jimenez et al (1996) evaluated the background serum levels of non-*ortho* PCBs in 11 unexposed people during 1993. The age of the donors

ranged between 19-55 years and the mean level found for non-*ortho* PCBs was 85.47 pg/g lipid. Calculated I-TEQ values were 7.03 pg I-TEQ/g lipid for non-*ortho* PCBs (PCB #126 plus PCB #169). In comparison, the mean WHO-TEQ for non-*ortho* PCBs (PCB #126 plus PCB #169) for the Australian population was 1.98 pg/g lipid.

Covaci et al (2001) analysed concentrations of PCBs in 47 pooled human serum samples from 200 women between 50-65 years living in two areas of Flanders, Belgium in 1999. The women sampled were not at risk from occupational exposure to PCBs or dioxins and resided in either a rural or a suburban area of Antwerp. The mean WHO-TEQ value for PCBs was 25.8 pg/g fat and ranged from 20.3-32.4 pg/g. The mean total PCB WHO-TEQ (sum of 12 congeners) for Australian women aged > 46 years (averaged across 46-60 and >60 years age groups; see Table 3-2) was 6.4 pg WHO-TEQ/g lipid, which is substantially less than the level in Belgian women.

Johansen et al (1996) determined the concentrations of 19 PCB congeners in whole blood samples from 24 consumers of crabs and 10 referents in a contaminated fjord area in Norway. The subjects included in this study were all males aged between 40-54 years. The TEQ for PCBs was approximately 45 pg WHO-TEQ/g fat compared to 3.7 pg WHO-TEQ/g lipid for Australian males aged 31-60 years.

In Germany, Päpke et al (1996) analysed 104 blood samples in 1994 for PCB #77, #126 and #169 where the mean age of the participants was 38.5 years. The mean blood concentrations for the 3 congeners were 16.1 pg/g, 80.3 pg/g and 101.8 pg/g lipid, respectively. The authors did not provide TEQ values and also reported that the levels of PCB #77 may be affected by an outside contamination. For Australians aged between 31 to 45 years, the mean serum concentrations of PCB #126, PCB#169 and PCB #77 were 14.0, 10.5 and 25.9 pg/g lipid, respectively.

In another German study, Wuthe et al (1996) measured the blood fat concentrations of PCBs in pooled samples from children and individual samples from adults. The sample of children consisted of 142 boys and 144 girls aged <12 years. For the 15 adults, the mean blood values of PCB #126 and PCB #169 were 67.3 and 116.2 ng/g lipid, respectively. The children were from 3 different areas in Southern Germany, an urban industrial area, an industrial area within a rural setting, and a rural area. The mean sum value of PCB #126 for the 3 regions were, 44.8 ng/g, 45.2 ng/g and 41.9 ng/g lipid, respectively. For PCB #169, the levels were 29.4 ng/g, 30.3 ng/g and 34.0 ng/g lipid. The authors did not calculate TEQ values. In comparison, Australians aged <16 years exhibited PCB #126 and #169 serum levels of 13.1 and 5.3 pg/g lipid, respectively, while Australians aged 19-60 years had PCB #126 and #169 serum levels of 14.9 and 11.2 pg/g lipid, respectively.

3.1.1.3(b)(iii) Asian studies

In a study of 50 “normal” Japanese women aged ca. 20 years and without children, Iida et al (1999) reported a mean WHO-TEQ for coplanar PCBs was 4.9 pg/g lipid for samples collected between 1993-1994. In this current study, Australian females aged 16-30 years had a mean total PCB TEQ of 2.4 pg WHO-TEQ/g lipid. In the Japanese study, levels of PCB126 and PCB169 were 46 and 23 pg/g lipid respectively a mean

non-*ortho*-PCB concentration (ie. PCB 77, PCB81, PCB126 and PCB169) of 15 pg/g lipid in the Australian study.

A study of 253 Japanese subjects (112 women and 131 men), conducted by the Environment Agency of Japan in fiscal year 1998 (Ueda, 1999), reported a mean WHO-TEQ for coplanar PCBs of 7.3 pg TEQ/g fat with a range of 0.33-32 pg/g fat. There were no significant differences in PCB levels detected between 234 subjects who resided in "normal environmental regions" and 19 who resided in the vicinity of waste incineration facilities. In the Australian study, individuals aged between 16-60 years had a coplanar PCB serum concentration of approximately 26.5 pg/g lipid and a mean WHO-TEQ of 1.7 pg/g lipid (averaged across 16-30, 31-45 and 45-60 year age groups; see Table 3-2).

3.1.1.3(b)(iv) New Zealand studies

Buckland et al (2001) analysed 1,834 samples for levels of PCBs. Samples were obtained from people of both sexes, aged >15 years, Maori and non-Maori. The samples were pooled according to age, ethnicity, sex and geographic location to give 60 pools. The weighted mean levels of PCB #126 and PCB #169 were 30 and 20 pg/g lipid respectively. The total PCB TEQ (including ½ LODs) was 6.86 pg WHO-TEQ/g lipid.

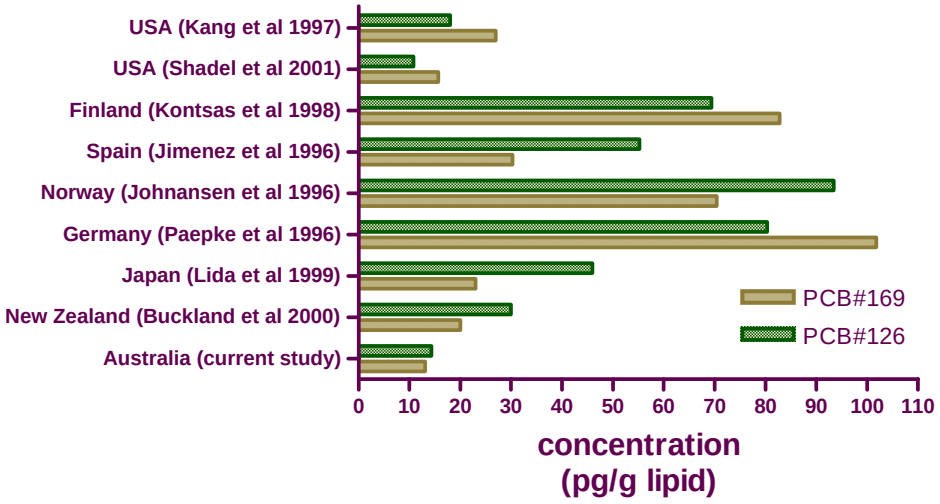

Figure 3-6 International comparison of blood serum levels of PCB #169 and #126 in non-occupationally exposed populations (pg/g lipid).

Data are reported on a lipid weight basis.

3.1.1.4 Derivations of body burden of PCDD/Fs and PCBs

For appraising the health risks of PCDD/Fs and PCBs to Australians, it is useful to also consider the concentrations of PCDD/Fs and PCB normalised for body weight and percent body fat (body burden). Estimation of the total body burden takes advantage of the fact that highly lipophilic, bioaccumulative compounds are relatively evenly

distributed in all lipid in the body. Measuring the dioxin concentrations in the lipid content of blood provides an estimation of dioxin concentration in all fat stores in the body. Data on the percentage of total body weight which is fat can then be used to estimate total body burdens.

3.1.1.4a Body Mass Index and Percent Body Fat

For the derivation of body burdens, an average percent total body fat for each region and age group was required. Ideally percent total body fat is measured using a variety of methods such as skin fold measurements or bioimpedance readings. Unfortunately for the Australian population, empirical percent total body fat data corresponding to the stratification criteria used in the dioxin serum level study was not available. Consequently percent total body fat for the Australian population was derived from the body mass index (BMI[25]) data, as this data was available for the different age and regions employed in this study. The Australian Bureau of Statistics provided mean BMI data collected using two different surveys. The 2001 National Health Survey (NHS, 2001) provided BMI data for individuals aged >16 years and the National Nutrition Survey conducted in 1995 (NNS, 1995) provided BMI data for individuals <16 years. The geographical stratification between the 2 different surveys was similar, but not identical (Table 3-3, Appendix V). However given the small differences in the mean BMI data between regions (Table 3-3), the differences in geographical stratification between the two national surveys were inconsequential.

Table 3-3 Body Mass Index data, by gender, age group and region.

Region[$]		**Northeast Urban**	**Southeast Urban**	**South Urban**	**West Urban**	**Rural**	**Average ± SD**
NNS (1995)		Metro QLD	Metro NSW/ACT	Metro VIC/TAS/VIC	Metro WA	Rural and NT	
NHS (2001)		Major urban QLD	Major urban NSW/ACT	Major urban VIC/TAS/SA	Major urban WA	Rural balance all states and territories	
Sex	**Age (years)**						
Male	<16#	20.10	20.50	20.50	20.50	20.80	20.48 ± 0.23
	16-30*	24.28	24.47	24.40	24.35	24.67	24.43 ± 0.15
	31-45*	26.95	26.43	26.16	26.38	26.96	26.58 ± 0.36
	46-60*	27.48	27.0	26.93	26.98	27.20	27.12 ± 0.27
	>60*	26.77	26.52	26.10	25.89	26.24	26.30 ± 0.25
Female	<16#	20.50	20.50	21.80	21.10	21.00	20.98 ± 0.54
	16-30*	23.48	23.10	22.52	22.83	23.66	23.12 ± 0.47
	31-45*	24.64	24.89	25.03	24.11	25.24	24.78 ± 0.43
	46-60*	26.32	25.95	26.72	25.47	27.05	26.30 ± 0.62
	>60*	25.72	26.01	25.60	26.42	25.73	25.90 ± 0.33

NNS (1995), * NHS (2001)

[$]Regions correspond to the geographical stratification used in the Australian study.

3.1.1.4(b) Model derivation and verification

[25] Body Mass Index (BMI, kg/m^2) is defined as the percent body weight per body area and is calculated by dividing body weight (kg) by the square of body height (m^2).

The derivation of percent body fat content from BMI data was performed using a modified literature model initially designed for white Americans (Equation 1) (Gallagher et al, 2000). The modified model was developed and verified using a limited data set containing percent body fat and BMI for the Australian population provided by the International Diabetes Institute (IDI) (Jonathan Shaw, Personal communication, 2004). This limited data set measured percent body fat by bioimpedance and calculated the BMI by standard methods. The data were stratified by age (25-34, 35-44, 45-54, 55-64 and 65-74 years) and sex, but not by regions. The equations used to derive percent body fat (%BF) from the BMI data for Australian males (Equation 2) and females (Equation 3) were as follows:

Equation 1: White Americans (Gallagher et al, 2000)

$$\%BF = 64.5 - 848 \times (1/BMI) + 0.079 \times AGE - 16.4 \times SEX + 0.05 \times AGE \times SEX + 39.0 \times SEX \times (1/BMI)$$

Where SEX = 1 for males and 0 for females

Equation 2: Australian Male [Sex = 1]

$$\%BF = 74.5 - 848 \times (1/BMI) + 0.079 \times Age + 0.05 \times Age + 39.0 \times (1/BMI) - 0.131 \times Age$$

Equation 3: Australian Female [Sex = 0]

$$\%BF = 64.5 - 848 \times (1/BMI) + 0.079 \times Age + 0.048 \times Age$$

Without modification and using the IDI data, equation 1 gave %BF values that were up to 5% lower than the actual %BF measured by bioimpedance. (Average standard error of estimate [SEE] values were 1.79% for males and 2.79% for females.) The limited data set illustrated that the %BF of Australians increased with increasing age to a greater extent than that predicted by the model of Gallagher et al (2000), hence the model was modified to accommodate the greater dependence of %BF on age. The derived %BF values using the modified algorithms and BMI data provided by the IDI are shown in Table 3-4. The derived %BF values had R^2 and average SEE values of 0.53 and 0.33% [males], and 0.51 and 1.39% [females].

Table 3-4 Verification of algorithm to derive %BF from BMI data for a limited data set

Age (years)	Male				Female			
	BMI[#]	%BF[#]	Calc. %BF[$]	SEE* (%)	BMI[#]	%BF[#]	Calc. %BF[$]	SEE* (%)
25-34	26.24	23.41	23.58	-0.17	24.58	36.54	39.37	-2.83
35-44	26.79	24.28	24.19	0.09	25.92	38.44	38.34	0.10
45-54	27.27	24.73	24.69	0.04	27.18	41.12	40.17	0.95
55-64	27.68	25.43	25.11	0.33	28.18	43.04	41.42	1.62
65-74	27.32	24.04	25.08	-1.04	27.89	41.20	42.65	-1.45
R^2 value				0.53				0.51
SEE (%)*				0.33				1.39

*SEE = Standard error of the estimate

[#] IDI data (%BF calculated from bioimpedance measurements, BMI calculated by standard methods).

$ Derived %BF using equations 2 or 3.

These algorithms were then used to derive %BF values from the BMI data supplied by ABS for the 5 regions and 5 age groups. These derived %BF values are reported in Tables 3-6 – 3-10 in the following section, and in appendices VII and VIII.

3.1.1.4(c) Dioxin body burdens using derived %BF values

The maximum and mean body burden of total dioxins expressed as ng WHO-TEQ/kg bw for both genders and the 5 age groups averaged across the 5 regions are listed in Table 3-5.

Table 3-5 Serum concentrations and body burden of total dioxin (PCDD/Fs plus PCBs) WHO-TEQ in Australians by gender, and age group, averaged across all regions.

Sex	Age (years)	Serum concentration (ng WHO-TEQ/kg lipid)#*		Body burden (ng WHO-TEQ/kg bw)	
		Maximum	Mean	Maximum	Mean
Male	<16	8.60	6.32	0.61	0.53
	16-30	7.50	5.69	1.41	1.21
	31-45	10.50	8.02	2.18	1.92
	46-60	14.80	12.44	3.30	3.05
	>60	21.60	18.51	4.68	4.35
Female	<16	8.30	6.05	2.14	1.72
	16-30	8.10	6.06	2.30	1.86
	31-45	13.50	8.88	4.30	3.11
	46-60	15.60	12.09	5.79	4.71
	>60	28.00	21.39	11.34	9.61

TEQs calculated using the 1997 WHO TEFs. Data reported includes LODs for non-detected congeners (i.e. upper bound TEQ).

* Maximas and means were calculated using data from individual pools.

Body burdens for PCDD/Fs, PCBs and total dioxins (PCDD/Fs plus PCBs), for males and females for each age group and region are presented in Tables 3-6 – 3-10 in the following section.

3.1.1.6(c)(i) Effects of gender on the body burden of PCDD/Fs and PCBs

The body burden data (Table 3-5) show a strong gender difference, with, on average a 54% (range 34-110%) higher body burden in females compared to males for the same age group (Figure 3-7). Generally, serum concentrations were similar for males and females within the same age group, except for the older age group, where women appeared to have higher concentrations. However, when normalised for body weight, women exhibited higher total dioxin body burdens across all age groups (Figure 3-7). This appears to be primarily influenced by the higher body fat content in women compared to that of men. As shown in Tables 3-6 – 3-10, body fat was on average 40% higher in women compared to men for the same age group.

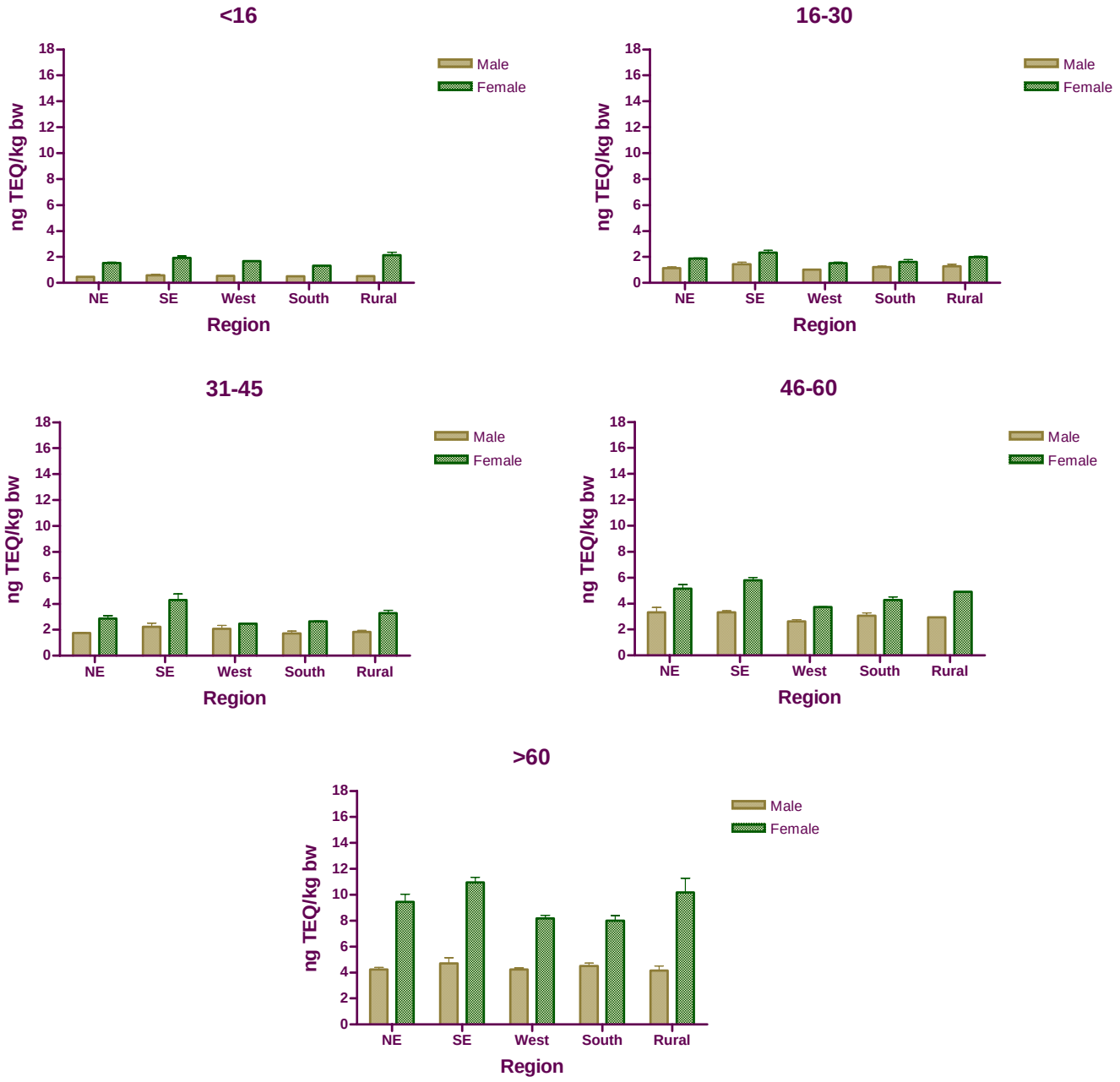

Figure 3-7 Mean body burden of total dioxins (WHO-TEQ/kg bw) in a representative group of the Australian population, by sex, age group and region.

Data shown represent mean body burdens for males and females from the all regions over the five age groups. Regions are Southeast urban (SE), Northeast urban (NE), South urban, West urban and rural.

3.1.1.4(c)(ii) Effects of age on the body burden of PCDD/Fs and PCBs

The trend of increasing total WHO-TEQ (PCDD/Fs plus PCBs) serum concentrations with age across all regions was also noted for total dioxin body burden (Figure 3-8). In males and females, there was a 6 to 8-fold increase in the total dioxin body burden of individuals aged >60 years when compared with the younger strata. Females >60 years had the highest mean dioxin body burden of 9.80 ng WHO-TEQ/kg bw compared to men of similar age (4.35 ng WHO-TEQ/kg bw) (Figure 3-8). Note that this difference in body burden (ie. amount per kg body weight) is a reflection of the significantly increased amount of body fat per unit bodyweight in females than in males (see %BF values in Tables 3-6 to 3-10); mean levels per unit lipid were similar for males and females.

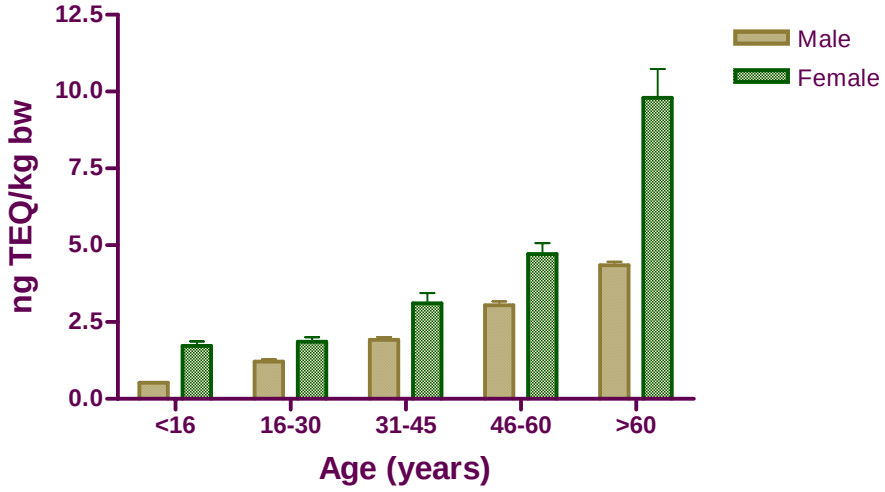

Figure 3-8 Mean body burden of total dioxins (WHO-TEQ/kg bw) in a representative group of the Australian population by sex and age group.

Data shown represent body burdens for males and females from the 5 age groups averaged across 5 regions.

3.1.1.4(c)(iii) Effects of region on the body burden of PCDD/Fs and PCBs

The individual body burden profiles of the Australian population for the 5 regions are shown in Appendix VI. Small geographical variations were observed, with total dioxin (PCDD/Fs plus PCBs) body burden tending to be marginally higher in the Southeast region (Sydney, Canberra, Wollongong, Newcastle and other major population centres in NSW) compared to other regions. This finding is unlikely to reflect an actual difference in exposure of the population in this region. With the exception of rural females, aged >60 years, there were no differences in body burden values between the urban or rural regions for either sex. For older women (>60 years; 10.2 ng WHO-TEQ/kg bw) residing in the rural region, body burden values were approximately 10% higher than similar aged urban females (9.1 ng WHO-TEQ/kg bw).

3.1.1.5 Derivation of the average lifetime daily exposure (ALDE)

Assuming steady-state conditions, the following expression can be used to estimate an approximate human daily intake to achieve the calculated body burden.

Intake (ng/kg bw/day) = body burden (ng/kg bw) x (0.693/half-life)/f

Where f is the fraction of the intake dose that is absorbed. Half-life is the average half-life of dioxins in the human body, assumed to be 7.5 years.

Dioxin compounds are absorbed through the gastrointestinal tract, skin and lungs. The degree of absorption varies with each congener, the route of absorption and the vehicle in which the dioxin is ingested. For the general population, oral intake of trace levels of these contaminants in foods accounts for 90% or more of the total intake. Findings in experimental animals indicate that oral exposure to TCDD in the diet or in an oil vehicle results in absorption of >50%, and often closer to 90% of the administered dose. More soluble congeners are almost completely absorbed, whilst extremely insoluble congeners, such as octachlorodibenzo-p-dioxin (OCDD) are poorly absorbed. Limited data from a single human volunteer suggest a high level (>85%) of absorption of TCDD in corn oil from the gastrointestinal tract. Thus, in the following calculations, the fraction of the dose that is absorbed was assumed to be 90% or f = 0.9. This value is in agreement with that used to model the ALDE for the New Zealand population, but is higher than the 50% value used by the WHO.

The WHO, in its 1998 re-evaluation of the tolerable daily intake, used a half-life of 7.5 years to estimate human intakes from animal body burden data (Van Leeuwen et al, 2000; Van Leeuwen & Younes, 2000). In the current risk appraisal, the half-life value used by WHO of 7.5 years has been used to calculate average lifetime daily intakes of dioxin compounds from body burden estimates[26].

The estimates of the equivalent daily intake of dioxin compounds for Australians by region, age and sex are reported in Tables 3-6 to 3-10.

It should be noted that the ALDE estimates in Tables 3-6 to 3-10 are calculated according to a simple steady-state model. As stated above, the calculations assume a half-life of 7.5 years for all dioxin-like compounds, assume that this half-life is constant over a person's lifetime, and assume a constant fraction absorbed. None of these assumptions are likely to be correct. For example, the average half-life probably increases with age (see 3.2.3 and discussion at 3.7.2). There is no perfect way to present these calculations, given all the uncertainties and the desire to use a simple rather than a very complex model. Therefore, these calculated figures are approximate estimates of dioxin intake at different ages and it should be borne in mind that significantly different values could be calculated using somewhat different assumptions for the half-life or the fraction absorbed for the different age groups.

[26] A recent analysis indicated mean half-lives of 6.9 years for the slower elimination period (measured from 3 to 16.35 years after exposure) in Seveso adults and 6.9 years for the slower elimination period for Ranch Hand veterans (9 to 33 years after exposure) (Michalek et al, 2002); both groups had an initial more rapid elimination phase, consistent with a two-compartment open model.

The ALDE estimates for total dioxins (PCDD/Fs plus PCBs) are similar to those reported for New Zealand (Buckland et al, 2001), with a minimum value of 0.13 pg WHO-TEQ/kg bw/d for males <16 years in the northeast urban region of Australia to a maximum of 2.96 pg WHO-TEQ/kg bw/d for women >60 years in the southeast urban region. The mean ALDE for all data was estimated as 1.32 pg WHO-TEQ/kg bw/d. (The mean ALDE estimated from New Zealand data for ages 15-65+ was 1.4 pg WHO-TEQ/kg/bw/d).

Table 3-6 Serum concentration, body burden and ALDE for PCDD/Fs, PCBs and total dioxins (PCDD/Fs plus PCBs) for Australians by gender and age for the Northeast urban region.

Sex	Dioxin	Age (years)	Mean [serum][1] (ng WHO-TEQ/kg lipid wt)	%BF[2]	Body burden (ng WHO-TEQ/kg bw)	ALDE[3] (pg TEQ/kg bw/d)
Male	PCDD/F	<16	3.95	8.24	0.33	0.09
	PCBs		1.70		0.14	0.04
	Total		5.65		0.47	0.13
	PCDD/F	16-30	3.55	21.1	0.75	0.21
	PCBs		1.80		0.38	0.11
	Total		5.35		1.13	0.32
	PCDD/F	31-45	4.70	24.37	1.15	0.32
	PCBs		2.50		0.61	0.17
	Total		7.20		1.75	0.49
	PCDD/F	46-60	8.20	24.91	2.04	0.57
	PCBs		5.05		1.26	0.35
	Total		13.25		3.30	0.93
	PCDD/F	>60	10.25	24.09	2.47	0.69
	PCBs		7.15		1.72	0.48
	Total		17.50		4.22	1.19
Female	PCDD/F	<16	3.40	28.44	0.97	0.27
	PCBs		2.00		0.57	0.16
	Total		5.40		1.54	0.43
	PCDD/F	16-30	4.00	31.31	1.25	0.35
	PCBs		1.95		0.61	0.17
	Total		5.95		1.86	0.52
	PCDD/F	31-45	5.85	34.19	2.00	0.56
	PCBs		2.50		0.85	0.24
	Total		8.35		2.85	0.80
	PCDD/F	46-60	8.60	39.01	3.35	0.94
	PCBs		3.90		1.52	0.43
	Total		12.50		4.88	1.37
	PCDD/F	>60	14.00	40.17	5.62	1.58
	PCBs		9.55		3.84	1.08
	Total		23.50		9.44	2.66

1. TEQs calculated using the 1998 WHO TEFs. Data reported includes LODs for non-detected congeners (i.e. upper bound)
2. Percent body fat was derived from BMI data obtained from the National Health Survey (NHS, 2001) (>16 years) and the National Nutrition Survey (NNS, 1995) (<16 years) by the ABS, using a modified literature algorithm.
3. Averaged lifetime daily exposure (ALDE) was calculated from:

Intake (ng/kg bw/d) = Body burden (ng/kg bw) x 0.693/half-life/f

where the half-life is taken as 7.5 years and f, the fraction of dose that is absorbed, is assumed to be 0.9.

Table 3-7 Serum concentration, body burden and ALDE for PCDD/Fs, PCBs and total dioxins (PCDD/Fs plus PCBs) for Australians by gender and age for the Southeast urban region.

Sex	Dioxin	Age (years)	Mean [serum][1] (ng WHO-TEQ/kg lipid wt)	%BF[2]	Body burden (ng WHO-TEQ/kg bw)	ALDE[3] (pg TEQ/kg bw/d)
Male	PCDD/F	<16	4.40	8.42	0.37	0.09
	PCBs		2.50		0.21	0.08
	Total		6.90		0.58	0.17
	PCDD/F	16-30	4.10	21.36	0.88	0.25
	PCBs		2.60		0.56	0.16
	Total		6.70		1.43	0.40
	PCDD/F	31-45	5.40	23.78	1.28	0.36
	PCBs		3.95		0.94	0.26
	Total		9.35		2.22	0.63
	PCDD/F	46-60	7.60	24.39	1.85	0.52
	PCBs		5.95		1.45	0.41
	Total		13.55		3.30	0.93
	PCDD/F	>60	10.95	23.81	2.61	0.73
	PCBs		8.80		2.10	0.59
	Total		19.75		4.70	1.32
Female	PCDD/F	<16	3.05	28.44	0.87	0.24
	PCBs		3.75		1.07	0.30
	Total		6.80		1.93	0.54
	PCDD/F	16-30	3.45	30.71	1.06	0.30
	PCBs		4.15		1.27	0.36
	Total		7.60		2.33	0.66
	PCDD/F	31-45	5.80	35.26	2.05	0.58
	PCBs		6.40		2.26	0.63
	Total		12.20		4.30	1.21
	PCDD/F	46-60	7.95	38.55	3.06	0.86
	PCBs		7.10		2.74	0.77
	Total		15.05		5.80	1.63
	PCDD/F	>60	16.00	40.53	6.48	1.82
	PCBs		10.50		4.26	1.20
	Total		26.00		10.54	2.96

1. TEQs calculated using the 1998 WHO TEFs. Data reported includes LODs for non-detected congeners (i.e. upper bound)
2. Percent body fat was derived from BMI data obtained from the National Health Survey (NHS, 2001) (>16 years) and the National Nutrition Survey in 1995 (<16 years) by the ABS (NNS, 1995), using a modified literature algorithm.
3. Averaged lifetime daily exposure (ALDE) was calculated from:

Intake (ng/kg bw/d) = Body burden (ng/kg bw) x 0.693/half-life/f

where the half-life is taken as 7.5 years and f, the fraction of dose that is absorbed, is assumed to be 0.9.

Table 3-8 Serum concentration, body burden and ALDE for PCDD/Fs, PCBs and total dioxins (PCDD/Fs plus PCBs) for Australians by gender and age for the South urban region.

Sex	Dioxin	Age (years)	Mean [serum][1] (ng WHO-TEQ/kg lipid wt)	%BF[2]	Body burden (ng WHO-TEQ/kg bw)	ALDE[3] (pg TEQ/kg bw/d)
Male	PCDD/F	<16	4.60	8.30	0.38	0.11
	PCBs		1.50		0.12	0.04
	Total		6.10		0.51	0.14
	PCDD/F	16-30	3.80	21.27	0.81	0.23
	PCBs		1.90		0.40	0.11
	Total		5.70		1.21	0.34
	PCDD/F	31-45	5.20	23.46	1.22	0.34
	PCBs		2.05		0.48	0.14
	Total		7.25		1.70	0.48
	PCDD/F	46-60	8.75	24.31	2.13	0.60
	PCBs		3.90		0.95	0.27
	Total		12.65		3.08	0.86
	PCDD/F	>60	13.00	23.32	3.03	0.85
	PCBs		6.30		1.47	0.41
	Total		19.30		4.50	1.27
Female	PCDD/F	<16	3.10	28.37	0.88	0.25
	PCBs		1.40		0.40	0.11
	Total		4.60		1.31	0.37
	PCDD/F	16-30	3.80	29.77	1.13	0.32
	PCBs		1.60		0.48	0.13
	Total		5.40		1.61	0.45
	PCDD/F	31-45	5.60	35.51	1.99	0.56
	PCBs		1.85		0.66	0.18
	Total		7.45		2.65	0.74
	PCDD/F	46-60	7.60	39.49	3.00	0.84
	PCBs		3.20		1.26	0.36
	Total		10.80		4.26	1.20
	PCDD/F	>60	14.00	40.01	5.60	1.58
	PCBs		6.10		2.44	0.69
	Total		20.00		8.00	2.25

1. TEQs calculated using the 1998 WHO TEFs. Data reported includes LODs for non-detected congeners (i.e. upper bound)
2. Percent body fat was derived from BMI data obtained from National Health Survey (2001) (>16 years) and the National Nutrition Survey in 1995 (<16 years) by the ABS, using a modified literature algorithm.
3. Averaged lifetime daily exposure (ALDE) was calculated from:

Intake (ng/kg bw/d) = Body burden (ng/kg bw) x 0.693/half-life/f

where the half-life is taken as 7.5 years and f, the fraction of dose that is absorbed, is assumed to be 0.9.

Table 3-9 Serum concentration, body burden and ALDE for PCDD/Fs, PCBs and total dioxins (PCDD/Fs plus PCBs) for Australians by gender and age for the West urban region.

Sex	Dioxin	Age (years)	Mean [serum][1] (ng WHO-TEQ/kg lipid wt)	%BF[2]	Body burden (ng WHO-TEQ/kg bw)	ALDE[3] (pg TEQ/kg bw/d)
Male	PCDD/F	<16	4.50	8.30	0.37	0.11
	PCBs		1.90		0.16	0.04
	Total		6.40		0.53	0.15
	PCDD/F	16-30	3.10	21.20	0.66	0.18
	PCBs		1.65		0.35	0.10
	Total		4.75		1.01	0.28
	PCDD/F	31-45	6.20	23.72	1.47	0.41
	PCBs		2.55		0.60	0.17
	Total		8.75		2.08	0.58
	PCDD/F	46-60	6.80	24.36	1.66	0.47
	PCBs		4.05		0.99	0.28
	Total		10.85		2.64	0.74
	PCDD/F	>60	11.50	23.06	2.65	0.75
	PCBs		6.85		1.58	0.44
	Total		18.35		4.23	1.19
Female	PCDD/F	<16	4.30	28.41	1.22	0.34
	PCBs		1.60		0.45	0.13
	Total		5.90		1.68	0.47
	PCDD/F	16-30	3.65	30.28	1.11	0.31
	PCBs		1.40		0.42	0.12
	Total		5.05		1.53	0.43
	PCDD/F	31-45	5.00	34.15	1.71	0.48
	PCBs		2.20		0.75	0.21
	Total		7.20		2.46	0.69
	PCDD/F	46-60	6.70	37.94	2.54	0.72
	PCBs		3.10		1.18	0.33
	Total		9.80		3.72	1.05
	PCDD/F	>60	13.50	41.04	5.54	1.56
	PCBs		6.45		2.65	0.74
	Total		19.95		8.19	2.30

1. TEQs calculated using the 1998 WHO TEFs. Data reported includes LODs for non-detected congeners (i.e. upper bound)
2. Percent body fat was derived from BMI data obtained from National Health Survey (2001) (>16 years) and the National Nutrition Survey in 1995 (<16 years) by the ABS, using a modified literature algorithm.
3. Averaged lifetime daily exposure (ALDE) was calculated from:

Intake (ng/kg bw/d) = Body burden (ng/kg bw) x 0.693/half-life/f

where the half-life is taken as 7.5 years and f, the fraction of dose that is absorbed, is assumed to be 0.9.

Table 3-10 Serum concentration, body burden and ALDE for PCDD/Fs, PCBs and total dioxins (PCDD/Fs plus PCBs) for Australians by gender and age for the rural region.

Sex	Dioxin	Age (years)	Mean [serum][1] (ng WHO-TEQ/kg lipid wt)	%BF[2]	Body burden (ng WHO-TEQ/kg bw)	ALDE[3] (pg TEQ/kg bw/d)
Male	PCDD/F	<15	4.20	8.34	0.35	0.10
	PCBs		2.05		0.17	0.05
	Total		6.25		0.52	0.15
	PCDD/F	16-30	3.90	21.63	0.84	0.24
	PCBs		2.05		0.44	0.12
	Total		5.95		1.29	0.36
	PCDD/F	31-45	5.20	24.38	1.27	0.36
	PCBs		2.35		0.57	0.16
	Total		7.55		1.84	0.52
	PCDD/F	46-60	7.45	24.61	1.83	0.52
	PCBs		4.45		1.10	0.31
	Total		11.90		2.93	0.82
	PCDD/F	>60	10.35	23.48	2.43	0.68
	PCBs		7.30		1.71	0.48
	Total		17.65		4.14	1.17
Female	PCDD/F	<15	3.85	28.41	1.09	0.31
	PCBs		3.70		1.05	0.30
	Total		7.55		2.14	0.60
	PCDD/F	16-30	3.50	31.58	1.11	0.31
	PCBs		2.80		0.88	0.25
	Total		6.30		1.99	0.56
	PCDD/F	31-45	6.10	35.73	2.18	0.61
	PCBs		3.10		1.11	0.31
	Total		9.20		3.29	0.92
	PCDD/F	46-60	7.95	39.88	3.17	0.89
	PCBs		4.35		1.73	0.49
	Total		12.30		4.91	1.38
	PCDD/F	>60	15.50	40.18	6.23	1.75
	PCBs		9.85		3.96	1.11
	Total		25.35		10.19	2.86

1. TEQs calculated using the 1998 WHO TEFs. Data reported includes LODs for non-detected congeners (i.e. upper bound)
2. Percent body fat was derived from BMI data obtained from National Health Survey (2001) (>16 years) and the National Nutrition Survey in 1995 (<16 years) by the ABS, using a modified literature algorithm.
3. Averaged lifetime daily exposure (ALDE) was calculated from:

$$Intake\ (ng/kg\ bw/d) = Body\ burden\ (ng/kg\ bw) \times 0.693/half\text{-}life/f$$

where the half-life is taken as 7.5 years and f, the fraction of dose that is absorbed, is assumed to be 0.9.

3.1.1.8 Conclusions

Whilst the serum study is an important assessment of the levels of dioxin compounds in the Australian population, it has a number of limitations. In particular, by pooling samples, it is not possible to examine the distribution of contaminant levels among individuals. Additionally, because of the use of de-identified samples there was no means by which the length of residence in a particular area could be verified. Nevertheless, the study has enabled a number of important conclusions to be made.

1. **National averages:** the National average serum concentration and body burden for dioxin compounds was 10.9 ng WHO-TEQ/kg lipid and 3.22 ng WHO-TEQ/kg bw, respectively. The mean ALDE for all data was estimated as 1.32 pg WHO-TEQ/kg bw/day.

2. **Age variations:** Serum concentrations of PCDD/Fs and PCBs were found to increase with age. Thus, the mean serum concentration of PCDD/Fs ranged from 3.54 ng WHO-TEQ/kg lipid for <16 year old females, to 14.30 ng WHO-TEQ/kg lipid for the >60 year old females. For PCBs, the mean serum concentration ranged from 2.11 ng WHO-TEQ/kg lipid for <16 year old males, to 9.99 ng WHO-TEQ/kg lipid for the >60 year old females. For total dioxin compounds (PCDD/Fs plus PCBs), the mean serum concentration ranged from 6.05 ng WHO-TEQ/kg lipid for <16 year old males, to 24.26 ng WHO-TEQ/kg lipid for the >60 year old females. As noted elsewhere, older people are likely to have experienced higher exposures due to higher environmental levels of dioxin-like compounds in the mid-20th Century; since then, environmental levels have been decreasing (see further discussion on this below).

Similarly when normalised to body weight, serum concentrations increased with age. Thus the mean body burdens for total dioxins (PCDD/Fs plus PCBs) ranged from 0.47 ng WHO-TEQ/kg bw for <16 year old males to 4.70 ng WHO-TEQ/kg bw for >60 year old males, and from 2.14 ng WHO-TEQ/kg bw for <16 year old females to 11.34 ng WHO-TEQ/kg bw for >60 year old females. The higher body burden in older people is likely to reflect higher historical environmental exposures to dioxin compounds in the 1960s and 70s, and the fact that these compounds are only slowly metabolised and excreted from the body. Additionally, given that older people have higher percent total body fat compared to the younger strata, the higher body burden also results from the continuous deposition of dioxin compounds in adipose tissue.

3. **Geographical variations:** Small geographical variations were observed, with total dioxin (PCDD/Fs plus PCBs) serum concentrations and body burdens tending to be marginally higher in the Southeast region (Sydney, Canberra, Wollongong, Newcastle and other major population centres in New South Wales) compared to other 3 urban (South, West and Northeast) and rural regions, with the exception of older rural women (>60 years). For older women (>60 years; 10.2 ng WHO-TEQ/kg bw) residing in the rural region, body burden values were approximately 10% higher than similar aged urban females (9.1 ng WHO-TEQ/kg bw). These findings are unlikely to reflect any actual differences in exposure of the population in these regions.

4. **Sex variations:** Generally no clear differences in serum concentrations were found between males and females, although women from the oldest age group (>60 years) appear to have higher concentrations then similar aged men. However when expressed as body burdens, women consistently had higher amounts of dioxin compounds per kilogram body weight than men for the same age group. This was probably largely due to the higher total body fat in females compared to males. It could reasonably be expected that breast-feeding might help reduce serum levels of dioxins; however this study which used pooling of a limited

number of pathology samples across a range of age groups would not be likely to detect such an effect.

The study also found that, on average, PCBs accounted for approximately 30-40% of the total TEQ associated with the general population exposures to dioxin compounds.

5. **International comparisons:** In the Australian population, the blood serum levels of PCDD/Fs expressed as WHO-TEQ pg/g lipid were generally lower than those observed in American, European or New Zealand studies, and similar to values reported in Asian studies.

For the majority of studies, the concentrations of PCB #169 and PCB #126 in blood sera from the Australian population was lower than that reported for subjects from America, Europe, Asia or New Zealand. Moreover, in some studies the level of PCB #126 or PCB #169 was up to 10-fold lower than that reported in some European countries (Norway, Germany or Finland).

3.1.2 Breast milk analysis

Dioxin-like compounds are lipid soluble, poorly eliminated and thus can accumulate in human fat, including the lipids of human milk. Since PCDD/F concentrations in blood and human milk are reasonably similar when concentrations are expressed on a lipid basis, human milk levels can provide a monitoring tool for exposure of a given population in a particular area (Päpke, 1998). Recently a reasonably comprehensive study on levels of PCDD/Fs and dioxin-like PCBs in human milk samples from Australian primiparous mothers has been published (Müller et al, 2003a); these results are considered below, with respect to estimating levels of exposure of the Australian population to dioxin-like compounds.

The objective of the study by Müller et al (2003a) was to investigate the levels of dioxins and dioxin-like compounds (PCDD/Fs and PCBs) in pooled human milk samples of cohorts from Australian urban, industrial and rural environments. The protocol used was identical to that used by the World Health Organization (WHO) in international studies conducted during 1987/88, 1992/93 and 2003. Once lactation was established, about 100 ml of milk was collected by each of the study participants, from which aliquots of 30 ml from each of ca. 10 mothers were pooled to give samples of about 300 ml, representing 12 regions. Besides exposure, the key factors affecting the levels of dioxin-like compounds in human breast milk are the number of children that have been breast fed by an individual (Fürst et al. 1989; Yang et al, 2002), the duration of the lactation period and maternal age (Fürst et al, 1992b). The first two factors were controlled by limiting participants to primiparous mothers breastfeeding an infant aged between 2 and 8 weeks post-partum. The mean age ($\pm$ SD) of mothers in the study was 30.7 $\pm$ 4.5 years, with the individual pools ranging from 26.8 $\pm$ 5.4 to 34.0 $\pm$ 3.4 years.

Pooled samples from Adelaide (2 separate pools), Brisbane, Darwin Hobart, Melbourne (4 pools), Perth and Sydney (2 pools) represented urban environments, Newcastle and Wollongong each provided a pooled sample representing more industrialised urban environments, while samples from the regional centres of Dalby and Bendigo/Ballarat/Lakes Entrance provided two pools representing rural regions. In total,

173 samples were collected from 12 regions between October 2001 and September 2003. Of these, 16 were excluded because they were found to have violated the inclusion/exclusion criteria. The remaining 157 samples were analysed as 17 pooled samples.

In addition to these samples a further 24 "historical" samples that were collected in 1993 were obtained from the Faculty of Life Sciences, School of Medical Sciences at RMIT University, Melbourne (courtesy of Prof. Jorma Ahokas). They were analysed as three pools of eight samples, to give a total of 20 pooled samples for analysis.

All pooled samples were assayed by the Australian Government Analytical Laboratories (AGAL), Sydney, and two duplicate samples were sent to the State Laboratory of Nordrhein-Westfalen, Münster, Germany. Both laboratories are accredited for dioxin analysis.

Dioxin-like chemicals were detected in all pooled samples. It should be noted that because of good assay sensitivity and the fact that a significant number of the congeners of the PCDD/F and PCBs were detected in the samples, the differences between lower-, middle- and upper-bound means and medians in this study were quite small. For samples collected during 2001-2003, the mean and median upper-bound levels of summed PCDD/Fs and PCBs, were 9.0 and 8.9 pg WHO-TEQ/g lipid, respectively (see Appendix IX). The average lipid concentration of all pooled samples was 3.7 $\pm$ 0.5%.

Of all analysed samples, PCDD and PCDF congeners were detected in 93% and 62%, respectively. The levels of TCDD detected in all samples were very low and ranged from <0.6 pg/g lipid in the Wollongong sample to 1.4 pg/g lipid detected in one of the two pooled Sydney samples. The average contribution of TCDD to the total WHO-TEQ for all pooled samples was 8.7%. On a concentration pg/g lipid basis, OCDD was the PCDD/F congener with the highest concentration in all pooled breast milk samples. Table 3-11 below lists the congeners making the most contribution to total WHO-TEQ in the breast milk and blood plasma (see Section 3.1.1). On average, the PCBs contributed about 30% of the total WHO-TEQ in breast milk.

Table 3-11 Main congeners contributing to total WHO-TEQ - breast milk and blood

Congener	Breast Milk (1993)	Breast Milk (2001-2003)	Blood Plasma
TCDD/Fs			
1,2,3,7,8-PeCDD	26.9%	25.5%	19.0%
2,3,4,7,8-PeCDF	12.8%	13.8%	8.1%
1,2,3,6,7,8-HxCDD	10.4%	9.6%	11%
non-ortho-PCBs			
PCB126	12.7%	18.9%	18.0%
mono-ortho-PCBs			
PCB156	5.9%	7.0%	9.2%

In breast milk collected in or close to an industrial area of Wallonia in Belgium (Focant et al, 2002) 2,3,7,8-TCDD, 1,2,3,7,8-PeCDD, 2,3,4,7,8-PeCDF and PCB-126 accounted for more than 90% of the WHO-TEQ. In breast milk from two areas in Korea, 2,3,4,7,8-PeCDD was the predominant PCDD/PCDF congener, with 2,3,7,8-TCDD being less than 3% of total PCDDs/PCDFs (Yang et al, 2002).

No obvious or systematic differences were observed in the levels of dioxin-like chemicals in breast milk samples collected from different regions of Australia during 2001-2003. Thus there were no significant difference between samples taken from urban and regional rural centres or between industrialised urban and other centres (see Appendix X). Levels, expressed as upper bound WHO-TEQs varied by a factor of 2.5, from a minimum value of 6 pg WHO-TEQ/g lipid in the rural Queensland sample to 15.2 pg WHO-TEQ/g lipid in the Brisbane sample (one pool from this city). The lowest concentrations were found in samples from a rural centre in Queensland, Wollongong (a quite heavily industrialised city), Adelaide (one of the two pools from this city), and Hobart. The higher value in the Brisbane sample was somewhat unexpected since in a previous study carried out as part of the worldwide WHO study on dioxins in breast milk, levels in a Brisbane sample were found to be close to the mean level observed of 8.3 pg WHO-TEQ/g lipid. The present result reflects an unusually low lipid content of 2.8% in the Brisbane sample, cf. 3.8 ± 0.5% for all remaining 16 samples. For results that are expressed on a lipid basis, a reduced lipid content can cause an overestimation of the actual concentration. If lipids are degraded in a sample (eg. when a sample is not adequately stored), an increase in the levels of dioxin-like compounds per unit lipid may be expected. The sampling design of this study relied on mothers collecting and storing samples themselves. Although instructions were provided, the study authors stated that it was unknown whether these instructions were always followed explicitly.

For samples collected from Melbourne women in 1993, the mean and median levels (upper bound) of PCDD/Fs and PCBs were 16 and 16.4 pg WHO-TEQ/g lipid, respectively (see Appendix IX). The average lipid concentration of these pooled samples was 3.9 $\pm$ 0.7%.

A comparison of the samples collected from Melbourne women in 1993 with those collected for the present study (2001 - 2003) clearly shows that the levels of dioxin-like compounds decreased over the ten-year time period. This is apparent if the comparison is done with all pooled samples from 2001 -2003 or just with the 4 Melbourne pools, for which the mean and median levels (upper bound) were 9.3 and 8.8 pg WHO-TEQ/g lipid. It should be noted that details of maternal parity and infant age at date of collection was not available for the older samples. However, despite this limitation, a clear decrease in the levels of these compounds over time was observed. The concentration decreased by approximately 45% between 1993 and 2001-2003. Consistently, PCDD/Fs as well as PCBs decreased in the samples.

Table 3-12 Change in WHO-TEQs in breast milk over 10 years

pg WHO-TEQ per g lipid	1993 Samples	2001-2003 Samples	
	Melbourne (3 pools)	Australia (17 pools)	Melbourne (4 pools)
Mean	16.0	9.0	9.3
Median	16.4	8.9	8.8

Data are upper bound means and medians.

A plot of the WHO-TEQ versus average age of donor mothers found no significant correlation ($r^2 = 0.16$). Similarly, the New Zealand breast milk study did not identify any relationship ($r^2 = 0.10$) between age and dioxin levels (Bates et al, 2001). Other studies have found a positive correlation between increasing maternal age and the levels of dioxin-like compounds (Fürst et al, 1992b; Beck et al, 1989); the lack of such a correlation in the Australian and New Zealand populations could possibly be due to the lower overall levels of dioxin-like compounds compared with breast milk levels in Europe and North America. Nevertheless, this relationship would be better assessed by examining individual rather than pooled samples.

The 1987/88 and 1992/93 international comparison studies organised by the WHO indicated that levels of dioxins in human milk were relatively high in industrialised countries when compared with non-industrialised countries (Liem et al, 2000). However, these international studies noted an average decline of breast-milk dioxin levels between the 2nd round investigation in 1992/1993 and the 3rd round in 2003 of about 40% (Malisch & Van Leeuwen 2003), with the largest declines in countries with the highest initial levels (Van Leeuwen & Malisch, 2002). In Japan, assays of breast milk samples collected in Osaka between 1973 - 1996 and stored frozen showed that the concentrations of dioxin-like compounds decreased by 50% over that period (Hirayama, 2000). Consistent with worldwide trends, the levels of dioxin-like compounds in the breast-milk of Australian mothers have significantly decreased over a ten-year period from 1993 to 2003.

As noted above, no consistent trends were observed between pools obtained from rural, industrial or urban regions of Australia. This is in agreement with results obtained in other studies in New Zealand (Bates et al, 2001) and Europe (Fürst et al, 1992b, Deml et al, 1996).

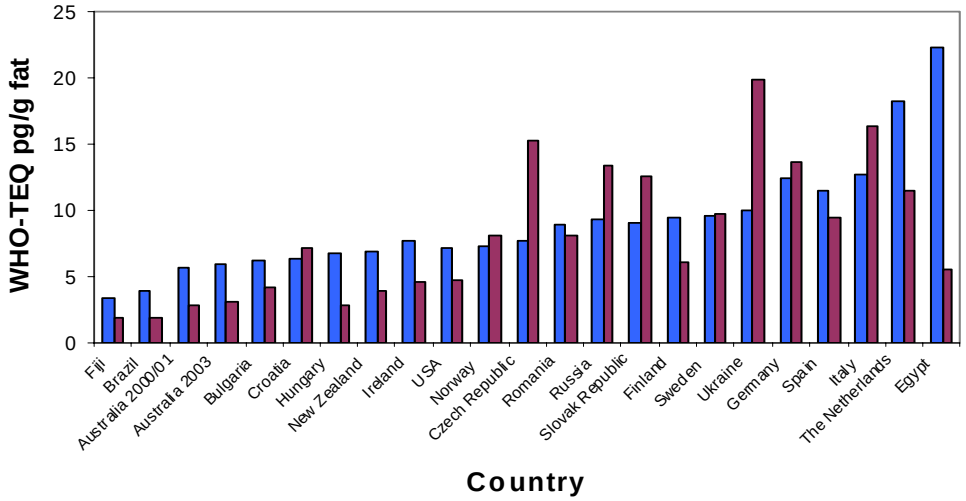

Figure 3-9 Comparison of levels of PCDD/Fs and PCBs in pooled human milk. (The first column for each country represents PCDD/Fs and the second, PCBs.)

Figure 3-9 graphically presents a comparison of PCDD/Fs and PCBs (as WHO-TEQ pg/g lipid) from the 3rd round WHO study from 2003. The lowest levels of PCDD/Fs and dioxin-like PCBs were found in the Southern hemisphere (Fiji, Brazil, Australia and New Zealand); in fact, after Fiji and Brazil, Australia had the third lowest levels of the 22 countries included in the comparison. Egypt had the highest WHO-TEQ levels for PCDD/Fs and the Ukraine had the highest WHO-TEQ for PCBs (Malisch & Van Leeuwen, 2003). Van Leeuwen & Malisch (2002) noted that for only a few countries (Australia, Brazil, Bulgaria and Hungary) were the observed levels for all three groups of compounds (PCDD/Fs, dioxin-like PCBs and indicator PCBs) consistently lower than other countries.

Higher levels than reported above have been reported from mothers living near heavily industrialised sites. Thus, relatively high levels of dioxin-like compounds have been reported in 20 non-pooled breast milk samples collected in or close to an industrial area of Wallonia in Belgium (Focant et al, 2002); PCDD/F concentrations ranged between 16.0 - 52.1 pg WHO-TEQ/g fat, with a mean of 29.4 pg TEQ/g fat. If coplanar PCBs (77, 126, 169) were included, levels ranged between 22.2 - 100.2 pg TEQ/g fat, with a mean of 40.8 pg TEQ/g fat. Similarly, the mean content of dioxins in seven pooled samples of human milk (40 individual trials) from Chapaevsk in Russia was 42.26 pg TEQ/g fat; Chapaevsk, in the Samara Region, is home to the Middle Volga chemical plant which produced hexachlorocyclohexane (lindane) and related chemicals from 1967 to 1987 (Revich et al, 2001).

Breast milk and blood have both been used to estimate body burdens of dioxin-like compounds in humans. Results of previous studies indicate that congener profiles differ somewhat between the two media. For the present study, no blood samples were collected from the participants and so the results obtained from blood serum study (Harden et al, 2004; see Section 3.1.1) were used for comparative purposes. Blood serum data were modelled to take into account age and then compared with predicted results on the basis of the average age of the donor mothers in each milk pool; overall, there was reasonably good agreement between the results from breast milk and plasma (for further details see Müller et al, 2004).

Despite the overall good comparability of the data from the blood and the breast milk study it may be noted that the PCDD/F and PCB congener profiles in the breast milk samples are slightly different from those observed in the blood study of the same age group. Specifically, PCBs and lower chlorinated dibenzodioxins occurred at similar or higher concentrations in breast milk samples compared to the blood samples. However with increasing level of chlorination (i.e. increasing hydrophobicity), there was a shift towards higher concentrations of congeners in the blood compared with breast milk.

In conclusion, the levels of dioxin-like chemicals in the breast milk of Australian women are similar across all regions of Australia but low by international standards. Consistent with world-wide trends, the levels of dioxin-like compounds have decreased over a ten-year period from 1993 to 2003, reflecting a global trend over recent decades of declining levels of dioxin-like compounds in the environment and in human tissues.

Since breast-milk levels can be taken to indicate the extent of exposure to dioxin-like compounds (after controlling for the number of children that have been breast fed by an individual, the duration of lactation, and maternal age), the international comparison of breast-milk levels of PCDD/Fs and PCBs for 22 countries indicates that Australian population exposures (including mothers and their breast-fed infants) are close to the lowest end of the scale.

Infants' dietary intake of PCDD/Fs and PCBs from breast milk is considered in Section 3.2.3.

3.2 Dietary Intake

As demonstrated by a variety of international risk assessments for dioxins, dietary exposure is expected to represent the greatest proportion of the overall intake of dioxins. Food Standards Australia New Zealand (FSANZ) conducted a survey of dioxins in a range of foods, which are representative of the total diet, in order to estimate the dietary exposure of Australians to dioxins (FSANZ, 2004). The contribution of dietary intake to the overall intake of dioxins and a comparison of the estimated dietary intake with the TMI are included in Chapter 4, Section 4.1.

3.2.1 Food Intake assessment

3.2.1.1 Survey of Australian foods for dioxin levels

Since no data existed in Australia on dioxin concentrations in food, an analytical survey was required before a dietary exposure assessment could be conducted.

Dioxin concentration data were obtained from the analysis of a range of foods sampled. A total of 168 composite samples of 22 different foods were analysed. Details of these foods are given in Appendix XI. Foods likely to have higher levels of dioxins (*eg.* meat, fish and dairy products) and those foods that are central to the Australian diet ('core foods' such as bread, potatoes, orange juice) were analysed.

Each sample analysed for dioxins was made up of a composite of four food purchases for core foods, or three food purchases for all other foods. Where appropriate, the composite food samples were prepared to a 'table ready' state before analysis, thus best representing the amounts of dioxins that would be consumed. For example, meat and eggs were cooked, while no additional preparation occurred for composite milk or bread samples. Details of the preparation undertaken for each food are available in the Supplementary Information (Part 5) to the 20th ATDS on the FSANZ web site (www.foodstandards.gov.au).

The methods used for the analysis of dioxins in food were based on the United States Environmental Protection Agency (US EPA) *Method 1613 Revision B* for PCDDs/PCDFs and *Method 1668 Revision A* for PCBs. Both methods use the technique of isotope dilution with high-resolution mass spectrometry for dioxin determination. These methods are available on the US EPA web site (www.epa.gov).

Survey samples were analysed for the 29 PCDD, PCDF and PCB congeners for which the WHO derived toxic equivalency factors (TEFs) for human risk assessment. WHO Toxic Equivalents (WHO-TEQs) (picograms/gram) were calculated by summing the weighted concentrations for each of the 17 specified PCDD/F and 12 PCB congeners, on both a fresh weight and lipid weight basis, for each food analysis. For foods with very low levels of lipid (*eg.* orange juice), WHO-TEQs were determined on a fresh weight basis only. Results were reported as both the lower bound and upper bound WHO-TEQs for each food sample (see introductory section for Chapter 3), noting that in this study the limit of quantitation (LOQ) rather than the limit of detection (LOD) was used and the LOQ is higher than the LOD.

No analysis of drinking water was carried out as a part of this survey. Given the exceedingly low water solubility of dioxins, there is virtually no exposure from drinking water, whether or not the water is chlorinated.

A summary of the mean PCDD/F and PCB concentrations for each food used in the dietary modelling is shown in Table 3-13. Individual composite sample PCDD/F and PCB summary results are available from FSANZ (FSANZ, 2004).

Peanut butter was selected for inclusion in the dioxin survey as it is a relatively high fat product, and can be a high consumption food in the diet of children. While still at a relatively low level, the lower and upper bound results for one peanut butter sample were unexpectedly high in PCDD/F (0.14-0.32 pg WHO-TEQ/gram) compared to other foods analysed in the survey. The high result was still included in the dietary modelling because it was from random samples of peanut butter available on supermarket shelves for purchase and consumption by the general public. The mean value of the four peanut butter analyses was used for the dietary modelling.

Of the ten composite fish fillet samples analysed, one sample contained greater amounts of PCBs than all the other composite samples. The high result was still included in the dietary modelling because it was from random samples of fish fillets available in supermarket for purchase and consumption by the general public. The mean value of the ten fish fillet analyses was used for the dietary modelling.

Table 3-13 Mean levels of PCDD/Fs and PCBs in Australian food

Food	Number of composite samples	PCDD/Fs		PCBs	
		Lower Bound pg WHO-TEQ/g	Upper Bound pg WHO-TEQ/g	Lower Bound pg WHO-TEQ/g	Upper Bound pg WHO-TEQ/g
Bacon	10	0.0135	0.0613	0.0117	0.0214
Baked beans	3	0.0002	0.0139	0.0011	0.0024
Bread, white	3	0.0004	0.0210	0.0003	0.0045
Butter	10	0.0105	0.1984	0.0173	0.0697
Chicken breast	11	0.0006	0.0156	0.0038	0.0057
Eggs	13	0.0026	0.0447	0.0062	0.0121
Fish fillets	10	0.0803	0.1269	0.5097	0.5100
Fish portions	9	0.0013	0.0183	0.0175	0.0204
Hamburger	10	0.0002	0.0197	0.0003	0.0069
Infant formula	5	0.0016	0.0150	0.0019	0.0027
Lamb chops	11	0.0004	0.0360	0.0040	0.0091
Leg ham	9	0.0004	0.0137	0.0012	0.0030
Liver pate	4	0.0005	0.0325	0.0020	0.0104
Margarine	6	0.0006	0.0508	0.0019	0.0071
Milk chocolate	1	0.0029	0.0440	0.0048	0.0120
Milk, whole	13	0.0010	0.0065	0.0013	0.0060
Minced beef	14	0.0008	0.0328	0.0046	0.0148
Orange juice	3	0.0000	0.0071	0.0002	0.0004
Peanut butter	4	0.0350	0.2350	0.0003	0.0132
Potatoes	3	0.0002	0.0127	0.0001	0.0016
Sausage	11	0.0013	0.0407	0.0083	0.0171
Tuna, canned	5	0.0024	0.0142	0.0269	0.0272

All samples are composites of three or four purchases.
All results are reported on a fresh weight basis.

3.2.1.2 International comparison of dioxin levels in food

Comparison of dioxin concentrations in food across different monitoring programs is difficult since there are differences in foods sampled, analytical methodologies and calculation and reporting of TEQs. Furthermore, some data may have been collected up to a decade ago and dioxin intakes would have fallen in the last decade. Therefore, a comparison of contemporary data with older data should be done cautiously. However, Tables 3-14 and 3-15 give some indication of the measured concentrations of dioxins in selected Australian foods compared with those measured in foods from other areas of the world. Data for the tables were derived from data reported by the European Commission (2000), the Codex Alimentarius Commission (2003), the US EPA (2000) and the Buckland et al (1998a), unless otherwise indicated. It should be noted that the Australian values reported in Table 3-14 are WHO-TEQs, which are 10-20% higher than the I-TEQs reported for other areas of the world.

Generally, Australian foods have levels of PCDD/Fs and PCBs that are similar to those reported in New Zealand and lower than those reported from other areas of the world.

Table 3-14 A comparison of PCDD/F concentrations in selected foods from different areas of the world.

Food	Mean PCDD/F I-TEQ (pg/g lipid weight)				
	Australia[1]	New Zealand[2]	USA	Europe[9]	Asia[9]
Beef	0.0006-0.24	0-0.11	0.89-2.86[5]	0.68	1.0
Pork	0.05-0.22[3]	0-0.20[4]	0.64-3.97[5]	0.26	0.8
Lamb	0.004-0.25	0-0.07	-	-	-
Poultry	0.02-0.53	0.037-0.29	0.10-5.17[5]	0.524	0.67
Fish	1.56-3.04	0.33-0.41	2.45-21.1[5]	9.92	0.002-10.2[6]
Eggs	0.013-0.42	0.017-0.12	0.8	1.19	-
Milk	0.04-0.23	0.019-0.16	0.98[7]	0.97	0.3-1.8
Bread/cereals[6]	0.00039-0.021	0.0012-0.0059	-	0.019	-
Fruit/ vegetables[6]	0.000023-0.013	0.0012-0.0016[8]	-	0.029	-

[1]-Values are WHO-TEQs which are 10-20% higher than I-TEQs and are reported as range of lower bound to upper bound
[2]-All New Zealand values reported a range of lower bound to medium bound
[3]- Assumes bacon is representative of all pork products
[4]-Pork meat
[5]- Values reported in Schecter et al (1997)
[6]- On a fresh wt basis
[7]- Calculated from fresh wt assuming 3.2% fat
[8]- Includes fried potatoes
[9]- Whether values represent lower and upper bound means was not reported

Table 3-15 A comparison of PCB concentrations in selected foods from different areas of the world.

Food	Mean PCB WHO-TEQ (pg/g lipid weight)				
	Australia[1]	New Zealand[2]	USA	Europe	Asia
Beef	0.03-0.11	0.0036-0.092	0.49	0.914	-
Pork	0.04-0.07[3]	0.15-0.43[4]	0.06	0.09-0.81[5]	-
Lamb	0.02-0.06	0.01-0.045	-	-	-
Poultry	0.18-0.24	0.018-0.14	0.29	0.59-0.7[5]	-
Fish	9.46-9.5	0.77	30[7]	35.3	0.004-2.0[5]
Eggs	0.04-0.11	0.05-0.11	0.87[10]	0.44-1.5[5]	-
Milk	0.04-0.11	0.027-0.15	0.5[9]	1.25	-
Bread/ cereals[6]	0.0003-0.005	0.00099-0.004	-	0.11	-
Fruit/ vegetables[6]	0.00006-0.0016	0.0012-0.0025[8]	-	0.03-0.12[5]	-

[1]-Values are reported as range of lower bound to upper bound
[2]-All New Zealand values reported a range of lower bound to medium bound
[3]- Assumes bacon is representative of all pork products
[4]-Pork meat
[5]-Range of min-max values reported
[6]- On a fresh wt basis
[7]- Calculated from fresh wt of fresh water fish and shellfish assuming 4% fat
[8]- Includes fried potatoes
[9]- Calculated from fresh wt, assumes 3.2% fat
[10]-Calculated from fresh wt, assumes 11.5% fat

3.2.1.3 Dietary exposure assessment

The dietary exposure assessment was conducted using dietary modelling techniques that combine food consumption data with dioxin concentration data to estimate the exposure to dioxins from the diet. The dietary exposure assessment was conducted using FSANZ's dietary modelling computer program, DIAMOND (for Dietary Modelling of Nutritional Data). This program is based on individual dietary records from a very large number of respondents. It contains a range of databases including:

- food consumption data from single 24-hour recall surveys (3 national dietary surveys conducted in Australia between 1983 and 1995 [2 years old and above surveyed], plus a 1997 New Zealand dietary survey [15+ years old])

- food chemical concentration data (MRLs for pesticide residues, Maximum Levels for contaminants, Maximum Permitted Levels for food additives; pesticide residue levels in food commodities from supervised field trials, surveys for levels of pesticide residues and contaminants in raw and processed food; manufacturers' data for levels of food additives)

- a recipe database (used to split prepared food into its constituent raw commodities).

Utilising its databases, this program can rapidly calculate, for different population subgroups, whether the dietary intake of a chemical in food exceeds the established health standard.

The exposure to dioxins was estimated by combining usual patterns of food consumption, as derived from the 1995 national nutrition survey (NNS) data, with concentrations of dioxins in foods as determined by the FSANZ analytical survey.

The age-gender groups assessed were infants (9 months), toddlers (2-4 years), boys and girls aged 4-15 years, males and females aged 16-29 years, males and females aged 30-44 years, males and females aged 45-59 years and males and females aged 60 years and over. In addition, exposure to dioxins was estimated for males, females and both genders combined from 2 years of age and above.

As there were no food consumption data available from the NNS on children under 2 years, a diet was constructed to enable dietary exposure to dioxins for infants at 9 months of age to be calculated. The recommended energy intake for a 9 month old boy at the 50th percentile weight was used as the basis for the model diet (WHO, 1983). Boys' weights were used because boys tend to be heavier than girls at the same age and therefore have higher energy and food requirements. It was assumed that 50% of the energy intake was derived from milk and 50% from solids (Hitchcock et al., 1986). The patterns of consumption of solid foods for a 2 year old child from the NNS were scaled down and used to determine the solid portion of the nine-month-old's diet. Certain foods such as nuts, coffee and alcohol were removed from the infant diet since nuts can be a choking risk (NHMRC, 2003) and coffee and alcohol are unsuitable foods for

infants (ACT Community Care, 2000). All milk consumption was assumed to be in the form of infant formula.

Only mean exposure to dioxins for this 9-month old age group was calculated. The 9-month old average diet was constructed by making a number of assumptions regarding energy intake and extrapolations from a 2-year old's diet. In constructing a 95th percentile diet for infants at 9 months, it could be assumed that a high consuming infant at 9 months would eat the same foods as a high consuming toddler at 2 years. However, this is unlikely to be the case, as a high consuming infant at nine months would eat more energy-dense foods. There was not enough information from references to enable a diet for a high consuming infant to be derived, and there are no individual food consumption data on high consuming infants from nutrition surveys. Therefore, there was no evidence to validate any extrapolations and assumptions for a high consuming infant. Consequently, estimated 95th percentile exposures for infants at 9 months were not calculated.

The 22 foods surveyed and analysed were matched (or mapped) to the foods reported as consumed in the NNS. This process assigns the levels of dioxins in the surveyed foods to the appropriate food consumption data to estimated dietary exposure to dioxins. In the mapping it was assumed that:

- all cereal products have the same PCDD/F and PCB concentration as white bread;
- crustaceans and molluscs have the same PCDD/F and PCB concentration as fish fillets;
- all vegetables have the same PCDD/F and PCB concentration as potatoes;
- all fruit and fruit juices have the same PCDD/F and PCB concentration as orange juice.

Given that it is impractical to analyse all foods in the food supply, a single food may be assumed to represent a whole groups of foods. For mixed foods, recipes were used to assign their ingredients to the appropriate survey food. Dioxins in some raw foods were also assumed to be carried over into the processed food proportional to the amount of fat in the product.

In the dietary modelling some general assumptions were made including:

- where a food containing PCDD/Fs and PCBs was included in a particular food group, all foods in that group contain the chemicals at the specified concentration for that group;
- any foods not analysed or included in a particular food group (*eg*. sugar, tea, coffee, soft drinks and alcoholic beverages), are assumed to contain no dioxins due to their extremely low fat content, except if they were mixed foods and their ingredients were analysed;

- for upper bound estimates of exposure, the concentrations of each of the congeners was taken as the LOQ for all cases where dioxin concentrations were reported as less than the LOQ;
- consumption of foods as recorded in the NNS represents current food consumption patterns; and
- consumers eat the same every day of the month.

There are several limitations associated with the dietary modelling including:

- monthly intakes of dioxins are based on 24-hour food consumption data (this is more of a limitations for foods not consumed daily, such as fish);
- exposures for high consumers are likely to be overestimated due to the use of 24-hour food consumption data; and
- the small number of foods analysed and the small number of random samples taken provides only a small subset of data on dioxin concentrations in the Australian food supply.

The DIAMOND program multiplies the specified concentration of dioxin by the amount of food that an individual consumed in order to estimate the exposure to each food. The exposures of each individual were then ranked and population exposures (mean and 95th percentile) were derived. To estimate dietary exposures on a per kilogram of body weight basis, each individual's total dietary exposure to dioxins from all foods was divided by their own body weight (as reported in the NNS), the results for all individuals were ranked, and population statistics (mean and 95th percentile exposures) were derived. Daily exposures, in picograms WHO-TEQ per kilogram of body weight, were multiplied by 30 to estimate monthly exposures.

Exposures to PCDD/Fs were calculated separately to PCBs for each population group. The exposure to total dioxins from all foods for each population group was then determined by summing the separate PCDD/F and PCB exposures.

Percentage contributions of each food group to total estimated exposures were calculated by dividing the sum of all consumers' exposures from one food group by the sum of all consumers' exposures from all foods containing dioxins, and multiplying this by 100.

Because the foods that were surveyed represent a wide range of foods commonly consumed as a part of the Australian diet, all dietary survey respondents were considered to be consumers of dioxins. Therefore, all results are reported on an 'all respondent' basis. Mean estimated monthly dietary intake data for PCDD/Fs and PCBs per kilogram of body weight for each population group are given in Table 3-16. Figure 3-10 shows the mean upper and lower bound estimates of total dioxin intake per kilogram bodyweight for each of the age groups. The 95th percentile estimated monthly intakes of PCDD/Fs and PCBs per kilogram of body weight are given in Appendix XII (except for infants because a 95th percentile was not calculated for this age group).

Table 3-16 Mean estimated monthly dietary exposure to dioxins

Sex	Age Group	PCDD/Fs (pg WHO-TEQ/kg bw/month)		PCBs (pg WHO-TEQ/kg bw/month)		Total Dioxins (pg WHO-TEQ/kg bw/month)	
		Lower Bound	Upper Bound	Lower Bound	Upper Bound	Lower Bound	Upper Bound
All	2+	0.9	10.2	2.8	5.4	3.7	15.6
Males	2+	0.9	10.9	3.1	5.9	4.1	16.9
Females	2+	0.8	9.5	2.6	5.0	3.4	14.5
Infants	9 months	4.5	49.0	7.3	11.8	11.8	60.8
Toddlers	2-4	1.9	25.0	4.3	11.8	6.2	36.7
Males	4-15	1.4	17.4	3.6	8.5	4.9	25.9
Females	4-15	1.2	14.8	3.1	7.1	4.2	21.9
Males	16-29	0.9	10.5	3.0	5.7	3.9	16.2
Females	16-29	0.7	8.8	2.4	4.6	3.1	13.4
Males	30-44	0.9	9.1	3.2	5.4	4.1	14.6
Females	30-44	0.7	8.0	2.4	4.3	3.1	12.3
Males	45-59	0.8	8.5	2.9	4.9	3.7	13.3
Females	45-59	0.7	7.6	2.7	4.5	3.4	12.1
Males	60+	0.7	7.9	2.8	4.6	3.5	12.5
Females	60+	0.6	7.6	2.3	4.1	3.0	11.6

Total dioxins = sum of intakes of PCDD/Fs and PCBs. Total dioxins may not equal the sum of the separate intakes due to rounding.

Estimated mean and 95th percentile exposures to total dioxins decreased with age due to food consumption being greater relative to body weight for children.

The difference between the upper bound and lower bound estimates of dietary exposures results from limitations of the analytical method and the high proportion of results that were reported as less than the limit of quantitation. It should be noted that the upper bound estimate is likely to be a very conservative overestimate and the actual dietary exposure for total dioxins lies somewhere between the lower and upper bound estimates (see introductory section of Chapter 3).

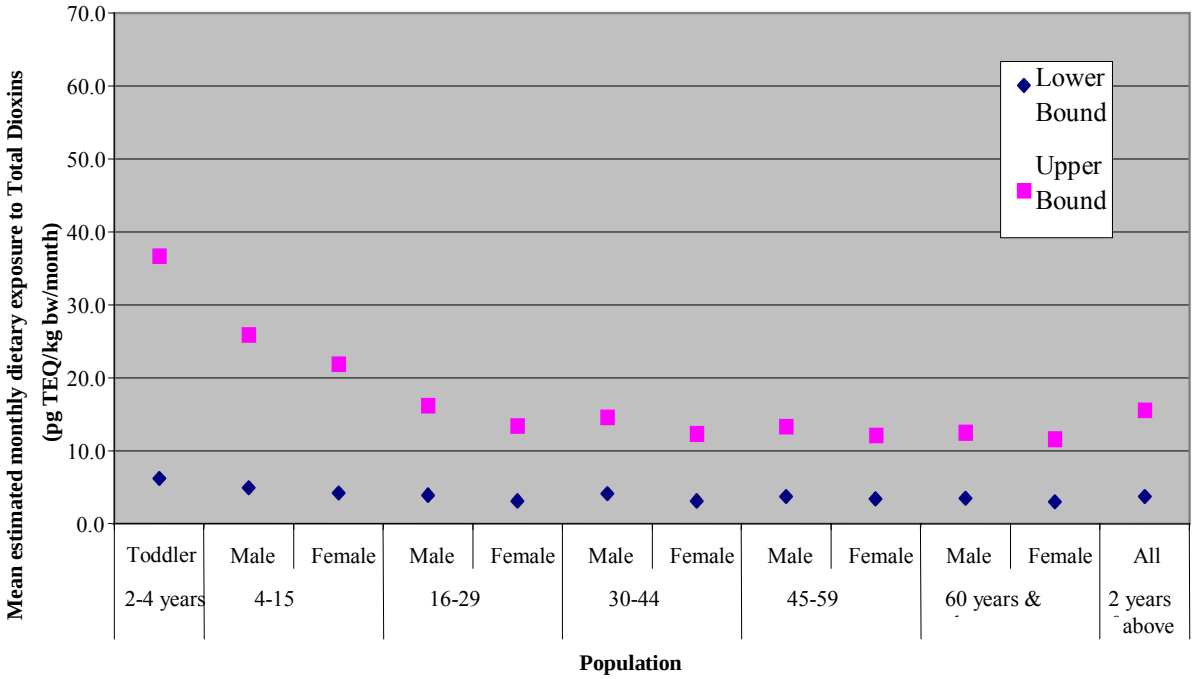

Figure 3-10 Mean estimated monthly dietary exposure to dioxins per kilogram of body weight.

The major contributors to both PCDD/F and PCB exposures were fish fillets (including crustaceans and molluscs) and milk products (including cheese, ice cream etc) in all age groups except infants. Figures 3-11 and 3-12 show the contribution of various food groups to PCDD/F and PCB intake respectively. As expected, in infants the major contributor to both PCDD/F and PCB exposures was infant formula, since it forms the major part of the diet in this age group.

The major foods that contributed to PCDD/Fs exposure differed slightly between adults and children, with milk being the major contributor for children (4-15 year old boys and girls and 2 –4 year old toddlers), and fish for adults (30-44, 45-59 and 60+ year old males and females). The contribution to PCDD/Fs exposure from fish and dairy products was almost equal in the 16-29 year age group.

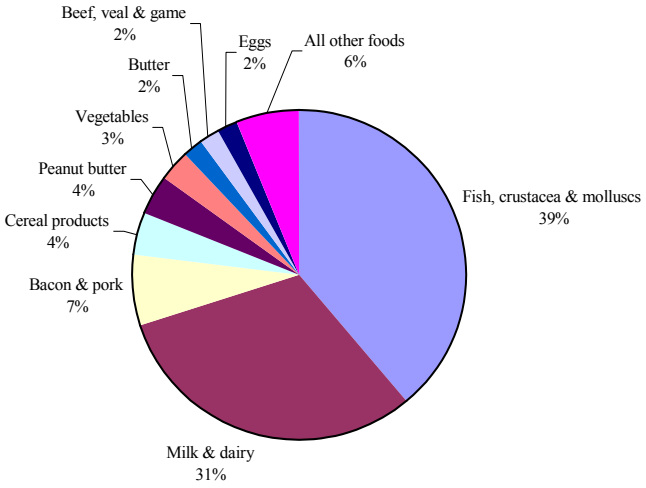

Figure 3-11 Percent contribution of major food contributors to PCDD/F dietary exposures for the population aged 2+ years

The major contributor to exposure to PCBs for all age groups except infants was fish fillets. Of the ten composite fish fillet samples analysed, one sample contained significantly greater amounts of PCBs. FSANZ performed additional dietary modelling using a mean value of PCBs for fish calculated excluding the one high value. In this scenario, fish remained the highest contributor to PCB exposure for adults. This may be attributed to the fact that people who consumed fish as a part of the 24-hour recall in the NNS were assumed to have consumed fish for 30 days when calculating the monthly exposures, which is unlikely because fish is not consumed every day by the majority of the population. However, milk was the highest contributor to PCB exposure for children and toddlers.

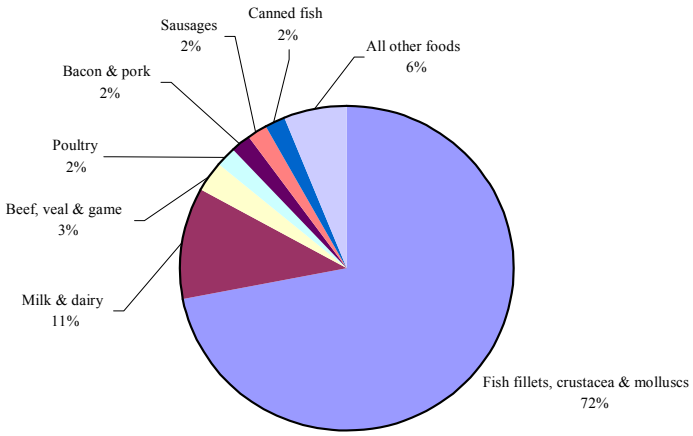

Figure 3-12 Percent contribution of major contributors to PCBs dietary exposures for the population aged 2+ years

The food groups that contributed to PCDD/F and PCBs dietary exposure for infants aged 9 months are shown in Appendices C and D respectively. The major contributors to PCDD/F exposure for infants were infant formula (78%), milk (from ice cream, cheese and infant desserts: all other milk consumption is assumed to be in the form of infant formula) (10%) and fish fillets (6%). Major contributors to PCBs exposure for infants were infant formula (61%) and fish fillets (26%).

3.2.1.3 International comparison of dietary intake of dioxins

Direct comparison of different dietary exposure assessments conducted by different countries is problematic for a number of reasons including differences in dietary survey design, age groups surveyed, different methods of determining food consumption for the population and different methods of collecting food data. In addition there can be quite different patterns of food consumption in different areas of the world and there may be differences in calculating and reporting of TEQs. Furthermore, some data may have been collected up to a decade ago and dioxin intakes would have fallen in the last decade. Therefore, a comparison of contemporary data with older data should be done cautiously. Nonetheless, Table 3-17 gives a comparison of the mean estimated dietary exposure for adults of different countries/regions of the world for the purpose of providing some indication of the dietary exposure of the Australian population relative to that of the populations of other countries.

In general terms, the estimated intake of dioxins by Australians is comparable to that of New Zealand and lower than that of most other industrialised nations.

Table 3-17 An international comparison of mean estimated dietary intakes of dioxins

Country/region	Reference	PCDD/Fs (pg WHO-TEQ/kg bw/month)	PCBs (pg WHO-TEQ/kg bw/month)	Total Dioxins (pg WHO-TEQ/kg bw/month)
Australia[1]	(this study)	0.9-10.2	2.8-5.4	3.7-15.6
New Zealand[2]	Buckland et al 1998a, Smith and Lopipero 2001	6.6	4.5	11.1
UK[3,4]	Food Standards Agency 2003	9	9-12	15-21
USA[6]	Schecter et al 1994a, 1996b US EPA, 2000	9-90 16.7	30 10.1	- 26.8
Europe[4]	European Commission 2000	12-45	24-45	36-90
Canada[5,6]	Birmingham et al 1989a	60	-	-
	Codex 2003	24	7.8	31.8
Germany[5,6]	Beck et al 1992	56		
The Netherlands	Freijer et al 2001	20.7	18.6	39

[1]-Range is lower bound to upper bound for all persons 2+years of age
[2]-Medium bound estimate for adult males
[3]-Range is lower bound to upper bound for average adult
[4]-Sum of PCDD/F and PCB may not equal sum of separate intakes due to rounding
[5]-Assuming a 70 kg person
[6]-I-TEQs. WHO-TEQs are 10-20% higher than I-TEQs

3.2.2 Agricultural commodities

The Australian Government Department of Agriculture, Fisheries and Forestry (DAFF) conducted a dioxin testing program through a joint arrangement between the Australian Government Department of the Environment and Heritage (DEH) and participating industry bodies.

In 2002, the National Residue Survey (NRS), managed by DAFF, arranged for the collection of approximately 220 samples from meat and fish products (DAFF, 2003). The collection of 19 milk samples was organised by the Australian Dairy Industry Corporation and a contract analytical laboratory carried out the analysis of all samples for PCDD/Fs and PCBs.

Table 3-18 shows the measured PCDD/F, PCB and total dioxins in the tested Australian agricultural commodities. Except for salmonids, there is a large difference between the lower bound and upper bound estimates. This is because only a small number of samples had detectable levels of dioxins and the assumption of non-detects being at the Limit of Detection (LOD) was by far the major contributor to the upperbound estimates. Therefore, the upper bound results are overestimates of dioxins present in the commodities.

Table 3-18 Mean dioxin concentrations in Australian agricultural commodities

Commodity	PCDD/F (pg WHO-TEQ/g fat)			PCB (pg WHO-TEQ/g fat)			Total dioxins (pg WHO-TEQ/g fat)		
	Lower bound	Medium bound	Upper bound	Lower bound	Medium bound	Upper bound	Lower bound	Medium bound	Upper bound
Beef	0.104	0.331	0.557	0.0731	0.181	0.289	0.177	0.512	0.847
Milk	0.0277	0.231	0.434	0.028	0.107	0.186	0.0557	0.338	0.620
Pigs	0.0029	0.167	0.331	0.0106	0.127	0.244	0.0212	0.294	0.575
Poultry	0.0012	0.166	0.330	0.0173	0.133	0.249	0.0184	0.299	0.579
Sheep	0.112	0.342	0.572	0.0346	0.133	0.231	0.147	0.475	0.803
	PCDD/F (pg WHO-TEQ/g fresh weight)			PCB (pg WHO-TEQ/g fresh weight)			Total dioxins (pg WHO-TEQ/g fresh weight)		
Salmonids[1]	0.173	0.201	0.228	0.398	0.500	0.602	0.571	0.701	0.830

[1]-aquacultured

Despite the inconsistency of methods and sampling of international dioxin data, it is useful to compare Australian data to international findings and international standards. A comparison was made between data generated in this study and the dioxin data for geographical regions in the recent Codex Commission on Food Additives and Contaminants (CCFAC) position paper (Codex Alimentarius Commission, 2003). It is important to note that these results are not directly comparable and the testing conducted for the Australian study includes more species and more compounds (i.e. PCDD/F, PCBs and Total WHO-TEQ) than data presented in the CCFAC paper. Therefore, several species/compound comparisons are not possible. Those that are possible are included Appendix XV and are presented as upperbound ranges of dioxins in the various species. In most cases the maximum PCDD/F and PCB concentrations in all Australian agricultural commodities was lower than that of other regions of the world.

In addition, the results of the current study were compared to the EU standard for PCDD/Fs in agricultural commodities. Table 3-19 shows that both the mean and the maximum values for all of the tested Australian commodities were below the EU standard.

Table 3-19 A comparison of PCDD/Fs in Australian agricultural commodities with the EU Standard for PCDD/Fs

Species	EU standard Maximum pg WHO-TEQ /g *	Mean** result from this study	Maximum** result from this study
Beef	3	0.557 (18.6%)	1.77 (59.0%)
Fish (salmonids)	4	0.228 (5.7%)	0.350 (8.75%)
Milk	3	0.434 (14.5%)	0.749 (25.0%)
Pig	1	0.331 (33.1%)	0.551 (55.1%)
Poultry	2	0.330 (16.5%)	0.529 (26.45%)
Sheep	3	0.572 (19.1%)	2.83 (94.3%)

* on a fat basis except for fish which is on a muscle basis. Where a congener is not detected, the EU standard assumes the LOD for that congener.

** mean and maximum results are upperbound concentrations expressed as pg WHO-TEQ/g. Values in parentheses are expressed as a percentage of the EU standard for that species).

Since "table ready" food products derived from the agricultural commodities sampled in this study were also included in the dietary survey and dietary modelling conducted by FSANZ, the potential human health risks of dioxin contaminated agricultural commodities will not be further discussed in this section. Section 3.2.1 contains details of the Australian population's estimated dietary exposure to dioxins.

3.2.3 Intake from human milk

Section 3.2.1 includes the estimated dioxin intake for infants (9-months old) fed 50% of their energy requirements from infant formula and 50% from solids and gives measured concentrations of dioxins in infant formula sampled in Australia. Section 3.1.2 outlines the results of a study by Müller et al (2003a) which investigated the current levels of dioxins in the breast milk of Australian mothers. Using the results of these analyses and the measured concentrations of dioxins in infant formula, the intake of dioxins by breast-fed and non-breast fed infants can be estimated.

In order to assess the dietary exposure to dioxins for infants at three months of age that are fully breast-fed, the quantity of breast milk consumed needed to be determined. Butte et al (2002) found that infants at 3 months of age from presumably well-nourished populations, including Australia, consumed a mean amount of 750 g of breast milk per day (weighted for sample size). The median (50^{th} percentile) weight for a male infant at three months is 6 kg (WHO, 1983). Boys' weights were used because boys tend to be heavier than girls at the same age and therefore have higher energy and food requirements. Therefore, using these figures, and multiplying by 30 to provide a monthly consumption, a fully breast fed infant at three months of age consumes 3800 g breast milk/kg bw/month. The mean concentrations of dioxins in breast milk used for this dietary exposure assessment were taken from the recent study of Müller et al (2003a).

As there were no food consumption data available from the NNS on children under two years, a diet was constructed to enable dietary exposure to dioxins for infants at nine months of age to be calculated. Details of the constructed diet for infants at 9 months are available in Section 3.2.1. In this constructed diet, milk was assumed to provide half of the infant's energy requirements. In order to determine the dietary exposure to dioxins for breast fed infants at 9 months, this same constructed diet was used, and all milk consumption was assumed to be breast milk. All other assumptions relating to the construction of the diet remained the same. As for infants at 3 months, the dioxin concentrations for breast milk used for calculating dioxin exposure for infants at 9 months were taken from Müller et al (2003a). As milk was assumed to only provide 50% of the energy requirements of an infant at 9 months, dioxin concentrations for all other foods, making up the other 50% of energy requirements were derived from the FSANZ dioxin total diet survey, which is outlined in Section 3.2.1.

The aim of the dietary exposure assessment was to make as realistic an estimate of dietary exposure to dioxins as possible. However, where significant uncertainties in the data existed, conservative assumptions were generally used to ensure that the dietary exposure assessment did not underestimate exposure.

For breast fed infants, the following assumptions were made:

- milk was the only food consumed for infants at 3 months;
- all milk consumed was breast milk for infants at 3 and 9 months;
- the dioxin concentration of breast milk for infants at 2-8 weeks is the dioxin concentration of breast milk for the whole term of breast-feeding each infant;
- the dioxin concentration for breast milk was the same for all infants, irrespective of the number of breast-fed siblings; and
- one gram of breast milk is equal to one millilitre of breast milk.

Table 3-20 gives the estimated lower and upper bound mean intakes of PCDD/Fs, PCBs and total dioxins for breast-fed and non-breast-fed Australian infants at 3 and 9 months of age.

Table 3-20 Estimated monthly intake of dioxin for Australian breast-fed and non-breast-fed infants

Compound	Bound	Estimated intake (pg WHO-TEQ/kg bw/month)			
		Breast-fed		Non-breast-fed	
		3 months	9 months	3 months	9 months
PCDD/F	Lower	807	490	5.9	4.4
	Upper	831	518	54.1	49.0
PCB	Lower	427	261	6.9	7.3
	Upper	427	264	9.7	11.8
Total dioxins	Lower	1234	751	12.8	11.8
	Upper	1258	782	63.9	60.8

As is the case with other aspects of this exposure assessment, comparison of different estimates of dioxin intake as a result of breast feeding is difficult because factors such as the sampling of breast milk, assumed intake of breast milk, infant age and percent of diet assumed to be from breast milk will differ between studies. Compared with intake estimates for breast-fed infants from other countries, the intake estimates for Australian infants were the lowest amongst those countries for which data were readily available (see Figure 3-13 for an international comparison of intake estimates for breast-fed infants). Smith and Lopipero (2001) estimated intake of total dioxins for New Zealand infants breast-fed for periods up to 12 months and calculated an average intake of between 37 and 52 pg WHO-TEQ/kg bw/day (equal to 1110-1560 pg WHO-TEQ/kg bw/month). Dioxin intakes for breast-fed Dutch infants (age not specified) were estimated by Liem and Rappe (1998) to be 115 pg WHO-TEQ/kg bw/day (equal to 3450 pg WHO-TEQ/kg bw/month). The estimate of Liem and Rappe (1998) was very similar to the 112-118 pg WHO-TEQ/kg bw/day (3360-3540 pg WHO-TEQ/kg bw/month) intake estimate of Patandin et al (1999b) for Dutch infants fed breast milk for 6 months. Estimated lower bound total dioxin intake of 76 pg WHO-TEQ/kg bw/day (2280 pg WHO-TEQ/kg bw/month) for Belgian infants that were breast-fed (Focant et al, 2002) was similar to that of Dutch infants. Two estimates of total dioxin intakes from breast milk by Korean infants were 60 and 85 pg WHO-TEQ/kg bw/day (1800 and 2550 pg WHO-TEQ/kg bw/month) (Yang J et al, 2002; Yang Y-H et al, 2002). The US EPA

(2000) estimated an average total dioxin intake of 92 pg WHO-TEQ/kg bw/day (2760 pg WHO-TEQ/kg bw/month) by US infants breast-fed for 12 months.

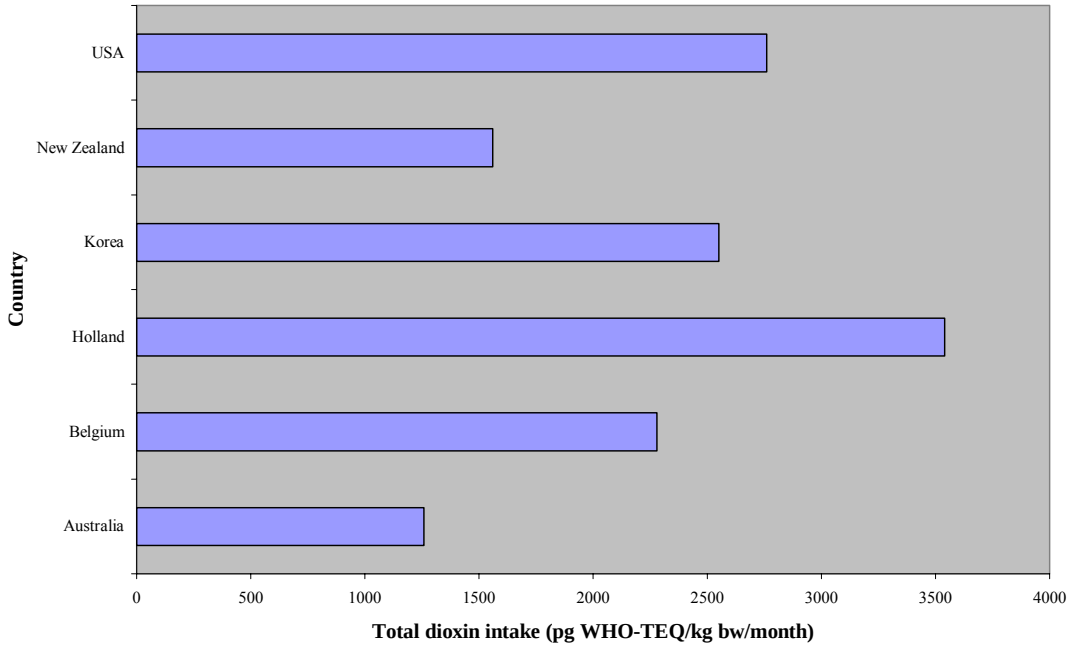

Figure 3-13 An international comparison of estimated dioxin intakes for breast-fed infants

[Maximum reported intakes (as given in above text) for solely breast-fed infants from each country. Australian value is upper bound estimate at 3-months.]

The estimated intake of dioxins during breast feeding of Australian infants was considerably higher than estimated dietary intakes of dioxins for the rest of the Australian population (3.7-15.6 pg WHO-TEQ/kg bw/month; see Section 3.2.1). Similar differences between the dioxin intake of breast-fed infants and the rest of the general population were also reported for the Dutch (Liem & Rappe, 1998), New Zealand (Smith & Lopipero, 2001) and the US populations (US EPA, 2000).

Estimated dietary exposure to dioxins for infants at 9 months is much less than for infants at 3 months as approximately half the energy requirements of a 9-month old infant are derived from foods other than breast milk, that have significantly lower dioxin concentrations. Exposure to dioxins from breast milk occurs for a very short time in a person's life. As the 1995 National Health Survey (NHS) did not survey children under the age of two, it is difficult to obtain data on the consumption of infant formula in Australia. However, a report based on the results of the NNS on the introduction of breast milk substitutes and solid foods to Australian children between 1992 and 1995 revealed that by the age of 26 weeks, the majority of children had been given infant formula (56.9%) (Donath & Amir, 2002).

The pattern of infant feeding at four weeks, 12 weeks and 24 weeks of life, using a sub-sample of children aged over six months, is shown in Table 3-21.

Table 3-21 Patterns of feeding for the first six months of a child's life

	At 4 weeks	At 12 weeks	At 24 weeks
Breast milk only	70.3%	57.8%	17.5%
Infant formula[a] only	25.1%	32.2%	15.8%
Breast milk and infant formula[a]	2.7%	3.1%	2.2%
Breast milk and solid food	0.7%	2.7%	23.3%
Infant formula[a] and solid food	1.0%	4.2%	36.2%
Breast milk, infant formula[a] and solid food	0.0%	0.1%	3.2%

[a] Includes milk substitutes other than infant formula
from Donath and Amir, 2002.

In addition to changes in the infant diet that reduce the intake of dioxins as an infant grows, the intake of dioxins by growing infants may also be reduced by changes in the dioxin concentration of breast milk. The estimates of intake given in Table 3-20 assume that dioxin concentrations in breast milk are constant over the nursing period. However, the dioxin concentration in maternal milk has been observed to decrease during lactation (Lakind, 2000; Fürst 1989). The modelling studies of the US EPA (2000) and Lorber and Phillips (2002) took into account the reduction in breast milk concentrations during lactation and predicted a decrease in infant intakes of dioxins during lactation (without accounting for any dietary changes). Therefore, the intake estimate given in Table 3-20 for 9-month old infants is likely to be an overestimate.

The dioxin intakes of breast-fed Australian infants were also considerably higher than those of non-breast-fed infants. This difference is due to the lower dioxin concentrations in infant formula, largely as a result of infant formulas containing vegetable fats rather than animal milk fats. Patandin et al (1999b) reported a similar difference with the mean daily dioxin intake per kilogram bodyweight for breast-fed Dutch infants being 50 times higher than that of non-breast-fed infants.

Although the intake of dioxins by breast-fed infants is considerably higher than the estimated adult and non-breast-fed infant intakes, the impact of breast feeding on the body burden in infants is likely to be lower. This can be attributed to the rapidly increasing body weight and lipid volume of the growing infant and the higher rate of dioxin excretion in infants compared with adults (see discussion below on body burden modelling). In the study of Kreuzer et al (1997) the difference in body burden between breast-fed and non-breast-fed infants was less than an order of magnitude and similarly, the study by the US EPA (2000) showed a difference in body burden between breast-fed and non-breast-fed infants of only two times at one year of age.

Several modelling studies have been conducted to investigate the impact of dioxin intake from breast feeding on body burdens of infants and the lifetime intake in adults (Kreuzer et al, 1997; Pantandin et al, 1999; Lorber & Phillips, 2002; US EPA, 2000). Although breast-fed infants were shown to have higher body burdens of dioxins during nursing, the body burden of breast-fed and non-breast-fed children was predicted to be similar after several years and to remain similar for the rest of life. The study by

Kreuzer et al (1997) is discussed below to examine the predicted impacts of dioxin intakes by infants on body burden over a lifetime.

Using data from their own study and other values reported in the literature, the authors have modelled TCDD levels in adipose tissue over a lifetime, in breast-fed (6 months) and non-breast-fed subjects. Figure 3-14 shows the time-course of the predicted concentrations of TCDD in lipids of adipose tissue or blood of a male subject from birth to 60 years of age. Note that this model is for TCDD only since to model related compounds would require consideration of different rates of bioaccumulation and biotransformation, and different rates and extent of protein binding. There is evidence that trans-placental transport from the mother to the fetus is close to 100%, leading to the treatment of the whole organism (mother/fetus) as a one-compartment model. Thus, based on a simulated initial maternal TCDD concentration of 2.23 ng/kg lipid), the TCDD concentration in the body of the newborn at the time of delivery was also taken to be the same, viz. 2.23 ng/kg lipid, a value also taken to be the level in breast milk.

For elimination of TCDD, the model takes into account excretion of TCDD in faecal lipids as well as its metabolic transformation. With respect to faecal excretion, data suggest that the faecal TCDD concentration reflects its concentration in lipids of the organism. The half-life of faecal elimination is proportion to the ratio of the volume of body lipids to the mass of lipids in faeces excreted per unit time; since the volume of body lipids increases at least 40 times during ageing but the mass of lipids in faeces excreted per unit time increases only about 1.7-times, the calculated half-life of faecal elimination changes considerably with age, from only ca. 0.42 years in newborns to ca. 9.5 years in 40-year old adults. The half-life of metabolic elimination is proportional to the total volume of body lipids and inversely proportional to liver surface area. Calculated half-lives for metabolic elimination were 1.5 years for newborns and about 10 years at age 40. However, according to the model, most TCDD is eliminated unchanged in the faeces during childhood and youth, whilst metabolic removal becomes more important with age. (With respect to increasing elimination half-life with age, it may be noted that the decline in TCDD levels in adipose tissue of young rhesus monkeys (0.3 - 2 years) revealed a mean half-life of ca. 180 days cf. 391 days in adults (Bowman et al, 1989b; 1990).

The upper curve of Figure 3-14 was computed assuming breast feeding for the first 6 months of life, followed by formula up to one year of age. The lower curve considers intake of only feeding formula for the same time period. For both scenarios, further nutrition was simulated to consist of common diet. The curves predicted for both feeding conditions differ considerably during the first years of life. Over the first year, predicted TCDD concentrations decrease for a non breast-fed subject, subsequently increasing to a maximum at ca. 16 years. The initial decrease reflects less uptake of TCDD from formula than during pregnancy when the foetus was in equilibrium with the mother's body burden.

For breast-fed infants, the simulation yields a rapid increase of TCDD in body lipids due to TCDD uptake from mother's milk. After weaning, the concentrations decrease during the following 3 or so years and the curves merge at about the age of 7 years. [Kreuzer et al (1997) noted that simulated TCDD levels in breast fed infants did not

exceed actual measurements of lipid TCDD levels in adults, which show a wide spread of values in different samples.]

Thus the model for TCDD levels in body lipids demonstrates that even relatively high concentrations of TCDD which may be reached after 6 months of breast feeding do not lead to a raised lifetime body burden. This is a reflection of the fact that the half-life due to metabolic transformation and faecal elimination is considerably shorter in infants than in older subjects. In addition, there is dilution of concentration by growth in body mass and the significant increase in total body fat volume.

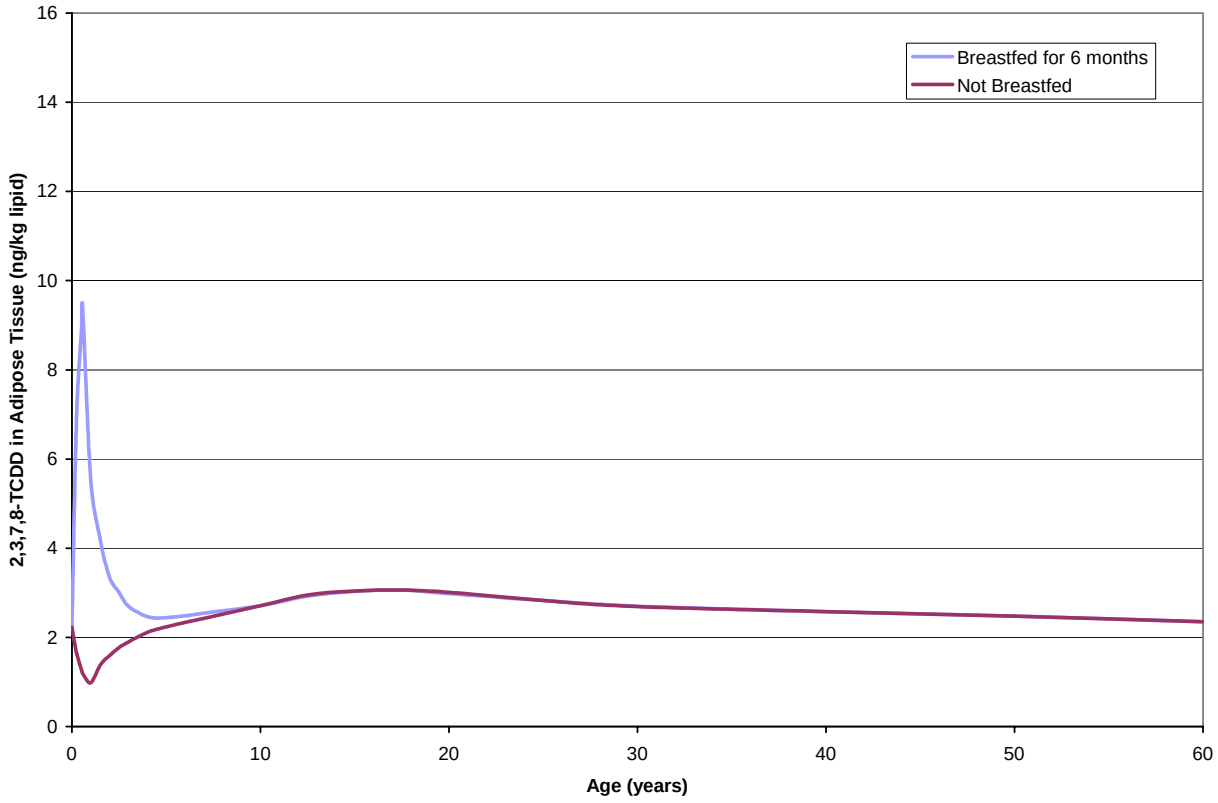

Figure 3-14 TCDD concentrations in lipid tissue of breast-fed and non-breast-fed infants

3.3 Intake from Air

The generation of dioxins results predominantly from combustion processes and atmospheric transport represents the primary route for transport of dioxins into the environment. A review of sources of dioxins in Australia (Pacific Air and Environment Pty Ltd, 2002b) identified a range of possible sources including bushfires and prescribed burning, residential wood combustion and industrial processes. This review was updated recently using United Nations Environment programme standardised protocols for estimating dioxin emissions to air, water and land. In this update, uncontrolled combustion processes which include biomass burning such as forest,

grassland and harvest residue fires and waste burning and accidental domestic/industrial fires were shown to represent the largest single category contributor to dioxins in air (Bawden et al., 2004).

In this section, discussion of dioxin contributions from motor vehicles is based on data from an Environment Australia report commissioned to assess dioxins emissions from motor vehicles (Pacific Air and Environment Pty Ltd, 2002a). Comment on the contribution of bushfires to dioxin air levels is made predominantly from a report on dioxin release from bushfires, commissioned by DEH (Meyer & Beer, 2004). Similarly, comment on the contribution of wood heaters to dioxin air levels in Australia is made from two technical reports on the use of firewood and solid fuel burning appliances also commissioned by DEH (Gras, 2002; Todd, 2002).

As well as commenting on main sources of air dioxins, this section provides a dioxin inhalation exposure assessment for different population subgroups based on data from a project, which determined ambient air levels of dioxins in Australia. The Australian dioxin ambient air level study (Gras & Müller, 2003) measured dioxin levels in urban, rural and remote airsheds. Based on these data, estimated daily inhalational exposures to dioxins were calculated for 5 separate Australian population subgroups - newborn, infant (one year), child (10 years), adult woman and adult man. Daily inhalation exposures per kg body weight were based on data for inhalation rates and body weights from the draft Australian Exposure Assessment Handbook (EnHealth, 2003).

3.3.1 Ambient air

Data on dioxins in ambient air were provided by the DEH ambient air project (Gras & Müller, 2003) which sampled air from a total of 10 sites representing three different airsheds:

1. Urban (residential, light and heavy industrial areas in State capital city sites and large regional centres), consisting of:
    - Kwinana, Perth, WA (industrial);
    - Duncraig, Perth, WA (mid-sized urban);
    - Darwin, NT (small urban within a remote rural region);
    - Eagle Farm, south-east Qld (light industrial);
    - Westmead, Sydney, NSW (major urban, some light industry impact from mixed industrial/urban air shed);
    - Alphington, Melbourne, Vic (major urban area, Yarra Valley);
    - Netley, Adelaide, SA (light industrial).

2. Rural (grazing, cropping and intensive horticulture areas) consisting of:
    - Mutdapilly, south-east Qld (agricultural/grazing)
    - Boorolite, lower north-east Vic (agricultural/grazing), and

3. Remote Reference Area
    - Cape Grim, Tasmania

Sampling was usually conducted monthly over a 12-month period to establish possible seasonal variations in dioxin concentration related to emissions from sources such as wood heaters and bushfires. At two sites (Mutdapilly and Netley), the sampling period was 12 months, collected at intervals of two months.

Samples were collected using high volume samplers designed to collect both gas and particle-phase dioxins. Subsequent extractions and analyses for a total of 29 dioxin and dioxin-like congeners and homologues were conducted at the Australian Government Analytical Laboratories, Sydney.

Data for each of the three air sheds were averaged over the year and combined as WHO-TEQs for PCDD/Fs, PCBs or total dioxins. Lower bound, middle bound and upper bound limits were determined by differing treatment of dioxin concentrations below the limit of detection (LOD), set at three times the sample blank noise standard deviation (0.6 fg WHO-TEQ_{DF}/m^3). For lower bound limits, values below the LOD were assumed to be zero. For middle bound limits, values below the LOD were assumed to be half the LOD. Upper bound limits were calculated by assuming values below the LOD were equal to the LOD.

Summarised air data from the DEH ambient air project are depicted in Appendix XVI. Across all three airsheds, PCDD/Fs were present in much higher concentrations than PCBs. As expected, urban airsheds showed the highest levels of dioxins (total dioxins, mean lower and upper bound limits 13.61 – 14.37 fg WHO-TEQ/m^3). Total dioxin levels were approximately five to six times higher than those for rural airsheds (mean lower and upper bound limits 1.94 – 2.82 fg WHO-TEQ/m^3) and an order of magnitude higher than those for the remote reference site (mean lower and upper bound limits 0.73 – 1.47 fg WHO-TEQ/m^3).

Comparisons to levels reported overseas show that Australian ambient air concentrations are relatively low. Mean concentrations of PCDD/Fs for rural sites are 1.52 – 2.35 fg WHO-TEQ/m^3 (lower and upper bound limit), lower than the mean of 3.77 fg I-TEQ/m^3 for the lowest reported New Zealand rural site (Buckland et al, 1999), and much lower than the 12 fg I-TEQ/m^3 reported for rural locations in the USA (Cleverly et al, 2000).

Similarly, mean concentrations of dioxins for Australian urban sites are 11.8-12.50 fg WHO-TEQ/m^3 (lower and upper bound limit), comparable to New Zealand rural locations (4 – 16 fg I-TEQ/m^3) (Buckland et al, 1999) and lower than many urban sites across Europe (for detail, see Gras & Müller, 2003).

Inhalation Exposure Assessment

Inhalation exposures for five population subgroups were calculated using exposure factor data from the draft Australian Exposure Assessment Handbook (AEAH). Body weights for adult women and adult men were taken as those for individuals 25-44 years of age. The weight for a child (10 years) was the average of values given for male and female children. For infants and newborn for which data are lacking in the draft AEAH, infant weights (1 year) were assumed to be half the average weight for 2-3 year old

males and females. Newborn weights were assumed to be half the weight of infants (3.8 kg).

Table 3-22 Inhalation rates and body weights of population subgroups

	Inhalation Rate (m^3/day)	Body Weight (kg)
Newborn[+]	0.8	3.8
Infant (1 year)[#]	3.8	7.7
Child (10 years)	15.0	35.7
Adult Woman[*]	21.0	67.3
Adult Man[*]	23.0	82.4

+ assumed to be one-half the body weight of infants
# assumed to be one-half the body weight of 2-3 year olds
* 25-44 years of age

There is a paucity of data on human absorption of dioxins from inhalation exposure. ATSDR (2000) notes the study of Wolff (1985) examining capacitor workers exposed to PCBs. This study claims the inhalation route as responsible for up to 80% of the absorbed PCB levels in adipose tissue.

In rats, at least 95% of a single dose of 2,3,7,8- tetrachlorodibenzo-p-dioxin (TCDD) was reported to be absorbed following intratracheal application. In this study, pulmonary absorption was greater than oral absorption (Diliberto et al, 1996). In a single human volunteer, > 87% absorption was reported following a single oral dose of 2,3,7,8-TCDD (Poiger & Schlatter, 1986). Notwithstanding species differences, taken together, these data would suggest extensive absorption of dioxins via the inhalation route in humans.

Differences in absorption are expected between dioxins in the gaseous (vapour) dissolved liquid and solid (particulate) states. On the basis of animal data and information on the fate of particles in the respiratory system, the US EPA estimated that the fraction of 2,3,7,8-TCDD absorbed into the human body from inhalation of soil particles ranges from 0.25-0.29 (US EPA, 1984b).

The ambient air data from the DEH Ambient Air Project do not distinguish between gaseous and particulate dioxins. Overall, therefore, in the absence of detailed information on pulmonary deposition and absorption of dioxins of different material states and of the different congeners and homologues in humans, this exposure assessment assumes 100% pulmonary deposition and absorption for all dioxin species. This assumption is in line with policy of the US Department of Health and Human Services (DHHS) which, in the absence of bioavailability information, assumes 100% bioavailability for health effects evaluations (DHHS, 2002).

Inhalation exposures to dioxins were estimated using urban and rural ambient airshed data. Lower and upper bound exposure estimates were calculated according to the following formula using lower and upper bound mean ambient air dioxin concentrations (Gras & Müller, 2003) and standard values for air intakes and body weights from the Australian Exposure Assessment Handbook:

Estimated Daily Dioxin Intake (fg WHO-TEQ/kg bw/day**)** =

[dioxin ambient air concentration (fg/m^3) x daily inhalation rate (m^3/day)]/ body weight (kg)

Inhalation exposure estimates using urban and rural airshed data are depicted in Tables 3-23 and 3-24.

Table 3-23 Mean estimated monthly inhalation exposure to dioxins (pg WHO-TEQ/kg bw/day) - Urban airshed

	PCDD/Fs		PCBs		Total Dioxins	
	Lower Bound	Upper Bound	Lower Bound	Upper Bound	Lower Bound	Upper Bound
Newborn	0.074	0.079	0.012	0.012	0.086	0.091
Infant (1 year)	0.174	0.185	0.027	0.028	0.202	0.213
Child (10 years)	0.148	0.157	0.023	0.024	0.172	0.181
Adult Woman	0.110	0.117	0.017	0.018	0.127	0.134
Adult Man	0.098	0.105	0.015	0.016	0.114	0.120

Table 3-24 Mean estimated monthly inhalation exposure to dioxins (pg WHO-TEQ/kg bw/month) - Rural airshed

	PCDD/Fs		PCBs		Total Dioxins	
	Lower Bound	Upper Bound	Lower Bound	Upper Bound	Lower Bound	Upper Bound
Newborn	0.010	0.015	0.003	0.003	0.012	0.018
Infant (1 year)	0.022	0.035	0.006	0.007	0.029	0.042
Child (10 years)	0.019	0.030	0.005	0.006	0.024	0.035
Adult Woman	0.014	0.022	0.004	0.004	0.018	0.026
Adult Man	0.013	0.019	0.004	0.004	0.016	0.024

As expected, given significant anthropogenic sources of dioxins such as fossil fuel combustion, inhalation exposure to dioxins is approximately 5-6 times higher in the urban compared to the rural environment.

Amongst the 5 population subgroups assessed, dioxin intake per kg body weight per day was highest for infants and children. The values for infant appear slightly higher than those for child, but are dependent on the assumption of body weight in the absence of weight information for infants in the AEAH. Weight data for adult men and women were available in the AEAH and the calculated dioxin intake for women was slightly greater than that for men. This reflects the fact that women have a significantly lower average body weight than men although the volume of air they breathe per day is only slightly smaller.

For the lower measured levels of dioxins in rural and remote region air compared to urban air, assumptions regarding measurements below the LOD have a greater relative

impact. As a percentage of absolute mass estimates, differences between lower and upper bound values are much greater for rural compared to the urban environments because measured levels are closer to the LOD.

3.3.2 Motor vehicles

Dioxins are formed by combustion processes. In a study commissioned to determine sources of dioxins in Australia, Bawden et al (2004) noted that anthropogenic sources, particularly industrial combustion processes, are significant contributors to environmental dioxin levels.

In the light of dioxin generation from vehicles, Environment Australia commissioned a study to estimate the total contribution to environmental dioxins from motor vehicle use in Australia. In this study, a survey of international dioxin inventories identified emissions from motor vehicles as important sources (Pacific Air and Environment Pty Ltd, 2002a).

Although it is recognised that dioxins are formed during combustion, the mechanisms of formation are poorly or incompletely understood. Production processes in which chlorine and a carbon source are present at temperatures greater than 200°C are potential dioxin sources. Although no specific data on dioxin formation within vehicle engines or exhausts were found (Pacific Air and Environment Pty Ltd, 2002a), the general formation mechanisms that are known to apply during combustion are assumed to apply to internal combustion engines. For example, studies show particular dioxin formation in the cooler zones of waste incinerator systems where catalytic surfaces, excess oxygen, organic matter and appropriate temperatures (approximately 300°C) are present. These conditions are assumed analogous to environmental conditions in exhaust systems of diesel and petrol engines (Bacher et al., 1991; Jones, 1993). Also, whereas high temperatures and long residence times in furnaces lead to complete combustion and lower dioxin emissions, the incomplete combustion in internal combustion engines, as suggested by low efficiency and significant emissions of incomplete combustion products such as hydrocarbons and carbon monoxide, indicates a potential for dioxin formation.

In the absence of Australian data, Pacific Air and Environment Pty Ltd (2002a) presents data from international studies of vehicle dioxins emissions for different vehicle classes. Most data were in the form of fuel-based emission factors (as pg/L fuel). In order to estimate total dioxin emissions, fuel-based emission factors were combined with Australian fuel economy data for varying vehicle types to account for differences in fuel economy between countries, and then combined with use (kilometres travelled) data for different vehicle types from the Australian Bureau of Statistics (ABS) and the National Environment Protection Council. Alternatively, the fuel-based emission factors were combined with total fuel consumption data for each vehicle type from the ABS to derive total dioxin emissions. Lastly, as a worst case estimate which includes off-road traffic and non-road traffic dioxin emissions, emission factors were combined with total fuel use statistics from the Department of Industry, Tourism and Resources (DoITR) (Table 3-25).

Table 3-25 Dioxin emissions estimates using different vehicle use/fuel datasets

Data Source	Total Dioxins Emissions (g I-TEQ/year)
Vehicle fuel economy/activity data (ABS)	0.7-16.5
Vehicle total fuel consumption data (ABS)	0.6-17.3
Total fuel use statistics (DoITR)	0.7-24.3

From Pacific Air and Environment Pty Ltd, 2002a.

On the basis of Australian fuel economy and activity (kilometres) data, total dioxin emissions from Australian road traffic were estimated at 0.7-16.5 g I-TEQ per year. On the basis of total individual vehicle type fuel consumption data, total dioxin emissions from Australian road traffic were estimated at 0.6-17.3 g I-TEQ per year. On the basis of total fuel use statistics, (which then includes off-road traffic and non-road traffic emissions), worst case estimates of 0.7-24.3 g I-TEQ per year were obtained.

Using a current inventory estimate of total dioxin air emissions in Australia of 500 g WHO-TEQ per annum (Pacific Air and Environment Pty Ltd, 2002b) the above figures represent a contribution from vehicle use of 0.12-4.9% of total dioxin emissions to air.

These estimates are accompanied by significant uncertainties. Unfortunately, there is a lack of measured data internationally on dioxin emissions from road traffic. Despite the variety and number of vehicles currently in operation worldwide, relatively few test data on dioxin emissions are available. Studies generally only consider small numbers of vehicles with estimates sensitive to factors such as driving conditions, fuel quality and ambient temperatures. Overall, assumptions only allowed the estimation of emission factors ranges and not average emission factors (Pacific Air and Environment Pty Ltd, 2002a).

3.3.3 Bushfires

The generation of dioxins *via* combustion processes and the high frequency of bushfires, prescribed fires and agricultural waste burning suggest these events as noteworthy sources of dioxins discharged to air in Australia (Pacific Air and Environment Pty Ltd, 2002b). Although measured data on emissions from small scale controlled burns are available (eg. woodheaters), the complexity of dioxin chemistry precludes the extrapolation of data from such studies to the characterisation of combustion processes in the field. Therefore, on the basis of a lack of measured data on emissions from bushfires, prescribed fires and agricultural waste burning in Australia, a study was commissioned to determine the emissions of dioxins from field fires (Meyer & Beer, 2004).

Dioxin emissions were measured from 21 field burns and 19 laboratory burns designed to replicate combustion processes of open fires. Field burns comprised 13 fuel reduction fires, 2 cane burns, 4 fires in tropical savannah woodlands and 2 wildfires. Cereal straw, native sorghum, sugar cane trash and forest leaf litter were subject to laboratory burns in a dedicated test corridor at the CSIRO fire testing laboratory. As well as dioxin emissions, total suspended particulate matter and carbon dioxide concentrations were measured so that emission factors relating dioxin concentrations to combusted fuel masses (expressed per gram of carbon) could be derived.

For field burns, mean emission rates for total dioxins were calculated for fuel reduction fires, savannah fires, sugar cane fires and wildfires were 1.8, 2.3, 2.1 and 1.0 pg WHO-TEQ/g carbon respectively.

In contrast, most emission rates measured in laboratory burns were much higher than field burns. Mean emission rates for straw, sorghum and sugar cane were 33, 69 and 9.8 pg WHO-TEQ/g carbon respectively. However, emission rates from laboratory leaf litter burns were much lower with a mean of 1.7 pg WHO-TEQ/g carbon. These emission factors incorporate middle bound estimates where values below the limit of detection (LOD) were assumed to be half the LOD.

Congener profiles observed in laboratory burns were different to those observed in field burns, but consistent with emissions measured from wood combustion in domestic heaters. Overall, laboratory burns produced a wide range of PCDD/F congeners with lower chlorinated species most abundant. Furans were substantially more abundant than dioxins. In contrast, field burns produced predominantly dioxins with higher chlorinated species most abundant.

The contrast between emissions measured in the laboratory and in the field were thought to arise from differences in the durations at which smoke plumes remain at high temperatures necessary for heterogeneous dioxin synthesis. In laboratory tests, as in domestic heating appliances, gases and particulates are thought to be retained in the combustion space in a temperature environment above 200°C which is optimal for dioxin synthesis. In contrast, in field burns, air entrained in the smoke plume rapidly cools below this temperature and thus extensive dioxin synthesis is prevented. These observations preclude laboratory tests as appropriate surrogates for emissions testing in the field (Meyer & Beer, 2004).

Emission rates derived from field measurements were combined with National Greenhouse Gas Inventory (NGGI) algorithm and activity data to derive total emissions of dioxins/furans and PCBs from different types of field fires. Using NGGI data, total emissions of PCDD/Fs and PCBs from agricultural, forest and savannah fires were estimated at 152 g WHO-TEQ/year for 1994 and 233 g WHO-TEQ/year for 2001. The increase was due to increased fire activity (Meyer & Beer, 2004).

Using a current estimate of total dioxin air emissions in Australia of 500 g WHO-TEQ per annum (Bawden et al, 2004), the comparable emissions figure for 2001 represents a best estimate contribution from field fires of 47% of total dioxin emissions to air.

3.3.4 Wood heaters

Studies of atmospheric fine particulates in Australian cities suggest that residential wood combustion for heating is a major source of winter aerosol mass (Gras & Müller, 2003).

One of the findings of a recent Australian dioxin ambient air level study (Gras & Müller, 2003) was a strong seasonal cycle in dioxin concentrations both as mass concentrations and TEQ. A winter concentration maximum was measured for all major

population centres studied. Moreover, the period of enhanced concentrations was shorter in northern locations compared to southern locations. This seasonal variation in dioxin levels and correlation with aerosol non-sea-salt potassium as a tracer for biomass burning indicate residential wood smoke as the source of winter increases (Gras & Müller, 2003). The particular seasonal patterns of dioxin congeners and homologues show strong correlation to patterns found in studies of wood smoke emissions from residential wood heaters in New Zealand (Buckland et al, 1999) and more recently in Australia (Gras, 2002; Gras & Müller, 2003).

Residential combustion (furnaces, stoves, fireplaces) was identified as a potential source of air dioxins also in a source survey of dioxin air emissions in Australia (Pacific Air and Environment Pty Ltd, 2002b). In this study, dioxin emission factors for residential combustion activities were derived. However, because of a lack of Australian emissions data, estimates were based on information from the US, UK and the Netherlands and, as well as wood, fossil fuels such as oil or coal were also considered. However, stoves burning wood have a greater potential for dioxin emissions due to increased chlorine and/or dioxin precursors present in wood compared to oil or coal (Pacific Air and Environment Pty Ltd, 2002b). For example, much higher dioxin emissions are estimated for wood treated with pentachlorophenol (PCP) preservative.

Based on international data, Australian emission factors for PCDD/Fs of 1-3 and 1-29 µg I-TEQ /tonne fuel burned for stoves and fireplaces respectively burning clean wood were derived. Emission factors were higher for "treated" wood: 10-50 and 100-500 µg I-TEQ /tonne fuel burned for stoves and fireplaces respectively. The latter figure of 500 µg I-TEQ /tonne fuel directly reflects data from the Netherlands for combustion of wood containing PCP.

Using these emission factors and estimations of wood burning activities for different installations i.e. stoves versus fireplaces (combined total of 4000 ktonnes wood/year), the Pacific Air and Environment Pty Ltd (2002b) report estimated a total release of PCDD/Fs from residential wood combustion of 15-98 g I-TEQ/year.

With controlled burns in the emissions study, no detectable emissions of PCDD/Fs were detected above background (1 ng/kg fuel) for softwood fuel, whereas, overall, levels of 7.5 ng/kg fuel were detected for hardwood fuel. Accounting for operating parameters derived from the survey of wood burning appliance users which considered heater types, fuel types, fuel moisture content and appliance fuel loading, a final best-estimate emission factor of 4.1 ng WHO-TEQ/kg fuel was calculated. Wood treated with preservative was not tested in this study (Gras, 2002). This figure is comparable to and at the lower end of emissions factors ranges estimated previously by Pacific Air and Environment Pty Ltd (2002b) of 1-3 and 1-29 µg I-TEQ /tonne fuel for stoves and fireplaces respectively based on overseas data.

Although information on the types of wood used for heating was obtained from the users survey, this study did not provide a figure for total wood consumed. However, figures for total firewood consumed per year of 3-5.5 million tonnes was provided in the companion study by Todd (2002) on residential firewood use. This conforms well with the 4000 ktonnes/year estimate of Pacific Air and Environment Pty Ltd (2002b).

Assuming this upper figure of 5.5 million tonnes of wood combusted for residential purposes, the total release of dioxins based on the recent best-estimate emission factor from measurements from controlled burnings of Australian wood would be 22.6 g WHO-TEQ/year.

Using a current inventory estimate of total dioxin air emissions in Australia of 500 g WHO-TEQ per annum (Bawden et al, 2004) the above figure represents a contribution from residential wood combustion of 4.5% of total dioxin emissions to air.

Summary

In a response to the lack of quantitative Australian data on the composition of emissions arising from the use of domestic combustion heaters, Environment Australia commissioned separate companion studies reviewing residential wood fuel use, wood smoke and air toxics (Todd, 2002) and emissions from domestic solid fuel heating appliances (Gras, 2002). The studies comprised a review of residential firewood combustion, solid-fuel appliances, surveys of the number and type of wood burning appliances and fuels in use in southern Australia and the collection and analysis of emissions from controlled burns of different Australian wood fuels in different heaters.

Motor vehicles represent an anthropogenic source of dioxins. Combining overseas dioxin vehicle emission factors, Australian motor vehicle economy and activity data, fuel consumption data and total fuel use statistics, dioxin emissions of 0.6 - 24.3 g I-TEQ/year were estimated to result from motor vehicle use. Compared to the current total dioxin air emission estimation of 500 g WHO-TEQ per annum (Bawden et al., 2004) contributions from vehicle use represent between 0.1-5% of total dioxin emissions to air.

A study of dioxins in ambient air (Gras & Müller, 2003) showed a strong seasonal cycle in dioxin air concentrations. A winter concentration maximum was measured for all major population centres studied with periods of enhanced concentrations shorter in northern locations compared to southern locations. Studies of atmospheric fine particulates in Australian cities suggest that residential wood combustion for heating is a major source of winter aerosol mass. A study of emissions from wood heaters (Gras, 2002) showed that accounting for heater types, fuel types, fuel moisture content and appliance fuel loading, a final best-estimate emission factor of 4.1 ng WHO-TEQ/kg fuel was calculated for Australian wood heaters. Assuming a total of 5.5 million tonnes of total wood combusted for residential purposes (Todd, 2002), the total release of dioxins from burnings of Australian wood for heating was estimated at 22.6 g WHO-TEQ/year, representing around 4.5% of total dioxin emissions to air.

A report of the impact of bush fires on dioxin emissions established emission factors based on measurements of field fires and laboratory burns of different fuels (Meyer & Beer, 2004). Both the dioxin congener patterns and quantities of release differed considerably between the field and laboratory. In general, emission rates measured in laboratory burns were much higher than field burns. Congener patterns in laboratory burns showed the production of a wide range of dioxin/furans with furans

predominating. On the other hand, congener patterns for field fires showed predominantly formation of dioxins.

Differences in emission rates and congener patterns were explained by variations in the residence time of gases and particulates at a temperature range within the combustion space suitable for widespread dioxin/furan formation. In general, the limited heterogeneous dioxin/furan release seen in field fires was attributed to air entrainment and rapid cooling of emissions within the smoke plumes. Using National Greenhouse Gas Inventory data, total emissions of dioxins/furans/PCBs from agricultural, forest and savannah fires were estimated at 152 g WHO-TEQ/year for 1994 and 233 g WHO-TEQ/year for 2001. When compared to the current total release inventory of 500 g WHO-TEQ per annum (Bawden et al, 2004), the 2001 best estimate of this release is 46.6% of total dioxin emissions to air.

It should be noted that since bushfires, grass and scrub fires have been part of the Australian landscape for aeons, humans and the environment have been exposed to low levels of dioxin-like compounds and human metabolism has been coping with dioxin compounds for thousands of years.

An Australian dioxin ambient air study (Gras & Muller, 2003) measured dioxin levels in urban, rural and remote airsheds. Based on these data, estimated daily inhalational exposures to dioxins were calculated for 5 separate Australian population subgroups-newborn, infant (one year), child (10years), adult woman and adult man. Daily inhalation exposures per kg body weight were based on data for inhalation rates and body weights from the draft Australian Exposure Assessment Handbook (EnHealth Council, 2003)

As expected, inhalation of urban air provides a greater dioxin exposure than rural air. Of the separate subgroups examined, infants (one year) were assessed with the highest total dioxin inhalation intake per kilogram body weight (urban air, 0.174-0.178 pg WHO-TEQ/kg bw/month), followed by child (10 years) (0.148-0.157 pg WHO-TEQ/kg bw/month). Women had a marginally higher inhalation exposure per kg bodyweight to dioxins (0.017-0.018 pg WHO-TEQ/kg bw/month) than men (0.015-0.016 pg WHO-TEQ/kg bw/month), reflecting their lower body weight as compared with males but relatively similar air intake volume per unit time.

3.4 Intake from Soil

Humans may be exposed to dioxins from environmental or occupational sources or as a result of industrial accidents. Dietary intake is generally considered to account for approximately 95% of the human intake of dioxins in Australia. The remainder of human intakes of dioxins occurs via other routes such as inhalation and ingestion of contaminated air particles, soil ingestion and dermal contact with soil, air particles or water.

Dioxins have very low water solubility, high octanol-water partition coefficients and low vapour pressure. In soils, these physical and chemical properties of dioxins cause them to absorb strongly to soil organic matter and therefore they have limited mobility

within the soil profile. The possible environmental fates of dioxins sorbed to soil particles include burial, resuspension as dust or erosion by water to ultimately form a part of sediments lying beneath water columns. Dioxins may also volatilise from soils into the air. Due to their chemical stability and resistance to biodegradation, dioxins persist in soils.

3.4.1 Ambient levels of dioxins in Australian soils

Under the information gathering phase of the National Dioxins Program, the Department of Environment and Heritage commissioned a study to determine ambient environmental levels (air, water, soils and fauna) of dioxins in Australia. This section uses the data from the study designed to determine dioxin levels in Australian soils to estimate human intakes of dioxins as a result of exposure to soil.

The overall objective of the study by Müller et al (2003b) was to determine ambient environmental levels of dioxins in Australian soils across a range of landforms, climates and land-uses. Samples were collected from 86 locations representing urban, industrial, agricultural and remote sites across Australia. Urban sites were concentrated in capital cities and major towns, including coastal and inland population centres. Industrial sites were concentrated in areas dominated by industry, but no specific industries were targetted. Agricultural sites included areas used for sugarcane, cotton, grazing, forestry, cereals or horticulture. Remote sites sampled included open forest, closed forest, inland areas, coastal areas, regions subject to regular burning and regions where fire is excluded. The sampling locations covered three different regions in Australia; north, south-east and south-west with samples covering all land-use types. In addition, historical evidence of soil dioxin contamination was determined through analysis of ten samples collected from the same agricultural plot at the Waite Agricultural Research Institute, South Australia. These soil samples were collected in 1925, 1935, 1945, 1950, 1956, 1963, 1973, 1981, 1983, and 2001. Figure 3-15 shows details of the sites sampled by Müller et al (2003b).

A summary of the sampling strategy is described in Table 3-26. The sampling protocol was designed for the determination of the concentrations of dioxins in soil across a range of environments and land-uses. Sites which may have been subject to specific local contamination were avoided.

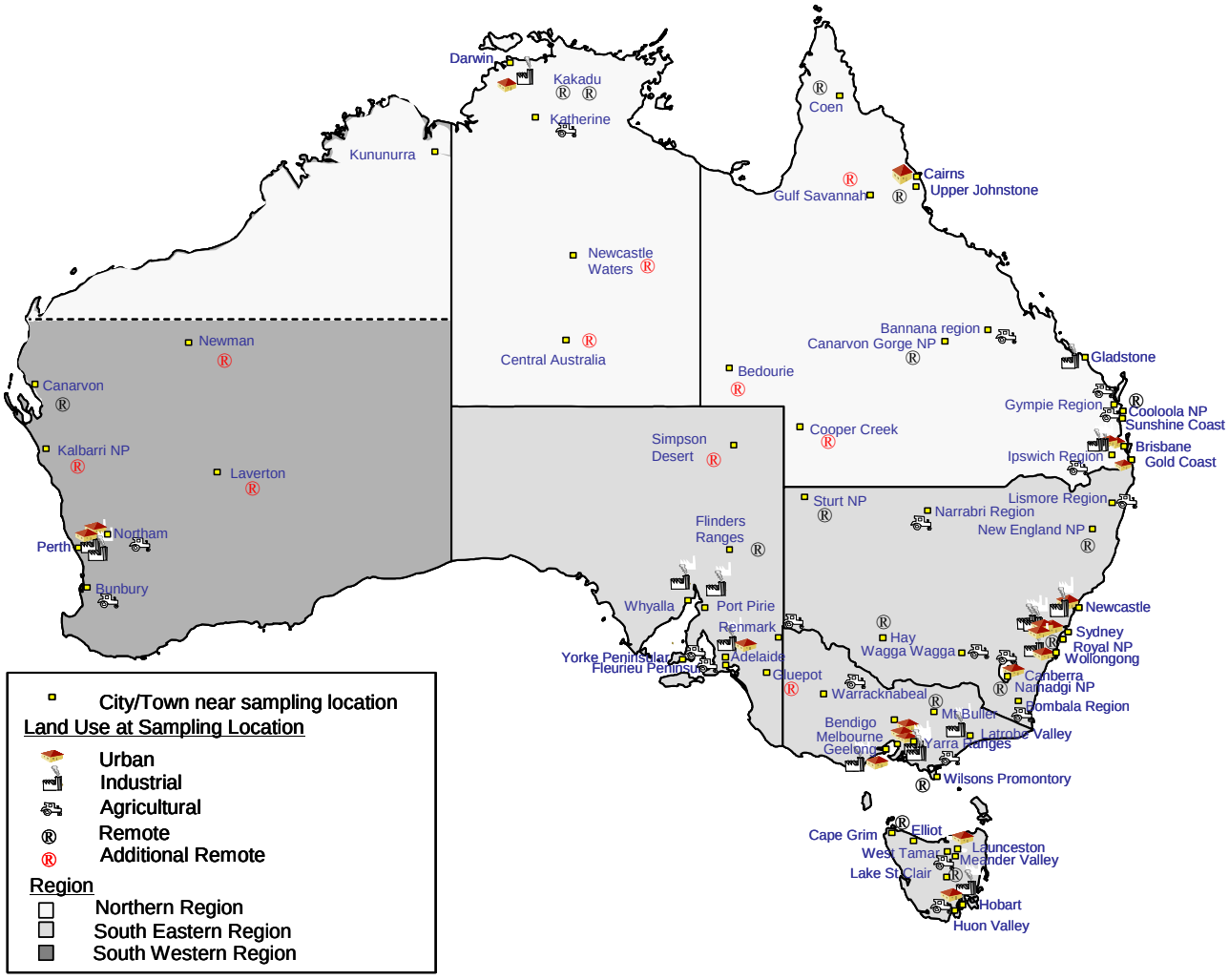

Figure 3-15 Details of sites sampled as a part of the study to determine dioxin levels in Australian soils.

From Müller et al, 2003

Table 3-26 Summary of the sampling strategy and number of samples analysed for the study.

Land Use	Region			
	Northern	South-Eastern	South-Western	Total
Industrial	6	18	3	27
Urban	6	18	2	26
Agricultural	5	16	2	23
Remote	6	10	3	19
Additional Remote[1]	6	2	1	9
Total	29	64	11	104

[1] Additional remote sampling locations were selected to specifically cover inland regions.

The analytical methodology for the determination of PCDD/Fs and PCBs was based on quantification of the analytes through isotopic dilution techniques and is modified from those described by the US EPA methods 1613B and 1668A, respectively. The study design allowed determination of both analytical and sampling reproducibility. A component of the study involved an inter-laboratory calibration in which samples that had been analysed by AGAL were analysed the Dioxin Laboratory of Environment Canada. PCDD/Fs and PCBs were reported as pg/g soil on a dry weight basis. Total toxic equivalents for PCDD/Fs (WHO-TEQ_{DF}), PCBs (WHO-TEQ_{P}) and total toxic equivalents for PCDD/Fs and PCBs (WHO-$TEQ_{DF\&P}$) were calculated using the WHO Toxic Equivalents Factors (TEFs).

Dioxins were detected in all but 1 of the 114 different soil samples analysed. Concentrations of PCDD/Fs and PCBs expressed as TEQs ranged from below the limit of detection (about 0.05 pg/g dry weight (dwt) depending on the specific sample) to 43 pg/g dwt. Dioxin concentrations in soils of north and south-east regions were similar, whereas the concentration in the soils from the south-west region was lower. The median concentration of total dioxins expressed as WHO-$TEQ_{DF\&P}$ were 0.98, 0.74 and 0.21 pg/g dwt in the north, south-east and south-west regions respectively. The highest concentrations of dioxins were found in soils near the centres of population within the south-eastern coastal regions of Australia, whereas those in western Australia and remote and inland areas were low.

The major finding from this study was that land use is a key determinant of dioxin concentrations in Australian soils. Four key land-use types were sampled in this study: industrial, urban (non-industrial), agricultural and remote. Table 3-27 gives the lower and upper bound estimates of PCDD/F, PCBs and total dioxins across land use types. The data clearly demonstrate that mean concentrations of dioxins are substantially higher in soils from urban or industrial locations than in those from agricultural and remote locations. However, mean concentrations in soils from urban and industrial locations were similar, as were those from soils from agricultural and remote locations.

One of the urban sites sampled in Hobart, Tasmania, had the highest PCDD/F concentration (approximate 43 pg WHO-TEQ/g dwt) measured in this study. When this site was re-sampled, the PCDD/F concentration was reported as 1.5 pg WHO-TEQ/g dwt. Both the original “high” value and the re-sampled value were included in the calculation of dioxin TEQs for urban soils. These TEQs were then used in the estimation of human exposure from urban soils, since the use of these “high” values would represent a “worst-case” for dioxin exposure as a result of contact with Australian soils. Table 3-27 summarizes the levels of PCDD/Fs, PCBs and total dioxins (as TEQs) in soil from different land use areas. For comparison, the mean and range of dioxin concentrations calculated from results of analyses of soils samples taken between 1925 and 2001 are also given in Table 3-27.

Table 3-27 Dioxin concentrations Australian soils according to land use

Land use	Bound	PCDD/F (WHO-TEQ pg/g dwt)			PCB (WHO-TEQ pg/g dwt)			Total Dioxins (WHO-TEQ pg/g dwt)		
		Min.	Max.	Mean	Min.	Max.	Mean	Min.	Max.	Mean
Agricultural	Lower	0	4.0	0.40	0	0.087	0.0094	0	4.1	0.41
	Upper	0.054	4.4	0.64	0.007	0.092	0.021	0.061	4.5	0.66
Industrial	Lower	0.063	11	2.6	0.005	1.7	0.36	0.069	11	2.9
	Upper	0.177	11	2.8	0.025	1.9	0.38	0.20	11	3.2
Remote	Lower	0.00056	5.0	0.38	0	0.078	0.0054	0.00068	5.1	0.38
	Upper	0.073	5.2	0.62	0.002	0.08	0.017	0.08	5.3	0.63
Urban[1]	Lower	0.023	42	5.9	0	1.6	0.41	0.081	42	6.3
	Upper	0.20	43	6.0	0.011	1.6	0.41	0.26	43	6.4
Urban[2]	Lower	0.023	22.8	4.3	0	1.6	0.40	0.08	23.3	4.7
	Upper	0.20	23	4.6	0.011	1.6	0.41	0.26	23.5	5.0
Reference[3]	Lower	0.37	2.7	1.1	0.0035	1.1	0.16	0.39	3.8	1.3
	Upper	0.55	2.7	1.1	0.025	1.1	0.18	0.59	3.8	1.3

[1]-includes the "high" PCDD/F TEQ value and the re-sampled value for one site in Hobart

[2]- excludes the "high" PCDD/F TEQ value for one site in Hobart and includes the re-sampled value for that site

[3]- mean and range of results from 1925-2001

The results of the analysis of the reference site at the Waite Agricultural Research Institute are also shown in Figure 3-16. Interestingly, the oldest sample collected in the 1920s contained detectable concentrations of PCDD/Fs and also PCBs. The concentrations of dioxins in the sample from the 1920s are greater than in the samples from the 1930s and 1940s. It is uncertain whether the result is an artefact related to sampling or storage of the sample, although it is not clear how selective contamination of the oldest sample could have occurred. Furthermore, no explanation was available for the peak of dioxins observed in 1981.

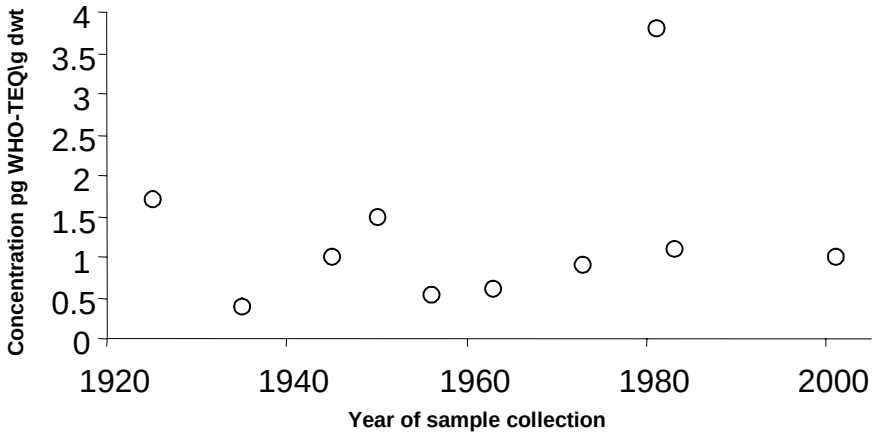

Figure 3-16 Total dioxin concentrations (as WHO-TEQ) in soil samples taken from the reference site between 1925 and 2001.

Modified from Muller et al, 2003b.

Typically in all samples (including the historical samples) that were collected in this study the PCDD/F homologue profile as well as the congener profiles were dominated by octachlorodibenzodioxin (OCDD). The soil congener profiles obtained from this study indicate that the dominance of the higher chlorinated PCDDs is less pronounced in samples from the more temperate regions. This result maybe seen as an indication that the domination of higher chlorinated PCDDs in samples from the tropical regions is at least in part related to fate processes of the chemicals where the least volatile and most persistent PCDDs accumulate specifically in tropical environments whereas the more volatile lower chlorinated PCDD/Fs are transported from these environment to colder climates where they remain.

The congener profile for PCBs was dominated by PCB 118 (ca.50 to 70%) followed by PCB 105 (10 to 20%). No apparent differences in PCB profiles were observed between soils from different locations.

Comparing results across different soil monitoring studies is difficult since there may be differences in the aims of the studies (e.g. determining background levels versus identification of contamination and potential hotspots), differences in the sampling regimens and methodology, and differences in the expression and reporting of results

(e.g. type of TEQs, expression - dry weight versus organic carbon basis, mean versus median, ranges). Nonetheless, Figures 3-17 and 3-18 compare dioxin concentrations across land uses from several countries, to give some indication of Australian soil levels of dioxins relative to other countries.

The concentrations of dioxins in urban and industrial locations sampled as part of the study by Müller et al (2003b) were similar to those reported in previous Australian studies (Buckland et al, 1994; Sund et al, 1993). Dioxin levels in agricultural and remote locations sampled by Müller et al (2003b) were also similar to results of previous Australian studies. However, Müller et al (1996) reported higher levels in some agricultural areas and the study by Buckland et al (1994) reported a higher maximum dioxin concentration in a bushfire-affected area. In general the dioxin levels in Australian soils were similar to those reported in the New Zealand Organochlorine Program (Buckland et al, 1998b). On the basis of toxic equivalents, concentrations of dioxins are on average much lower than those reported from many industrial sites globally and are among the lowest background concentrations internationally, across all land-uses.

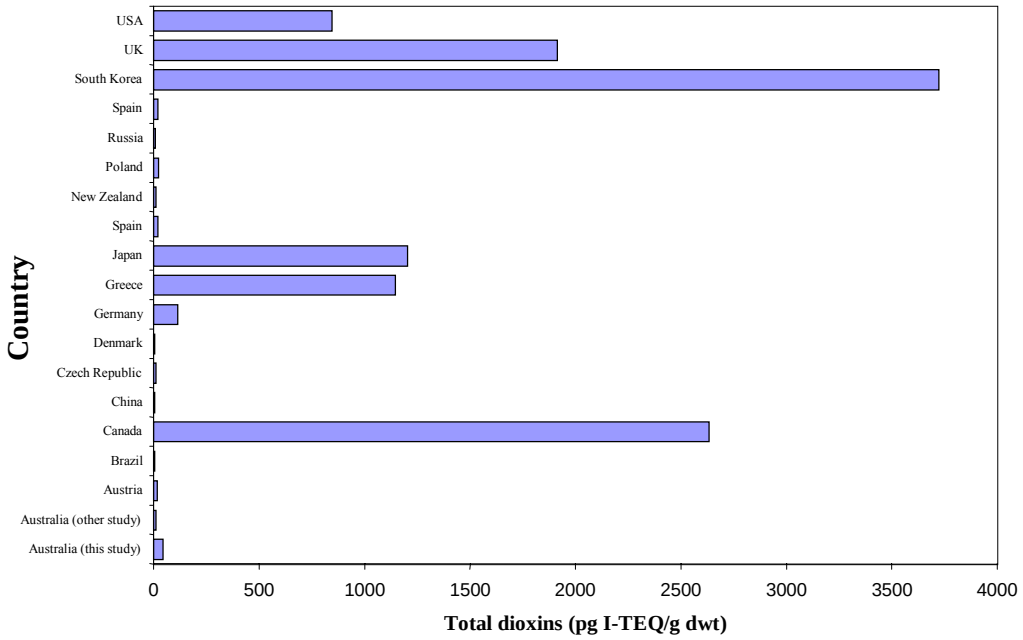

Figure 3-17 An international comparison of dioxin concentrations in soils from industrial and urban locations.

Data from Müller et al, 2003b.

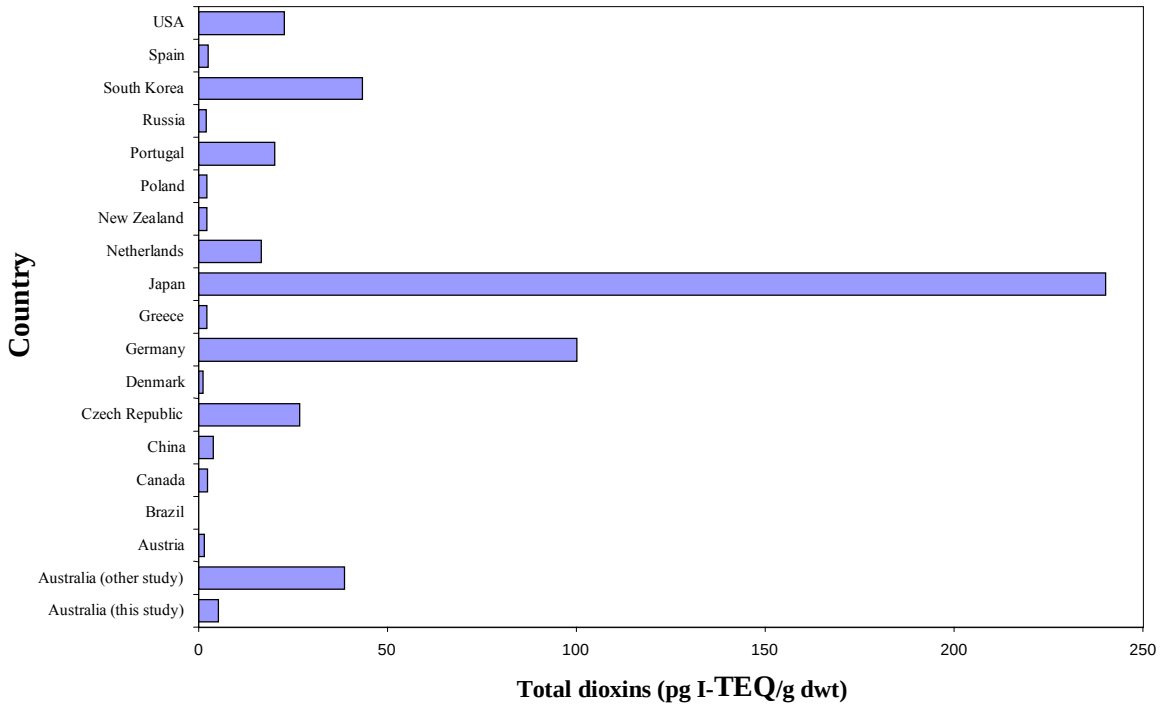

Figure 3-18 An international comparison of dioxin concentrations in soils from remote (reference) and agricultural land use sites.

Data from Müller et al, 2003b.

3.4.2 Estimation of dioxin intake from Australian soils

Direct human exposure to dioxins in soil can occur as a result of ingestion or by skin contact. Soil ingestion commonly occurs in young children during mouthing of toys or other objects, inadvertent hand-to-mouth transfer and as a consequence of non-sanitary eating habits. In addition, deliberate ingestion of soil (known as pica) has also been observed in young children. Although, soil ingestion also occurs in adults as a result of accidental hand-to-mouth transfer (eg. when eating or smoking), it occurs to a lesser extent in adults than in children. Direct skin contact with soils occurs in both adults and children with the extent of exposure dependent upon a number of factors including the surface area of exposed skin, the body part(s) exposed and the activity undertaken at the time of exposure.

Since a majority of the Australian population lives in urban areas that were sampled as a part of the study conducted by Müller et al (2003b), the mean lower and upper bound values for PCDD/F, PCB and total dioxins in urban soils were used to estimate the intake of dioxins from soil. The values used included the "high" PCDD/F TEQ and the resampled value for one of the sites in Hobart (see Table 3-27, row named "Urban[1]"). Formulae and assumptions used in the estimation of dioxin intakes from ingestion and estimated systemic exposure as a result of both ingestion and dermal contact with soils are given in Appendix XVII. Table 3-28 gives the estimate monthly intake of PCDD/F, PCB and total dioxins as a result of soil ingestion and Table 3-29 gives the estimated

mean monthly systemic exposure from both ingestion and dermal contact with soils and the total estimated exposure from soil.

Table 3-28 Estimated mean monthly intake of dioxins as a result of soil ingestion

Age	Bound	Mean monthly oral intake* (pg WHO-TEQ/kg bw/month)		
		PCDD/F	PCB	Total dioxins
Child	Lower	1.18	0.082	1.26
	Upper	1.20	0.082	1.28
Adult	Lower	0.063	0.0044	0.068
	Upper	0.064	0.0044	0.069

* 'oral intake' means amount ingested

Table 3-29 Estimated mean monthly exposure to dioxins as a result of soil ingestion and dermal contact with soil

Age	Bound	Mean monthly exposure* (pg WHO-TEQ/kg bw/month)								
		PCDD/F			PCB			Total dioxins		
		Oral	Dermal	Total	Oral	Dermal	Total	Oral	Dermal	Total
Child	Lower	0.59	0.141	0.73	0.041	0.046	0.087	0.63	0.187	0.82
	Upper	0.60	0.143	0.74	0.041	0.046	0.087	0.64	0.189	0.89
Adult	Lower	0.032	0.025	0.057	0.002	0.008	0.01	0.034	0.033	0.067
	Upper	0.032	0.025	0.057	0.002	0.008	0.01	0.034	0.033	0.067

* 'oral' exposure estimate assumes that 50% of dioxins ingested are systemically absorbed. See appendix XVI for formula and assumptions used for calculation of oral and dermal exposure.

The intake and systemic exposure estimates above are both likely to be overestimates since the mean TEQs for urban/industrial soils were higher than those for any other land uses sampled in the study by Müller et al (2003) and they included the "high" TEQ value from an urban site in Tasmania rather than excluding that value. Not all members of the general population would be exposed to soils containing dioxins at levels similar to those used for the intake/systemic exposure estimates. In addition, several conservative assumptions were used in calculating the intake/exposure estimates (eg. 24% or 30% of the total skin surface is exposed to the same amount of soil everyday for a lifetime).

As is the case with other components of this exposure assessment (eg. dietary exposure), comparisons between exposure assessments conducted by different groups/countries is complicated by differences in sampling, methodologies and assumptions used for intake estimates and calculating and reporting TEQs. Few other countries have undertaken soil monitoring and the estimation of dioxin intakes as a result of exposure to soil. Table 3-30 compares the intake estimates as a result of ingestion and dermal contact with soil (where available) from several countries.

The US EPA (2000) estimated exposure to dioxins from soil ingestion to be 0.063 pg WHO TEQ/kg/day (1.89 WHO-TEQ/kg/month) for children of 1-5 years of age and 0.0067 WHO TEQ/kg/day (0.201 WHO-TEQ/kg/month) for adults. A less recent

assessment conducted in the Netherlands estimated daily exposure to TCDD from ingestion of soil to be 0.1 pg I-TEQ/day (0.042 pg I-TEQ/kg/month for a 70 kg adult) (Theelen, 1991). Birmingham et al (1989) estimated intake of PCDD/Fs from soil ingestion by the Canadian population to be 0.02 pg I-TEQ/kg/day (0.6 pg I-TEQ/kg/month).

Exposure to dioxins as a result of dermal contact with soil in the USA was estimated as 0.0014 pg WHO-TEQ/kg/day (0.042 pg WHO-TEQ/kg/month) for children of 1-5 years of age and 0.0016 WHO-TEQ/kg/day (0.048 WHO-TEQ/kg/month) for adults (US EPA 2000). An assessment for the Dutch population estimated TCDD intake from dermal contact with soil as 0.15 pg I-TEQ/day (0.064 pg I-TEQ/kg/month for a 70 kg adult) (Theelen et al, 1991).

Table 3-30 An international comparison of dioxin intake estimates (for adults) as a result of contact with soils

Country	Mean monthly intake (pg WHO or I-TEQ/kg bw/month)		
	Oral	Dermal	Total
Australia (this report)[1]	0.069	0.033	0.102
Canada[2]	0.60	-	-
USA[1]	0.201	0.048	0.249
Netherlands[3]	0.042	0.064	0.106

[1]-total dioxins
[2]- PCCD/F only
[3]- TCDD only

3.5 Intake from Water and Sediments

Under the information gathering phase of the National Dioxins Program, the Department of Environment and Heritage commissioned a series of studies to determine the ambient environmental levels (air, water, soils and fauna) of dioxins in Australia. This section uses the data from the study that measured dioxin levels in the aquatic environment (Müller et al, 2003c) to assess human intakes of dioxins as a result of exposure to water, aquatic sediments and aquatic biota.

3.5.1 Water

One of the studies commissioned by the Department of Environment and Heritage measured ambient levels of dioxins in the aquatic environment in Australia. This study measured dioxin concentrations in aquatic sediment, but no water samples were collected for measurement of dioxins in water. Dioxins have very low water solubility and therefore dioxin concentrations in Australian water are expected to be very low and are unlikely to contribute significantly to the overall intake of dioxins.

In a recent human health and environmental risk assessment conducted in relation to an Australian site that may have been contaminated with dioxins (a decommissioned sewerage treatment plant), dioxin levels in ground water were insignificant. Therefore,

dioxins in ground water were not considered to be a significant source of human exposure (Gorman et al, 2003). This is supported by Canadian, German and American estimates of water intakes of PCDD/Fs of 0.1, 0.005 and 0.008 pg I-TEQ/day respectively (Liem and Rappe, 1998). These estimated intakes from water were one thousandth or less of the estimated overall intakes for dioxins. Furthermore, the US EPA's 2000 draft reassessment for dioxins reports dioxin levels in water as 0.0005 pg WHO-TEQ/L and estimates intake from water to be 0.000011 pg WHO-TEQ/kg/day. Therefore, the intake of dioxins from ingestion of water is considered to be negligible in Australia and will not be considered further in this report.

3.5.2 Sediments

The study to determine ambient levels of dioxins in the aquatic environment in Australia involved the collection of several thousand aquatic sediment cores from locations representative of major catchments according to priorities identified by the National Pollution Inventory. A range of samples were collected in freshwater, estuarine and marine locations. In addition to sediment samples, bivalve shellfish samples were also collected when available. Fish were also obtained through local commercial fishing industries with an emphasis on local catches of table species.

Dioxins were found in all Australian aquatic sediments analysed, with levels ranging from 0.002 pg WHO-TEQ/g dry weight (dwt) to 520 pg WHO-TEQ/g dwt. Highest levels were found in Sydney harbour in the sediments from the Parramatta River estuary (100 and 520 pg WHO-TEQ/g dwt) and the western section of Port Jackson (78 and 130 pg WHO-TEQ/g dwt), which is one of the most urbanised and industrialised regions of Australia. In addition, elevated concentrations were also found in other estuarine waters near Sydney (Botany Bay) as well as the estuaries in or near Brisbane, Melbourne, Hobart, Perth and Wollongong. Considering all sediment samples, the median concentrations were 0.2, 2.3 and 0.12 pg WHO-TEQ/g dwt in sediments from freshwater, estuarine and marine locations respectively. This is due to the association of higher densities of urban/industrial areas with estuarine waters compared to remote and agricultural areas (*i*.e. interaction between urban/industrial and estuarine waters). Urban/industrial locations had significantly greater levels of dioxin-like chemicals than samples from remote and agricultural locations. Further details of the dioxins in the aquatic environment are discussed in the environmental risk assessment.

Direct human exposure to aquatic sediments is not considered to be a widespread or frequent occurrence. If it does occur, the amounts of sediment to which people may be exposed is likely to be small and the duration of contact prior to removal is likely to be short. Therefore, the human health risk associated with exposure to dioxin contaminated sediments is likely to be negligible and will not be considered any further in this report. However, since aquatic biota may be exposed to contaminated sediment, there is potential for human dietary exposure to aquatic organisms such as fish and shellfish, which may bioaccumulate dioxins. Therefore, the results of the measurement of dioxins in fish and bivalves is considered, as follows.

Dioxins were detected in all 18 bivalve samples covering the different regions and various environments of Australia. Total dioxin levels ranged from 0.0068 – 3.4 pg

WHO-TEQ/g wet weight (wwt) with a mean of 0.69 pg WHO-TEQ/g wwt. Dioxins were detected in all 23 fish samples with levels ranging 0.054 to 0.85 pg WHO-TEQ/g wwt. As expected from the sediment results for the Sydney harbour area, highest levels of dioxin-like chemicals were found in a bivalve sample (1.2 pg WHO-TEQ/g wwt) and a fish sample (0.47 pg WHO-TEQ/g wwt) collected from Port Jackson. There was little difference between the lower bound and middle bound estimates for both bivalves and fish. A summary of dioxin concentrations in bivalves and fish collected as a part of this study is given in Table 3-31.

Table 3-31 Middle bound mean dioxin concentration in fish and shellfish in Australia (range of min-max)

Organism	PCDD/F (pg WHO-TEQ/g wet weight)	PCB (pg WHO-TEQ/g wet weight)	Total dioxins (pg WHO-TEQ/g wet weight)
Fish	0.083 (0.0051-0.48)	0.036 (0.0016-0.37)	0.12 (0.011-0.85)
Bivalves	0.27 (0.0041-1.3)	0.42 (0.0027-2.6)	0.69 (0.0068-3.4)

Although people would consume fish and shellfish caught in the areas covered by this study, the intake of dioxins from these sources has been considered as a part of the dietary intake assessment (Section 3.2.1.2). The dietary intake of fish assessed in that section incorporates both fish and shellfish. Therefore, it will not be further considered in this section. However, it is interesting to note that one of the fish fillets sampled in the food survey contained higher levels of dioxins than any of the fish samples measured in the aquatic monitoring study. Since the fish fillet with the high levels of dioxins was included in the dietary intake calculations, the intake from seafood taken from the most contaminated sites sampled in the aquatic monitoring study has been adequately modelled. Despite the higher levels of dioxins in seafoods as cf. other foodstuffs, the importance of including fish in a nutritious diet has been emphasized by many agencies and organisations (see eg. IOM, 2004).

3.6 Intake from Specific Exposure Sources

3.6.1 Industrial sources

The manufacture and use of chlorinated aromatic chemicals have been significant sources of dioxin-like compounds in the environment. In addition to the use of certain pest-control chemicals which were contaminated with dioxin-like compounds (see below), other chemicals such as the PCBs were deliberately manufactured and had industrial uses. Other industrial processes, such as the production of chlorine-bleached pulp, have also led to environmental contamination by PCDD/Fs as unwanted by-products.

Australia's National Pollutant Inventory (NPI) reports on estimates of emissions of chemical substances and where and from what sources they are generated. The NPI holds emission data reported by industrial facilities, and aggregated emission data collected by participating jurisdictions. Aggregated data cover smaller facilities that are not required to report, and mobile and non-industrial sources such as transport and

domestic activities. The accuracy of the NPI data varies according to the technique used to estimate releases. For the aggregated emissions data in particular, comparative analysis of the data may be misleading, because jurisdictions may have used different estimation techniques.

The Australian NPI provides an emission report for polychlorinated dioxins and furans; a summary of the data (reporting year 2002 - 2003) may be found *via* http://www.npi.gov.au/. 335 Facilities from 31 industry sources reported polychlorinated dioxins and furans emissions. Additional aggregated emission data were collected for 8 sources, for a total of 39 sources. Total mass emissions were estimated at 0.5 kg, of which virtually all was to air, less than 1% to land and virtually none to water. The percentage contribution from different sources was estimated to be as follows: backyard incinerators (31.6%); electrical equipment and appliance manufacturing (19.0%); basic non-ferrous metal manufacturing (10.3%); electricity supply (7.0%); burning (fuel reduction, regeneration, agriculture)/wildfires (5.2%); and 'other' (27.0%).

PCBs

The polychlorinated biphenyls or PCBs refer to a family of 209 congeners, that is, chemicals with the same basic structure, in which the biphenyl structure has chlorine atoms substituted for hydrogen atoms to varying degrees. Approximately 100 of these congeners are present in various technical mixtures of PCBs that were produced commercially in large quantities until the late 1970s. PCBs were used in electrical appliances, such as transformers and capacitors, hydraulic fluids, plasticisers and dye carriers. They are also generated and released into the environment as unintentional by-products of chemical manufacturing and incineration.

PCBs are amongst a broader group of harmful persistent organic pollutants (POPs) that are toxic, persist in the environment and animals, bioaccumulate through the food chain, and pose a risk of causing adverse effects to human health and the environment. Because of their physical characteristics, POPs are transported long distances and are often deposited in areas where they have never been used or produced. As discussed elsewhere in this document, some PCBs have dioxin-like characteristics. Concerns over the potential risks to health, food chain and environment led to a ban on the importation of PCBs and PCB-contaminated or PCB-containing equipment to Australia in the 1970s.

Australia has a PCBs Management Plan for disposal and destruction of PCBs. Details of the plan are available from the Department of the Environment and Heritage (DEH) website at www.deh.gov.au/industry/chemicals/scheduled-waste/pcbs/index.html.

3.6.2 Chlorinated pesticides - manufacture and use

The manufacture and use of chlorinated aromatic chemicals have been significant sources of PCDD/Fs in the environment. Such chemicals include the wood preservative and biocide pentachlorophenol (PCP) and the herbicide 2,4,5-trichlorophenoxyacetic acid (2,4,5-T).

Historically, higher-level exposures to PCDD/PCDFs in PCP and 2,4,5-T has probably been restricted to relatively small groups of people involved in the handling and use of the pesticides. For example, a study published in 1992 reported that the blood serum TCDD levels in pesticide applicators involved for many years in ground-level spraying of 2,4,5-T in New Zealand were significantly higher than those of a comparison group (Smith et al, 1992). PCP and 2,4,5-T are no longer approved for use in Australia.

2,4,5-T

The herbicide 2,4,5-T (2,4,5-trichlorophenoxyacetic acid) was introduced in the 1960s and was once used in Australia to control woody weeds such as blackberries. It is a relatively simple chemical that structurally mimics certain natural plant growth regulators. It is difficult to manufacture pure 2,4,5-T without some contamination by dioxins; TCDD alone is the major contaminant of 2,4,5-T (Schechter et al, 1998). Dioxin levels in 2,4,5-T were generally in the low ppm to high ppt range, with more recently produced batches typically contaminated at the lower levels. 2,4,5-T was withdrawn from use in the late 1980s and is no longer approved for use or marketed in Australia. Furthermore, 2,4,5-T with dioxin contamination is now strictly controlled in international trade through the UNEP Prior Informed Consent or PIC Procedure (the 'Rotterdam' Convention).

The links between dioxins and potential adverse health and environmental effects have been established for well over 20 years. With respect to dioxin contamination of 2,4,5-T, appropriate controls to protect human health were established in the early 1970s via standards set by the National Health and Medical Research Council (NHMRC). In 1975, the NHMRC established a maximum level of dioxin contamination in 2,4,5-T of 0.1 mg/kg (100 ppb). In 1982, this level was lowered 10-fold to 0.01 mg/kg, reflecting improved analytical capability to monitor dioxin levels in technical-grade 2,4,5-T. At the time, both these standards were considered adequate to protect the health of agricultural workers and the public. Illegally imported batches of chemical which have been the subject of a Western Australian (WA) investigation have been reported as containing 200 times the 1975 standard, although definitive evidence that such contaminated 2,4,5-T was used in the Agricultural Protection Board spraying program is lacking.

The Western Australian Parliament conducted an inquiry into a government weed control program undertaken by the Agriculture Protection Board (APB) from 1975 to 1985 in the Kimberleys and other regions of WA. It has been suggested that some of the 2,4,5-T used may have been heavily contaminated by dioxins, with some evidence indicating that contaminated stock may have been illegally imported from about 1969 to 1971. Apart from the formation of toxic dioxins during manufacture of 2,4,5-T, if pure 2,4,5-T is subjected to high temperatures (eg. as in a factory fire, which may have been the case with contaminated material imported into Western Australia), 2,4,5-T molecules can chemically combine to form dioxins. This is also the case with its immediate precursor, 2,4,5-trichlorophenol (TCP).

An Occupational Health Physician, Dr Andrew Harper, interviewed 90 former Agricultural Protection Board (APB) employees involved with this Government

spraying program. His report, the Kimberley Chemical Use Review (Harper, 2002), concluded that exposure to unregulated levels of dioxins could not be ruled out. Whilst Dr Harper acknowledged that the review was not a scientific investigation, he found an association between illness and exposure to herbicides and considered that about one third of those interviewed had developed a chronic disability that was possibly or probably attributable to these chemicals. He also suggested that longer serving workers may have been more commonly affected. The WA State Government considered that further evaluation was required before the conclusion of this review that "illness developed in association with the spray" could be accepted. Consequently, an Expert Medical Panel was appointed to evaluate the results of the review. The Panel, chaired by Bruce Armstrong, Adjunct Professor of Epidemiology at the University of Sydney and Director of the NSW State Cancer Council's Epidemiology Unit,
produced an interim progress report, the Interim Report of the Expert Medical Panel to Evaluate the Kimberley Chemical Use Review Recommendations , which was tabled in the WA Legislative Council on 13th March 2003. The Panel requested that additional work be undertaken, including further analysis of data on the health status of former APB employees, and a review of the risk assessment and adverse event reporting mechanisms for chemicals used in agricultural protection programs. The Panel subsequently re-convened to consider this information and a further report was forwarded to the WA Cabinet in February 2004. The final report of The Expert Medical Panel to Evaluate Recommendations of the Kimberley Chemical Use Review, dated December 2003, was published on the internet on 27th February 2004 (accessed via http://www.ministers.wa.gov.au).

The Panel concluded the following:

1. Based on published evidence identifying a 'probable' link between exposure to chlorphenoxy herbicides containing TCDD and an increased overall cancer risk; the likelihood that spray workers were highly exposed to the herbicide (which may or may not have contained unregulated levels of TCDD); and evidence that APB workers have experienced a somewhat higher incidence of cancer than the community overall, albeit not statistically significant, the Panel concluded that "APB workers may suffer or may have suffered already an increase in the risk of cancer due to their exposure to herbicides containing the dioxin TCDD in the spray program". With respect to cancers, 17 APW workers were matched to people on the WA Cancer Registry, with 18 cancers; only two cancers (non-Hodgkin lymphoma and one which might have been a retroperitoneal soft-tissue sarcoma) were of a type linked to exposure to chlorphenoxy herbicides or TCDD. With respect to all cancer incidence cf. a comparison Kimberley population, a high degree of uncertainty about the true difference is due to the small number of observed cancer cases in the APB cohort.

2. The symptoms of ill health that the APB workers reported do not form a pattern such as to suggest that they were directly caused by their exposure to herbicides during their employment in the spray program. Furthermore, the symptoms of anxiety and depression reported by the APB workers were no more prevalent in the APB workers than in the general community; hence they are unlikely to be due to their employment in the spray program.

3. Little evidence was available to determine whether or not the APB workers have experienced increased rates of a number of other conditions that might possibly be caused by exposure to chlorphenoxy herbicides containing dioxins. No cases of chloracne were reported to have been diagnosed in APB workers; a definitive diagnosis of this condition would have indicated exposure. For diabetes, possibly associated with exposure to dioxins (see Chapter 2), its prevalence in the Australian aboriginal population is high and any additional effect from dioxin exposure would be very difficult to distinguish. In fact, expected deaths from diabetes in the indigenous population was "appreciably" greater than that actually observed in APB workers.

4. On the basis of a best estimate Standardised Mortality Ratio (SMR) of 1.09 (95% CI = 0.79-1.42), the Panel concluded that there was no strong evidence to suggest that the mortality in APB workers was higher than in the general Kimberley population.

5. A majority of the Panel recommended that a survey of serum TCDD levels be conducted in APB workers and a comparison population in the Kimberley. The results of such a survey could strengthen the evidence for the Panel's conclusion that APB workers may suffer or may have already suffered an increase in the risk of cancer due to their exposure to herbicides.

In its response, the Government of WA advised that it would act expeditiously through the workers' compensation system to assist APB workers diagnosed with cancer. Specifically, "the Government employer (APB) and insurer (RiskCover) will accept that cancers diagnosed in a former worker in the Kimberley weed spraying program, now or in the future, and assessed as being linked to 2,4,5-T herbicide use, will be eligible for consideration for compensation".

Pentachlorophenol

The historical use of pentachlorophenol (PCP) in the timber industry has resulted in occupational exposure to PCDD and PCDFs for some timber workers. It appears that the higher chlorinated (five to eight chlorines) PCDDS and PCDFs are found at elevated levels (Schecter et al, 1998). PCP was widely used both for anti-sapstain treatment for the interim protection of freshly sawn timber against fungal staining and as a permanent timber preservative. In addition to acute health effects of PCP exposure (including eye irritation, upper and lower respiratory tract irritation and skin changes such as burning, irritation and dermatitis), effects of contaminants such as dioxins were of concern. Whilst there does not appear to be any firm evidence of significant long-term health effects from the use of PCP, the possibility of such effects cannot be excluded.

Chlorinated phenols such as PCP were widely used in Australia to protect softwood timber from decay. In 1996 the then Department of Health and Family Services provided written comments to the Australian Pesticides and Veterinary Medicines Authority (APVMA; then the National Registration Authority for Agricultural and Veterinary Chemicals, or NRA) on acceptable levels of microcontaminants in PCP. The

impurities of concern in PCP were hexachlorobenzene (HCB) and dioxins, in particular tetrachloro-dibenzodioxins (TCDDs) and hexachloro-dibenzodioxins (HCDDs). Impurity limits were proposed, in the interests of ensuring that the Australian standard for dioxins and HCB impurities were at the lowest levels that can be achieved in the manufacturing method. However, at that time, it appears that PCP and pentachlorophenoxide were exempt from NRA requirements for technical-grade active constituent approval and thus these recommendations were not further considered. A search of the APVMA's pesticide products database indicates that, whilst there were two old PCP-containing wood-treatment products on the database in 1996, there are now no such registered products on the Australian market. However, PCP may be available in Australia for industrial and manufacturing purposes, and inappropriate continued use from stored stocks cannot be discounted.

With regard to those workers who have been exposed to PCP contaminated with dioxins, it is likely that they have concentrations of these chemicals in their blood higher than those in the general population. Whether or not they have experienced symptoms and health effects at these concentrations is unknown. Although PCDD/Fs gradually break down and are eliminated from the body, because these chemicals have long half-lives these workers can continue to be exposed for quite some years after workplace exposure ceased.

Other pesticides

As part of an ongoing review of 2,4-D, targeted for completion in 2004, Canada's Pest Management Regulatory Agency (PMRA) has found that in addition to 2,4,5-T and pentachlorophenol (PCP), pesticides known to be contaminated with dioxins, several other pesticides currently used in Canada may contain traces of dioxin and furans. Dioxins were found in 2,4-D although not in amounts causing any environmental concern. Other pesticides reported as containing dioxin include chlorthal-dimethyl (also known as dimethyl tetrachloroterephthalate, Dacthal or DCPA), dicamba, dichlorprop (2,4-DP), hexaconazole, MCPA, mecoprop and quintozene. This issue is being examined by the Australia's pesticide regulator, The Australian Pesticide and Veterinary Medicines Authority (APVMA). A Canadian media report of the PMRA finding also listed "dichlorophenoxyl-phenol" as one of the pesticides; this appears to be an incorrect reference to 5-chloro-2-(2,4-dichlorophenoxyl) phenol (i.e. the disinfectant 'Triclosan') which may contain traces of several non-toxic dioxin congeners. The issue of impurities in Triclosan has been previously investigated by NICNAS within DoHA's Office of Chemical Safety.

3.6.3 Cigarettes

Dioxins are a natural product of the combustion of organic material. The amount of dioxins formed depends principally on: (1) high temperature processes and/or incomplete combustion; (2) the presence of organic carbon; and (3) the presence of chlorine (either in organic or inorganic form). The presence of materials containing dioxins will obviously also increase the release of these substances during the combustion process (UNEP Chemicals, 2003).

Tobacco leaf naturally contains both organic carbon and chloride ions (regardless of the presence or absence of pesticide residues or chemical/flavouring additives in the tobacco) and consequently, as for any thermal process, “combustion” of cigarettes and cigars produces dioxins.

Investigations of the ten most popular brands smoked in Germany gave “emissions” of 0.1 pg I-TEQ/cigarette (Ball et al, 1990). There were no results from cigars, but given the greater quantity of tobacco present in a cigar (2 - 20 times that of a cigarette), a value of approximately 0.3 pg I-TEQ is reasonable.

Lofroth and Zebuhr (1992) report dioxin concentrations in both mainstream and sidestream smoke from one brand of Swedish cigarettes as approximately 1 pg I-TEQ per cigarette for mainstream smoke (smoke from 20 cigarettes; one 2-second puff of 35 ml, each minute) and 2 pg I-TEQ per cigarette for sidestream smoke. No individual isomer made up more than 20% of the total dioxin content with most isomers below the detection limits of 0.3 – 1.3 pg. These values are about 10-times those reported in the German study, although the congener profiles were relatively similar. Dioxins have also been reported in tobacco smoke by Muto and Takizawa (1989).

In Australia, recent estimates (November 2002) suggest that approximately 1/5th (19.8%) of the population smoke (Wakefield & Bobevski, 2003). The average number of cigarettes smoked per day (factory made and 'roll-your-own'), including those who smoke on a daily or weekly basis, is 14.4 ($\pm$ 12.2 SD; n = 1,585) and for daily smokers, 15.7 + 12.2 (n = 1,414).

Assuming an intake per cigarette of between 0.1 - 0.5 pg TEQ (the upper value assuming inhalation of 50% of mainstream smoke containing 1 pg TEQ/cigarette; see above) would give a daily inhalation intake for an 'average' smoker of around 1.5 - 7.5 pg/day. Assuming 100% uptake *via* the lungs (see Section 3.3) means that the systemic exposure estimate would be the same. Ball et al (1990) estimated that smoking 20 cigarettes/day could result in a TEQ intake (PCDD/Fs) of up to 3 pg/day.

A daily inhalation intake for an 'average' smoker of around 1.5 - 7.5 pg/day is equivalent to ca. 0.5 - 3.0 pg/kg bw per month (assuming a bodyweight of 70 kg). While it is not clear whether the cigarette TEQs from the published literature are based on lower bound or upper bound estimates, they may be crudely compared with the mean estimated intake of PCDD/Fs from food in Australia of 0.9-10.2 pg WHO-TEQ/kg bw per month (lower bound and upper bound means for the population greater than 2 years old; see Section 3.2.1). This means that with an intake from smoking possibly being 1/3rd of that coming from food, smokers are likely to have a measurably elevated dioxin intake cf. non-smokers. This intake comparison is consistent with the US intake estimate, with PCDD/F exposure *via* cigarette smoking representing "over 10 percent of the average daily background dose of CDD/CDFs from soil, air, water and foods" (US EPA, 2000).

Non-smokers are also likely to be exposed to dioxins from passive intake of cigarette smoke. However, individual exposure to so-called 'sidestream' smoke is much more variable than the exposure of smokers themselves since it depends on a person's proximity to smokers, how often they are near smokers, and the extent of ventilation in

the smoking area. These extra uncertainties mean that it is not feasible to reasonably estimate the contribution of inhaled sidestream smoke to dioxin intake.

Whilst we do not have any experimental data in animals on the cancer risks from inhalation exposure to dioxins, available evidence suggests that for smokers, the health risks from other toxic and carcinogenic components of cigarettes far outweigh the likely health risk from the PCDD/Fs. However, it appears that encouraging people to give up smoking would help to reduce their body burden of dioxins; in young women in particular, smoking has the potential to increase their tissue levels of dioxins which can ultimately transfer to any future offspring *via* prenatal (transplacental) and postnatal (breast feeding) routes.

In view of the age of the available studies on dioxins in cigarette smoke (Ball et al, 1990; Lofroth & Zebuhr, 1992; Muto & Takizawa,1989), this could be an area for further investigation eg. laboratory experiments to accurately quantify release from burning cigarettes and epidemiology studies to see if cigarette smokers do indeed have higher body burdens of dioxins cf. matched controls (ie. to clearly ascertain whether cigarettes are a dioxin-source problem or not).

3.7 Exposure Estimates from All Sources

3.7.1 Estimated intake of dioxins from all sources

The total dioxin intake for the Australian adult population can be estimated by adding the estimated intakes from all sources of exposure. Table 3-32 gives the estimated PCDD/F, PCB and total dioxin intakes from air, food, soil and water, and the total estimated intake of dioxins for Australian adults. From this data it can be seen that intake from food represents between 95% and 99% of the total intake of dioxins, with intake from contact with soils and breathing of air representing 5% or less of the total intake of dioxins for Australian adults.

Table 3-32 Estimated exposure of Australian adults to dioxins from all sources

Source of exposure	Total intake (pg WHO TEQ/kg bw/month)					
	PCDD/Fs		PCBs		Total dioxins	
	Lower bound	Upper bound	Lower bound	Upper bound	Lower bound	Upper bound
Air[1]	0.104	0.111	0.016	0.017	0.120	0.127
Food[2]	0.9	10.2	2.8	5.4	3.7	15.6
Soil[3]	0.057	0.057	0.01	0.01	0.067	0.067
Water[4]	-	-	-	-	-	-
TOTAL	1.06	10.37	2.83	5.42	3.89	15.79

[1]- mean of adult male and female intake for urban airshed exposure
[2]- all Australians 2+ years of age, lower and upper bound estimates use LOQ rather than LOD
[3]- total of both dermal exposure and ingestion of soil from urban sites
[4]- intake from water was not estimated but is expected to be negligible (see Section 3.5.1)

The intake estimates given in Table 3-32 do not include an estimate of dioxin intake from cigarette smoking. Cigarette smokers will have a higher intake of dioxins than

non-smokers. Section 3.6.3 estimates a smoker's intake of PCDD/Fs from cigarette smoke as 0.5-3.0 pg
I-TEQ/kg bw/month, which is up to approximately one third of the upper bound PCDD/F intake estimated from food. No data were available on PCBs in cigarette smoke. Assuming that the PCB intake of a smoker is the same as a non-smoker, then a conservative upper bound estimation of the total dioxin intake of an average smoker is approximately 19 pg TEQ/kg bw/month.

Table 3-33 gives the estimated PCDD/F, PCB and total dioxin intakes from air, food, soil and water, and the total estimated intake of dioxins for young children in Australia. From this data it can be seen that intake from food represents between 86 and 97% of the total intake of dioxins, while intake from contact with soils and breathing of air represents between 3 and 14% of the total intake of dioxins.

The estimated total dioxin intakes of young Australian children are higher than those of the Australian adult population. This is expected since children have higher levels of food consumption relative to body weights than adults and intake from food represents the greatest source of exposure to dioxins. The estimated total dioxin intake from air is only slightly higher in young children than adults, but young children have significantly higher intakes of dioxins from soil since they have the potential to ingest much more soil than adults.

Table 3-33 Estimated exposure of young children in Australia to dioxins from all sources

Source of exposure	Total intake (pg WHO TEQ/kg bw/month)					
	PCDD/Fs		PCBs		Total dioxins	
	Lower bound	Upper bound	Lower bound	Upper bound	Lower bound	Upper bound
Air[1]	0.174	0.185	0.027	0.028	0.202	0.213
Food[2]	1.9	25.0	4.3	11.8	6.2	36.7
Soil[3]	0.73	0.74	0.087	0.087	0.82	0.83
Water[4]	-	-	-	-	-	-
TOTAL	2.80	25.92	4.41	11.91	7.22	37.74

1- intake of 1-year old child for urban airshed exposure
2- children 2-4 years of age, lower and upper bound estimates use LOQ rather than LOD
3- total of both dermal exposure and ingestion of soil from urban sites by a child 2-3 years of age
4- intake from water was not estimated but is expected to be negligible (see Section 3.5.1)

Other than the US EPA's (2000) comprehensive human exposure and health assessment, there are few recent, readily available multimedia dioxin health risk assessments that have been conducted by other countries. Liem and Rappe (1998) compared estimated daily exposures to PCDD/Fs in Canada, Germany, the Netherlands, the United Kingdom and the United States of America. However, these estimates were based on data collected in the late 1980s or early 1990s and several studies have shown that human exposures to dioxins have declined significantly since then, making it inappropriate to compare data collected approximately a decade apart (Codex Alimentarius Commission, 2003; European Commission, 2002; Food Standards Agency (UK) (2003); US EPA, 2000; Malish and Van Leewen, 2003).

Table 3-34 compares the recently estimated intake of dioxins in Australian and US populations with a US estimate of PCDD/F intake prepared in 1994 (US EPA, 1994). The data illustrate the decline in PCDD/F intake that has occurred in the USA since the early 1990s and shows that the current Australian dioxin intake estimates are lower than the recent US EPA estimates, even allowing for the fact that the Australian upper bound mean is being compared with the US middle bound mean. The PCDD/F intake estimates made in the late 1980s/early 1990s for 4 other countries and reported by Liem and Rappe (1998) were similar to those in the USA measured at about the same time (US EPA, 1994).

Table 3-34 Estimated adult intakes of dioxins from all sources: a comparison of recent Australian and American estimates with an American PCDD/F intake estimate from 1994.

Source of exposure	Total intake (pg WHO TEQ/kg bw/month)						
	PCDD/Fs			PCBs		Total dioxins	
	Australia 2004[1]	USA 2000[2]	USA 1994[3]	Australia 2004[1]	USA 2000[2]	Australia 2004[1]	USA 2000[2]
Air	0.111	0.69	0.94	0.017	-	0.127	0.69
Food[4]	10.2	16.7	49.7	5.4	10.2	15.6	26.76
Soil[5]	0.057	0.249	0.34	0.01	-	0.067	0.249
Water	-	0.0003	0.003	-	-	-	0.0003
TOTAL	10.37	17.7	51.4	5.42	10.2	15.79	27.9

[1]-upper bound mean
[2]-middle bound mean, except soil which is lower bound mean
[3]-middle bound I-TEQ estimate
[4]-total intake from all foodstuff
[5]-includes dermal and ingestion intakes for Australia 2004 and USA 2000 and soil ingestion for USA 1994

The intake estimates given in Tables 3-32 and 3-33 were calculated by combining the measured dioxin concentrations in environmental media and food with the estimated extent of contact (by ingestion, inhalation, dermal contact etc) with the media (see Sections 3.2 to 3.6). This approach gives the estimated current intake of dioxins in the Australian population.

Since dietary intake contributes by far the greatest proportion of the total intake of dioxins, the variability and uncertainty associated with the dietary intake assessment are the factors most likely to impact significantly on the overall intake assessment. In general terms, the major sources of uncertainty associated with the dietary intake assessment are those related to the analysis of dioxins in foodstuffs and those related to assumptions used in the dietary exposure modelling. Examples of some of the possible sources of uncertainty include the use of upper bound estimates (which generally leads to an overestimate of intake), the use of 24-hour recall survey data, the limited range of foodstuffs analysed and assumptions that certain foods that were not analysed contain dioxins at the same levels as similar foods that were analysed. For further details of some of the assumptions and uncertainties associated with dietary intake assessment see Section 3.2 and FSANZ (2004).

Other sources of uncertainty associated with the estimation of dioxin intake from all sources include the use of several default parameters for assessment of intakes from soils and air eg. assumptions about population average body weights and body fat percentages, air intake volumes, extent of contact with soils, the half- life of dioxins in the human body etc. Another potential source of uncertainty is the possible omission of a significant, but unidentified source of dioxin intake. Overall, the use of conservative assumptions, in particular the use of upper bound estimates for intake calculations, is most likely to have resulted in an overestimate of dioxin intake by the Australian population.

3.7.2 Estimating intake from measured body burdens

An alternative approach to investigating the exposure of the Australian population to dioxins is to estimate the average lifetime daily exposure (ALDE) from the measured body burdens of dioxin using a simple pharmacokinetic model. This approach to estimating dioxin intake is detailed in Section 3.1.1.5, and is based upon the fact that, assuming a steady-state between intake and excretion, a theoretical estimated average daily intake which would lead to a measured body burden can be calculated. Estimation of the total body burden of dioxins takes advantage of the fact that the concentration of these compounds in fat is constant throughout the body. Thus, whatever fat sample is used (eg. fat in blood or breast milk samples) gives an estimate of the concentration in all fat in the body. Then, using data on the percentage of total body weight which is made up of fat, the total body burden of dioxin can be easily estimated.

The ALDE estimated across all age groups to achieve the measured blood levels of dioxins was 1.3 pg WHO-TEQ/kg bw/day (40 pg WHO-TEQ/kg bw/month). This is approximately 2.5 times higher than the total dioxin intake estimate for adults calculated from current levels in food and the environment (15.7 pg WHO-TEQ/kg bw/month). The US EPA (2000) found daily dioxin intake estimated on the basis of blood serum data was approximately 2.2 times higher than the dioxin intake estimated from current levels in food and the environment. This difference is expected since the intake estimate based on blood serum measurement reflects past exposures to dioxin levels in food and the environment, which were higher than current levels (as outlined above and in Section 3.1). In addition, there is likely to be significant variability and uncertainty associated with each of the estimates.

It will be apparent that the calculations of TEQ intakes show that infants and children have higher intake rates than adults on a bodyweight basis (for reasons given in Section 3.7.1), yet simple ALDE calculations indicate the opposite. The reasons for this apparent discrepancy in the ALDE calculations include the fact that environmental levels of dioxin-like compounds were higher in the past than they are at present and thus adults have had proportionately greater exposure than younger people ie. given that the annual exposure to dioxin-like compounds has decreased over the decades, a back calculation using body burden in older age groups would be expected to yield a higher estimate of ALDE than one done for a younger age group that is only affected by more recent intakes. Furthermore, this simple steady-state model makes the assumption of constant half-life over the lifetime of an individual, an assumption which is very unlikely to be correct. If the average half-life increases with age, as expected with reduced fecal excretion and changing metabolism of dioxins (see discussion at Section 3.2.3), then a higher ALDE would be calculated for the younger, and a lower ALDE would be calculated for the older age categories ie. the discrepancy in ALDEs between the age groups would be much less apparent.

Thus, the use of a simple steady-state model which assumes a constant elimination half-life for dioxins in the human body regardless of its age or physiological status, can at best provide only a relatively crude back-estimate of a daily dioxin intake which may have led to a measured body burden at a particular time in life.

4. Health risk assessment

4.1 Health Risks for the General Population

4.1.1 Dietary exposure as a proportion of the Tolerable Monthly Intake (TMI)

Figure 4-1 shows the mean estimated monthly exposure to total dioxins for the range of population groups aged 2 years and above expressed as a percentage of the TMI. Appendix XVIII contains detailed tables of the mean and 95th percentile exposure results, as a percentage of the TMI, for PCDD/F, PCBs and total dioxins.

In all cases, the mean and 95th percentile estimated dietary exposure to total dioxins for all age-gender categories (from 2 years and above) were below the TMI of 70 pg WHO-TEQ/kg bw/month. Across all age groups from 2 years and above, the estimated mean exposure to total dioxins was between 5% (lower bound) and 22% (upper bound) of the TMI. The 95th percentile exposure for the same population was between 23% (lower bound) and 58% (upper bound) of the TMI. For the population groups representing the younger members of the population, the mean and 95th percentile dietary exposure estimates are higher percentages of the TMI, as a result of their lower bodyweights and a higher proportion of milk and dairy products in their diets.

The mean estimated dietary exposure for infants aged 9 months (fed 50% infant formula/ 50% solids, see Section 3.2.1.2) as a percentage of the TMI was considered separately from other population groups since this was derived using a different methodology and cannot be directly compared to other population groups. For this population group, the 95th percentile exposures were not calculated (see Section 3.3 for discussion). Estimated mean exposure to total dioxins for infants aged 9 months was 17% (lower bound) to 87% (upper bound) of the TMI. Infants at this age had the highest calculated mean exposure to total dioxins as a percentage of the TMI because of their high food consumption relative to body weight.

It is apparent that the estimated dietary intake vs age gives a different picture from that obtained when average lifetime daily exposures (ALDEs), which are back-calculated from measured dioxin body-burdens using a simple steady-state model, are plotted vs age. The errors and uncertainties in the simple model used for ALDE calculations are given in sections 3.1.1.5 and 3.7.

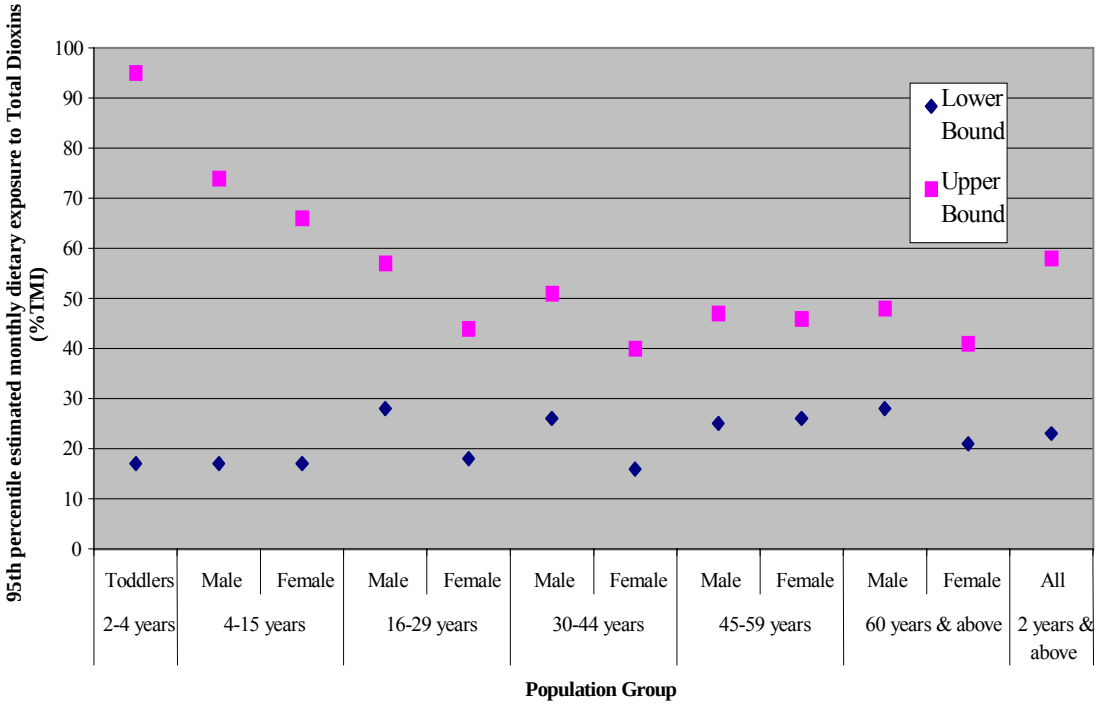

Figure 4-1 Mean estimated dietary exposure to total dioxins as a percentage of the TMI

Lower Bound – assumes results reported as being below the LOQ are zero.
Upper Bound – assumes results reported as being below the LOQ are at the LOQ.
Australian TMI = 70 pg TEQ/kg bw/month.
Dioxins = sum of intakes of PCDD/F and PCBs.
Estimated dietary exposures are based on food consumption data from the 1995 NNS

4.1.2 A comparison of intake from all sources with the TMI

The potential risk to the health of the general public as a result of exposure to dioxins can be estimated by comparing the current exposure estimates (outlined in Section 3.7) with the tolerable monthly intake (TMI) for dioxins. The upper bound mean total dioxin intakes for adults and young children (approx. 1-4 years of age) in Australia were 15.6 and 37.5 pg WHO-TEQ/ kg bw/month respectively. These estimates of intake represent 22% and 54% of the TMI of 70 pg WHO-TEQ/kg bw/day respectively. However, it should be noted that the upper bound intake estimates given in Section 3.7 are likely to be conservative overestimates, therefore the average intake by these two age groups is likely to be less.

Since the TMI is determined on the basis of the most sensitive adverse effects observed in animal studies and includes an appropriate safety factor, it is considered unlikely that the estimated average dioxin exposure of the Australian population (1+ years of age) would result in any appreciable health risk. However, because there are uncertainties in our understanding of the health effects that may be associated with exposure to dioxins, higher margins of safety are desirable to further reduce the potential for any possible risk to public health as a result of such exposure.

The intake from all sources was not calculated for children <1 year of age. However, the discussion in Section 4.1.1 about the dietary intake of a 9-month old infant fed 50% infant formula and 50% solids indicates that the total dioxin intake of this group of the population (fed this diet) is likely to be slightly lower than the TMI. It should be noted that the intake of infants is likely to have been overestimated and infants would only be exposed at these levels for a small proportion of the total lifetime. Section 4.2 includes further discussion of the potential for health risks in breast-fed infants.
In addition to the average exposures of the Australian population there may be certain segments of the population that could have exposures somewhat higher than the general population as a result of occupational exposure, smoking or elevated dietary exposure to certain foods that may contain high levels of dioxins. The potential health risk for segments of the population that may have elevated exposure to dioxins is detailed in Section 4.2.

4.1.3 Cancer risk

The IARC and other agencies/organisations have concluded that the available epidemiology data suggest that TCDD is likely to be a human carcinogen. Statistically significant increases in risks for all cancers were found in highly exposed workers with longer latency periods. Although the estimated Standardised Mortality Ratios (SMRs) for cancer were consistent across studies with the highest exposures, they were generally low.

A number of national agencies have endeavoured to provide quantitative estimates of cancer risk, based on low-dose extrapolation from both animal and human data. In view of the ongoing debate about the existence of a threshold level below which dioxins will not increase cancer risk, about the potency of the various dioxins, furans and PCBs in causing cancer, and the variability in various quantitative risk estimates, this assessment has not endeavoured to conduct a quantitative risk assessment. The available data from high dose animal studies and studies of human occupational and accidental exposures cannot be extrapolated quantitatively with any confidence down to values corresponding to the background exposures of the general population.

However, it is noted that the body burden of dioxins in the general population is several orders of magnitude lower than the body burdens of the most highly exposed industrial cohorts or by the neighbouring population during the industrial accidental exposure at Seveso (eg. Kogevinas, 2000), where there is evidence of some increased cancer risk. Although the excess cancer risk at the highest exposures in human epidemiology studies are statistically significant, most assessments of the cancer risks posed by dioxins note that these results need to be evaluated with caution as the overall risks are not high and the strongest evidence was for industrial populations with high exposures to dioxins, and also with heavy exposure to other chemicals. Furthermore, lifestyle factors such as smoking were not evaluated. JECFA also noted, *inter alia*, that there were few precedents of carcinogens that increase the risk for cancer at all sites combined, with no excess risk for any specific tumour predominating.

In the high-exposure industrial cohorts studied by IARC (IARC, 1997), blood lipid levels estimated to the last time of exposure were 2000 ng/kg (mean, with levels up to

32,000 ng/kg; US cohort), 1434 ng/kg (geometric mean, range 301 - 3,683 ng/kg; Dutch cohort), 1008 ng/kg (geometric mean; German workers with severe chloracne), and up to 2252 ng/kg (Boehringer cohort, Germany). The mean serum concentration across the Australian population was determined as 10.9 ng WHO-TEQ/kg on a lipid-adjusted basis (range: 4.6-28 ng WHO-TEQ/kg lipid). Thus, the workers in the industrial cohorts studied were exposed to TCDD levels two to three orders of magnitude higher than those experienced by the Australian population

The exposure of Australians to dioxins may also be compared to the levels required to cause tumours in laboratory animal studies. In 2001 the Joint FAO/WHO Expert Committee on Food additives (JECFA) noted that in a long-term carcinogenicity study in rats in which the incidence of liver tumours was increased over that in controls, the LOEL of 10 ng/kg bw/day for TCDD corresponded to a steady-state body burden of 290 ng/kg bw/day. In order for humans to attain a similar steady-state body burden, they would have to have a daily intake of 150 pg/kg bw (FAO/WHO, 2002), equivalent to 4,500 pg/kg bw per month. As estimated above, the upper bound mean total dioxin intakes by young children (1-4 years of age) and adults in Australia were 37.5 and 15.6 pg WHO-TEQ/ kg bw/month respectively. The margin of safety between these values is greater than immediately apparent if one takes into account the conclusion that rats are likely to be somewhat more sensitive than humans to the carcinogenic effects of TCDD (see 'Hazard Assessment' at Section 2) and the fact that the human intake is expressed as WHO-TEQ (total dioxin-like compounds) while the rats study was conducted using the most potent dioxin, TCDD.

As discussed in Section 2 ('Hazard Assessment') the Tolerable Monthly Intake value established on the basis of non-cancer effects is sufficiently protective to guard against any carcinogenic risk. This conclusion has been reached by the JECFA, the EC-SCF, the US SAB Panel, and other independent risk assessors.

4.2 Health Risks for Specific Population Sub-Groups

4.2.1 Breast-fed infants

As noted in Section 3.2.3, since infants have a high dietary intake and low bodyweight, they have higher exposures to food contaminants per kilogram of body weight than adults. Since human breast milk generally contains higher dioxin levels than infant formulas (which are based on plant-derived oils rather than animal fats), there are some concerns about breast-fed infants receiving a higher intake of dioxin-like compounds than formula-fed infants. However, data assessed in Section 3.2.3 indicate that, compared with intake estimates for breast-fed infants from other countries, estimates of intakes by Australian infants were the lowest amongst those countries for which data were retrieved.

Notwithstanding this, it is noted that during the breast-feeding period, absolute intake of dioxins is likely to be higher in breast-fed infants than formula-fed infants[27], while the

[27] A peer-review comment was that the breast milk comparison should be with "low levels/natural levels" in breast milk rather than with levels in formula. The difficulty arises in ascertaining what is a "natural"

estimated intake per kg bodyweight is clearly likely to be higher than dietary intakes of dioxins for the rest of the Australian population. Available evidence does suggest, however, that dioxin intake for breast-fed infants diminishes over time. This can be explained by the observations that the dioxin concentration in maternal milk decreases during lactation, that the excretion rate of dioxins is higher in infants than in adults, and the fact that food intake per unit body weight and per unit total body fat decreases with age (attributed to the rapidly increasing body weight and lipid volume of the growing infant).

At issue is whether there are likely to be any developmental consequences of a period of somewhat higher exposure to dioxin-like compounds during breast feeding as cf. formula-fed infants. In order to help answer this question, a number of studies have been conducted.

A 1997 Dutch review (Cuijpers et al, 1997) of four epidemiological studies published between 1984 and 1996 (referred to as the Michigan study, the Rotterdam/Groningen study, the Amsterdam study, and the North-Carolina study) led the reviewers to conclude that these studies did not indicate any adverse effect of postnatal exposure *via* mother's milk to dioxins, furans and PCBs on the postnatal development of children. While the authors of the reviewed studies suggested that neurotoxic effects in children exposed to relatively high prenatal levels of dioxins could not be excluded, Cuipers and co-authors opined that this conclusion remained to be demonstrated. At best, the results of the epidemiological studies served a function in the identification of possible hazards of dioxins but could not be used for any quantitative risk assessment purposes.

A large prospective follow-up study, the "Dutch PCB/Dioxin Study" was initiated in 1989. In 1993, this study became part of a multi-centre cohort study with Germany and Denmark, financed by the European Community. Of 418 'healthy' mother-infant pairs, fifty percent (n = 209) of the children were breast-fed and 50% were formula-fed during infancy. The cohort was also fairly evenly divided in location between a highly industrialised area and a semi-urban area. Subjects were followed from birth until 6 years of age. The primary goal of this study was to gain insight into possible toxic effects associated with environmental PCB and dioxin exposure and the contribution of prenatal *vs* postnatal exposure to neurobehavioural and cognitive outcomes (Patandin, 2001).

In considering the numerous papers published as a result of the Dutch PCB/Dioxin Study, it needs to be borne in mind that 'prenatal' exposure refers to direct transfer of dioxins to the developing foetus from the mother whereas 'postnatal' exposure refers to post-partum transfer *via* breast milk; thus both breast-fed and formula fed babies have equivalent prenatal exposures to dioxin-like compounds. Because of the fact that quite subtle developmental changes are being studied and because it may not have been possible to distinguish between pre- or postnatal exposures, some of the published findings from the Dutch PCB/Dioxin Study (see below) report on effects of peri-natal

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level; because of the limited numbers of samples taken, pooling of samples, and limited stratification of samples, no such samples could be clearly identified in this current study. Furthermore, it should be noted that no significant differences in dioxin levels were noted between rural, urban and industrialised urban areas in Australia.

exposure (exposure 'around' the time of birth) rather than specific pre- or post-birth exposures.

Prenatal PCB exposure was related to lower psychomotor scores at 7 months of age, poorer neurological condition at birth and at 18 months. At 42 months, prenatal PCB exposure was related to lower scores on the Kaufman Assessment Battery for Children, but no effect on the neurological condition was seen. Postnatal PCB and dioxin exposure through lactation was related to lower psychomotor development at 7 months (Vreugdenhil & Weisglas-Kuperus, 2000). Yet, in an assessment of play behaviour is school-age children, Vreugdenhil et al (2002b) reported more feminized play in boys as well as girls to be associated with higher prenatal dioxin levels, not with postnatal exposure to dioxin and PCBs through breast feeding.

Boersma and Lanting (2000) and Boersma et al (2001) investigated long-term effects of perinatal exposure to PCBs and dioxins on neurological and cognitive development in these infants from birth to 6 years of age. Data obtained suggested that prenatal exposure to PCBs may have subtle negative effects on early neurological and cognitive development of children but there were consistently beneficial effects of breast-feeding on brain development when children were studied from 18 months up to school age. Various possible mechanisms to explain the ability of breast feeding to counteract adverse developmental effects were suggested, including the transfer of hormones and biologically-active peptides, various long-chain fatty acids found in human milk which are important in supporting brain growth and development, as well as the psychosocial aspects of nursing. In a related component of the study which assessed the cognitive and motor abilities of school-age children using the McCarthy Scales of Children's Abilities, the authors (Vreugendhil et al, 2002) concluded that subtle cognitive and motor developmental delays from prenatal (perinatal?) PCB and dioxin exposure may persist into school age "when parental and home characteristics were less optimal", but such effects were not measurable in children raised in more optimal environments. That is, the intellectual stimulation provided by a more advantageous parental and home environment appeared to counteract any possible effects of prenatal exposure to PCBs and dioxins on cognitive and motor abilities. (Note that while half of this population was fully breast-fed for at least 6 weeks and the other half formula fed during infancy, the study focussed on linking effects to prenatal exposure.)

Weisglas-Kuperus et al (2000) suggested that prenatal exposure to PCBs and dioxins is associated with changes in the T-cell lymphocyte population in healthy Dutch infants, concluding that in Dutch preschool children the effects of perinatal background exposure to PCBs might be associated with a greater susceptibility to infectious diseases. However, the authors also hypothesized that this might lead to a lower prevalence of allergic diseases.

As appears to be the case in the Dutch PCB/Dioxin Study, a number of other studies (eg. Gladen et al, 1988; Jacobson et al, 1990; Huisman et al, 1995) also indicate that any neurological deficits associated with exposure to dioxins and other organochlorine contaminants appears to be associated with *in utero* exposure rather than breastfeeding, in spite of the higher doses received postnatally through breast milk than transplacentally.

A program established by the Japanese Ministry of Health and Welfare measured concentrations of dioxins in breast milk samples collected in Osaka over a 23-year period between 1973 - 1996 showed a decrease of approximately 50% in the level of dioxin-like compounds in the fat. It was reported that there were no changes in the health status of Japanese infants over this period (Hirayama, 2000). However, such a broad conclusion does not add significant information to the debate about effects of perinatal exposure of infants to dioxins.

Tsutsumi et al (2000) studied a cohort of Japanese females of reproductive age (2,281 control subjects and 567 patients with endometriosis) and reported that females who had been breast-fed had a lower incidence of endometriosis in adult life than non breast-fed infants. This unexpected finding led them to conclude that, if dioxin exposure was partly responsible for an increased incidence of endometriosis in women, it was not due to dioxin exposure during the breast-feeding period.

In two episodes of epidemic poisoning in Japan and Taiwan (so-called Yusho and Yu-Cheng incidents, respectively), developmental effects in infants and children born to mothers who had been exposed to PCDFs and PCBs included a higher incidence of natal teeth and later, missing permanent teeth, delayed eruption of permanent teeth, and disturbed root development (Ikeda, 1996; Rogan et al, 1988). A Finnish study (Alaluusua et al, 1996) concluded that long breast feeding may increase the risk of mineralization defects in children, possibly because of environmental contaminants (not identified). Further investigations (Alaluusua et al, 1999) suggested that such defects occurred more often and were more severe in children who had been exposed to higher amounts of polychlorinated aromatic hydrocarbons than in those exposed to lower amounts. Another Finnish study on 34,457 infants born in 1997-2000 (Alaluusua et al, 2002) indicated that the prevailing levels of PCDD/Fs and PCBs appeared to be below the threshold to cause perinatal eruption of teeth.
More recently, this Finnish research team has concluded that, despite findings that dioxins can have adverse effects on tooth development, breast feeding should not be restricted. This was made on the basis of observations that dioxin levels are declining and the fact that the benefits outweigh any possible risks (Alaluusua, 2004).

Hoover (1999) estimated the exposure of Canadian infants to persistent organochlorines in breast milk, using probabilistic methods. Although the levels of persistent compounds have been declining in Canadian breast milk, there were potential risks arising from exposure to dioxins, furans and PCBs. It was concluded that the well-documented benefits of breast-feeding qualitatively appeared to outweigh potential health concerns associated with organochlorine exposure. Furthermore, the risks of mortality from not breast-feeding as estimated by Rogan and colleagues (Rogan et al, 1991) exceeded any theoretical cancer risk estimated for infant exposure to potential carcinogens in Canadian breast milk. Rogan et al (1991) concluded that only extreme levels of contaminants could result in a greater health hazard than failure to breast feed. Thus, any recommendation to reduce or eliminate breast feeding would only be appropriate in isolated situations in which there was heavy exposure of the mother, such as might occur occupationally or from consumption of highly contaminated food (Rogan et al, 1991).

Despite evidence that breast-fed infants may initially have somewhat higher exposures to dioxin-like compounds than formula-fed infants, it has been widely concluded that, in addition to meeting nutritional needs, breast milk provides numerous immunological, developmental, psychological, economic, and practical advantages. Furthermore, a range of studies support the conclusion that breast-feeding may be related to the prevention of some adult-onset health problems such as diabetes and coronary heart disease. There are a large number of publications which catalogue specific benefits of breast feeding; some of these are outlined in the following Table.

Table 4-1 Some reported health benefits of breast feeding

Morbidity and mortality	Protection against otitis media, bacteraemia, meningitis, diarrhoea, necrotizing enterocolitis, gastro-intestinal disorders, anaemia, eczema, respiratory and urinary tract infections, Sudden Infant Death Syndrome (SIDs), Crohn's disease, celiac disease and Type I diabetes
Neurological effects	Long-chain fatty acids in breast milk are essential for brain development; Breast-fed infants score higher in a variety of neurodevelopmental tests and are at a lower risk for learning disability; Exclusively breast-fed infants show more advanced psychological and psychomotor development at one year of age; Pre-term infants fed breast milk (even by tube-feeding) had better IQ outcomes at age 7-8;
Immunological effects	Breast-fed infants are protected against a variety of immune-related disorders including auto-immune diseases, food allergies and allergic dermatitis; Immune systems of breast-fed infants appear to mature more quickly; Immunological protection afforded by breast milk reduces the overall morbidity in breast-fed infants.
Physical development	Enhances the maturation of the neonatal intestinal tract.
Vision	Fatty acids in breast milk are important for optimal retinal development and visual function.
Psychological	Provides an opportunity for mother/infant bonding, with implications for emotional development and adult psychoaffective behaviour.

Table adapted from Hoover (1999) and references therein.

The WHO estimated the percentage of lifetime intake of PCDD/Fs and PCBs that would be obtained from nursing and concluded that exposure is small in comparison to the benefits of breast feeding (WHO, 1988). After more recent extensive evaluation of the literature, the WHO has re-stated that current scientific evidence does not support altering its global public health recommendation of exclusive breast-feeding for 6 months, followed by safe and appropriate complementary foods, with continued breast-feeding, up to 2 years of age or beyond, as appropriate (Pronczuk et al, 2002). Nevertheless, it has also stated that further efforts to control environmental releases of these compounds is warranted, based on results of epidemiological studies showing the possibility of subtle clinical, endocrine and neurodevelopmental effects, in conjunction with related data obtained in experimental animals (Brouwer et al, 1998; AMAP 2003).

In conclusion, breast-fed infants are likely to have an intake of dioxins over the breast-feeding period which is somewhat higher than in formula-fed infants. However, by far the majority of evidence in the scientific literature suggests that any short-term adverse effects of this intake are far outweighed by the beneficial effects of breast feeding.

4.2.2 Workers exposed to chlorinated pesticides

Occupational exposure to the herbicide 2,4,5-T (2,4,5-trichlorophenoxyacetic acid) contaminated with TCDD is considered in some detail in Section 3.6.2. It appears that some heavily contaminated 2,4,5-T may have been illegally imported from about 1969 to 1971 and used in a government weed control program undertaken by the Agriculture Protection Board (APB) from 1975 to 1985, in the Kimberleys and other regions of WA. An inquiry was conducted by the Parliament of Western Australia; the final report of The Expert Medical Panel to Evaluate Recommendations of the Kimberley Chemical Use Review (made public on 27th February 2004; accessed via http://www.ministers.wa.gov.au) concluded that the cohort of APB workers examined may have experienced a somewhat higher incidence of cancer than the community overall, although the results were not statistically significant. Other signs and symptoms of ill health that the APB workers reported did not appear to be caused by their exposure to herbicides during their employment in the spray program. Thus, no cases of chloracne were reported to have been diagnosed (a condition which indicates exposure). Symptoms of anxiety and depression reported by the APB workers were no more prevalent than in the general community. For diabetes, possibly associated with exposure to dioxins (see Section 2), the expected diabetes-related death rate in the indigenous referent population was greater than that observed in APB workers. Further, there was no strong evidence to suggest that mortality in APB workers was higher than in the general Kimberley population. It is not possible to comment further on any link between cancer incidence and exposure to dioxins in this case, since no survey of serum dioxin levels has yet been conducted in APB workers involved in 2,4,5-T spraying programs. The results of such a survey, if performed, could indicate whether these workers had significantly higher historical exposures to dioxins than a control population. Thus, the available information from this study does not allow any assessment to be made of the likely increase in cancer risk from a given exposure to dioxins.

2,4,5-T and 2,4-D were manufactured in Sydney for more than 25 years at the Union Carbide site at Rhodes. DDT was manufactured there for almost 40 years. Unfortunately, information about the health of these workers does not appear to be available. However, there is information available about the site – particularly dioxin levels.

The historical use of pentachlorophenol (PCP) in the timber industry in Australia to protect softwood timber from decay has most likely resulted in occupational exposure to PCDD and PCDFs for some timber workers. Whether or not they have experienced symptoms and health effects due to such exposures is unknown. Whilst there does not appear to be any evidence of significant long-term health effects from the use of PCP, the possibility of such effects cannot be excluded.

4.2.3 Cigarette smokers

Very approximate estimates (Section 3.6.3) indicate that intake of PCDD/Fs by the average smoker could be around 1/3rd of that coming from food. Thus, smokers are likely to have a measurably elevated dioxin intake cf. non-smokers, with the potential for an increased body burden of dioxins. Smokers place themselves at significant health

risk from the many other toxic and carcinogenic components present in cigarette smoke, a risk which far outweighs the risk from intake of this level of dioxins. However, it appears that encouraging people to give up smoking would help to reduce body burdens of dioxins in the 1/5th of the Australian population which smoke; in young women in particular, smoking has the potential to increase their tissue levels of dioxins which could ultimately transfer to any future offspring *via* prenatal (transplacental) and postnatal (breast feeding) routes.

Non-smokers are also likely to be exposed to dioxins from passive intake of cigarette smoke. However, because individual exposure to so-called 'sidestream' smoke is much more variable than the exposure of smokers themselves, it is not feasible to reasonably estimate the extra contribution of inhaled sidestream smoke to dioxin intake *via* the lungs.

4.2.4 Subsistence and recreational fishermen

In Australia, indigenous populations which may consume diets high in seafood are located in northern coastal areas away from key population centres. Thus the seafood that they consume is unlikely to present a significant dietary source of dioxin-like compounds.

In considering the intake of recreational fishermen based in larger population centres, the typical dioxin concentrations in seafood and typical rates of consumption have been included in the dietary intake assessment conducted by FSANZ (see Section 3.2.1). The kinds of exposures likely to occur in Australian waters are addressed within the estimates of variability of the levels of dioxin-like compounds found, and are not considered to be likely to result in a population subgroup which would be significantly more exposed than the general population. Except in a place like Homebush Bay where the fish are significantly more contaminated due to the contamination of sediments resulting from the manufacture of 2,4,5-T. The sediments of Homebush Bay and the land where the chemicals were manufactured is about to be remediated. Currently, there is a ban on all types of fishing in the area to try and ensure that people don't get exposed to these fish that have significant levels of dioxins.

4.2.5 Indigenous populations

The Aboriginal and Torres Strait Islander population in Australia tends not to have a high intake of animal fats from wild-caught game, including land animals (kangaroos, wallabies, lizards etc) and marine species (eg. dugongs, turtles and crocodiles). Overall, indigenous diets would not generally rely more heavily on animal fats than the rest of the Australian population (advice from the Population Health Division of the Australian Department of Health and Ageing). In Australia with its temperate, tropical and hot climatic zones, the contamination of native Australian animals which may be food sources for the aboriginal population is not a significant problem cf. levels of persistent organic pollutants (including dioxins) found in the extensive fat stores of arctic mammals e.g. seals and polar bears. This arctic contamination arises from the trans-boundary migration of POPs in the northern hemisphere, with their volatilisation from tropical and temperate climate zones and subsequent precipitation in the polar zone of the Arctic Circle. An ecological risk assessment of dioxins in Australia (Gatehouse,

2004) also noted that only low levels of dioxins were found in Australian fauna, this being particularly so in low-trophic-level herbivores and in marine mammals living in the open ocean environments of this continent.

5. Recommendations

Although hundreds of epidemiology studies have looked at the human health effects of dioxin exposures, neither the full extent of dioxin contamination nor the magnitude of the associated human health risks are clearly understood (eg. Institute of Medicine, 2004). Because of this, and in the light of increasing scientific knowledge about the biological actions and effects of dioxin-like compounds, it would be prudent to continue efforts to reduce any potential risks to human health. Thus, a cautious and conservative approach should be adopted with respect to dioxin-like compounds.

5.1 Some Specific Risk Management Recommendations

The following are some suggested specific measures to help reduce population body-burdens of dioxins.

- Programs which have been introduced to reduce the release of dioxin-like compounds to the environment need to be on going.

- Ways to block the cycling of dioxins through the food supply need to be identified. Reducing the level of dioxins in feed given to livestock, poultry and aquaculture fish will help to reduce the levels of dioxins in the food supply. This may be achieved by reducing the amount of animal fat used as a growth enhancer in stockfeed, and sourcing fish-based aquaculture feed (eg. pilchards, sardines) from non-polluted environments.

- Since foods high in animal fats are a source of exposure to these chemicals, current efforts to promote lower saturated fat intake in the population should continue[28].

- The utility and feasibility of setting Maximum Limits (MLs), action levels and target values for dioxin-like compounds in those food groups which contribute most to the human body burden of dioxins could be considered by the health, food and agriculture portfolios. Exceeding action thresholds, if set, would instigate efforts to identify sources of contamination, whilst target values would be set lower than current average background levels.

- Current programs to discourage cigarette smoking should be maintained. In particular, any measures which reduce dioxin intake in young women are likely to help reduce their body burden of dioxins and ultimately, the amount of dioxins

[28] Note that the relative specific heath risks of exposure to dioxins are low compared to those arising from a high intake of saturated fats

which may be transferred to their offspring, both prenatally (*via* trans-placental transfer) and postnatally *via* breast milk[29].

- The population burden of dioxin-like compounds should be monitored periodically, to see whether risk reduction strategies are effective.

Note that these recommendations are preliminary risk management recommendations made by the Office of Chemical Safety and they will be further developed following discussions with other government agencies and consideration of public input.

[29] As for dietary intake of saturated fats, the specific health risks associated with dioxin exposure are low compared to the known adverse effects of smoking. This could be an area for further investigation eg. to ascertain whether smokers have higher body burdens of dioxins cf. matched controls.

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Appendices

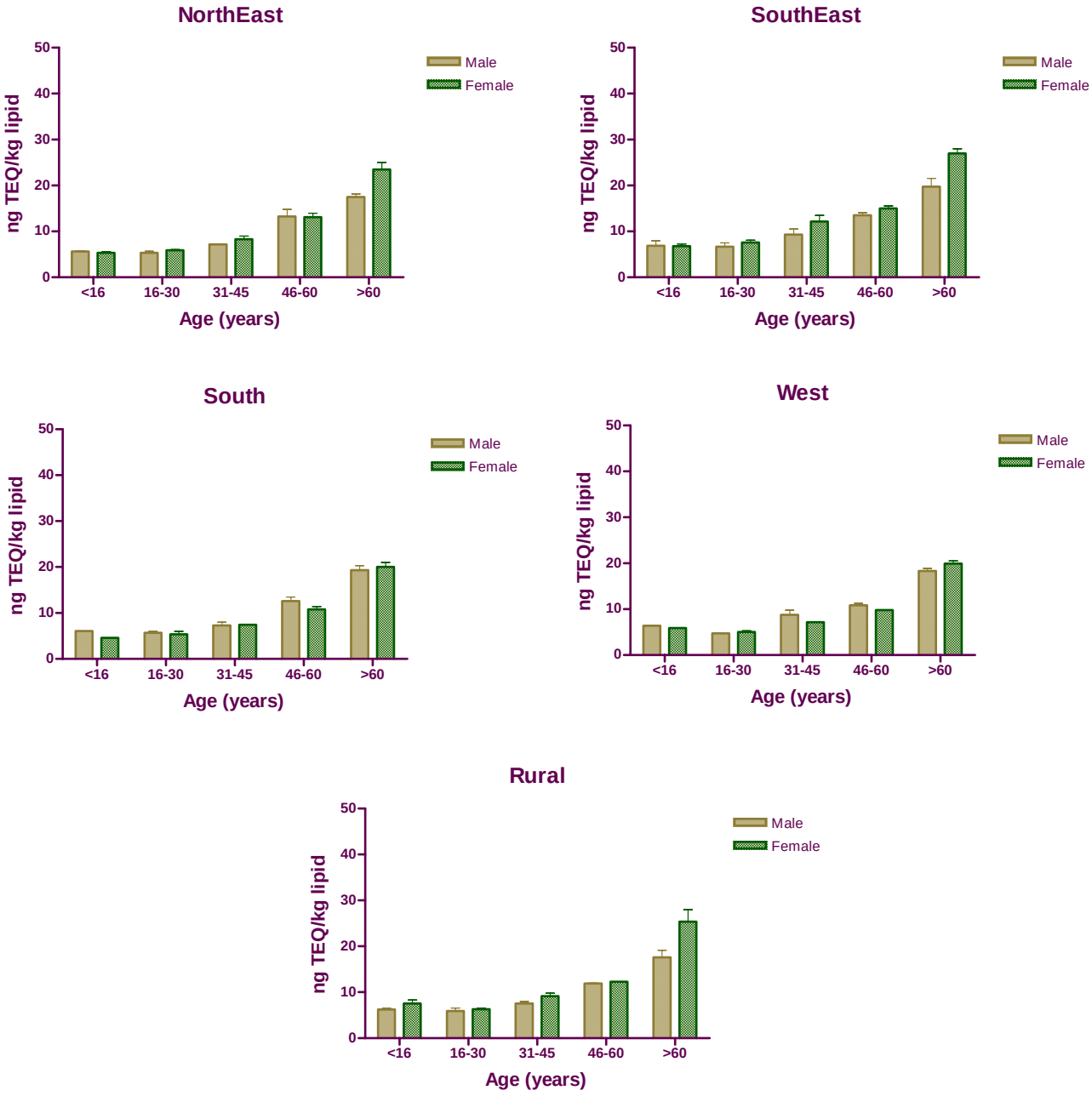
Appendix 1 Acronyms and Abbreviations

ALDE	Average Lifetime Daily Exposure
ATSDR	Agency for Toxic Substances and Disease Registry
BMI	Body Mass Index
DAFF	Australian Department of Agriculture, Fisheries & Forestry (formerly Agriculture, Fisheries & Forestry Australia, or AFFA)
bw	bodyweight
CAC	Codex Alimentarius Commission
CI	Confidence Interval
COT	UK Department of Health's Committee on the Toxicity of Chemicals in Food, Consumer Products, and the Environment
DEH	Australian Government Department of the Environment and Heritage (formerly 'Environment Australia', or EA)
DoHA	Australian Government Department of Health and Ageing
DRRS	The Dioxin Reassessment Review Subcommittee of the Executive Committee of US EPA's Science Advisory Board
EC	European Commission
EC-SCF	EC-Scientific Committee on Food
EHDI	estimated human daily intake
EHMI	estimated human monthly intake
FAO	Food and Agriculture Organization of the United Nations
FSANZ	Food Standards Australia New Zealand
GD	gestational day
IARC	International Agency for Research on Cancer
IC3	indole-3-carbinol
IgG	immunoglobulin G
ILO	International Labour Organization
IPCS	International Programme on Chemical Safety
I-TEQ	international toxic equivalence
JECFA	Joint Expert Committee on Food Additives
LO(A)EL	lowest observable (adverse) effect level
LOD	Limit of Detection
LOQ	Limit of Quantification (or Quantitation)
μg	microgram; 10^{-6} grams
MRL	minimal risk levels; also maximum residue limit
mRNA	messenger ribonucleic acid
ng	nanogram; 10^{-9} grams
NHMRC	National Health & Medical Research Council

NICNAS	National Industrial Chemicals Notification and Assessment Scheme
NIOSH	US National Institute for Occupational Safety and Health
NO(A)EL	no observable (adverse) effect level
OCS	Office of Chemical Safety, DoHA
OR	odds ratio
PAHs	polyaromatic hydrocarbons
PBDDs	polybrominated dibenzo-*p*-dioxins
PBDFs	polybrominated dibenzofurans
PCBs	polychlorinated biphenyls
PCDDs	polychlorinated dibenzo-*p*-dioxins
PCDFs	polychlorinated dibenzofurans
pg	picogram; 10^{-12} grams
ppt	parts per trillion (one in a million million, or 10^{-12})
PTMI	provisional tolerable monthly intake
RfD	reference dose
SAB	US EPA's Science Advisory Board
RR	relative risk
SMR	standardised mortality ratio
TCDD	2,3,7,8-tetrachloro-dibenzo-p-dioxin
TDI	tolerable daily intake
TEF	toxic equivalency factors
TEQ	toxic equivalence
TGA	Therapeutic Goods Administration
TMI	tolerable monthly intake
TWI	tolerable weekly intake
UNEP	United Nations Environment Programme
US EPA	United States Environmental Protection Agency
WHO	World Health Organization
WHO-ECEH	European Centre for Environmental Health

Appendix 2 Mean total WHO-TEQ (PCDD/Fs plus PCBs) in the serum of a representative group of the Australian population by age group, sex and region.

Data shown represent average upper bound WHO-TEQ values for pooled samples across 5 regions obtained for males and females from the 5 age groups.



Appendix 3 PCB loadings[30] for PCB #126 and PCB #169 for a representative sample of the Australian population.

		PCB Loading				
		<16 years	16-30 years	31-45 years	46-60 years	>60 years
South, Females	3,3',4,4',5-PeCB (126)	64.29%	56.25%	42.97%	42.19%	40.16%
	3,3',4,4',5,5'-HxCB (169)	2.57%	2.66%	3.78%	4.06%	3.77%
South, Males	3,3',4,4',5-PeCB (126)	73.33%	57.89%	41.46%	30.77%	34.92%
	3,3',4,4',5,5'-HxCB (169)	3.33%	3.79%	4.93%	4.74%	4.60%
RURAL, Females	3,3',4,4',5-PeCB (126)	64.86%	75.00%	50.00%	39.08%	41.62%
	3,3',4,4',5,5'-HxCB (169)	1.43%	1.54%	2.84%	3.45%	2.79%
RURAL, Males	3,3',4,4',5-PeCB (126)	56.10%	56.10%	44.68%	37.08%	39.04%
	3,3',4,4',5,5'-HxCB (169)	2.32%	2.88%	4.00%	3.71%	3.22%
North East, Females	3,3',4,4',5-PeCB (126)	67.50%	61.54%	44.00%	26.41%	36.65%
	3,3',4,4',5,5'-HxCB (169)	2.10%	2.33%	3.14%	3.72%	2.46%
North East, Males	3,3',4,4',5-PeCB (126)	64.71%	55.56%	38.60%	28.71%	36.36%
	3,3',4,4',5,5'-HxCB (169)	2.88%	3.42%	4.40%	3.66%	3.36%
West, female	3,3',4,4',5-PeCB (126)	75.00%	52.86%	44.55%	35.48%	45.74%
	3,3',4,4',5,5'-HxCB (169)	2.56%	3.50%	4.32%	5.00%	3.80%
West, male	3,3',4,4',5-PeCB (126)	52.63%	57.58%	39.80%	35.80%	42.34%
	3,3',4,4',5,5'-HxCB (169)	3.84%	4.30%	5.69%	5.31%	4.53%
South East, females	3,3',4,4',5-PeCB (126)	77.33%	74.70%	57.03%	55.63%	50.91%
	3,3',4,4',5,5'-HxCB (169)	1.35%	1.69%	1.80%	2.25%	1.95%
South East, males	3,3',4,4',5-PeCB (126)	60.00%	55.77%	51.90%	42.02%	40.91%
	3,3',4,4',5,5'-HxCB (169)	2.44%	3.54%	3.67%	3.70%	3.18%

[30] PCB loadings is defined as the serum concentration (WHO-TEQ pg/g lipid) divided by the total PCB WHO-TEQ.

Appendix 4 Comparisons of serum levels with international data

A comparison of Australian levels of PCDD/Fs (ng/kg lipid) with other countries

Country	Sampling year	No. of samples	Total PCDD/F	Total TEQ PCDD/F	Reference
Australia	2002/3	9090	291.1	6.68	Current study
U.S.	unknown	16	778.8^	19.1	Tepper (1997)
U.S.	1995/1996	5	491.0	12.1**	Schecter et al (1998)
	1995/1996	5	324.5	10**	Schecter et al (1998)
Finland	1993	18	893.7	50.4	Kontsas et al (1998)
Spain	1995	97	640.3	13.4	Gonzalez et al (2000)
	1997	91	na	16.7	Gonzalez et al (2000)
Spain	1993	11	582.0	15.7	Jimenez et al (1996)
Spain	unknown	20	na	27.0	Schuhmacher et al (1999)
Belgium	1999	47	na	48.6 *	Covaci et al (2001)
Norway	1992	10	631.1	21.4 #	Johansen et al (1996)
Germany	1989	228	942.2	43.7	Wittsiepe et al (2000)
	1992	157	703.2	38.1	Wittsiepe et al (2000)
	1993	17	534.5	29.1	Wittsiepe et al (2000)
	1994	74	376.7	29.1	Wittsiepe et al (2000)
	1995	69	431.6	24.1	Wittsiepe et al (2000)
	1997/1998	9	452.0	20.7	Wittsiepe et al (2000)
	1989-1998	744	671.7	35.6	Wittsiepe et al (2000)
Germany	unknown	16	na	18.5	Menzel et al (1998)
Germany	1994	134	508.8	19.1	Paepke et al (1996)
Germany	unknown	15	573.1	18.4	Wuthe et al (1996)
	unknown	45	326.7	7.3	Wuthe et al (1996)
	unknown	79	318.1	8.2	Wuthe et al (1996)
	unknown	39	303.4	10.0	Wuthe et al (1996)
	unknown	44	260.6	9.0	Wuthe et al (1996)
	unknown	46	289.0	9.3	Wuthe et al (1996)
	unknown	33	333.8	10.1	Wuthe et al (1996)
Japan	unknown	20	400.6	20.3**	Kumagai et al (2002)
Japan	1998	na	na	11*	Ueda et al (1999)
China	unknown	50	148.0	4.8	Schechter et al (1996)
	unknown	51	178.0	6.4	Schechter et al (1996)
New Zealand	1996/1997	1834	459.0	12.7*	Buckland et al (2001)
New Zealand	1992/1993	28	866.6	11.6 **	Hannah et al (1994)

Concentrations expressed in pg/g lipid and TEQ expressed using I-TEF unless otherwise specified
na = Not assessed
# = µg/L
* = ng/g lipid
*WHO-TEF
** TEF unknown
^ pg/g median

APPENDIX IV Continued

A comparison of Australian levels of PCBs (ng/kg lipid) with other countries

Country	Sampling year	No. of samples	PCB #126	PCB #169	TEQ non-ortho PCBs	TEQ total PCBs	Reference
Australia	2002/3	9090	14.3	13.1	1.6	4.0	Current study
U.S.	unknown	16	18	27	na	na	Kang et al (1997)
U.S.	1991/1993	7	na	na	na	na	Greizerstein et al (1999)
U.S.	1995/1996	5	21.7	9	2.26	na	Schecter et al (1998)
		5	16.3	6.7	1.7	na	Schecter et al (1998)
U.S.	1995	150	10.8	15.7	na	na	Shadel et al (2001)
Finland	1993	18	69.4	82.8	na	11.1*	Kontsas et al (1998)
Spain	1993	11	55.21	30.26	7.03*	na	Jimenez et al (1996)
Spain	1995	97	na	na	na	na	Gonzalez et al (2000)
	1997	91	na	na	na	na	Gonzalez et al (2000)
Belgium	1996/1998	96	na	na	na	na	Pauwels et al (2000)
Belgium	1999	47	na	na	na	25.8	Covaci et al (2001)
Norway	1992	10	93.4	70.1	na	45	Johansen et al (1996)
Germany	1994	104	80.3	101.8	na	na	Paepke et al (1996)
Germany	unknown	15	67.3*	116.2*	na	na	Wuthe et al (1996)
	unknown	45	37.6	24.6	na	na	Wuthe et al (1996)
	unknown	79	41.9	29.4	na	na	Wuthe et al (1996)
	unknown	39	52.6	37.4	na	na	Wuthe et al (1996)
	unknown	44	44.8	30.3	na	na	Wuthe et al (1996)
	unknown	46	49.4	36.7	na	na	Wuthe et al (1996)
	unknown	33	45.2	34	na	na	Wuthe et al (1996)
Japan	1993/1994	50	46	23	na	21	Iida et al (1999)
Japan	1998	253	na	na	7.3	na	Ueda et al (1999)
New Zealand	1996/1997	1834	30	20	na	6.86	Buckland et al (2001)

Concentrations expressed in ng/kg lipid unless otherwise specified (Note: ng/kg lipid is equivalent to pg/g lipid.)

TEQ expressed using WHO-TEF unless otherwise specified
na = Not assessed
# = µg/L
* = ng/g lipid
*I-TEQ

Appendix 5 The differences in geographical stratification and population (000s) between the two different dietary surveys NNS (1995) and NHS (2001).

National Health Survey (NHS, 2001)

Geographical stratification		Age (years) & population (000s)			
STUDY	SURVEY	16-30	31-45	45-60	>60
NORTHEAST URBAN	MAJOR URBAN QLD	198-201	198-201	147-157	119-132
Southeast Urban	Major urban NSW/ACT	503-507	500-501	395-419	282-338
South Urban	Major urban VIC/TAS/SA	440-444	467-479	370-371	305-370
West Urban	Major Urban WA	119-121	125-129	109-129	109-119
Rural	Rural balance all states and territories	508-565	621-692	476-580	491-508

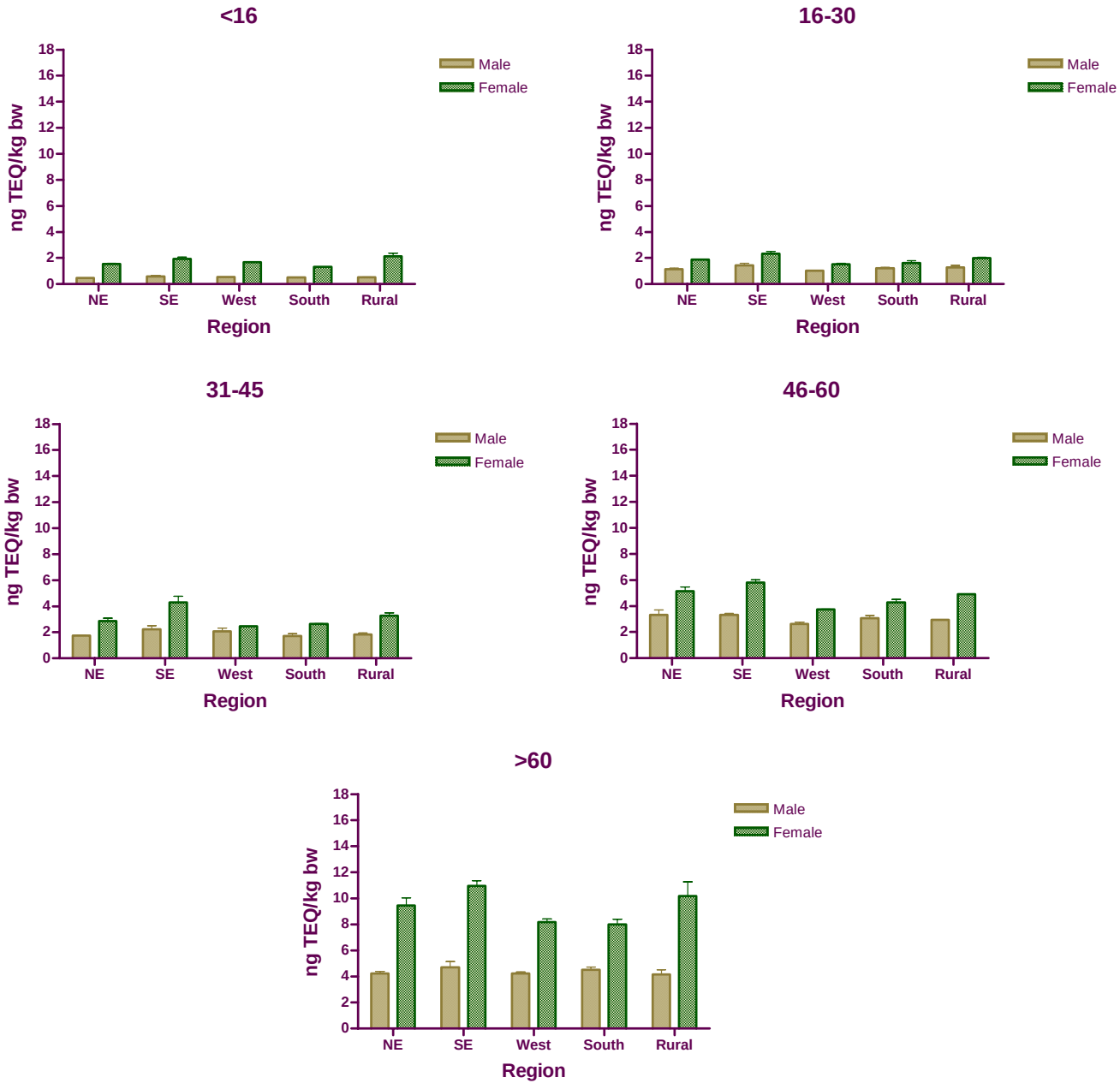
Major urban is classified as urban areas with a population > 100000

National Nutrition Survey (NNS, 1995)

Geographical stratification		Age (years) & population (000s)
STUDY	SURVEY	<16
NORTHEAST URBAN	METRO QLD	47-51
Southeast Urban	Metro NSW/ACT	110-117
South Urban	Metro VIC/TAS/SA	114-140
West Urban	Metro WA	39-47
Rural	Rural and NT	172-177

Appendix 6 Mean total PCDD/Fs and PCBs body burden of a representative group of the Australian population by age, sex and region.

Data shown represent average body burden values for pooled samples across 5 regions obtained for males and females from the 5 age groups.



Appendix 7 Upper bound blood serum concentrations, body burden and ALDE for PCDD/Fs, PCBs and total dioxins (PCCDD/Fs plus PCBs) for a representative sample of the Australian population by age group, sex and region.

Location / Sex	Dioxin	Age (years)	Plasma concentration (upper bound) (ng TEQ/kg lipid)				Fat Content	PCDD/F/PCB body burden (ng TEQ/kg bw)				PCDD/F & PCB ALDE
			POOL 1	POOL 2	MEAN	SD	(%)	POOL 1	POOL 2	MEAN	SD	(pg TEQ/kg bw/d)
NE Urban Male	PCDD/F	<16	4.00	3.90	3.95	0.07	8.24	0.33	0.32	0.33	0.01	0.09
	PCB		1.80	1.60	1.70	0.14		0.15	0.13	0.14	0.01	0.04
	Total		5.80	5.50	5.65	0.21		0.48	0.45	0.47	0.02	0.13
	PCDD/F	16-30	3.60	3.50	3.55	0.07	21.1	0.76	0.74	0.75	0.01	0.21
	PCB		2.10	1.50	1.80	0.42		0.44	0.32	0.38	0.09	0.11
	Total		5.70	5.00	5.35	0.49		1.20	1.06	1.13	0.10	0.32
	PCDD/F	31-45	4.50	4.90	4.70	0.28	24.37	1.10	1.19	1.15	0.07	0.32
	PCB		2.60	2.40	2.50	0.14		0.63	0.58	0.61	0.03	0.17
	Total		7.10	7.30	7.20	0.14		1.73	1.78	1.75	0.03	0.49
	PCDD/F	46-60	7.70	8.70	8.20	0.71	24.91	1.92	2.17	2.04	0.18	0.57
	PCB		4.00	6.10	5.05	1.48		1.00	1.52	1.26	0.37	0.35
	Total		11.70	14.80	13.25	2.19		2.91	3.69	3.30	0.55	0.93
	PCDD/F	>60	9.50	11.00	10.25	1.06	24.09	2.29	2.65	2.47	0.26	0.69
	PCB		7.10	7.20	7.15	0.07		1.71	1.73	1.72	0.02	0.48
	Total		16.80	18.20	17.50	0.99		4.05	4.38	4.22	0.24	1.19
NE Urban Female	PCDD/F	<16	3.60	3.20	3.40	0.28	28.44	1.02	0.91	0.97	0.08	0.27
	PCB		2.00	2.00	2.00	0.00		0.57	0.57	0.57	0.00	0.16
	Total		5.60	5.20	5.40	0.28		1.59	1.48	1.54	0.08	0.43
	PCDD/F	16-30	4.10	3.90	4.00	0.14	31.31	1.28	1.22	1.25	0.04	0.35
	PCB		1.70	2.20	1.95	0.35		0.53	0.69	0.61	0.11	0.17
	Total		5.80	6.10	5.95	0.21		1.82	1.91	1.86	0.07	0.52
	PCDD/F	31-45	6.70	5.00	5.85	1.20	34.19	2.29	1.71	2.00	0.41	0.56
	PCB		2.30	2.70	2.50	0.28		0.79	0.92	0.85	0.10	0.24
	Total		9.00	7.70	8.35	0.92		3.08	2.63	2.85	0.31	0.80
	PCDD/F	46-60	8.80	8.40	8.60	0.28	39.01	3.43	3.28	3.35	0.11	0.94
	PCB		3.90	3.90	3.90	0.00		1.52	1.52	1.52	0.00	0.43
	Total		14.00	12.30	13.15	1.20		5.46	4.80	5.13	0.47	1.44

	PCDD/F		14.00	14.00	14.00	0.00		5.62	5.62	5.62	0.00	1.58
	PCB	>60	11.00	8.10	9.55	2.05	40.17	4.42	3.25	3.84	0.82	1.08
	Total		25.00	22.00	23.50	2.12		10.04	8.84	9.44	0.85	2.66

APPENDIX VII Continued

Location Sex	Dioxin	Age (years)	Plasma concentration (upper bound) (ng TEQ/kg lipid)				Fat Content	PCDD/F/PCB Body burden (ng TEQ/Kg bw)				PCDD/F & PCB ALDE
			POOL 1	POOL 2	MEAN	SD	(%)	POOL 1	POOL 2	MEAN	SD	(pg TEQ/kg bw/d)
SE Urban	PCDD/F	<16	5.30	3.50	4.40	1.27	8.42	0.45	0.29	0.37	0.11	0.10
Male	PCB		2.70	2.30	2.50	0.28		0.23	0.19	0.21	0.02	0.06
	Total		8.00	5.80	6.90	1.56		0.67	0.49	0.58	0.13	0.16
	PCDD/F	16-30	3.60	4.60	4.10	0.71	21.36	0.77	0.98	0.88	0.15	0.25
	PCB		2.30	2.90	2.60	0.42		0.49	0.62	0.56	0.09	0.16
	Total		5.90	7.50	6.70	1.13		1.26	1.60	1.43	0.24	0.40
	PCDD/F	31-45	5.10	5.70	5.40	0.42	23.78	1.21	1.36	1.28	0.10	0.36
	PCB		3.10	4.80	3.95	1.20		0.74	1.14	0.94	0.29	0.26
	Total		8.20	10.50	9.35	1.63		1.95	2.50	2.22	0.39	0.63
	PCDD/F	46-60	7.30	7.90	7.60	0.42	24.39	1.78	1.93	1.85	0.10	0.52
	PCB		5.70	6.20	5.95	0.35		1.39	1.51	1.45	0.09	0.41
	Total		13.00	14.10	13.55	0.78		3.17	3.44	3.30	0.19	0.93
	PCDD/F	>60	12.00	9.90	10.95	1.48	23.81	2.86	2.36	2.61	0.35	0.73
	PCB		9.60	8.00	8.80	1.13		2.29	1.90	2.10	0.27	0.59
	Total		21.60	17.90	19.75	2.62		5.14	4.26	4.70	0.62	1.32
SE Urban	PCDD/F	<16	3.20	2.90	3.05	0.21	28.44	0.91	0.82	0.87	0.06	0.24
Female	PCB		3.10	4.40	3.75	0.92		0.88	1.25	1.07	0.26	0.30
	Total		6.30	7.30	6.80	0.71		1.79	2.08	1.93	0.20	0.54
	PCDD/F	16-30	3.50	3.40	3.45	0.07	30.71	1.07	1.04	1.06	0.02	0.30
	PCB		3.60	4.70	4.15	0.78		1.11	1.44	1.27	0.24	0.36
	Total		7.10	8.10	7.60	0.71		2.18	2.49	2.33	0.22	0.66
	PCDD/F	31-45	5.70	5.90	5.80	0.14	35.26	2.01	2.08	2.05	0.05	0.58
	PCB		7.80	5.00	6.40	1.98		2.75	1.76	2.26	0.70	0.63
	Total		13.50	10.90	12.20	1.84		4.76	3.84	4.30	0.65	1.21
	PCDD/F	46-60	8.40	7.50	7.95	0.64	38.55	3.24	2.89	3.06	0.25	0.86
	PCB		6.10	8.10	7.10	1.41		2.35	3.12	2.74	0.55	0.77
	Total		14.50	15.60	15.05	0.78		5.59	6.01	5.80	0.30	1.63
	PCDD/F	>60	15.00	17.00	16.00	1.41	40.53	6.08	6.89	6.48	0.57	1.82
	PCB		11.00	11.00	11.00	0.00		4.46	4.46	4.46	0.00	1.25
	Total		26.00	28.00	27.00	1.41		10.54	11.35	10.94	0.57	3.08

APPENDIX VII Continued

Location Sex	Dioxin	Age (years)	Plasma concentration (upper bound) (ng TEQ/kg lipid)				Fat Content	PCDD/F/PCB body burden (ng TEQ/kg bw)				PCDD/F & PCB ALDE
			POOL 1	POOL 2	MEAN	SD	(%)	POOL 1	POOL 2	MEAN	SD	(pg TEQ/kg bw/d)
S Urban	PCDD/F	<16	4.60		4.60	0.00	8.3	0.38	0.38	0.38	0.00	0.11
Male	PCB		1.50	N/A	1.50	0.00		0.12	0.12	0.12	0.00	0.04
	Total		6.10		6.10	0.00		0.51	0.51	0.51	0.00	0.14
	PCDD/F	16-30	3.90	3.70	3.80	0.14	21.27	0.83	0.79	0.81	0.03	0.23
	PCB		2.10	1.70	1.90	0.28		0.45	0.36	0.40	0.06	0.11
	Total		6.00	5.40	5.70	0.42		1.28	1.15	1.21	0.09	0.34
	PCDD/F	31-45	4.60	5.80	5.20	0.85	23.46	1.08	1.36	1.22	0.20	0.34
	PCB		1.90	2.20	2.05	0.21		0.45	0.52	0.48	0.05	0.14
	Total		6.50	8.00	7.25	1.06		1.52	1.88	1.70	0.25	0.48
	PCDD/F	46-60	9.30	8.20	8.75	0.78	24.31	2.26	1.99	2.13	0.19	0.60
	PCB		4.20	3.60	3.90	0.42		1.02	0.88	0.95	0.10	0.27
	Total		13.50	11.80	12.65	1.20		3.28	2.87	3.08	0.29	0.86
	PCDD/F	>60	12.00	14.00	13.00	1.41	23.32	2.80	3.26	3.03	0.33	0.85
	PCB		6.30	6.30	6.30	0.00		1.47	1.47	1.47	0.00	0.41
	Total		18.30	20.30	19.30	1.41		4.27	4.73	4.50	0.33	1.27
S Urban	PCDD/F	<16	3.10		3.10	0.00	28.37	0.88	0.88	0.88	0.00	0.25
Female	PCB		1.40	N/A	1.40	0.00		0.40	0.40	0.40	0.00	0.11
	Total		4.60		4.60	0.00		1.31	1.31	1.31	0.00	0.37
	PCDD/F	16-30	4.10	3.50	3.80	0.42	29.77	1.22	1.04	1.13	0.13	0.32
	PCB		1.90	1.30	1.60	0.42		0.57	0.39	0.48	0.13	0.13
	Total		6.00	4.80	5.40	0.85		1.79	1.43	1.61	0.25	0.45
	PCDD/F	31-45	5.60	5.60	5.60	0.00	35.51	1.99	1.99	1.99	0.00	0.56
	PCB		1.80	1.90	1.85	0.07		0.64	0.67	0.66	0.03	0.18
	Total		7.40	7.50	7.45	0.07		2.63	2.66	2.65	0.03	0.74
	PCDD/F	46-60	8.10	7.10	7.60	0.71	39.49	3.20	2.80	3.00	0.28	0.84
	PCB		3.30	3.10	3.20	0.14		1.30	1.22	1.26	0.06	0.36
	Total		11.40	10.20	10.80	0.85		4.50	4.03	4.26	0.34	1.20
	PCDD/F	>60	15.00	13.00	14.00	1.41	40.01	6.00	5.20	5.60	0.57	1.58
	PCB		5.90	6.30	6.10	0.28		2.36	2.52	2.44	0.11	0.69
	Total		21.00	19.00	20.00	1.41		8.40	7.60	8.00	0.57	2.25

APPENDIX VII Continued

Location Sex	Dioxin	Age (years)	Plasma concentration (upper bound) (ng TEQ/kg lipid)				Fat Content	PCDD/F/PCB body burden (ng TEQ/kg bw)				PCDD/F & PCB ALDE
			POOL 1	POOL 2	MEAN	SD	(%)	POOL 1	POOL 2	MEAN	SD	(pg TEQ/kg bw/d)
West Urban	PCDD/F	<16	4.50		4.50	0.00	8.3	0.37	0.37	0.37	0.00	0.11
Male	PCB		1.90	N/A	1.90	0.00		0.16	0.16	0.16	0.00	0.04
	Total		6.40		6.40	0.00		0.53	0.53	0.53	0.00	0.15
	PCDD/F	16-30	3.00	3.20	3.10	0.14	21.2	0.64	0.68	0.66	0.03	0.18
	PCB		1.70	1.60	1.65	0.07		0.36	0.34	0.35	0.01	0.10
	Total		4.70	4.80	4.75	0.07		1.00	1.02	1.01	0.01	0.28
	PCDD/F	31-45	5.30	7.10	6.20	1.27	23.72	1.26	1.68	1.47	0.30	0.41
	PCB		2.40	2.70	2.55	0.21		0.57	0.64	0.60	0.05	0.17
	Total		7.70	9.80	8.75	1.48		1.83	2.32	2.08	0.35	0.58
	PCDD/F	46-60	7.20	6.40	6.80	0.57	24.36	1.75	1.56	1.66	0.14	0.47
	PCB		4.10	4.00	4.05	0.07		1.00	0.97	0.99	0.02	0.28
	Total		11.30	10.40	10.85	0.64		2.75	2.53	2.64	0.16	0.74
	PCDD/F	>60	11.00	12.00	11.50	0.71	23.06	2.54	2.77	2.65	0.16	0.75
	PCB		6.80	6.90	6.85	0.07		1.57	1.59	1.58	0.02	0.44
	Total		17.80	18.90	18.35	0.78		4.10	4.36	4.23	0.18	1.19
West Urban	PCDD/F	<16	4.30		4.30	0.00	28.41	1.22	1.22	1.22	0.00	0.34
Female	PCB		1.60	N/A	1.60	0.00		0.45	0.45	0.45	0.00	0.13
	Total		5.90		5.90	0.00		1.68	1.68	1.68	0.00	0.47
	PCDD/F	16-30	3.40	3.90	3.65	0.35	30.28	1.03	1.18	1.11	0.11	0.31
	PCB		1.40	1.40	1.40	0.00		0.42	0.42	0.42	0.00	0.12
	Total		4.80	5.30	5.05	0.35		1.45	1.60	1.53	0.11	0.43
	PCDD/F	31-45	4.90	5.10	5.00	0.14	34.15	1.67	1.74	1.71	0.05	0.48
	PCB		2.30	2.10	2.20	0.14		0.79	0.72	0.75	0.05	0.21
	Total		7.20	7.20	7.20	0.00		2.46	2.46	2.46	0.00	0.69
	PCDD/F	46-60	6.70	6.70	6.70	0.00	37.94	2.54	2.54	2.54	0.00	0.72
	PCB		3.00	3.20	3.10	0.14		1.14	1.21	1.18	0.05	0.33
	Total		9.70	9.90	9.80	0.14		3.68	3.76	3.72	0.05	1.05
	PCDD/F	>60	13.00	14.00	13.50	0.71	41.04	5.34	5.75	5.54	0.29	1.56
	PCB		6.40	6.50	6.45	0.07		2.63	2.67	2.65	0.03	0.74
	Total		19.40	20.50	19.95	0.78		7.96	8.41	8.19	0.32	2.30

APPENDIX VII Continued

Location Sex	Dioxin	Age (years)	Plasma concentration (upper bound) (ng TEQ/kg lipid)				Fat Content	PCDD/F/PCB body burden (ng TEQ/kg bw)				PCDD/F & PCB ALDE
			POOL 1	POOL 2	MEAN	SD	(%)	POOL 1	POOL 2	MEAN	SD	(pg TEQ/kg bw/d)
Rural	PCDD/F	<16	4.30	4.10	4.20	0.14	8.34	0.36	0.34	0.35	0.01	0.10
Male	PCB		2.20	1.90	2.05	0.21		0.18	0.16	0.17	0.02	0.05
	Total		6.50	6.00	6.25	0.35		0.54	0.50	0.52	0.03	0.15
	PCDD/F	16-30	3.40	4.40	3.90	0.71	21.63	0.74	0.95	0.84	0.15	0.24
	PCB		1.90	2.20	2.05	0.21		0.41	0.48	0.44	0.05	0.12
	Total		5.30	6.60	5.95	0.92		1.15	1.43	1.29	0.20	0.36
	PCDD/F	31-45	4.80	5.60	5.20	0.57	24.38	1.17	1.37	1.27	0.14	0.36
	PCB		2.30	2.40	2.35	0.07		0.56	0.59	0.57	0.02	0.16
	Total		7.10	8.00	7.55	0.64		1.73	1.95	1.84	0.16	0.52
	PCDD/F	46-60	7.40	7.50	7.45	0.07	24.61	1.82	1.85	1.83	0.02	0.52
	PCB		4.40	4.50	4.45	0.07		1.08	1.11	1.10	0.02	0.31
	Total		11.80	12.00	11.90	0.14		2.90	2.95	2.93	0.03	0.82
	PCDD/F	>60	8.70	12.00	10.35	2.33	23.48	2.04	2.82	2.43	0.55	0.68
	PCB		7.40	7.20	7.30	0.14		1.74	1.69	1.71	0.03	0.48
	Total		16.10	19.20	17.65	2.19		3.78	4.51	4.14	0.51	1.17
Rural	PCDD/F	<16	3.60	4.10	3.85	0.35	28.41	1.02	1.16	1.09	0.10	0.31
Female	PCB		4.70	2.70	3.70	1.41		1.34	0.77	1.05	0.40	0.30
	Total		8.30	6.80	7.55	1.06		2.36	1.93	2.14	0.30	0.60
	PCDD/F	16-30	3.60	3.40	3.50	0.14	31.58	1.14	1.07	1.11	0.04	0.31
	PCB		2.50	3.10	2.80	0.42		0.79	0.98	0.88	0.13	0.25
	Total		6.10	6.50	6.30	0.28		1.93	2.05	1.99	0.09	0.56
	PCDD/F	31-45	5.60	6.60	6.10	0.71	35.73	2.00	2.36	2.18	0.25	0.61
	PCB		3.00	3.20	3.10	0.14		1.07	1.14	1.11	0.05	0.31
	Total		8.60	9.80	9.20	0.85		3.07	3.50	3.29	0.30	0.92
	PCDD/F	46-60	8.10	7.80	7.95	0.21	39.88	3.23	3.11	3.17	0.08	0.89
	PCB		4.20	4.50	4.35	0.21		1.67	1.79	1.73	0.08	0.49
	Total		12.30	12.30	12.30	0.00		4.91	4.91	4.91	0.00	1.38
	PCDD/F	>60	15.00	16.00	15.50	0.71	40.18	6.03	6.43	6.23	0.28	1.75
	PCB		7.70	12.00	9.85	3.04		3.09	4.82	3.96	1.22	1.11
	Total		22.70	28.00	25.35	3.75		9.12	11.25	10.19	1.51	2.86

Appendix 8 Lower bound blood serum concentrations, body burden and ALDE for PCDD/Fs, PCBs and total dioxins (PCCDD/Fs plus PCBs) for the Australian population.

Location Sex	Dioxin	Age (years)	Plasma concentration (lower bound) (ng TEQ/kg lipid)				Fat Content	PCDD/F/PCB body burden (ng TEQ/kg bw)				PCDD/F & PCB ALDE
			POOL 1	POOL 2	MEAN	SD	(%)	POOL 1	POOL 2	MEAN	SD	(pg TEQ/kg bw/d)
NE Urban Male	PCDD/F	<16	2.70	2.50	2.60	0.14	8.24	0.35	0.32	0.34	0.02	0.09
	PCB		0.65	0.65	0.65	0.00		0.08	0.08	0.08	0.00	0.02
	Total		3.45	3.15	3.30	0.21		0.45	0.41	0.43	0.03	0.12
	PCDD/F	16-30	1.30	2.30	1.80	0.71	21.1	0.27	0.49	0.38	0.15	0.11
	PCB		0.90	0.70	0.80	0.14		0.19	0.15	0.17	0.03	0.05
	Total		2.20	3.00	2.60	0.57		0.46	0.63	0.55	0.12	0.15
	PCDD/F	31-45	3.10	3.50	3.30	0.28	24.37	0.76	0.85	0.80	0.07	0.23
	PCB		1.50	2.40	1.95	0.64		0.37	0.58	0.48	0.16	0.13
	Total		4.60	5.90	5.25	0.92		1.12	1.44	1.28	0.22	0.36
	PCDD/F	46-60	6.70	7.60	7.15	0.64	24.91	1.67	1.89	1.78	0.16	0.50
	PCB		4.00	6.00	5.00	1.41		1.00	1.49	1.25	0.35	0.35
	Total		10.70	13.60	12.15	2.05		2.67	3.39	3.03	0.51	0.85
	PCDD/F	>60	8.70	9.30	9.00	0.42	24.09	2.10	2.24	2.17	0.10	0.61
	PCB		7.10	7.20	7.15	0.07		1.71	1.73	1.72	0.02	0.48
	Total		15.80	15.50	15.65	0.21		3.81	3.73	3.77	0.05	1.06
NE Urban Female	PCDD/F	<16	2.40	0.99	1.70	1.00	28.44	0.68	0.28	0.48	0.28	0.14
	PCB		0.74	0.57	0.66	0.12		0.21	0.16	0.19	0.03	0.05
	Total		3.24	1.60	2.42	1.16		0.92	0.46	0.69	0.33	0.19
	PCDD/F	16-30	3.10	2.90	3.00	0.14	31.31	0.97	0.91	0.94	0.04	0.26
	PCB		0.61	0.80	0.71	0.13		0.19	0.25	0.22	0.04	0.06
	Total		3.70	3.70	3.70	0.00		1.16	1.16	1.16	0.00	0.33
	PCDD/F	31-45	4.80	3.70	4.25	0.78	34.19	1.64	1.27	1.45	0.27	0.41
	PCB		1.40	1.40	1.40	0.00		0.48	0.48	0.48	0.00	0.13
	Total		6.20	5.10	5.65	0.78		2.12	1.74	1.93	0.27	0.54
	PCDD/F	46-60	8.20	7.70	7.95	0.35	39.01	3.20	3.00	3.10	0.14	0.87
	PCB		3.90	2.70	3.30	0.85		1.52	1.05	1.29	0.33	0.36
	Total		12.10	10.40	11.25	1.20		4.72	4.06	4.39	0.47	1.23
	PCDD/F	>60	13.00	13.00	13.00	0.00	40.17	5.22	5.22	5.22	0.00	1.47
	PCB		11.00	8.10	9.55	2.05		4.42	3.25	3.84	0.82	1.08
	Total		24.00	21.10	22.55	2.05		9.64	8.48	9.06	0.82	2.55

APPENDIX VIII Continued

Location Sex	Dioxin	Age (years)	Plasma concentration (lower bound) (ng TEQ/kg lipid)				Fat Content	PCDD/F/PCB body burden (ng TEQ/kg bw)				PCDD/F & PCB ALDE
			POOL 1	POOL 2	MEAN	SD	(%)	POOL 1	POOL 2	MEAN	SD	(pg TEQ/kg bw/d)
SE Urban	PCDD/F	<16	3.00	0.96	1.98	1.44	8.42	0.25	0.08	0.17	0.12	0.05
Male	PCB		1.30	0.79	1.05	0.36		0.11	0.07	0.09	0.03	0.02
	Total		4.30	1.80	3.05	1.77		0.36	0.15	0.26	0.15	0.07
	PCDD/F	16-30	2.80	3.60	3.20	0.57	21.36	0.60	0.77	0.68	0.12	0.19
	PCB		0.89	2.90	1.90	1.42		0.19	0.62	0.40	0.30	0.11
	Total		3.70	6.50	5.10	1.98		0.79	1.39	1.09	0.42	0.31
	PCDD/F	31-45	4.80	4.70	4.75	0.07	23.78	1.14	1.12	1.13	0.02	0.32
	PCB		3.10	4.80	3.95	1.20		0.74	1.14	0.94	0.29	0.26
	Total		7.90	9.50	8.70	1.13		1.88	2.26	2.07	0.27	0.58
	PCDD/F	46-60	7.10	7.50	7.30	0.28	24.39	1.73	1.83	1.78	0.07	0.50
	PCB		5.70	6.20	5.95	0.35		1.39	1.51	1.45	0.09	0.41
	Total		12.80	13.70	13.25	0.64		3.12	3.34	3.23	0.16	0.91
	PCDD/F	>60	11.00	9.40	10.20	1.13	23.81	2.62	2.24	2.43	0.27	0.68
	PCB		9.60	8.00	8.80	1.13		2.29	1.90	2.10	0.27	0.59
	Total		20.60	17.40	19.00	2.26		4.90	4.14	4.52	0.54	1.27
SE Urban	PCDD/F	<16	2.10	2.00	2.05	0.07	28.44	0.60	0.57	0.58	0.02	0.16
Female	PCB		3.10	4.40	3.75	0.92		0.88	1.25	1.07	0.26	0.30
	Total		5.20	6.40	5.80	0.85		1.48	1.82	1.65	0.24	0.46
	PCDD/F	16-30	3.00	3.30	3.15	0.21	30.71	0.92	1.01	0.97	0.07	0.27
	PCB		3.60	4.70	4.15	0.78		1.11	1.44	1.27	0.24	0.36
	Total		6.60	8.00	7.30	0.99		2.03	2.46	2.24	0.30	0.63
	PCDD/F	31-45	5.60	5.50	5.55	0.07	35.26	1.97	1.94	1.96	0.02	0.55
	PCB		7.80	5.00	6.40	1.98		2.75	1.76	2.26	0.70	0.63
	Total		12.40	10.50	11.45	1.34		4.37	3.70	4.04	0.47	1.14
	PCDD/F	46-60	8.10	6.90	7.50	0.85	38.55	3.12	2.66	2.89	0.33	0.81
	PCB		6.10	8.10	7.10	1.41		2.35	3.12	2.74	0.55	0.77
	Total		14.20	15.00	14.60	0.57		5.47	5.78	5.63	0.22	1.58
	PCDD/F	>60	13.00	14.00	13.50	0.71	40.53	5.27	5.67	5.47	0.29	1.54
	PCB		10.00	5.00	7.50	3.54		4.05	2.03	3.04	1.43	0.86
	Total		23.00	19.00	21.00	2.83		9.32	7.70	8.51	1.15	2.39

APPENDIX VIII Continued

Location Sex	Dioxin	Age (years)	Plasma concentration (lower bound) (ng TEQ/kg lipid)				Fat Content	PCDD/F/PCB body burden (ng TEQ/kg bw)				PCDD/F & PCB ALDE
			POOL 1	POOL 2	MEAN	SD	(%)	POOL 1	POOL 2	MEAN	SD	(pg TEQ/kg bw/d)
S Urban	PCDD/F	<16	2.50		2.50	0.00	8.3	0.21	0.21	0.21	0.00	0.06
Male	PCB		0.48	N/A	0.48	0.00		0.04	0.04	0.04	0.00	0.01
	Total		3.00		3.00	0.00		0.25	0.25	0.25	0.00	0.07
	PCDD/F	16-30	2.90	2.60	2.75	0.21	21.27	0.62	0.55	0.58	0.05	0.16
	PCB		2.00	0.63	1.32	0.97		0.43	0.13	0.28	0.21	0.08
	Total		4.90	3.23	4.07	1.18		1.04	0.69	0.86	0.25	0.24
	PCDD/F	31-45	3.60	4.90	4.25	0.92	23.46	0.84	1.15	1.00	0.22	0.28
	PCB		1.20	1.30	1.25	0.07		0.28	0.30	0.29	0.02	0.08
	Total		4.80	6.10	5.45	0.92		1.13	1.43	1.28	0.22	0.36
	PCDD/F	46-60	8.60	7.40	8.00	0.85	24.31	2.09	1.80	1.94	0.21	0.55
	PCB		4.20	3.60	3.90	0.42		1.02	0.88	0.95	0.10	0.27
	Total		13.00	11.00	12.00	1.41		3.16	2.67	2.92	0.34	0.82
	PCDD/F	>60	11.00	11.00	11.00	0.00	23.32	2.57	2.57	2.57	0.00	0.72
	PCB		6.30	6.30	6.30	0.00		1.47	1.47	1.47	0.00	0.41
	Total		17.30	17.30	17.30	0.00		4.03	4.03	4.03	0.00	1.13
S Urban	PCDD/F	<16	2.30		2.30	0.00	28.37	0.65	0.65	0.65	0.00	0.18
Female	PCB		0.50	N/A	0.50	0.00		0.14	0.14	0.14	0.00	0.04
	Total		2.80		2.80	0.00		0.79	0.79	0.79	0.00	0.22
	PCDD/F	16-30	3.40	2.50	2.95	0.64	29.77	1.01	0.74	0.88	0.19	0.25
	PCB		0.60	0.45	0.53	0.11		0.18	0.13	0.16	0.03	0.04
	Total		4.00	3.00	3.50	0.71		1.19	0.89	1.04	0.21	0.29
	PCDD/F	31-45	4.30	4.40	4.35	0.07	35.51	1.53	1.56	1.54	0.03	0.43
	PCB		0.95	1.90	1.43	0.67		0.34	0.67	0.51	0.24	0.14
	Total		5.25	6.30	5.78	0.74		1.86	2.24	2.05	0.26	0.58
	PCDD/F	46-60	7.50	5.80	6.65	1.20	39.49	2.96	2.29	2.63	0.47	0.74
	PCB		3.30	3.10	3.20	0.14		1.30	1.22	1.26	0.06	0.36
	Total		10.80	8.90	9.85	1.34		4.26	3.51	3.89	0.53	1.09
	PCDD/F	>60	14.00	12.00	13.00	1.41	40.01	5.60	4.80	5.20	0.57	1.46
	PCB		5.90	6.30	6.10	0.28		2.36	2.52	2.44	0.11	0.69
	Total		19.90	18.30	19.10	1.13		7.96	7.32	7.64	0.45	2.15

APPENDIX VIII Continued

Location Sex	Dioxin	Age (years)	Plasma concentration (lower bound) (ng TEQ/kg lipid)				Fat Content	PCDD/F/PCB body burden (ng TEQ/kg bw)				PCDD/F & PCB ALDE
			POOL 1	POOL 2	MEAN	SD	(%)	POOL 1	POOL 2	MEAN	SD	(pg TEQ/kg bw/d)
West Urban	PCDD/F	<16	1.20		1.20	0.00	8.3	0.10	0.10	0.10	0.00	0.03
Male	PCB		0.86	N/A	0.86	0.00		0.07	0.07	0.07	0.00	0.02
	Total		2.10		2.10	0.00		0.17	0.17	0.17	0.00	0.05
	PCDD/F	16-30	2.10	2.10	2.10	0.00	21.2	0.45	0.45	0.45	0.00	0.13
	PCB		0.74	0.64	0.69	0.07		0.16	0.14	0.15	0.01	0.04
	Total		2.84	2.74	2.79	0.07		0.60	0.58	0.59	0.01	0.17
	PCDD/F	31-45	4.10	6.40	5.25	1.63	23.72	0.97	1.52	1.25	0.39	0.35
	PCB		2.40	2.70	2.55	0.21		0.57	0.64	0.60	0.05	0.17
	Total		6.50	9.10	7.80	1.84		1.54	2.16	1.85	0.44	0.52
	PCDD/F	46-60	5.70	5.30	5.50	0.28	24.36	1.39	1.29	1.34	0.07	0.38
	PCB		4.10	4.00	4.05	0.07		1.00	0.97	0.99	0.02	0.28
	Total		9.80	9.30	9.55	0.35		2.39	2.27	2.33	0.09	0.65
	PCDD/F	>60	9.80	9.20	9.50	0.42	23.06	2.26	2.12	2.19	0.10	0.62
	PCB		6.80	6.90	6.85	0.07		1.57	1.59	1.58	0.02	0.44
	Total		16.60	16.10	16.35	0.35		3.83	3.71	3.77	0.08	1.06
West Urban	PCDD/F	<16	0.93		0.93	0.00	28.41	0.26	0.26	0.26	0.00	0.07
Female	PCB		0.43	N/A	0.43	0.00		0.12	0.12	0.12	0.00	0.03
	Total		1.36		1.36	0.00		0.39	0.39	0.39	0.00	0.11
	PCDD/F	16-30	2.40	2.60	2.50	0.14	30.28	0.73	0.79	0.76	0.04	0.21
	PCB		1.40	0.68	1.04	0.51		0.42	0.21	0.31	0.15	0.09
	Total		3.80	3.28	3.54	0.37		1.15	0.99	1.07	0.11	0.30
	PCDD/F	31-45	3.50	3.80	3.65	0.21	34.15	1.20	1.30	1.25	0.07	0.35
	PCB		2.30	2.10	2.20	0.14		0.79	0.72	0.75	0.05	0.21
	Total		5.80	5.90	5.85	0.07		1.98	2.01	2.00	0.02	0.56
	PCDD/F	46-60	5.10	6.00	5.55	0.64	37.94	1.93	2.28	2.11	0.24	0.59
	PCB		3.00	3.20	3.10	0.14		1.14	1.21	1.18	0.05	0.33
	Total		8.10	9.20	8.65	0.78		3.07	3.49	3.28	0.30	0.92
	PCDD/F	>60	12.00	13.00	12.50	0.71	41.04	4.92	5.34	5.13	0.29	1.44
	PCB		6.40	6.50	6.45	0.07		2.63	2.67	2.65	0.03	0.74
	Total		18.40	19.50	18.95	0.78		7.55	8.00	7.78	0.32	2.19

APPENDIX VIII Continued

Location Sex	Dioxin	Age (years)	Plasma concentration (lower bound) (ng TEQ/kg lipid)				Fat Content	PCDD/F/PCB body burden (ng TEQ/kg bw)				PCDD/F & PCB ALDE
			POOL 1	POOL 2	MEAN	SD	(%)	POOL 1	POOL 2	MEAN	SD	(pg TEQ/kg bw/d)
Rural	PCDD/F	<16	2.60	2.60	2.60	0.00	8.34	0.22	0.22	0.22	0.00	0.06
Male	PCB		1.00	0.66	0.83	0.24		0.08	0.06	0.07	0.02	0.02
	Total		3.60	3.30	3.45	0.21		0.30	0.28	0.29	0.02	0.08
	PCDD/F	16-30	2.30	3.00	2.65	0.49	21.63	0.50	0.65	0.57	0.11	0.16
	PCB		0.79	1.00	0.90	0.15		0.17	0.22	0.19	0.03	0.05
	Total		3.09	4.00	3.55	0.64		0.67	0.87	0.77	0.14	0.22
	PCDD/F	31-45	4.40	4.70	4.55	0.21	24.38	1.07	1.15	1.11	0.05	0.31
	PCB		2.30	2.40	2.35	0.07		0.56	0.59	0.57	0.02	0.16
	Total		6.70	7.10	6.90	0.28		1.63	1.73	1.68	0.07	0.47
	PCDD/F	46-60	7.10	6.90	7.00	0.14	24.61	1.75	1.70	1.72	0.03	0.48
	PCB		4.40	4.50	4.45	0.07		1.08	1.11	1.10	0.02	0.31
	Total		11.50	11.40	11.45	0.07		2.83	2.81	2.82	0.02	0.79
	PCDD/F	>60	8.20	11.00	9.60	1.98	23.48	1.93	2.58	2.25	0.46	0.63
	PCB		7.40	7.10	7.25	0.21		1.74	1.67	1.70	0.05	0.48
	Total		15.60	18.10	16.85	1.77		3.66	4.25	3.96	0.42	1.11
Rural	PCDD/F	<16	2.50	2.40	2.45	0.07	28.41	0.71	0.68	0.70	0.02	0.20
Female	PCB		4.70	0.95	2.83	2.65		1.34	0.27	0.80	0.75	0.23
	Total		7.20	3.35	5.28	2.72		2.05	0.95	1.50	0.77	0.42
	PCDD/F	16-30	2.60	1.10	1.85	1.06	31.58	0.82	0.35	0.58	0.33	0.16
	PCB		0.78	3.10	1.94	1.64		0.25	0.98	0.61	0.52	0.17
	Total		3.38	4.20	3.79	0.58		1.07	1.33	1.20	0.18	0.34
	PCDD/F	31-45	5.30	5.10	5.20	0.14	35.73	1.89	1.82	1.86	0.05	0.52
	PCB		1.40	1.60	1.50	0.14		0.50	0.57	0.54	0.05	0.15
	Total		6.70	6.70	6.70	0.00		2.39	2.39	2.39	0.00	0.67
	PCDD/F	46-60	7.80	7.50	7.65	0.21	39.88	3.11	2.99	3.05	0.08	0.86
	PCB		4.20	4.50	4.35	0.21		1.67	1.79	1.73	0.08	0.49
	Total		12.00	12.00	12.00	0.00		4.79	4.79	4.79	0.00	1.35
	PCDD/F	>60	14.00	15.00	14.50	0.71	40.18	5.63	6.03	5.83	0.28	1.64
	PCB		7.70	12.00	9.85	3.04		3.09	4.82	3.96	1.22	1.11
	Total		21.70	27.00	24.35	3.75		8.72	10.85	9.78	1.51	2.75

Appendix 9 Minimum, Maximum, Weighted Mean and Median Values for Breast Milk Samples - 1993 and 2001-2003 Studies

	1993 Breast Milk Sample Data				2003 Breast Milk Sample Data			
	Min	**Max**	**Wtd Mean**	**Median**	**Min**	**Max**	**Wtd Mean**	**Median**
WHO-TEF - PCDD/Fs								
Lower bound	8.4	11.8	10.3	10.6	3.7	9.7	5.7	5.5
Middle Bound	9.0	12.0	10.6	10.8	3.7	9.8	5.8	5.6
Upper Bound	9.6	12.2	10.9	11.0	3.7	9.9	5.9	5.7
WHO-TEF - PCBs								
Lower bound	3.7	7.4	5.1	4.2	1.8	5.4	3.1	2.6
Middle Bound	3.7	7.4	5.1	4.2	1.8	5.4	3.1	2.6
Upper Bound	3.7	7.4	5.1	4.2	1.8	5.4	3.1	2.6
WHO-TEF - Total								
Lower bound	14.3	15.9	15.4	15.9	6.0	15.1	8.8	8.9
Middle Bound	14.5	16.4	15.7	16.2	6.0	15.1	8.9	8.9
Upper Bound	14.6	17.0	16.0	16.4	6.0	15.1	9.0	8.9

Appendix 10 Mean PCDD/F, PCB and Total WHO-TEQs by Region - Industrial, Urban and Rural

	Mean Values (pg/g lipid)		
	Urban Regions (n=12)	**Industrial Regions (n=2)**	**Rural Regions (n=3)**
WHO-TEF - PCDD/F			
Lower bound	6.2	4.4	5.3
Middle Bound	6.2	4.6	5.4
Upper Bound	6.3	4.9	5.5
WHO-TEF PCB			
Lower bound	3.1	3.3	2.8
Middle Bound	3.1	3.4	2.8
Upper Bound	3.1	3.4	2.8
WHO-TEF Total			
Lower bound	9.3	7.7	8.1
Middle Bound	9.3	8.0	8.2
Upper Bound	9.4	8.2	8.2

Appendix 11 Foods analysed for dioxins

Food	Number of composite samples analysed	Number of Purchases included in each composite sample
Meat & Meat Products		
Bacon	10	3
Beef, minced	14	4
Hamburger	10	3
Lamb chops	11	3
Leg ham[1]	9	3
Sausages, meat, thick	11	3
Liver pate (chicken)	4	3
Dairy Products		
Butter[31]	10	3
Chocolate, milk[1]	1	3
Milk, whole[1]	13	4
Infant formula[1]	5	3
Margarine/Table spread	6	4
Fish		
Fish fillets[1]	10	3
Fish portions	9	3
Tuna, Canned[1]	5	3
Poultry & Eggs		
Eggs[1]	13	4
Chicken breasts[1]	11	3
Cereal Products		
Bread, white[1]	3	4
Other Foods		
Baked beans[1]	3	3
Orange juice[1]	3	4
Peanut butter[1]	4	3
Potatoes[1]	3	4
Total Samples (Total foods)	**165** (22)	

[1]Additional sample collection performed by AGAL.

Appendix 12 95th percentile estimated monthly dietary exposure to dioxins per kilogram of body weight.

Sex	Age group	PCDD/Fs (pg WHO-TEQ/kg bw/month)		PCBs (pg WHO-TEQ/kg bw/month)		Total Dioxins (pg WHO-TEQ/kg bw/month)	
		Lower Bound	Upper Bound	Lower Bound	Upper Bound	Lower Bound	Upper Bound
All	2+	2.9	23.7	13.2	16.9	16.1	40.6
Males	2+	3.2	25.0	14.5	18.4	17.7	43.3
Females	2+	2.7	22.4	12.1	16.0	14.8	38.4
Toddlers	2-4	4.0	43.6	8.0	22.6	12.1	66.2
Males	4-15	3.5	33.2	8.3	18.7	11.8	51.9
Females	4-15	3.2	29.0	8.5	17.4	11.7	46.4
Males	16-29	3.5	21.3	15.8	18.6	19.3	39.9
Females	16-29	2.2	17.7	10.4	13.3	12.6	31.0
Males	30-44	3.0	18.1	15.4	17.3	18.4	35.4
Females	30-44	2.2	16.1	9.3	11.9	11.5	28.0
Males	45-59	2.9	16.5	14.9	16.6	17.8	33.1
Females	45-59	2.8	14.8	15.6	17.4	18.4	32.2
Males	60+	3.0	14.9	16.7	18.8	19.7	33.6
Females	60+	2.3	14.8	12.5	14.0	14.9	28.8

TMI = 70 pg TEQ/kg bw/month
Total dioxins = sum of intakes of PCDD/Fs and PCBs. Total dioxins may not equal the sum of the separate intakes due to rounding.
Estimated dietary exposures are based on food consumption data from the 1995 NNS

Appendix 13 Percent contribution of food groups to PCDD/F mean dietary exposures for each population group

Food Name	9 months	2+ years			2-4 years	4-15 years		16-29 years		30-44 years		45-59 years		60+ years	
	All	All	Males	Females	All	Males	Females	Males	Females	Males	Females	Males	Females	Males	Females
Fish fillets, including crustacea and molluscs	6	39	40	38	18	26	24	35	35	45	39	44	46	47	44
Milk (full fat) including cheese, icecream and infant dessert	10	31	30	33	55	45	44	33	35	25	31	25	28	24	29
Bacon	1	7	8	6	2	5	6	9	7	8	7	7	7	8	6
White bread, including all cereal products	2	4	4	4	5	5	5	4	5	4	5	4	4	4	4
Peanut butter	0	4	5	4	8	5	7	4	5	5	4	5	3	3	3
Potatoes, including all vegetables	1	3	3	4	2	2	3	3	3	3	4	3	4	3	4
Butter	0	2	2	2	1	1	2	2	2	2	2	2	2	3	3
Beef, minced	0	2	2	2	1	1	1	2	2	2	2	2	1	2	1
Eggs	0	2	2	2	1	2	2	2	2	2	2	2	2	2	2
Milk chocolate	1	1	1	1	2	2	3	2	2	1	2	1	1	0	1
Chicken breasts	0	1	1	1	1	1	1	1	2	1	1	1	1	1	1
Sausages, meat, thick	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Margarine, table spread	0	1	1	1	0	1	1	1	1	0	0	0	0	1	1
Infant formula	78	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Percentage food contributions to PCDD/F and PCB exposure based on ‘lower bound’ values.

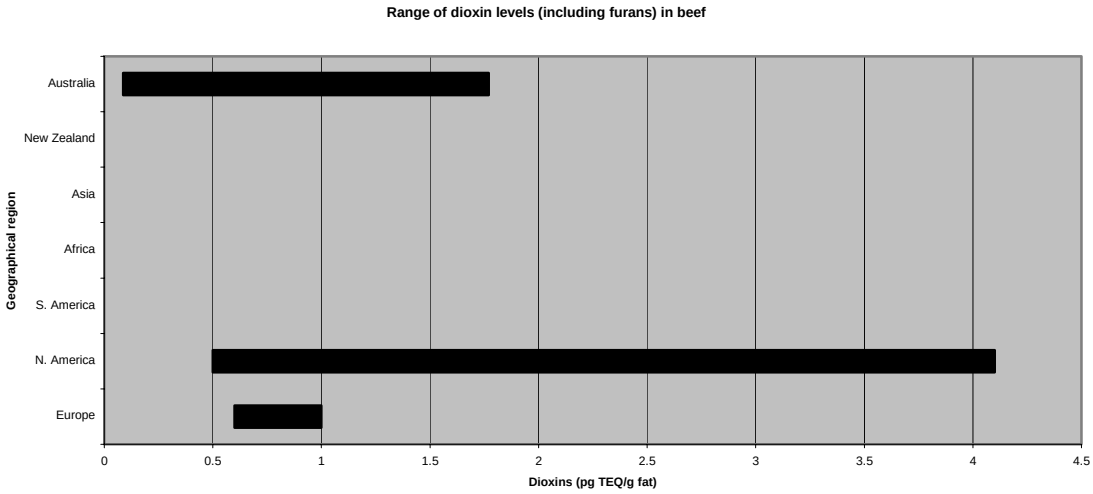
Appendix 14 Percent contribution of food groups to PCB mean dietary exposures for each population group

Food Name	9 months	2+ years			2-4 years	4-15 years		16-29 years		30-44 years		45-59 years		60+ years	
	All	All	Males	Females	All	Males	Females	Males	Females	Males	Females	Males	Females	Males	Females
Fish fillets, including crustacea and molluscs	26	72	73	71	49	60	57	68	68	76	72	75	77	78	76
Milk (full fat) including cheese, icecream and infant dessert	4	11	11	12	30	21	21	13	13	9	11	8	9	8	10
Beef, minced	1	3	3	3	2	3	3	4	3	3	3	3	2	3	2
Chicken breasts	1	2	2	2	2	2	2	3	3	2	2	2	1	1	2
Bacon	1	2	2	2	1	2	2	2	2	2	2	2	2	2	1
Sausages, meat, thick	1	2	2	1	3	3	3	2	1	1	1	2	1	1	1
Tuna, canned	1	2	1	2	1	1	2	1	2	1	2	2	2	1	2
Eggs	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Butter	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1
White bread, including all cereal products	1	1	1	1	2	1	1	1	1	1	1	1	1	1	1
Lamb chops	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Orange juice, including all fruit	2	1	1	1	2	1	1	1	1	0	1	1	1	1	1
Milk chocolate	1	1	1	1	1	1	2	1	1	0	1	0	0	0	0
Margarine, table spread	0	0	0	0	1	1	1	1	1	0	0	0	0	0	0
Infant Formula	61	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Baked beans	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0

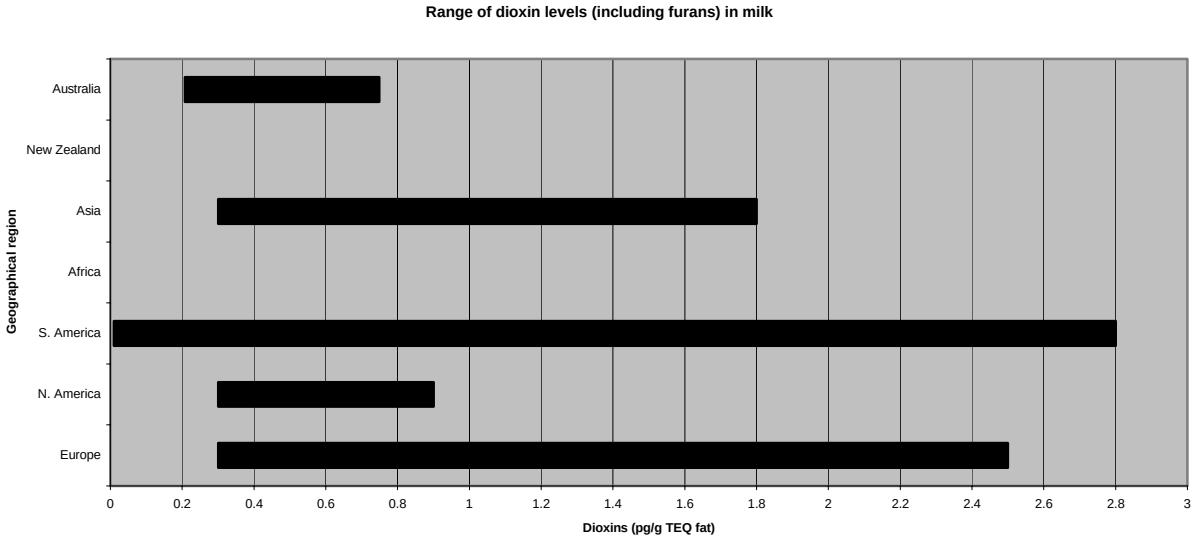
Percentage food contributions to PCDD/F and PCB exposure based on ‘lower bound’ values.

Appendix 15 An international comparison of the range of dioxins in agricultural commodities

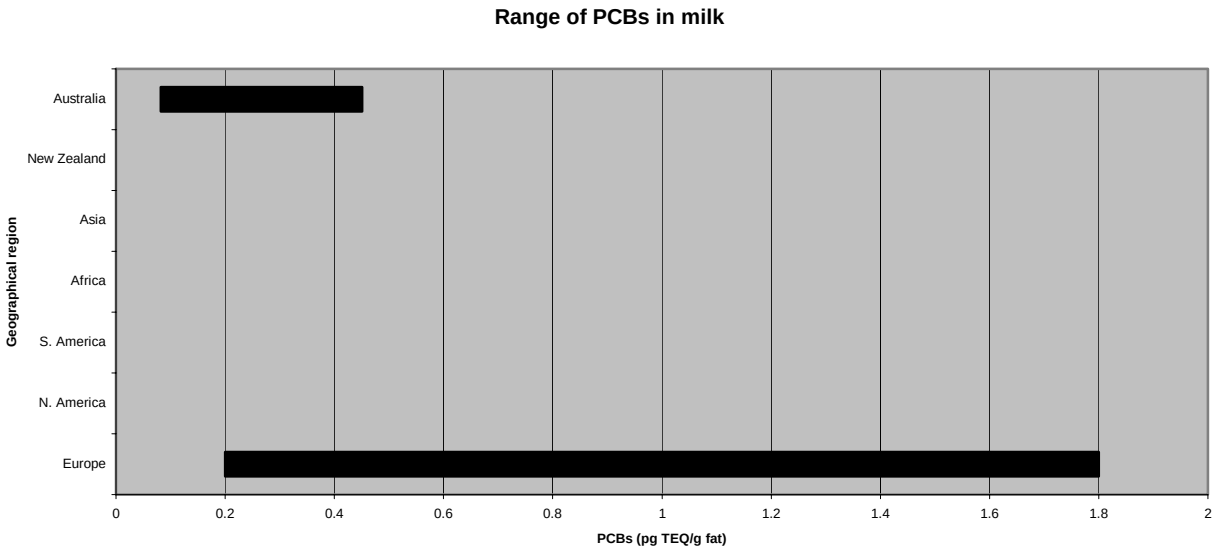
Range of PCDD/Fs in beef



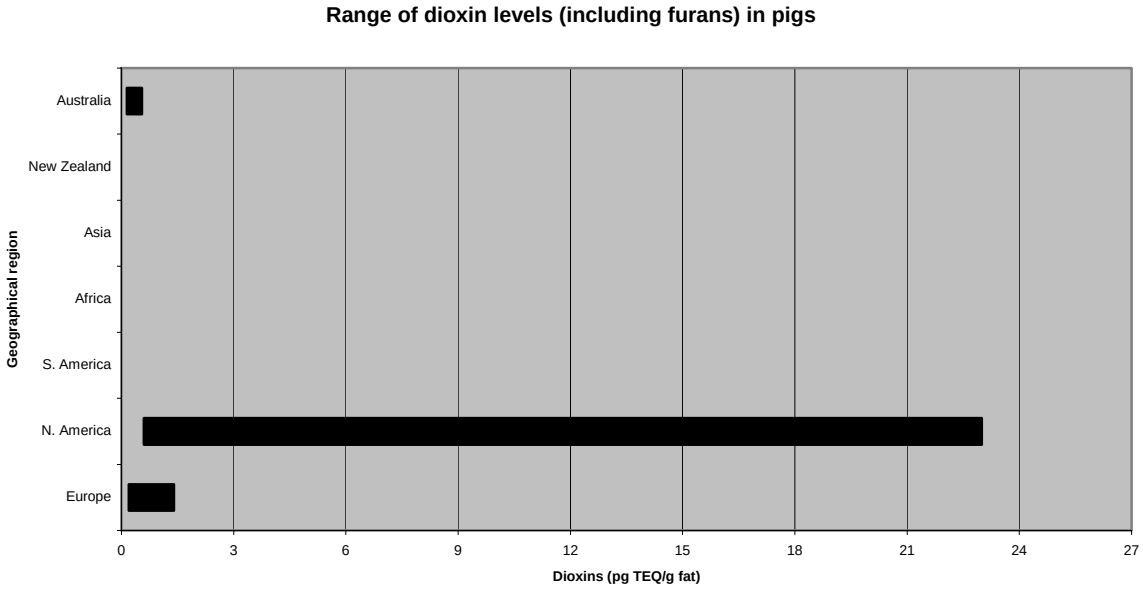
Range of PCDD/Fs in milk



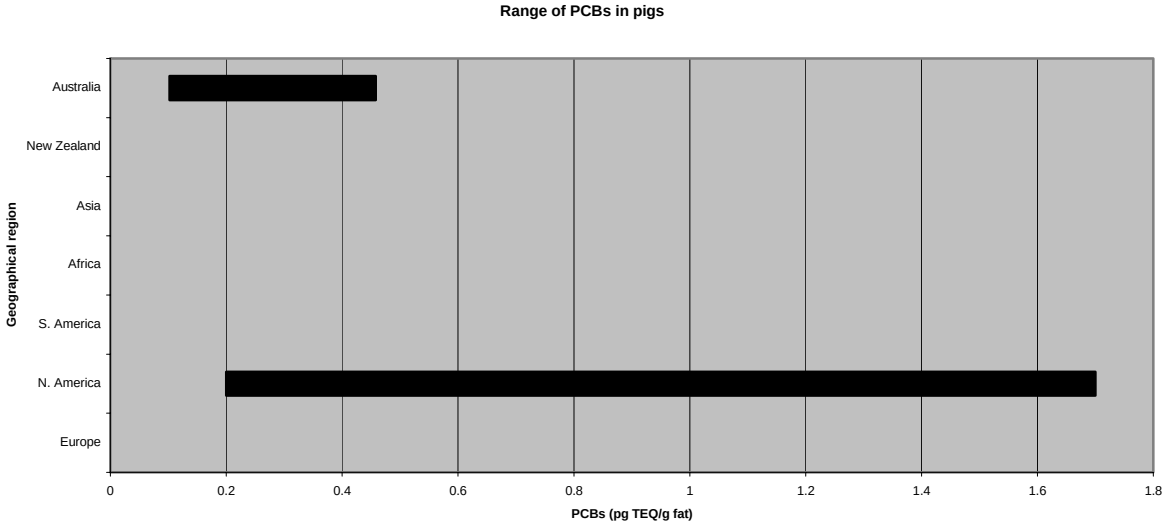
Range of PCBs in milk



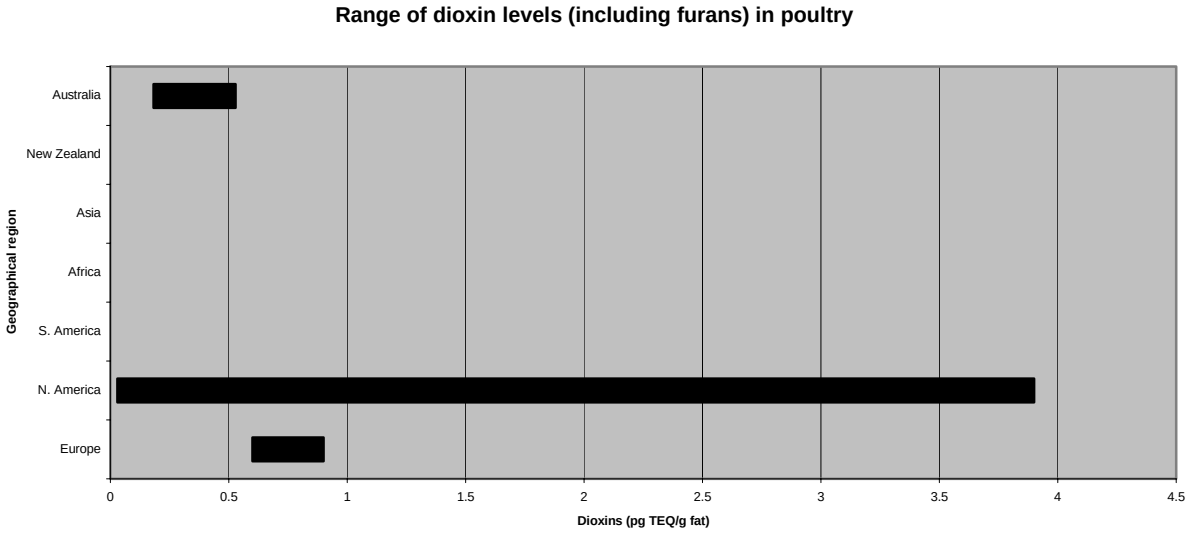
Range of PCDD/Fs in pigs



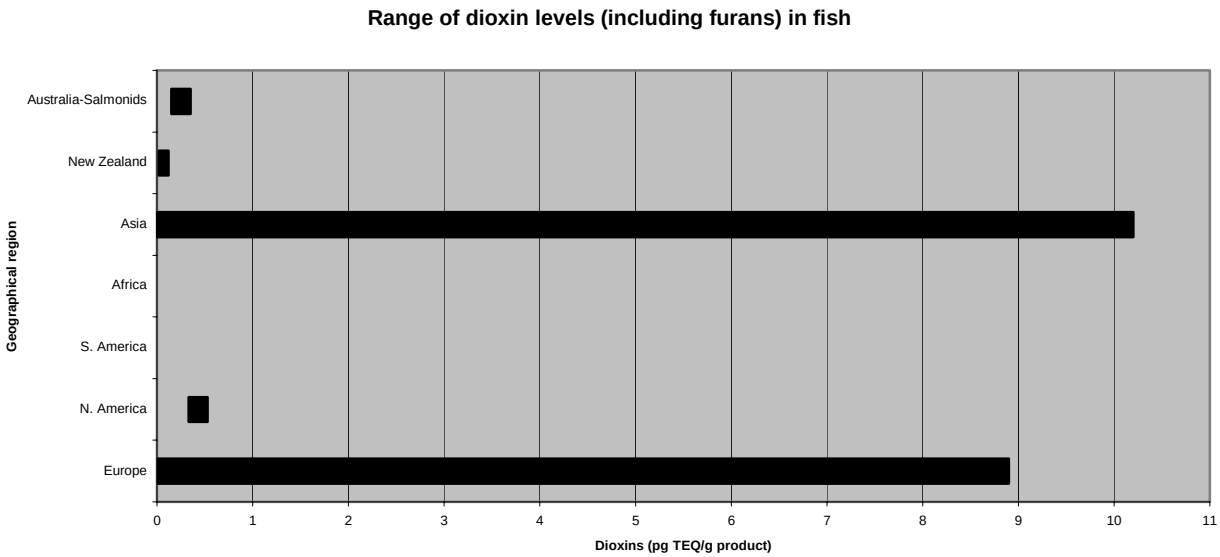
Range of PCBs in pigs



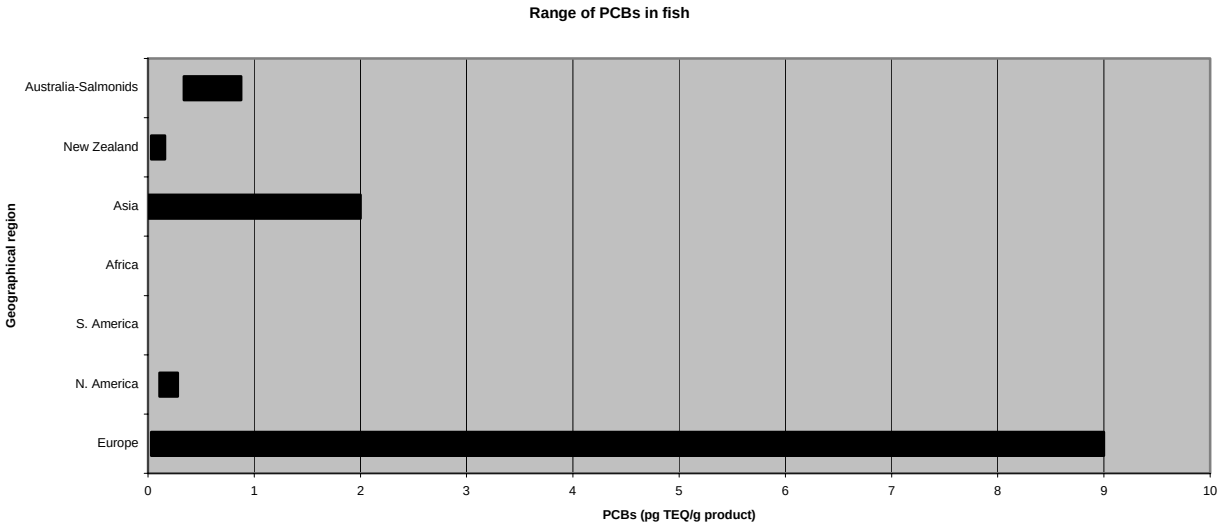
Range of PCDD/Fs in poultry



Range of PCDD/Fs in fish



Range of PCBs in fish



Appendix 16 Summarised Ambient Air Data from the DEH Ambient Air Study

		LOWER BOUND			MID BOUND			UPPER BOUND		
		DF	**PCB**	**DFPCB**	**DF**	**PCB**	**DFPCB**	**DF**	**PCB**	**DFPCB**
URBAN	**min**	0.14	0.14	0.38	0.37	0.19	0.75	0.58	0.24	1.09
	max	63.42	12.31	65.12	63.42	12.33	65.12	63.42	12.32	65.12
n=76	**mean**	11.77	1.84	13.61	12.14	1.86	14.00	12.49	1.88	14.37
	median	4.80	1.49	7.22	4.98	1.50	7.59	5.36	1.60	7.91
	SD	15.01	1.95	15.28	14.88	1.94	15.13	14.72	1.93	14.96
RURAL	**min**	0.01	0.08	0.15	0.31	0.10	0.65	0.47	0.12	0.81
	max	15.70	1.70	15.78	16.01	1.70	16.11	16.31	1.70	16.43
n=19	**mean**	1.52	0.42	1.94	1.93	0.45	2.38	2.35	0.47	2.82
	median	0.31	0.28	0.74	0.70	0.33	1.02	1.21	0.38	1.48
	SD	3.55	0.41	3.54	3.53	0.40	3.53	3.54	0.39	3.54
REMOTE	**min**	0.00	0.01	0.04	0.23	0.03	0.35	0.42	0.04	0.63
	max	4.43	0.41	4.67	4.43	0.40	4.68	4.44	0.41	4.68
n=10	**mean**	0.64	0.09	0.73	1.00	0.11	1.11	1.34	0.13	1.47
	median	0.07	0.04	0.12	0.48	0.07	0.62	0.95	0.09	1.01
	SD	1.37	0.13	1.42	1.27	0.12	1.30	1.24	0.11	1.26

Appendix 17 Formulae and Assumptions Used in Estimating the Intake and Systemic Exposure to Dioxins from Soil

Intake from ingestion of soil was calculated according to following formula:

$$\frac{\text{Dioxin concentration in soil x amount of soil ingested/day x 30}}{\text{Body weight}}$$

Systemic exposure from ingestion of soil was calculated according to following formula:

$$\frac{\text{Dioxin concentration in soil x amount of soil ingested/day x fraction absorbed x 30}}{\text{Body weight}}$$

For both the intake and systemic exposures, the amount of soil ingested was assumed to be 100 mg/day for child (1-5 years old) and 25 mg/day for adult. Body weights used were 15 kg for a 3 year old child and 70 kg for an adult (EnHealth, 2003; EnHealth, 2002; US EPA, 2002). The fraction of dioxins absorbed from soil was taken as 0.5, which was considered appropriate on the basis of results reported in animal and *in vitro* studies (Shu et al, 1988, Ruby et al, 2002)

Monthly systemic exposure from dermal contact with soil was estimated according to the following formula:

$$\frac{\text{Dioxin concentration in soil x area of exposed skin x dermal adherence x fraction absorbed x 30}}{\text{Body weight}}$$

Body weights used were as outlined above. Areas of exposed skin used were:
Child 1992 cm^2 =30% of total skin surface area (EnHealth, 2003; US EPA, 2002)
Adult 4700 cm^2 =24% of total skin surface area (EnHealth, 2003)

Since the draft Australian Exposure Assessment Handbook lacks dermal adherence factors for both children and adults, the dermal adherence factors used were 0.2 mg/cm^2 for a child and 0.07 mg/cm^2 for an adult (US EPA, 2001b). The fraction of PCDD/Fs absorbed was 0.03 and the fraction of PCBs absorbed through the skin was 0.14 (US EPA, 2001b). It was also assumed that dermal contact with soils occurred to the same extent every day of the year over a lifetime.

Appendix 18 Estimated monthly dietary exposures to PCDD/F, PCBs and total dioxins, as a percentage of the TMI.

Sex	Age group	PCDD/F (% TMI)		PCBs (% TMI)		Total Dioxins (% TMI)	
		Lower Bound	Upper Bound	Lower Bound	Upper Bound	Lower Bound	Upper Bound
All	2+	1	15	4	8	5	22
Males	2+	1	16	4	8	6	24
Females	2+	1	14	4	7	5	21
Infants	9 months	7	77	10	17	17	87
Toddlers	2-4	3	36	6	17	9	52
Males	4-15	2	25	5	12	7	37
Females	4-15	2	21	4	10	6	31
Males	16-29	1	15	4	8	6	23
Females	16-29	1	13	3	7	4	19
Males	30-44	1	13	5	8	6	21
Females	30-44	1	11	3	6	4	18
Males	45-59	1	12	4	7	5	19
Females	45-59	1	11	4	6	5	17
Males	60+	1	11	4	7	5	18
Females	60+	1	11	3	6	4	17

TMI = 70 pg TEQ/kg bw/month

Total dioxins = sum of intakes of PCDD/F and PCBs. Total dioxins may not equal the sum of the separate intakes due to rounding.

95th percentile dietary exposure to dioxins as a percentage of the TMI

Sex	Age group	PCDD/F (% TMI)		PCBs (% TMI)		Total Dioxins (% TMI)	
		Lower Bound	Upper Bound	Lower Bound	Upper Bound	Lower Bound	Upper Bound
All	2+	4	34	19	24	23	58
Males	2+	5	36	21	26	25	62
Females	2+	4	32	17	23	21	55
Toddlers	2-4	6	62	11	32	17	95
Males	4-15	5	47	12	27	17	74
Females	4-15	5	41	12	25	17	66
Males	16-29	5	30	23	27	28	57
Females	16-29	3	25	15	19	18	44
Males	30-44	4	26	22	25	26	51
Females	30-44	3	23	13	17	16	40
Males	45-59	4	24	21	24	25	47
Females	45-59	4	21	22	25	26	46
Males	60+	4	21	24	27	28	48
Females	60+	3	21	18	20	21	41

TMI = 70 pg TEQ/kg bw/month
Total dioxins = sum of intakes of dioxins-furans and PCBs. Total dioxins may not equal the sum of the separate intakes due to rounding.
Estimated dietary exposures are based on food consumption data from the 1995 NNS
Infant estimated dietary exposures are based on a constructed infant diet (see Section 3.2.2).

Appendix 19 Toxic Equivalency Factors (TEFs)

Congener		EPA/87[a]	NATO/88[b]	WHO/94[c]	WHO/98[d]
PCDDs					
2,3,7,8-TCDD		1	1		1
1,2,3,7,8-PeCDD		0.5	0.5		1
1,2,3,4,7,8-HxCDD		0.04	0.1		0.1
1,2,3,7,8,9-HxCDD		0.04	0.1		0.1
1,2,3,6,7,8-HxCDD		0.04	0.1		0.1
1,2,3,4,6,7,8-HpCDD		0.001	0.1		0.01
1,2,3,4,6,7,8,9-OCDD		0	0.001		0.0001
PCDFs					
2,3,7,8-TCDF		0.1	0.1		0.1
1,2,3,7,8-PeCDF		0.1	0.05		0.05
2,3,4,7,8-PeCDF		0.1	0.5		0.5
1,2,3,4,7,8-HxCDF		0.01	0.1		0.1
1,2,3,7,8,9-HxCDF		0.01	0.1		0.1
1,2,3,6,7,8-HxCDF		0.01	0.1		0.1
2,3,4,6,7,8-HxCDF		0.01	0.1		0.1
1,2,3,4,6,7,8-HpCDF		0.001	0.01		0.01
1,2,3,4,7,8,9-HpCDF		0.001	0.01		0.01
1,2,3,4,6,7,8,9-OCDF		0	0.001		0.0001
PCBs					
IUPAC #	**Structure**				
77	3,3',4,4'-TCB			0.0005	0.0001
81	3,4,4',5-TCB			-	0.0001
105	2,3,3',4,4'-PeCB			0.0001	0.0001
114	2,3,4,4',5-PeCB			0.0005	0.0005
118	2,3',4,4',5-PeCB			0.0001	0.0001
123	2',3,4,4',5-PeCB			0.0001	0.0001
126	3,3',4,4',5-PeCB			0.1	0.1
156	2,3,3',4,4',5-HxCB			0.0005	0.0005
157	2,3,3',4,4',5'-HxCB			0.0005	0.0005
167	2,3',4,4',5,5'-HxCB			0.00001	0.00001
169	3,3',4,4',5,5'-HxCB			0.01	0.01
170	2,2',3,3',4,4',5-HpCB			0.0001	-
180	2,2',3,4,4',5,5'-HpCB			0.00001	-
189	2,3,3',4,4',5,5'-HpCB			0.0001	0.0001

[a] US EPA, 1987
[b] NATO/CCMS, 1988
[c] Ahlborg et al, 1994
[d] van den Berg et al, 1998