5.0. POTENTIALLY ELEVATED EXPOSURES

5.1. INTRODUCTION

Certain groups of people may have higher exposures to the dioxin-like compounds than the general population. The following sections discuss higher exposures that may result from dietary habits, localized impacts, and cigarette smoking. Other population segments can be highly exposed due to occupational conditions or industrial accidents. For example, several epidemiological studies have evaluated whether elevated dioxin exposure has occurred to certain workers in the chemical industry, members of the Air Force who worked with Agent Orange, and residents of Seveso, Italy, who were exposed as a result of a pesticide plant explosion. These epidemiological studies are fully discussed in the Epidemiology Chapter of the Dioxin Health Reassessment Document (U.S. EPA, 1996) and should be consulted if further details are desired. This chapter, however, does not address occupational or accidental exposure. Instead, it focuses on elevated exposures among the general population from dietary habits such as breast feeding or high rates of fish ingestion, localized sources, or cigarette smoking.

5.2. NURSING INFANTS

Nursing infants may be exposed to dioxin-like compounds via consumption of breast milk. These compounds are deposited in the fatty tissues (i.e., adipose tissue, blood lipids, and breast milk) of the mother and may be transferred to the infant during nursing. Based on data from 1989, approximately 52 percent of U.S. mothers initiate breastfeeding with their newborn infants, and 40 percent continue breastfeeding for 3 months or longer (NAS, 1991). At 5 to 6 months of age, only about 20 percent of infants are breast-fed (NAS, 1991). This section will show how breast milk ingestion exposures, which are higher during breast-feeding, on a body weight basis, than during any other period in an individual's life, impact lifetime exposures and body burdens. First, data showing the impact of breast milk ingestion to the infant body burden of CDD/CDF/PCBs are reviewed. Then, an estimate of the dose (average daily dose, ADD, and lifetime average daily dose, LADD) to the infant via breast milk is made. The section will close by developing, testing, and applying a model on the impact of breast-feeding to body burdens for growing infants.

5.2.1. The Impact of Breast Feeding on Infant Body Burden

Abraham et al. (1994, 1995) studied CDD/CDF/PCB levels in the blood of a breast-fed and a formula-fed infant at 11 and 25 months of age. Sampling of blood showed that the body burden of dioxin-like compounds was more than an order of magnitude higher for the breast-fed infant than the formula-fed infant during both time periods, with CDD/CDF ranging from 34.7 (11 months) to 43.9 (25 months) ppt TEQ_{DF}-WHO_{98} lipid-basis in the breast-fed infant compared to 2.7 to 3.3 ppt TEQ_{DF}-WHO_{98} for the formula-fed infant. Dioxin-like PCB concentrations were similarly an order of magnitude different, with the breast-fed infant having a concentration of 31.4 ppt TEQ_{P}-WHO_{98}, compared to 2.5 ppt TEQ_{P}-WHO_{98} for the formula-fed infant at 11 months (PCB 126 not measured at 25 months, so a comparison for that age is not informative). The full congener profiles for these results are shown in Table 5-1. The increase in the lipid-based CDD/CDF TEQ concentration in the blood of the breast-fed infant at 25 months was attributed to the relative decrease in body fat mass during the period between sampling and slight increases in body burden concentrations.

Abraham et al. (1994) also analyzed mother's milk at 1 month and mother's blood along with the infants' blood at 11 months. They found mother's milk to contain 23.5 ppt TEQ_{DF}-WHO_{98} at 1 month and mother's blood to contain 14.2 ppt TEQ_{DF}-WHO_{98} at 10 months. If blood and milk concentrations in a mother during lactation are the same at any given time, then these data suggest a reduction of about 40 percent in TEQ concentration in the mother between the 1st and 10th month of lactation. The reduction in mother's milk concentration of dioxins during nursing is discussed further in Section 5.2.3 below.

Kreuzer et al. (1997) developed and tested a toxicokinetic model of human lifetime body burden of TCDD, starting with a model for breast-feeding. To support their model, they presented adipose tissue and liver data on 3 stillborn and 17 infants who had died from sudden infant death syndrome (SIDS). Nine of the 17 infants had spent some portion of their lives breast-feeding, while the other 8 infants were formula-fed. Average congener and TEQ concentrations for these three groups are shown in Table 5-2. The highest TEQ concentrations were found in the infants who had some breast-feeding, with adipose concentrations at 15.9 ppt TEQ_{DF}-WHO_{98}, as compared to formula-fed infants who had concentrations at 4.3 ppt TEQ_{DF}-WHO_{98}. The breast-fed infants' concentrations included four infants who were weaned several weeks prior to their death from SIDS.

This may have generally led to reductions in their body burdens as their higher daily intake from breast-feeding was reduced after weaning. The average TEQ concentration for the five infants who died while still breast-feeding was 20.1 ppt TEQ_{DF}-WHO_{98}. The highest concentration found was for the infant who was breast-fed the longest at 19 weeks, and who died at that time; the TEQ concentration was 35 ppt TEQ_{DF}-WHO_{98}. Other breast-fed infants, however, did not have as much impact - infants who died while breast-feeding at 12 and 16 weeks had concentrations of 9 and 7.5 ppt TEQ_{DF}-WHO_{98}. While Kreuzer et al. (1997) concluded that breast-fed infants had elevated concentrations compared to formula-fed infants, they also observed that breast-fed infants had adipose TEQ concentrations that were within the range or lower than the values published for adults.

Abraham et al. (2000) reported on a study in Germany in which the blood of 80 breast-fed infants between the ages of 4 and 11 months were analyzed for the 17 CDD/CDFs . Of these 80 infants, 27 were from a region where a copper recycling plant led to elevations in the mother's milk. The I-TEQ_{DF} blood concentration in this group of 80 children at 11 months ranged between 2.0 and 107 pg/g lipid-basis, with a median of 25.3 ppt. Of these children, 6 had I-TEQ_{DF} concentrations greater that 50 ppt, and 5 of these 6 were from the region impacted by the copper recycling plant. From a control group of 21 children who had been formula-fed, individual dioxin measurements were performed in 5 children. Concentrations were found to range narrowly from 1.9 to 3.2 ppt I-TEQ_{DF} lipid-basis at 11 months. With several measurements over time, Abraham et al. (2000) found the blood concentrations of the breast-fed infants to increase over time. Infant or time-specific concentration data were not presented in Abraham et al. (2000). However, they did show the ratio between the concentration of specific compounds, as well as the I-TEQ_{DF} concentrations, in the children's blood and the blood of the mothers. When the ratio exceeded 1.0, this meant that the child's concentration was higher than the mother's. Abraham et al. (2000) showed the I-TEQ_{DF} ratio to increase from 1.12 at 16-24 weeks (n = 11 meaning there were 11 paired measurements at that time) to 2.12 at 25-32 weeks (n = 29) to 3.20 at 33-40 weeks (n = 33) to 3.73 at 41-48 weeks (n = 7). This was the most comprehensive data set found in the literature, although it was not fully described in the Abraham et al. (2000) abstract.

Patandin et al. (1997) looked at the plasma levels of four polychlorinated biphenyls (PCBs) in 173 Dutch children 3.5 years of age, 91 of which had been breast-fed and 82

of which had been formula-fed. Children in the breast-fed group had significantly higher median PCB levels in plasma ($p < 0.0001$) than children in the formula fed group. The four PCBs measured were 118, 138, 153, and 180. The median sums of these four PCBs in the two groups of children were 0.75 µg/L in the breast-fed group versus 0.21 µg/L in the formula fed group. By means of an extensive questionnaire on dietary history, combined with data on the concentrations of dioxin and PCBs in foods provided by the Dutch National Institute of Public Health and the Environment, Pantadin et al. (1997) were able to determine that the TEQ intake via the diet was virtually indistinguishable in the two groups. They found that PCB levels in the breast-fed children were significantly correlated with the period of breast-feeding ($r = 0.63$), milk PCB levels ($r = 0.39$), and the total TEQ in breast milk ($r = 0.36$). They concluded that the plasma PCB levels in Dutch children were the result of exposure through breast milk and in utero exposure, and that the influence of dietary intake of PCBs after weaning is small compared to the intake during breast-feeding.

5.2.2. Calculation of an Average Daily Dose from Breast-Feeding

Using the estimated dioxin concentration in breast milk, the administered dose to the infant can be estimated as follows:

$$ADD_{infant} = \frac{C_{milk\ fat} * f_3 * IR_{milk} * ED}{BW_{infant} * AT} \qquad \text{(Eqn. 5-1)}$$

where,

ADD_{infant} = Average daily dose to the infant (pg/kg-d);
$C_{milk\ fat}$ = Concentration in milk fat (pg/g);
IR_{milk} = Ingestion rate of breast milk (kg/d);
ED = Exposure duration (yr);
BW_{infant} = Body weight of infant (kg);
AT = Averaging time (yr); and
f_3 = Fraction of fat in breast milk.

The administered dose can be converted to an absorbed dose by multiplying by the fraction of ingested contaminant that is absorbed.

This approach assumes that all pertinent parameters, including the body weight of the infant, the infant ingestion rate of breast milk, and perhaps most importantly, the contaminant concentration in milk, represent the average over the breast feeding time period.

Smith (1987) reported that a study in Britain found that the breast milk ingestion rate for 7- to 8-month old infants ranged from 677 to 922 mL/d and that a study in Houston measured the mean production of lactating women to range from 723 to 751 g/d. Smith (1987) also reported that breast milk ingestion rates remain relatively constant over an infant's life. For purposes of estimating the dose to breast feeding infants, a milk ingestion rate of 800 mL/d was assumed in the analysis presented in this section. Smith (1987) also assumed that mother's milk has a 4 percent fat content, and that 80 percent of the ingested contaminant are absorbed. The infant weight varies with time. For example, a typical infant (average of male and female data) weighs about 3.3 kg at birth, 7.9 kg at 6 months, and 10.2 kg at 1.0 year (U.S. EPA, 1997; Walker and Watkins, 1997).

The concentration of dioxin in the mother's milk is also expected to change, since lactation provides a significant avenue of depuration. Lakind et al. (2000) cite several references where measurements of breast milk concentrations of lipophilic compounds (PCBs, DDE, DDT, CDD/CDFs) were shown to decline during the course of lactation. They fit available data on 2,3,7,8-TCDD to a curve, and their resulting relationship showed an 86 percent loss over 6 months. This is comparable to a modeling effort by Kreuzer et al. (1997), who modeled a 70 percent decline in TCDD concentrations after 6 months. Their model was more mechanistic, and added the loss by breast milk to an overall female body burden model which included inputs by food consumption and outputs by metabolic and non-metabolic pathways. Patandin et al. (1999), in their modeling of dioxin exposures from infancy to adulthood, cited data from Germany and England to conclude that breast milk concentrations of TCDD decline by 20 percent every 3 months. The data described in the previous section by Abraham et al. (1994) suggest a decline of 40 percent of TEQs from 1 month to 10 months of lactation.

For assignment of $C_{milk\ fat}$ in Equation 5-1, therefore, one would have to assign a concentration at birth and consider a decline in that concentration over time. For purposes of this discussion, a concentration of 25 ppt TEQ_{DFP}-WHO_{98} on a lipid basis is assumed for mother's milk when lactation begins (which is the average tissue concentration derived from recent studies of dioxins in blood in background settings of the US, reviewed in Chapter 4). It is then assumed to linearly drop by 50 percent after 6 months, with an additional linear drop of 50 percent by the end of 12 months, for a total decline of 75 percent from initial concentrations. These assignments in concentration decline are in the middle of the range reported above. They translate to concentrations of 12.5 ppt TEQ_{DFP}-WHO_{98} after 6 months and 6.3 ppt TEQ_{DFP}-WHO_{98} after a year, given a starting concentration of 25 ppt TEQ_{DFP}-WHO_{98}.

The proper way to derive an average dose to the child is to integrate Equation 5-1 over the time period of interest. At birth, for example, with a mother's milk concentration of 25 ppt TEQ_{DF}-WHO_{98}, an infant body weight of 3.3 kg, an average ingestion rate of 800 g/d breast milk, the administered dose is predicted to be 242 pg TEQ_{DF}-WHO_{98}/kg bw/day [(25 pg/g x 0.04 x 800 g/d) / (3.3 kg) = 242 pg/kg-d]. Table 5-3 shows infant body weights, as well as doses of dioxin TEQ_{DF}-WHO_{98} expressed in terms of pg/day for each of the first 12 months of life. These body weight data are the averages for male and female infants (U.S. EPA, 1997; Walker and Watkins, 1997), and along with other data, were used in the pharmacokinetic exercise described in the next section. Calculating monthly doses on the basis of body weight for each of the first twelve months of life and then dividing by 12, results in an average dose to the infant of 87 pg TEQ_{DF}-WHO_{98}/kg bw/day.

This value is much higher than the estimated average background TEQ_{DFP}-WHO_{98} dose for adults of approximately 1 pg TEQ_{DFP}-WHO_{98}/kg-d. However, if a 70 year averaging time is used for this one-year nursing scenario, then the LADD (Lifetime Average Daily Dose, calculated as ADD * ED/LT where LT is lifetime typically assumed to be 70 years) is estimated to be 1.2 pg TEQ_{DFP}-WHO_{98}/kg-d ([87 pg/kg-d] * 1 yr/70 yr). This is close to the adult background dose of 1.0 pg TEQ_{DFP}-WHO_{98}/kg-d. However, this can be misleading because it ignores the difference in daily intake during potentially sensitive stages in development. Also, it does not consider any exposures past the first year of life. In order to calculate a true lifetime average daily dose, one needs to incorporate the

changes in dose over various life stages. Using the estimates of dose derived in Chapter 4 for various ages in children: 1-5: 3.3 pg TEQ_{DFP}/kg-d, 6-11: 1.9 pg TEQ_{DFP}/kg-d, and 12-19: 1.1 pg TEQ_{DFP}/kg-d, the following calculates the LADD for lifetime background exposures considering one year of breast-feeding:

$$\text{LADD} = 87 \frac{1\text{yr}}{70\text{yrs}} + 3.3 \frac{4\text{yrs}}{70\text{yrs}} + 1.9 \frac{6\text{yrs}}{70\text{yrs}} + 1.1 \frac{8\text{yrs}}{70\text{yrs}} + 1.0 \frac{51\text{yr}}{70\text{yr}} \quad \text{(Eqn. 5-2)}$$

$$\text{LADD} = 2.45 \frac{\text{pg TEQ}_{DFP}}{\text{kg- day}} \quad \text{(Eqn. 5-3)}$$

On a mass basis, the cumulative dose to the infant after a year is about 238 ng TEQ_{DFP}-WHO_{98} (87 pg/kg-d x 7.5 kg x 365 d x ng/1,000 pg; 7.5 kg is an average annual weight based on the average of 12 monthly body weights). Using the age-dependent doses derived in Chapter 4 with assumed body weights, a dose from year 1 to year 70 in a 70-year lifetime is estimated to be about 1,687 ng TEQ_{DFP}-WHO_{98}, so that a total lifetime dose is 1,925 ng TEQ_{DFP}-WHO_{98} (1,687 + 238). This suggests that about 12 percent of lifetime dose (238/1925 * 100 percent) may occur as a result of breast feeding, if that feeding occurred for one year.

This exercise describes accumulated dose over a lifetime, given a year of breast-feeding. It was found that about 12 percent of lifetime dose came from breast-feeding. It was also found that the LADD for this scenario, including average dioxin doses after the first year until year 70, was 2.45 pg TEQ_{DFP}-WHO_{98}/kg-day. The issue of accumulative dose is explored in more detail in the next section, where the quantity, "area under the curve" is defined and used to assess overall exposure during a lifetime, or portions of a lifetime, under different breast-feeding scenarios as well as a formula-only scenario where the infant experiences only background exposures.

5.2.3. Modeling the Impact of Breast-Feeding on Infant Body Burden

The previous section described an approach to estimate doses received by an infant due to breast-feeding, which included a starting concentration in mother's milk, a decline of that concentration over time (and the resulting decline in dose delivered to the child),

and the child's changing body weight. That information will be used in this section to evaluate the impact of breast feeding on an infant's body burden of dioxins.

To better evaluate the impact of nursing on infants, a one-compartment non-steady state pharmacokinetic model was used to evaluate dioxin tissue levels. As described below, this model was validated using paired mother/child data on breast milk and infant blood concentrations of TEQ_{DF}-WHO_{98}. Following this validation, several breast-feeding scenarios were modeled and compared with a formula-feeding only scenario. Specifically, changes in infant TEQ_{DFP}-WHO_{98} tissue concentration over time were modeled for these scenarios: formula only, 6 weeks nursing, 6 months nursing, 1 year nursing, and 2 years nursing. The section closes with sensitivity analyses exercises which describe the model response to changes in the key parameters describing the dose received by the infant via breast milk and the rate of dissipation of dioxin TEQs in the infant.

5.2.3.1. *Description of the Model*

The pharmacokinetic model was based on the following differential equation describing the mass balance of dioxin in lipids (Pinsky and Lorber, 1998):

$$da(t)/dt = f\,D(t) - k(t)\,a(t) \qquad \text{Eqn. (5-4)}$$

$$c(t) = \frac{a(t)}{1000\,V(t)} \qquad \text{Eqn. (5-5)}$$

where:

- a(t) = total mass of dioxins in lipid (pg) at time t;
- c(t) = concentration of dioxins in lipid (pg/g) a time t;
- D(t) = ingested dose of dioxins (pg/yr) at time t;
- V(t) = lipid weight (kg) at time t;
- k(t) = elimination rate constant (yrs^{-1}) at time t;
- t = time (yrs); and
- f = fraction of ingested dose absorbed into lipid compartment (unitless).

The lipid weight, V(t), is calculated as the product of the percent body lipid and the full body weight of the infant, both of which are provided in Walker and Watkins (1997) for infant boys and girls. This section demonstrates the approach using the average for infant boys and girls. The dose regime for tested scenarios in this section, the body weight, lipid fraction, and assumed half-lives of TEQ_{DFP}-WHO_{98}, are shown with other model parameters in Table 5-3. The body lipid and body weight are also shown graphically in Figure 5-1, for the 70 year life span and in more detail for the early years of life.

One key assumption of this simplistic framework is that dioxins are instantaneously distributed to all body lipids. This is a common assumption for TCDD PK modeling in humans, adopted by the multi-compartment model of van der Molen et al. (1996), and the single-compartment models in Kreuzer et al. (1997), Campbell et al. (1996), and Lakind et al. (2000). The model of Carrier et al. (1995a,b) alternately has a nonlinear response to doses, with different partitioning to the liver and other body lipids as a function of body concentration; when the overall body concentration is high, more of the dioxin dose is partitioned to the liver, whereas at lower body concentrations, the partitioning to the liver is lower.

The other key and important assumption for the model is that the TEQ_{DFP}-WHO_{98} behaves as a single compound in humans, and can be described by a single dissipation half-life. Ayotte et al. (1994) modeled TEQ body burdens from infancy to adulthood, but it was unclear whether they modeled individual congeners or TEQs as one compound. Campbell et al. (1996) used a framework similar to the one used here and modeled individual congeners for an industrial exposure study.

The elimination rate constant, k(t), was developed in similar fashions by Pinsky and Lorber (1998), Michalek et al. (1996), and Flesch-Janys et al. (1996), for 2,3,7,8-TCDD. All three research groups derived a relationship in which the elimination rate constant was a function of percent body fat. All three also curve-fit their empirical algorithms for k(t) on data from adult individuals, whose percent body fat was about 25 percent. With body fat percent increasing over time, particularly in older individuals, the elimination rate constant decreased (equivalently, the half-life increased) significantly. Given a range of body fat over time, from about a low of 15 percent to a high over 40 percent (for elderly females), the relationship in Pinsky and Lorber (1998) results in a half-life of 2,3,7,8-TCDD ranging from about 6 to over 20 years.

None of these efforts, however, identified processes or factors critical for infants, other than percent body fat. With a body fat of around 15 percent at birth, the half-life is calculated to be about 6.4 years using the relationship in Pinsky and Lorber (1998). Kreuzer et al. (1997), however, developed a procedure for modeling the elimination half-lives for 2,3,7,8-TCDD in infants which considerd metabolic, t_m (breakdown by enzymes), and non-metabolic, t_f (fecal elimination) processes. Kreuzer et al. (1997) combined these two half-lives to solve for an overall half-life, $t_{1/2}$. Other key parameters included total body lipid mass and liver volumes, which change over time, and a reference half-life for an adult. For their "reference adult" at age 40, they cited an overall half-life of 5 years, based on information in Geyer et al. (1986). The Kreuzer et al. (1997) model showed a rise in half-lives from a low of less than 0.5 years at birth to a high of 5 years at the total body lipid mass of 20 kg. With their parameter assignments, perhaps most importantly this assignment of a 5 year half-life for a reference adult, the half-life will not go far beyond 5 years (as a function of body lipid mass, it would exceed 5 years when body lipid mass exceeds 20 kg), which makes the model of Kreuzer et al. (1997) importantly different than that of Pinsky and Lorber (1998), Michalek et al. (1996), and Flesch-Janys et al. (1996), all of whom have half-lives varying from a value of 6 to over 20 years. In short, the model of Kreuzer et al. (1997) has half-lives which mostly never exceed 5 years, while the other approaches have half-lives for TCDD which never go below 6 years.

As noted, the model of Kruezer et al. (1997) suggests relatively short half-lives for infants. For infants, the overall half-life is driven by non-metabolic processes and the resulting half-life for newborns is calculated to be about 0.4 years. It rises to about 2.0 years when the total body fat weight is about 5 kg, which occurs around ages 8-10 years (25-35 kg overall body weight, about 20 percent body fat). Very clearly, this rapid a half-life of dioxin intake will have an important impact on the accumulation of dioxin residues during breast-feeding as compared to a model showing a 6 year or higher half-life. Lakind et al. (2000) adopted the Kruezer et al. (1997) approach in their evaluation of the impacts of breast-feeding on the 2,3,7,8-TCDD body burdens of infants.

For purposes of this assessment, it was assumed that the overall half-life for the early years of life more closely follows the trend as derived in the modeling exercises by Kruezer et al. (1997). For later years, it was felt that the empirical data upon which Pinsky and Lorber (1998), Michalek et al. (1996), and Flesch-Janys et al. (1996) derived

the half-life relationship for 2,3,7,8-TCDD is more valid. Therefore, a hybrid of these assumptions, as shown in Figure 5-2, was adopted for this effort. The half-life at birth starts at the low value of 0.4 yr and then slowly rises to the levels as modeled by Pinsky and Lorber (1998) by about age 20. It is noted that had Kreuzer et al. (1997) established reference half-lives for 40 year-olds more in the 6-20 year range, they would still have had very low half-lives at birth, rising to these higher half-lives with age. The half-life assumptions remain an obvious uncertainty for this type of modeling approach. Not only is there a disparity in the literature with regard to this critical assumption, but the literature is also only specific to 2,3,7,8-TCDD, not TEQ_{DFP}-WHO_{98}. The impact of this assumption is examined later in the sensitivity analysis exercises.

The final assumption for the model is the initial lipid concentration in the infant. It was assumed to be 10 ppt TEQ_{DFP}-WHO_{98}, which was reasonably similar to the 11.9 ppt TEQ_{DF}-WHO_{98} found in stillborn adipose tissue in Kreuzer et al. (1997). All other assumptions and parameter assignments for this modeling exercise, including the half-life change over time, are shown in Table 5-3, and Figures 5-1 and 5-2.

5.2.3.2. *Validation of the Model*

While demonstrating the impact of breast-feeding, the studies reviewed in Section 5.2.1. do not contain the type of information needed for model validation. What is needed are breast milk concentrations that are taken at the same time infant body burden measurements are taken. The breast milk concentrations are used to provide the "independent" model driving term, the dose term, and the body burden measurements provide the "dependent" model prediction, the infant body lipid concentration.

One study had a set of this kind of data. Abraham et al. (1998) studied CDD/CDF/PCB levels in the blood of 6 breast-fed infants as well as the breast milk of the mothers of these infants. A portion of this data set had been reported in their earlier articles (Abraham et al., 1994; 1995). This analysis will focus on the TEQ_{DF}-WHO_{98} concentrations reported in Abraham et al. (1998), since PCB concentrations were not uniformly available for mother's milk and infant blood for all six mother/child pairs.

Two of the infants were the second children from mothers whose first child was also tracked by Abraham and colleagues. It was interesting to note that, for these two second children, both the mothers' milk and the infants' body burdens were significantly

lower. Specifically, the comparison of first and second children, respectively, were: 34.7 ppt TEQ_{DF}-WHO_{98} lipid compared to11.9 ppt TEQ_{DF}-WHO_{98}, and 44.2 ppt TEQ_{DF}-WHO_{98} compared to 18.8 ppt TEQ_{DF}-WHO_{98}. The comparison of the mothers' milk from the first to second children was similarly disparate: the first mother had concentrations ranging from 14 to 24 ppt TEQ_{DF}-WHO_{98} lipid for the first child, but 13 to 14 ppt TEQ_{DF}-WHO_{98} lipid only for the second child. The other mother showed a range of 15 to 27 ppt TEQ_{DF}-WHO_{98} lipid for the first child, but only 13 to 18 ppt TEQ_{DF}-WHO_{98} lipid for the second. Apparently, breast-feeding of the first child resulted in a higher body burden for this infant as compared to the second infant, and a lower body burden for the mother when the second infant was breast-fed.

Table 5-4 shows the observed data that were available in Abraham et al. (1998) for this model validation exercise. There were two concentrations measured in breast-milk for each of 5 of 6 children. The one child whose mother had only one measurement was only breast-fed for 7 weeks; all other children were breast-fed for periods ranging narrowly from 26 to 32 weeks. Concentrations within the breast-feeding period were linearly extrapolated from the two available data points. For example, for the first mother/child pair listed in Table 5-4, mother's milk was analyzed during month 2 and month 11. TEQ concentrations were 23.5 and 14.0 ppt TEQ_{DF}-WHO_{98} lipid, respectively. These concentrations were extrapolated backwards to give an estimated concentration at birth of 24.6 ppt TEQ_{DF}-WHO_{98}. Likewise, forwards extrapolation gave an estimated concentration for month 3 of 22.4 TEQ_{DF}-WHO_{98}, assuming linear decline. The infant body burden was ascertained by blood measurements at about 1 year of age for each child. The amount of time of full breast-feeding was supplied by Abraham et al. (1998), and this is also listed in Table 5-4.

Other assumptions for modeling the infant body burden were outlined above, and these include the intake rate of mother's milk (IR = 800 ml/d), the fraction of fat in mother's milk (0.04), the rate of absorption of dioxins (0.80), and the changing infant body weight and lipid fraction (and hence lipid volume, V(t); Table 5-3). After weaning, the dose to the infant was assumed to be 50 pg TEQ_{DF}-WHO_{98}/d. This is the dose developed for the age range of 1-5 in Chapter 4. The dose by formula feeding or other foods the infants may be consuming after weaning may be lower or higher, as little

information is available on the dioxin content of baby formula or baby food. The assumed initial body burden of the infant was 10 ppt TEQ_{DF}-WHO_{98}, as noted above.

The rate of dissipation of dioxin residues was identified as a principal uncertainty for this model. Two lines of thought discussed above include the rapid dissipation (half-life < 1 year) of TCDD residues in infants modeled in Kreuzer et al. (1997) and later adopted by Lakind et al. (2000), and the much longer dissipation (half-life around 7 years) of TCDD in adults described in Pinsky and Lorber (1998), Michalek et al. (1996), and Flesch-Janys et al. (1996). The model validation exercise described in this section tested the appropriateness of the lower infancy half-life approach adopted in this model, as shown in Figure 5-2, against an assumption of a constant 7 year half-life for TEQ_{DF}-WHO_{98} during the first year of life.

Table 5-4 shows the final results of this exercise. As seen, the model predictions at the selected and more rapid dissipation rate were significantly nearer to observations as compared to the predictions with the longer half-life. The average predicted concentration for the rapid dissipation rate for the 6 infants was 26 ppt TEQ_{DF}-WHO_{98} lipid, compared to the average observed concentration of 23.5 ppt TEQ_{DF}-WHO_{98} lipid. With a longer 7-year half-life, the predicted concentrations were all higher, with an average of 39 ppt TEQ_{DF}-WHO_{98} lipid. The model also seemed very adequately responsive to lower or higher infants' exposures. For the infant who was breast-fed for only 7 weeks with a low concentration in the mother's milk, the blood concentrations measured 5.0 ppt TEQ_{DF}-WHO_{98} lipid at 13 months, compared to a predicted 10 ppt TEQ_{DF}-WHO_{98} lipid (with the rapid dissipation assumption). The infant exposed to the highest mother's milk concentration had the highest body burden measurement at 44.2 ppt TEQ_{DF}-WHO_{98} lipid and also the highest predicted concentration at 36 ppt TEQ_{DF}-WHO_{98} lipid.

In summary, it appeared that, even with the key uncertainties identified above, including the use of a simple, one-compartment pharmacokinetic model and the modeling of TEQ_{DFP}-WHO_{98}s as though they were a single compound, this approach appears to predict infant TEQ_{DFP}-WHO_{98} body burdens within the range observed, and is adequately responsive to the different conditions of high and low exposure via breast-feeding.

5.2.3.3. *Scenario Evaluation*

The scenarios evaluated include: formula only, 6 weeks of breast-feeding, 6 months of breast-feeding, 1 year of breast-feeding, and 2 years of breast-feeding. These scenarios encompass current trends. In comprehensive documentation of statistics for children born between 1990 and 1993, CDC (1997) reported that 55 percent of all babies breastfed, with about half of those breastfeeding beyond 5 months. The average duration of breastfeeding was 28.7 weeks. In a policy statement, the American Academy of Pediatrics (1997) stated that exclusive breastfeeding is ideal nutrition and sufficient to support optimal growth and development for 6 months after birth. They recommend that breastfeeding continue for at least 12 months, and thereafter for as long as mutually desired. Ryan (1997) documented a resurgence in breastfeeding between 1989 and 1995. In comprehensive surveys conducted in 1989 and 1995, he found a 14 percent increase in the number of mothers who breastfed in the hospital, rising from 52 percent in 1989 to 59 percent in 1995. He also found a 19 percent increase in mothers who continued to breastfeed at 6 months, rising from 18 percent in 1989 to 22 percent in 1995.

The specifics of these scenarios are:

Scenario #1: Formula Only: In this scenario, the dose to the infant was assumed to be 50 pg TEQ_{DFP}-WHO_{98}/d. This is the dose developed for the age range of 1-5, as described in Chapter 4. The dose by formula feeding may be lower or higher, as little information is available on the dioxin content of baby formula. TEQ_{DFP}-WHO_{98} doses among individuals from 6 to 11, 12 to 18, and greater than 18 years of age were 54, 65, and 66 pg TEQ_{DFP}-WHO_{98}/d, respectively, as developed for these age ranges in Chapter 4.

Scenario #2: Six-Week Nursing: The dose to the infant was assumed to be a function of the starting concentration of dioxins in the mother's milk, 25 pg TEQ_{DFP}-WHO_{98}/g lipid, and other assumptions that have been described in this section: 800 g/day milk ingestion, 4 percent lipids in milk, resulting in an initial dose of 800 pg TEQ_{DFP}-WHO_{98}/d. This drops to 733 after 1 month, and then to 667 pg TEQ_{DFP}-WHO_{98}/d, when nursing stops. Doses from then are as in Scenario #1.

Scenario #3: Six-Month Nursing: It was assumed that the dose drops linearly from 800 to an ending dose of 400 pg TEQ_{DFP}-WHO_{98}/day at month 6. From there, doses are as in Scenario #1.

Scenario #4: It was assumed that the doses drop linearly from 800 to 400 at 6 months and then linearly again to 200 pg TEQ_{DFP}-WHO_{98}/day at the end of one year. From there, doses again are as in Scenario #1.

Scenario #5: The 1 year dose of 200 pg TEQ_{DFP}-WHO_{98}/day assumes a mother's milk concentration of 6.25 ppt TEQ_{DFP}-WHO_{98} lipid, which represented a drop from an initial concentration of 25 ppt TEQ_{DFP}-WHO_{98} lipid. For purposes of this demonstration, it was assumed that the mother's milk concentration stays at 6.25 ppt TEQ_{DFP}-WHO_{98} lipid for the second year of breast-feeding. From there, doses again are as in Scenario #1.

The results from this exercise are shown in Figures 5-3 and 5-4, which show the lipid concentrations and the body burdens from birth up to 70 years of age (on Figure 5-3), and then these two quantities for the narrower time frame of from birth to 10 years of age (Figure 5-4). The body burden, defined as the whole body concentration, is simply calculated as the lipid concentrations times the lipid fraction. Other results for these 5 scenarios are provided in Table 5-5, including the peak TEQ_{DFP}-WHO_{98} concentrations in the infant, the time when the peak occurred, the "area under the curve" (AUC), corresponding to different times, and the ratio of that AUC for the breast-feeding scenarios and the AUC for formula feeding only. The AUC is defined as:

$$\mathbf{AUC} = \mathbf{\Sigma\ c(t)} \qquad \text{Eqn. (5-6)}$$

where:

AUC = area under the curve, ppt TEQ_{DFP}-WHO_{98}-day

c(t) = lipid-based concentration in the infant each day, ppt TEQ_{DFP}-WHO_{98}

The AUC is a measure of accumulated exposure. For example, a year at a lipid-based concentration of 10 ppt TEQ_{DFP}-WHO_{98} would yield an AUC of 3,650 ppt TEQ_{DFP}-WHO_{98}-day (10 ppt * 365 days). A lifetime at an average body lipid concentration of 10 ppt would yield an AUC of 255,500 ppt TEQ_{DFP}-WHO_{98}-day (10 ppt * 70 yrs * 365 days/yr). The AUC provides a parameter to compare accumulated exposure for different scenarios. For that reason, the ratios of the AUCs of the various breast-feeding scenario and the formula-only scenario are provided in Table 5-5. A ratio for a particular breast-feeding scenario of 6, for example, would mean that the accumulated exposure for that scenario is 6 times that of the breast-feeding only scenario. This can easily be translated to a

corresponding measure of percent above or below the baseline scenario of formula feeding only. For example, if the ratio is 6, this is equivalent to saying that the accumulated exposure for the breast-feeding scenario is 500 percent higher than the formula-only scenario ((6-1)*100 percent); if the ratio is 0.7, this is equivalent to saying that the accumulated exposure for the breast-feeding scenario is 30 percent lower than the formula-only scenario (-(0.7-1)*100 percent).

The lipid concentrations are predicted to rise to about 44 ppt TEQ_{DFP}-WHO_{98} for the 6-month,1-year, and 2-year scenarios. The time that these peaks occur is uniformly at 9 weeks. For the 6 week breast-feeding scenario, the peak is at 34 ppt and it occurs at the 6 week mark. Body burdens follow a similar trend, rising to about 9 ppt TEQ_{DFP}-WHO_{98} for both the 6-month, 1-year, and 2-year scenarios at 9 weeks. The body burdens decline for these breast-feeding scenarios, but the decline is slower as the duration of time for breast-feeding increases. For the 2-year scenario, the body lipid concentration stays near 40 ppt past 2 years of age (Figure 5-4). The six-week scenario shows a rise in infant body burden to above 30 ppt TEQ_{DFP}-WHO_{98}, but then shows a rapid decline, tracking the formula-only scenario fairly well after about age 2. From Figure 5-3, it appears that all four scenarios begin to merge at about age 10 years. The rise in concentrations seen in the later years in Figure 5-3 is due to the rise in body fat percent and the subsequent rise in half-life as predicted by elimination rate model of Pinsky and Lorber (1998).

The AUC results in Table 5-5 show how the accumulated exposure is higher for each of the breast-feeding scenarios as compared to the formula-only scenarios. This exceedance after one year is about a factor of 6 for breast-feeding for 6 months or more. Even for the first 10 years of life, the accumulated exposure is about 2 times higher for these breast-feeding scenarios as compared to formula feeding only. After a lifetime, the ratios suggest that breast feeding results in a lifetime exposure only 1.03-1.18 times higher than formula feeding, or expressed in terms of a percentage, from 3 to 18 percent higher than formula feeding only.

5.2.3.4. *Sensitivity Analysis*

A brief sensitivity analysis was conducted to study the impact of key parameters and assumptions on this exercise. Sensitivity analysis exercises typically focus on the parameters with these two characteristics: those that are the most uncertain and those

that have an important impact on the results. It was ascertained that the parameters: absorption, body weight, and lipid fraction, while important, are reasonably well known and assigned appropriate mid-range values for this exercise. The initial concentration in the infant at birth of 10 ppt TEQ_{DFP}-WHO_{98} lipid is an unknown, but testing showed that infant concentrations rapidly declined to about 5 ppt regardless of the initial concentration. Therefore, this parameter does not appear to influence results like peak concentrations or accumulated exposures. The two most important parameters, or groups of parameters, were those used to determine dose to the infant - mother's milk concentration initially and over time, and the dissipation rate of dioxin-like compounds in the infant. To test the influence that these parameters have on results, six sensitivity analyses were devised. These were all variations on a baseline scenario selected to be the 6-month breast-feeding scenario. The six scenarios were:

Scenario #1: Use of the Pinsky and Lorber (1998) lipid-based function for dissipation rate instead of the hybrid function used. The Pinsky and Lorber (1998) lipid-based function is shown in Figure 5-2. This is expected to result in an increase in the predictions of infant and childhood body impacts.

Scenario #2: Use of the Kreuzer et al. (1997) modeled dissipation rate throughout life instead of the hybrid function used. The Kreuzer et al. (1997) function is shown in Figure 5-2. This is expected to result in a decrease in predictions of infant, childhood, and adult impacts.

Scenario #3: Use of the assumption that mothers' milk concentrations do not decline from 25 ppt TEQ_{DFP}-WHO_{98} lipid during the 6 months of breast-feeding. This will obviously result in an increase in the impact to the infant.

Scenario #4: Use of the assumption that mothers' milk concentrations begin at 15 ppt TEQ_{DFP}-WHO_{98} and decline to 7.5 ppt TEQ_{DFP}-WHO_{98} after 6 months (instead of using concentrations that begin at 25 ppt TEQ_{DFP}-WHO_{98} and decline to 12.5 ppt TEQ_{DFP}-WHO_{98} after 6 months). The assignment of an initial concentration of 25 ppt TEQ_{DFP}-WHO_{98} is based on the finding that this represents a reasonable average of adult body concentrations of the sum of dioxin, furan, and dioxin-like PCB TEQs, described in Chapter 4. However, this average includes a wide age range of populations, including older individuals. As will be discussed in the next chapter on trends, higher exposures in the past have resulted in higher concentrations in older adults compared to today's younger

adults. It may be more reasonable to assume a woman of child-bearing age today would have concentrations closer to 15 ppt TEQ_{DFP}-WHO_{98} rather than the full adult population average of 25 ppt TEQ_{DFP}-WHO_{98}. Also, for children after the first-born, reduction in a woman's body burden of dioxin-like compounds could occur from prior breast-feeding.

Scenario #5: For this scenario, both assumptions that would lead to a higher impact - use of the Pinsky and Lorber (1998) lipid-based function for dissipation rate and the assumption of mother's milk concentration not declining from 25 ppt TEQ_{DFP}-WHO_{98} lipid - were used.

Scenario #6: In contrast to Scenario #5, both assumptions that would lead to a lower impact - the use of the Kreuzer et al. (1997) modeled dissipation rate and the assumption of mothers' milk concentrations beginning at 15 ppt TEQ_{DFP}-WHO_{98} and declining to 7.5 ppt TEQ_{DFP}-WHO_{98} after 6 months - were used.

Results from this sensitivity analysis exercise are shown in Table 5-6 and Figure 5-5. It is seen that all results range from a reduction of 40 percent (AUC ratio of 0.6) from baseline or an increase of 160 percent (AUC ratio of 2.6). The peak concentration can rise as high as 54 ppt TEQ_{DF}-WHO_{98}, as seen in Table 5-6 for Scenario #5 or as low as 28.5 ppt TEQ_{DF}-WHO_{98} for Scenario #6. Perhaps the biggest impact is seen in assuming the higher dissipation rate (lower half-life) for the childhood years. This is seen in Scenarios #4 and #6, with the lowest peak concentration and the steepest reduction from baseline: 30-40 percent. While the results displayed on Table 5-6 focus on the difference between the baseline 6-month scenario and sensitivity analysis scenarios, also of note is the difference between the two extremes as modeled by Scenarios #5 and #6. The peak concentration predicted for Scenario #5 (infant impact maximized) is about twice that of Scenario #6 (infant impact minimized): 54.0 versus 28.5 ppt TEQ_{DFP}-WHO_{98}. More importantly, the accumulated exposure from Scenario #5 is significantly higher than from Scenario #6. This can be seen In Figure 5-5, where the body concentrations are higher in Scenario #5 than #6 throughout the modeled lifetime, particularly for the first 10 years of life. After 10 years, the accumulated exposure, as measured by AUC, is about 4 times higher for Scenario #5 as compared to #6 (this results from the 10-year ratios of 2.6 and 0.7 displayed on Table 5-6, divided by each other; 2.6/0.7 = 3.7).

In short, when using this modeling approach to evaluate exposure-related impacts to infants from breast feeding, the assessor needs to be aware that assumptions relating

to the dissipation of dioxin-like compounds from infants, and the dose they receive through breast milk, are the two most important inputs. Data should be sought to further validate the selected modeling procedure and parameters, if possible.

5.3. SPORT AND SUBSISTENCE FISHERS

The possibility of high exposure to dioxin as a result of fish consumption is most likely to occur in situations where individuals consume a large quantity of fish from one location where the dioxin level in the fish is elevated above background levels. Most people eat fish from multiple sources, and even if large quantities are consumed, they are not likely to have unusually high exposures. However, individuals who fish regularly for purposes of basic subsistence are likely to obtain their fish from one source and have the potential for elevated exposures. Such individuals may consume large quantities of fish. U.S. EPA (1997) presents studies that indicate that Native American subsistence fishermen consume 59 g fish/day (as a mean) and 170 g fish/day (as an upper estimate). Wolfe and Walker (1987) found Native American subsistence fish ingestion rates up to 770 g/day in a study conducted in Alaska. Assuming that subsistence fishermen consume 59 to 170 g of freshwater fish per day as their primary source of protein (i.e., no meat or eggs are consumed) adult daily intake of CDD/CDFs/PCBs would be 2.2 to 5.7 pg/kg-day (Table 5-7). This estimate is based on the same CDD/CDF/PCB media concentrations exposure assumptions, and exposure algorithms as those presented in Chapter 4. The estimated values for subsistence fishermen are two to six times higher than the adult general population mean daily intake from all food sources of 0.94 pg/kg-day, as estimated in Chapter 4. It should be noted that fish ingestion rate data for subsistence fishermen are limited. The ingestion rate values used here pertain only to Native American subsistence populations (U.S. EPA, 1997), but are used to demonstrate the potential for elevated exposures among groups of individuals whose diets are known to consist of higher proportions of fish than the general population. Fish ingestion rates for sports fishermen would generally be lower than for the Native American subsistence population, but higher than for the general population.

Studies are underway to evaluate whether Native Americans living on the Columbia River in Washington have high dioxin exposures as a result of fish consumption. These Tribes consume large quantities of salmon from the river. As cited in U.S. EPA (1997), a

study conducted by the Columbia River Intertribal Fish Commission (1994) suggested that these individuals have an average fish consumption rate of 59 g/day and a 95th percentile rate of 170 g/day. These data were used in the estimated dietary intake calculations for subsistence fishermen, as shown above. Currently, studies are underway to measure dioxin levels in fish from this region.

Svensson et al. (1991) found elevated blood levels of CDDs and CDFs in high fish consumers living near the Baltic Sea in Sweden. Three groups were studied: nonconsumers (n = 9), moderate consumers (n = 9, 220 to 500 g/wk), and high consumers (n = 11, 700 to 1,750 g/wk). The high consumer group was composed of fishermen or workers in the fish industry who consumed primarily salmon (30 to 90 pg I-TEQ_{DF}/g) and herring (8 to 18 pg I-TEQ_{DF}/g) from the Baltic Sea. The I-TEQ_{DF} blood level was found to average about 60 pg I-TEQ_{DF}/g lipid among the high consumers and 20 pg I-TEQ_{DF}/g lipid for the nonconsumers. This difference was particularly apparent for the PeCDFs.

Asplund et al. (1994) also found elevated plasma levels of dioxin-like PCBs in Swedish fishermen who consumed large amounts of fish. A total of 37 individuals with varying intake rates of fish from the Baltic Sea was studied. These individuals were categorized as high-fish eaters, moderate fish-eaters, and nonfish-eaters. The estimated weekly intake of fish correlated positively with plasma PCB levels among this group (Table 5-8).

Cole et al. (1995) reported on CDD/CDFs and PCBs in 132 serum samples (pooled to 14) from Ontario Great Lakes anglers and control populations. Based on a preliminary survey, anglers from the communities of Cornwall and Mississauga, Canada, were categorized based on the numbers, species, and locations of fish caught and kept for consumption, and on data reflecting the contaminant levels for the fish in these areas. Individuals categorized as having the highest and lowest potential for having elevated body burdens of CDD/CDFs and PCBs were selected for biological sampling. Individuals who did not consume fish served as controls. Study participants were further categorized by age (i.e., <38 years, 38-50 years, and >50 years). The results, however, indicated that mean I-TEQ_{DF} levels were similar for both eaters and noneaters of Great Lakes' fish in these communities. I-TEQ_{DF}s ranged from 20.8 to 41.2 ppt for fish eaters and 24.7 to 36.8 ppt for noneaters. In general, mean I-TEQ_{DF}s increased with age (Table 5-9). PCBs 77, 126, and 169 were also evaluated in the serum samples collected from Cornwall

residents. Mean TEQ_P-WHO_{98}s ranged from 2.6 to 17.3 ppt for fish eaters and noneaters combined. Again, significant differences between the two groups were not observed and the serum CDD/CDF and PCB levels are within the range of values observed for the general population, as presented in Chapter 4.

Health departments of five Great Lakes states: Wisconsin, Michigan, Ohio, Illinois, and Indiana, formed a consortium to study blood levels of chemical residues in fish consumers of three Great Lakes: Michigan, Huron, and Erie. Anderson et al. (1998) reported on a feasibility study to determine which compounds might be found in very frequent Great Lakes sport fish consumers. Anderson et al. (1998) selected 32 angling enthusiasts who reported eating at least one sport fish meal per week from one of three Great Lakes (i.e., 11 Lake Huron anglers, 11 Lake Erie anglers and 10 Lake Michigan anglers). The analysis included examination of serum levels of 7 CDDs, 10 CDFs, 4 coplanar PCBs (i.e., 77, 81,126, and 169), and 32 other PCB congeners. One individual was excluded from the data summary due to unusually high occupational/environmental exposures. The blood CDD/CDF/PCB levels for these anglers were compared to CDD/CDF/PCB blood levels for a comparison group (n = 70) from Jacksonville, Arkansas. Data for this Arkansas population are discussed in Chapter 4. The comparison groups represented the general population with no known exposure to the contaminants of concern (Anderson et al., 1998). The mean CDD/CDF lipid adjusted serum concentrations for both the sport fishing populations and the comparison group used by Anderson et al. (1998) are shown in Table 5-10. The mean coplanar and other PCB lipid adjusted serum concentrations are reported in Table 5-11. The average lipid-based I-TEQ_{DFP} concentration for Great Lakes fish consumers was calculated at 56.8 ppt, with the breakdown as follows: I-TEQ_D = 27.5 ppt; I-TEQ_F = 11.9 ppt, and TEQ_P-WHO_{94} = 17.4 ppt. Anderson et al (1998) suggested that these values were higher than the background population used in the comparison.

The Anderson et al. (1998) study led to a larger study, in which the blood of 100 additional sport fishers were sampled, and a comparison population of 100 other individuals were sampled. Falk et al. (1999) reported on the results of the blood sampling from 96 (of the 100) additional sport fishers. Results for the 100 comparison population were not provided. Falk et al. (1999) presented results in terms of I-TEQ_{DF} and TEQ_P - WHO_{94} (congener-specific data were not provided), and also examined relationships

between the CDD/CDF/PCB measurements in blood and factors such as: age, gender, which Great Lakes the fish came from, the type of sport fish consumed, and amount of sport fish consumed, as reported by the participants. The median lipid-based TEQ_{DFP}-WHO_{94} from the 96 participants was 21.3 ppt, with the breakdown as follows: I-TEQ_D = 9.6 ppt; I-TEQ_F = 7.4 ppt, and TEQ_P-WHO_{94} = 4.3 ppt. This finding of 21.3 ppt TEQ_{DFP}-WHO_{94} appears significantly lower than the original finding of 56.7 TEQ_{DFP}-WHO_{98}. One reason for this is that the lower finding from the 96 participants was a *median*, while the finding from the 31 individuals in the pilot study was a *mean*. It also appears that the smaller population had a few individuals with very high levels of dioxins which resulted in a higher mean concentration. Other differences that could be identified from Anderson et al. (1998) and Falk et al. (1999) include: 1) the time of sampling of the two studies; 2) the age of the participants; and 3) the sport fish consumption rates. Anderson et al. (1998) reported that sampling of the initial 31 individuals in the pilot study occurred in 1993. Although Falk et al. (1999) did not identify the date at which the followup study occurred, it appears likely to have been in 1995 or 1996. Although not expected to be a large factor explaining the differences in the populations, it is possible that average body burdens within the population decreased during this time period. The mean age of the 31 participants in the pilot study was 52 years (range 36 to 76), while the mean age in the second population of 96 participants was 46 years (range 27-67). A clear age relationship has been demonstrated in other studies, showing that older individuals have higher body burdens of dioxins. The followup study population of 96 individuals clearly showed lower consumption of Great Lakes fish as compared to the pilot population of 31 individuals, as evidenced by questionnaire response data. The followup study population reported an average of 52 fish meals consumed per year, while the pilot group reported an average of 77 fish meals per year. Likewise, consumption of Great Lakes fish was lower for the followup group than the pilot group: 43 Great Lakes fish meals per year and 49 Great Lakes fish meals per year, respectively. Also, the followup group reported a lower number of years consuming Great Lakes sports fish (26 years) than the pilot group (33 years). In summary, while the larger population of 96 sport fishers in the full survey appeared to show a much lower body burden of dioxin-like compounds as compared to pilot population of 31 sport fishers, the differences could be explained by factors of data description (median vs. mean), year of sampling, age of participants, and exposure to dioxins in fish.

Another observation from the Anderson et al. (1998) study was that Lake Erie sport fish consumers had consistently lower CDD/CDF/PCB serum concentrations than consumers of sport fish from Lakes Michigan and Huron. Serum levels observed for the Lake Michigan and Lake Huron fish consumers were similar and higher than those observed in consumers of Lake Erie sport fish. These interlake differences parallel the pattern observed in previously reported EPA sport fish tissue monitoring data from the respective lakes (Anderson et al., 1998) and indicate that serum concentrations may also be affected by variations in fish concentrations among the lakes.

Kolic et al. (2000) reported on sampling of fish for dioxin-like CDD/F/PCBs conducted by the Ontario Ministry of the Environment between 1996 and 1998 in the Ontario Great Lakes region. Table 5-12 presents the data on this sampling effort as it was reported in Kolic et al. (2000). A total of 193 samples are reported on in Table 5-12. TEQ concentrations were calculated using the WHO 1998 TEF scheme, with zero values used for non-detects. When no congeners were detected in the sample, the value was reported as zero. Fish were sampled for the Ontario Sports Fish Program. This program monitors sport fish in the Ontario fresh water lakes and issues consumption advisories through its biannual guide. Because of this purpose, the fish sampled are typically larger and from suspect areas in order to obtain positive results and therefore be able to set consumption advisories (Reiner et al., 1995). An initial set of data on CDD/CDFs from this program were reported on in Reiner et al. (1995). Sampling reported there occurred between 1991 and 1994. Kolic et al. (2000) examined the data taken between 1996 and 1998 for purposes of studying the relationship between dioxin-like PCBs and CDD/CDFs in the fish. They observed PCB TEQ concentrations substantially greater that CDD/CDF TEQ concentrations in most locations, as is evident from Table 5-12. Over all lakes, they observe an average ratio of 6.5 (omitting the large value of 86 from the Welland River, as well as all circumstances when CDD/CDF TEQ concentrations are zero).

Also noteworthy is that the concentrations reported for these fish are substantially higher than the fish concentrations used for background exposure calculations in Chapter 5. CDD/CDF concentrations for marine and freshwater sources were 1.0 and 0.26 pg/g whole weight TEQ_{DF}-WHO_{98}, respectively. PCB concentrations were 1.2 and 0.25 pg/g whole weight TEQ_{P}-WHO_{98}, respectively. In contrast, the overall concentrations for this Great Lakes data set were 5.4 and 26.6 TEQ_{DF}-WHO_{98}/g whole weight for CDD/CDFs and

PCBs, respectively. As observed by Kolic et al. (2000), CDD/CDF concentrations appeared to be declining since their earlier reporting in 1995. At that time, Reiner et al. (1995) reported on 198 samples, and the average I-TEQ_{DF} concentration was 11.5 pg/g whole weight.

Hong et al. (1994) analyzed PCBs in human milk from Mohawk and control women to evaluate the potential effect that relatively high levels of environmental contamination may have had on the body burdens of lactating Mohawk women in New York. PCBs were found to be present in fish and wildlife in the vicinity of the Mohawk Reservation, and the Mohawk people formerly depended on local fish and wildlife for food. However, no significant differences were observed between the mean total dioxin-like PCB levels in milk from 30 Mohawk women and the 20 control women. The mean PCB concentrations for these women were 49 ppb and 55 ppb, respectively. The age of the mother, the length of the nursing period, and the number of breastfed children were found to influence PCB levels in human milk. Older women, mothers of first born children, and smokers had higher levels of PCBs. PCB levels were also higher at the onset of lactation and in earlier samples during a breastfeeding session.

Dewailly et al. (1994) observed elevated levels of dioxin-like PCBs in the blood of fishermen on the north shore of the Gulf of the St. Lawrence River who consume large amounts of seafood. Of the 185 study samples, the 10 samples with the highest total PCB levels were analyzed for dioxin-like PCBs. Samples from Red Cross blood donors in Ontario served as controls. Dioxin-like PCB levels were 20 times higher among the 10 highly exposed fishermen than among the controls (Table 5-13). Based on these results of the 10 highest samples, Dewailly et al. (1994) estimated that for the entire fishing population studied, dioxin-like PCB levels would be eight to ten times higher than the control group. Dewailly et al. (1994) also observed elevated levels of dioxin-like PCBs in the breast milk of Inuit women of Arctic Quebec. The principal source of protein for the Inuit people is fish and sea mammal consumption. Breast milk samples were collected from 109 Inuit women within the first 3 days after delivery and analyzed for di-ortho-dioxin-like PCBs during 1989 and 1990. Subsets of 35 and 40 randomly selected samples were analyzed for mono-ortho dioxin-like and non-ortho dioxin-like PCBs, respectively. Samples from 96 Caucasian women from Quebec served as controls. The levels of non-ortho dioxin-like PCBs for Inuit women ranged from 24.7 to 220.9 ppt.

These values were three to seven times higher than those observed in the control group. For mono-ortho and di-ortho dioxin-like PCBS, the levels among the Inuit women were three to ten times higher than in the control group.

Humphrey et al. (2000) reported on an elevation in the PCB concentrations in serum of humans consuming Great Lakes fish. They described a careful identification of "sport fish eaters" and "non-sport fish eaters," or controls, from 11 Lake Michigan shoreline communities during the years 1979 and 1982. Sport fish eaters were defined as those individuals who consumed 26 or more pounds of sport-caught fish annually, while non-sport fish eaters consumed less than 6 pounds of sport-caught fish annually. This cohort was revisited a second time in 1992 for a study of individuals over the age of 50. Blood sampling occurred in 1993-1995 for 101 fish-eaters and 78 controls. These samples were measured to 90 PCB congeners, including dioxin-like PCB congeners 77, 105, 118, 123, 157, 169, and 180. They found that sport fishers had significantly higher PCB concentrations as compared to controls. The mean concentration of total PCBs (sum of the 90 measured) in the fish-eaters was 14.26 ppb whole weight, while for the controls, the concentration was 4.56 ppb. They found that 22 of the congeners explained most of the concentration, and dioxin-like PCBs 105, 118, and 180 were among those 22. The whole weight concentrations (ppb) of these three PCBs in sport and control fishers were 2.00 (fishers) vs. 0.79 (control) for PCB 180; 0.26 vs. 0.02 ppb for PCB 105; and 0.83 vs. 0.06 for PCB 118.

5.4. LOCALIZED IMPACTS

Data have been collected that demonstrate that localized impacts may occur from emissions of dioxins from incinerators and other potential sources. "Localized impacts" are defined as measurements of CDD/CDFs in environmental (air, soil) or biotic (vegetation, animal tissue) samples near incinerators or other sources that show elevation above typical background levels for the area being studied. Therefore, "impacts," as used below, refer to elevation above background. These localized impacts may result in elevated exposure among some members of the population. Most of the data on localized impacts originate from studies conducted outside the United States, specifically from the European countries of England, Switzerland, Germany, Austria, The Netherlands, Belgium, and France. Data collected include concentrations of dioxins in air and soil, biota including

grass and cow's milk, as well as human blood and hair samples. This section reviews several of these studies, primarily discussing results in terms of TEQs from CDD/CDFs only. Following a review of the studies, the principal findings with regard to localized impacts are summarized.

Goldman et al. (2000) compared serum concentrations of CDD/CDFs among residents of 2 homes where contaminated home-produced eggs and beef were consumed to residents of a similar rural area that did not consume home-produced eggs and beef. The contaminated eggs and beef originated from a residence located near the site of a 1987 fire at a wood preservative plant. The chicken eggs had an I-TEQ_{DF} mean concentration of 10 pg I-TEQ_{DF}/g; beef fat contained 27 pg I-TEQ_{DF}/g. These concentrations are 10- to 100-fold higher than the results observed in samples of commercial foods. The soil near the home where contaminated eggs were observed contained CDD/CDF levels ranging from 30 to 40 pg I-TEQ_{DF}/g, and the soil CDD/CDF profile was similar to that observed in the eggs. Serum samples were collected from 9 individuals residing in homes where contaminated eggs and beef were consumed. I-TEQ_{DF} concentrations in serum were 26.7 ppt for the 4 individuals who had consumed eggs from the contaminated site over a 2-year period and 63.7 ppt for the 5 individuals who had consumed both eggs and beef from the contaminated site for up to 15 years, compared to 17.0 ppt for the comparison group.

Beck et al. (1990) sampled milk from a rural and an industrial area in Germany, and from dairies near a metals reclamation plant in Austria. Beck et al. (1990) observed average lipid-based concentration of 0.9 pg I-TEQ_{DF}/g in rural, background milk, 2.5 pg I-TEQ_{DF}/g in "industrial milk," and 9.6 pg I-TEQ_{DF}/g in the milk obtained from dairies near the metals reclamation plant. The dairy nearest the metals reclamation plant was located about a kilometer in the downwind direction and had the highest milk concentration (i.e., 14 pg I-TEQ_{DF}/g).

The Austrian metals reclamation plant described above has also been studied for impacts to air, soil, vegetation, and human blood by another research team (Riss et al., 1990; Riss, 1993). The plant was located in a rural Alpine river valley in Tyrol, Austria, in a mostly agriculture area. Although emissions data were unavailable, air concentrations measured near the incinerator were 1.2 to 2.3 pg I-TEQ_{DF}/m^3 (Riss, 1993). These data suggest very high emissions, because typical urban air concentrations are approximately

0.10 pg/m^3 in Europe as well as in the United States, and rural air concentrations are typically less than 0.05 pg I-TEQ_{DF}/m^3. (See Chapter 3.) Soil concentrations averaged 420 pg I-TEQ_{DF}/g at the site of the incinerator, 170 pg/g within 200 meters of plant, and 46 ppt about 2 km in the downwind direction (Riss et al., 1990). This compares with typical urban soil concentrations of approximately 10 to 20 pg I-TEQ_{DF}/g in both Europe and the United States and rural soil concentrations of less than 5 pg I-TEQ_{DF}/g. (See Chapter 3.)

A dairy farm was located between 1,400 and 2,100 meters from the same metals reclamation site in the downwind direction, and members of that farming family consumed milk from their own cows. Samples of the cows milk ranged from 20.1 to 69.5 pg I-TEQ_{DF}/g on a lipid basis. Given a general background level of milk in the low to sub ppt level on a lipid basis, it is clear that the milk showed elevated dioxin levels. (See Chapter 3.) Samples in the grass and hay from that farm were also elevated at 13 to 36 pg I-TEQ_{DF}/g dry weight. This compares to typical grass samples found in rural areas at the low to sub ppt levels (Reed et al., 1990; Kjeller et al., 1991; 1996). Blood samples from two farmers who consumed this milk were also elevated. Their blood CDD/CDF concentrations were 152 and 946 pg I-TEQ_{DF}/g on a lipid basis. Subsequent samples from three additional family members were also slightly elevated above typical levels at 41, 66, and 77 pg TEQ_{P}-WHO_{94}/g lipid.

The Austrian samples described above were taken in the late 1980s, before emission controls and other practices (i.e, removal of some plastics) were undertaken to reduce emissions from these plants. Riss (1993) reported on reductions in both cow's milk and fodder from this nearby farm in the early 1990s and speculated that they resulted from reductions in incinerator emissions. CDD/CDF concentrations in cows' milk dropped steadily from a high in 1987/88 samplings, averaging 49 pg I-TEQ_{DF}/g fat, to an average of 5 pg I-TEQ_{DF}/g fat in the 1992/93 sampling. Grass concentrations similarly dropped from 33 pg I-TEQ_{DF}/g dry weight to 4 pg I-TEQ_{DF}/g dry weight between the two sample dates. This trend demonstrates an important expectation with regard to environmental responses to reductions in emissions from tall industrial stacks. Specifically, vegetation appears to respond immediately to reduced air concentrations, and if dairy cows are being fed with vegetation that has reduced concentrations, cow's milk should similarly respond in a rapid manner. Fries and Paustenbach (1990) stated that a

steady state is reached in cow's milk with a constant dietary input of dioxins after about 30 to 60 days. Therefore, reductions in emissions will result in both a reduction in vegetation and cow's milk concentrations almost simultaneously.

Another study was conducted in Austria by Moche and Thanner (1997). The study evaluated ambient air patterns and CDD/CDF concentrations in a vicinity of steel production plants in Leoben/Donawitz. Samples were collected from sites in the immediate vicinity of the production plants, in an area that was expected to be impacted by the production plants, and in an area that was shielded by mountains in the northwest. Sampling occurred over four periods to address the potential influence of the summer and winter fluctuations in CDD/CDF concentration. The CDD/CDF concentrations in these samples were compared to previous data collected in the three Austrian conurbations Graz, Linz, and Wien. The previous data suggested average summer levels of CDD/CDFs in the range of 20 to 40 fg I-TEQ_{DF}/Nm^3 and winter levels in the range of 50 to 220 fg I-TEQ_{DF}/Nm^3. The data collected at Leoben/Donawitz indicated higher ambient air levels of CDD/CDF concentrations. Only the levels in the area shielded by mountains fall within the levels of the previously reported data. In addition, the CDD/CDF profiles of the Leoben/Donawitz sites indicated a high contribution of the lower chlorinated CDFs (tetra- through hexachlorinated CDFs as the most abundant). The patterns were in good agreement with emission profiles of metallurgical processes reported by Hagenmaier et al. (1994) (Moche and Thanner, 1997).

Liem et al. (1991) reported on the analysis of over 200 samples of cow's milk that were taken in various regions in The Netherlands, including some that were near municipal solid waste incinerators and metals reclamations plants, and some identified as background sites. Background levels ranged from 0.7 to 2.5 pg I-TEQ_{DF}/g lipid. The highest levels were found approximately 2 km from the largest municipal solid waste incinerator identified at the time, with concentrations ranging from 2.8 to 12.6 pg I-TEQ_{DF}/g lipid. Higher than background levels were also found in samplings near other incinerators. The researchers did a principal component analysis on congener profiles in the milk samples to determine if there were any discernable differences among groupings of samples. Liem et al. (1991) observed a distinct pattern for samples around the metals reclamation plant compared to samples around municipal solid waste facilities. A higher CDF/CDD ratio was found around the metals reclamation plant (i.e., higher furan

concentrations were in the milk near the metals reclamation plant than near the municipal solid waste incinerator). Liem et al. (1991) speculated that metals reclamation plants process cables that contain PVC, and according to Christmann et al. (1989), furans are predominantly formed in the combustion of PVC. Subsequently, the higher levels of furans would be taken up into vegetation and then into cow's milk. Liem et al. (1991) also found distinct patterns in samples associated with other facilities, as characterized by the relative amounts of lower and higher chlorinated congeners. Two of the incinerators were closed in April of 1990, and a marked decrease in sample concentrations associated with these two incinerators was noted between the February and August 1990 sampling. This supports the expectation described above regarding the response of vegetation and milk to changes in nearby source emissions.

A limited sample from six cows in Switzerland showed similarly elevated CDD/CDFs in association with incinerators or manufacturing sites. Higher CDD/CDF concentrations were observed in milk samples that were within 1,000 meters of an incinerator (two samples) and those that were within 1,000 meters of a production site for various chlorinated samples (one sample) than samples from a background farm (one sample) and from local dairies that pooled milk from several farms (two samples) (Rappe et al., 1987). Insufficient information was available in this report to calculate I-TEQ_{DF} concentrations.

De Fre and Wevers (1998) evaluated paired CDD/CDF deposition and cow's milk data from several locations in Belgium to evaluate the relationship between deposition rates and milk levels, and the potential impact that elevated deposition rates may have on local milk supplies. CDD/CDF deposition ranged from approximately 2 ng I-TEQ_{DF}/m^2/year to 45 ng I-TEQ_{DF}/m^2/year, and CDD/CDF concentrations in milk fat ranged from approximately 1 pg I-TEQ_{DF}/g to 19 pg I-TEQ_{DF}/g. The correlation coefficient (R) for CDD/CDF deposition rates and milk fat concentrations was 0.69. The results of a regression analysis using these data indicated that milk fat concentrations of I-TEQ_{DF}s could be predicted from deposition rates using the equation $y = 0.3332x$, where y is the milk fat concentration of CDD/CDFs in units of pg TEQ_{DF}/g and x is the CDD/CDF deposition rate in units of ng TEQ_{DF}/m^2/y.

In France, the Ministry of Agriculture and Fisheries investigated CDD/CDF concentrations in cow's milk sampled from farms in a downwind direction within 11 km, but mostly within 5 km, of 26 industrial facilities (Defour et al., 1998). These industries

included: steel manufacturing, secondary lead and aluminum smelting, copper refining, chemical and oil refining industries, electricity production, and municipal waste incinerators. Of the 49 milk samples analyzed, 46 samples had CDD/CDF concentrations that were less than 3 pg I-TEQ_{DF}/g fat with an average of 1.53 pg I-TEQ_{DF}/g on milk fat basis. One milk sample collected from a site near a chemistry industry was found to contain 3 to 5 pg I-TEQ_{DF}/g fat, and two milk samples collected 250 m and 1 km downwind of incinerators had concentrations higher than 5 pg I-TEQ_{DF}/g fat. The average concentration in milk and diary products in France assessed through a 1996 survey conducted by the Ministry of Agriculture and Fisheries was 1.33 pg I-TEQ_{DF}/g fat (Defour et al., 1998).

Abraham et al. (1998) reported on the levels of CDD/CDFs in the human milk of 10 mothers who lived within a radius of 8 km of Ilsenburg, Germany. The town was identified as an area highly contaminated with CDD/CDFs reportedly resulting from emissions from a copper plant. At the time of sample collection (i.e., 1997) the plant had been closed for approximately 6 years, Abraham et al. (1998) compared the findings to the results of a previous study of human milk levels conducted in 1990/1991 when the plant was still in operation. The 1990/1991 human milk samples contained a mean I-TEQ_{DF} of 59 ppt, lipid based (n = 9). The 1997 human milk samples contained a mean I-TEQ_{DF} of 41 ppt, lipid based (n = 10). Abraham et al. (1998) documents that this decrease in CDD/CDFs is lower than the decline reported in general background concentrations in human milk from Western Germany in recent years. These values are somewhat higher than the values reported in Chapter 4 for the general population of the United States.

An extensive study was undertaken in the Pontypool environment of South Wales (Ball et al., 1993; Ball et al., 1994a; Ball et al., 1994b; Ball et al., 1995). Evidence of the impact of emissions from waste incineration at Rechem International Ltd. (a chemical company) prompted extensive investigations into impacts from emissions of PCBs and CDD/CDFs to nearby and regional media including soil, grass, water, air, fruit/vegetables, cow's milk, duck meat, and eggs from chicken and ducks. The region has a combination of residential and industrial uses, with very little agricultural uses. The greatest impact was found at a residence adjacent to the site, located only about 100 meters away. The soil at Rechem International averaged 810 pg I-TEQ_{DF}/g (n = 4), while at this nearby

residence, the concentration averaged 66 pg I-TEQ_{DF}/g (n = 8). Other areas evaluated ranged from 4 to 24 pg I-TEQ_{DF}/g. Data were not available on CDD/CDF emissions, but air measurements at this residence suggested high emission rates. For five air samples taken at the residence, air concentrations ranged from 1.6 to 14.8 pg I-TEQ_{DF}/m^3. This compares to air concentrations ranging from 0.02 to 0.68 pg I-TEQ_{DF}/m^3 taken from a site about 2,500 meters away in the same direction from the Rechem site. The researchers also compared these air concentrations to average air concentrations ranging from 0.21 to 0.67 pg I-TEQ_{DF}/m^3 in four other UK urban areas. Concentrations of CDDs/CDFs in grass were found to be elevated at the same residence, but described as more typical for other grass sampling sites. Perhaps most importantly, samples of duck and bantam eggs from this residence showed concentrations that exceeded other duck and bantam egg samples in the area by a factor of 10. Duck and bantam egg concentrations in the area, but not at this residence, were described as typical of background. Duck meat at the impacted residence was not described as elevated compared to duck meat from nearby settings. Sampling of sediments in a nearby reservoir did not indicate elevated concentrations of dioxins or PCBs. There was no sampling of human blood or tissue. However, a simple exposure exercise showed that consumption of duck eggs, duck meat, apples, inhalation, and incidental soil ingestion at this impacted residence would result a daily intake of 165 pg I-TEQ_{DF}/day, compared to a background intake from these pathways of 43.2 pg I-TEQ_{DF}/day (consumption rates described as typical derived from consumption data from the Ministry of Food and Fisheries in the UK).

Foxall et al. (1997) also reported geographical variations in environmental levels and human exposure to CDD/CDFs and PCBs of the above study. The data indicated a particular impact in a 200-meter wide strip of land around the boundary of the incineration plant owned by Rechem International Ltd. This location is predominantly downwind from the incinerator and there had been evidence suggesting that fugitive emissions from the plant contributed to the environmental impacts. Marked differences were noted between the CDD/CDF and PCB content of samples (i.e., air, soil, and foods) collected at the impacted site and those collected at rural background locations. Intakes of CDD/CDFs (pg I-TEQ_{DF}/day) and PCBs (μg/day) were estimated using mean daily food consumption rates, inhalation and soil ingestion rates of 20 m^3/day and 100 mg/day, respectively, and the median concentrations of CDD/CDFs and PCBs found in the samples. These estimates

indicated that exposure to CDD/CDFs and PCBs at the impacted site was much higher than for background levels and the main contributors to these higher levels were residues in bantam and duck eggs. The estimated intake of CDD/CDFs from ingestion of bantam or duck eggs at the impacted site were 204 pg I-TEQ_{DF}/day and 103 pg I-TEQ_{DF}/day, respectively; levels that are substantially higher than the average UK dietary intake of 88 pg I-TEQ_{DF}/day from all food sources. Based on a body mass of 60 kg, these egg intakes (i.e., 3.4 and 1.7 pg I-TEQ_{DF}/kg body mass/day) would represent 34 and 17 percent of the WHO (World Health Organization) TDI (Total Dietary Intake) value of 10 pg I-TEQ_{DF}/kg body mass. Similarly, the corresponding PCB intake of 7.3 and 6.3 μg/day would represent 73 and 63 percent, respectively, of an average dietary intake (10 μg/day) of PCBs.

Lovett et al. (1998) performed additional analysis of chicken, bantam, and duck eggs; and also duck meat collected from the vicinity of the Rechem incinerator and compared the results to PCB and CDD/F levels of comparable foodstuffs collected from rural areas in the same Welsh district. Poultry produced at the impacted residence displayed a congener profile with noticeable variations compared to those collected from nearby rural sites. A prominence of higher chlorinated congeners in the egg and duck meat samples for the residence located near the incinerator was observed. Analysis of 46 PCB congeners resulted in a median fresh mass total PCB concentration in duck eggs of 191 μg/kg (n = 2), 341 μg/kg in bantam eggs (n = 2), and 43 μg/kg in duck meat (n = 2) from samples collected in the impacted area. Observations from rural areas showed fresh mass based total PCB concentrations of 14 μg/kg for duck eggs (n = 6), 22 μg/kg for bantam eggs(n = 4), and 25 μg/kg for duck meat (n = 6).

A second location in the United Kingdom, the Derbyshire area in central England, has shown elevations in cow's milk and other animal tissues. Initially, samples of cow's milk were taken by the Ministry of Agriculture, Fisheries, and Food (MAFF) from individual farm tanks on 11 farms in 1990. When 2 of the samples showed high concentrations of 40 and 42 ng I-TEQ_{DF}/kg fat (the other 9 showed more typical concentrations in the 1.1 to 7.1 ng I-TEQ_{DF}/kg fat), the sampling was expanded to 30 farms. These original two farms, plus an additional farm, continued to show high concentrations in the milk. Testing continued in milk through 1994. Milk concentrations dropped at one farm, but overall concentrations appeared to remain high (i.e., 29 ng I-TEQ_{DF}/kg) for the most recently

reported sampling in July of 1994 (Harrison et al., 1996). As a result of these findings, MAFF tested animal tissue from the three farms. Calves from one of the three farms had extremely elevated levels of dioxins and furans, with concentrations ranging from 2.5 to 6.9 ng I-TEQ_{DF}/kg whole weight (i.e., not lipid basis) in muscle tissue (MAFF, 1992a). This compares, for example, with I-TEQ_{DF} concentrations approximately 0.20 ng I-TEQ_{DF}/kg in the United States beef supply (from the national study on beef back fat, assuming 19 percent fat in whole beef (Winters et al., 1996). Egg samples were taken from one of the three farms and a second "free range" supplier. The concentrations found were reported as 2.2 and 2.1 ng I-TEQ_{DF}/kg in whole eggs. A second sample from one of the farms taken a year later showed a lower concentration of 0.8 ng I-TEQ_{DF}/kg whole weight. These would appear to be elevated, considering that eggs found in a background setting in Mississippi (Cooper et al., 1995), had concentrations less than 0.10 ng I-TEQ_{DF}/kg whole weight.

MAFF (1992b) also sampled leafy herbage (grass, hay, etc.) from the three farms described above. Concentrations ranged from about 2 to 14 ng I-TEQ_{DF}/kg dry weight. This appears elevated, considering that samplings of background grass in England showed 0.89 ng I-TEQ_{DF}/kg dry weight, as reported in 1991 (Kjeller et al., 1991) and 0.57 ng I-TEQ/kg dry weight in 1996 (Kjeller et al., 1996). The evidence suggests that the impacts were due to nearby industrial emissions from a fuel plant and chemical waste incineration. Her Majesty's Inspectorate of Pollution (HMIP) conducted additional studies to evaluate this possibility. These included stack testing of the Coalite Fuels, Ltd. and the Coalite Chemicals, Ltd. (which were adjacent to one of the farms and near the other two), air dispersion modeling, and soil monitoring. No results were available to evaluate the stack testing, but the air dispersion modeling predicted that the three impacted farms would be in the sectors having the highest air concentrations. The soil sampling on the three farms showed concentrations ranging from 10 to 90 ppt. This can be considered elevated above typical rural background and in the range or even higher than typical urban concentrations. Specifically, this compares with typical urban soil concentrations of 10 to 20 pg I-TEQ_{DF}/g in both Europe and the United States, and rural soil concentrations typically less than 5 pg I-TEQ_{DF}/g. (See Chapter 3.) Also, these concentrations are similar to concentrations found near incinerators emitting very high concentrations of dioxins in Tyrol, Austria, as described above, and in Columbus, Ohio, as described below. The

National Rivers Authority sampled sediment upstream and downstream of the effluent discharge pipe of the Coalite Chemicals, Ltd site. Samples collected about 1.5 km downstream of the discharge site had CDD/CDF levels that were 1,000 times greater than background samples collected 1.5 km upstream of the discharge point (these studies reported in MAFF, 1992a).

Another interesting finding associated with the samplings of foods and environmental media in the Derbyshire area were the congener profiles. Compared to background milk samples, the samples from the three impacted farms had proportionally higher concentrations of lower chlorinated dioxins, particularly 2,3,7,8-TCDD and 1,2,3,6,7,8-HxCDD. The background samples of milk tended to be dominated by OCDD (MAFF, 1992b). Blood samples were also collected from residents of these three impacted farms and analyzed for CDD/CDFs (Startin et al., 1994). The I-TEQ_{DF} concentrations for the 10 individual blood samples ranged from 49 pg/g to 291 pg/g on a lipid basis. In contrast, the two control samples had I-TEQ_{DF} concentrations of 16 pg/g and 26 pg/g on a lipid basis. The Derbyshire samples were dominated by OCDD, followed by 1,2,3,4,6,7,8-HpCDD, 2,3,7,8-TCDD, and 1,2,3,6,7,8-HxCDD.

Sandalls et al. (1998) analyzed soil concentrations around the site of a chemical waste incinerator near Bolsover, Derbyshire, United Kingdom. At each of 46 sites, five surface soil samples were collected, at varying depths up to a depth of 5 centimeters, every 1 square meter. All 46 sample sites had total TCDD concentrations exceeding background concentrations. Higher concentrations of TCDD were observed at locations closer to the incinerator and there was a strong correlation between the TCDD concentration in a given quadrant and the amount of time that the wind was blowing in that direction. At four quadrants around the site, TCDD soil concentrations were reported as 603 ppt for the northeast (approximately 42 percent of the total deposition); 315 ppt for the southeast (22 percent of the total); 269 ppt for the southwest (19 percent of the total); and 244 ppt (17 percent of the total) for the northwest. The results of the spatial distribution of CDD/CDFs implicated the incinerator as the likely source, and the correlation between deposition and wind direction suggested that these compounds reached the ground via the atmosphere. Also, 42 of the 46 sample sites showed similar CDD/CDF congener ratios to the flue gas of the waste incinerator. Soil concentrations were well in excess of background concentrations, up to 5 kilometers around the site.

Ohta et al. (1997) studied levels of CDD/CDF and non-ortho coplanar PCBs in soil at a high cancer-rate area close to a batch-type municipal solid waste (MSW) incinerator in Japan. Sixty-one soil samples were collected around the MSW incinerator. Among them, 52 samples were radially collected within 2 km from the center of the MSW incinerator, and 9 samples were collected across the high cancer-rate area. High concentrations of CDD/CDFs and coplanar PCBs were observed in all the soil samples from the leeward side of the MSW incinerator. Total concentrations ranged from 5,303 to 32,167 pg/g; mean = 13,934 pg/g. On the other hand, all but one sample on the windward site showed high contamination. Among the 61 samples analyzed, the total concentration was greater than 2,000 pg/g in 45 of the 61 samples and the TEQ_{DFP}-WHO_{94} concentration was over 10 pg/g in 39 of the 61 samples. In addition, the levels of CDD/CDFs and coplanar PCBs at a distance of 0 to 1.1 km from the MSW incinerator was compared with that of the area 1.1 to 2.0 km from the MSW incinerator. The area closer to the incinerator contained a higher ratio of samples with contamination over 5,000 pg/g (63.2 percent) than in the area further away from the MSW incinerator (38.5 percent). Similarly, the area closer to the incinerator had a higher percentage of samples with CDD/CDF/PCB levels over 30 pg TEQ_{DFP}-WHO_{94}/g (26.3 percent) than the area further away from the incinerator (15.3 percent).

Miyata et al. (1998) collected blood samples from residents living within 2 km from a batch-type municipal solid waste incinerator in Japan where soil concentrations of CDD/CDFs and PCBs were shown to be elevated. Eighteen blood samples were collected from 13 men, aged 23 to 63 years old (average age = 45 years), and 5 women, aged 30 to 72 years old (average age = 46 years) in March 1996. The results indicated that the average lipid-based TEQ_{DFP}-WHO_{94} concentrations found in blood samples ranged from 34 pg/g to 200 pg/g with a mean of 81 pg/g for men, and from 22 pg/g to 463 pg/g with a mean of 149 pg/g for women. These mean TEQ_{DFP}-WHO_{94} values are higher than those reported for the general population of various countries (the mean value estimated in Chapter 4 of this document is 55 pg/g).

Local impacts around a waste-to-energy municipal solid waste incinerator in Columbus, Ohio, were undertaken by the Ohio Environmental Protection Agency, and the U.S. Environmental Protection Agency (Lorber et al., 1998). This incinerator operated between 1983 and 1994. A stack test was taken in 1992, and when the results were

extrapolated to typical operation of the incinerator, annual emissions were calculated at 985 g I-TEQ/yr. This is a very high emission rate, and compares to total emissions from several European countries. It is about one-tenth of the national emissions estimated for all United States sources. (See Volume 1.) Process modifications were undertaken in the winter of 1993/94. A stack test was conducted which indicated that annual emissions were reduced to 267 g I-TEQ_{DF}/yr. The U.S. EPA undertook a soil testing program in December of 1995. Results showed a definite impact to soils at the site of the incinerator, with an average concentration of 356 pg I-TEQ_{DF}/g (n = 4). Of the four samples collected, three of the samples averaged 458 pg I-TEQ_{DF}/g and the fourth was much lower at 50 g I-TEQ_{DF}/g. Just offsite in the downwind direction, a cluster of four samples within 1,000 meters also showed some elevation of CDD/CDFs with an average concentration of 49 pg I-TEQ_{DF}/g. Fourteen additional samples, generally within 2 miles of the site, averaged 10 pg I-TEQ_{DF}/g. Three soil samples at a background site 28 miles away in the upwind direction averaged 1 pg I-TEQ_{DF}/g. These latter two clusters of urban and background samples have concentrations that are typical of urban and background situations. The urban results suggests that, despite large emissions from this source, soil impacts above typical levels appeared to be restricted to within 1,000 meters of the incinerator.

The Ohio EPA conducted air monitoring in 1994 and 1995 (OEPA, 1994; Lorber et al., 1998). Monitoring in 1994 occurred after process modifications were undertaken to reduce dioxin emissions. A stack test conducted just prior to the air sampling showed reductions of 75 percent from the levels measured in 1992. Wind rose data were taken on an hourly basis during the 1994 sampling. This showed that two samples from a sampler located about 2 miles away were in the downwind direction during the 48-hour sampling period. Eight other samples from four samplers (which were between 1 and 2 miles from the incinerator) were clearly not in the downwind direction. The two downwind samples averaged 0.26 pg I-TEQ/m^3 CDD/CDFs, while the eight upwind samples averaged 0.05 pg I-TEQ_{DF}/m^3. The incinerator shut down in December 1994. Five samples taken in 1995 showed an average of 0.05 pg I-TEQ_{DF}/m^3 CDD/CDFs. This air sampling suggests the following: (1) the typical background urban air CDD/CDF concentration in Columbus is probably around 0.05 pg I-TEQ_{DF}/m^3; and (2) when the incinerator is emitting dioxins typical of the rate measured in the 1994 stack test (not the

1992 stack test), air concentrations about 2 miles away are higher, perhaps by a factor of 5. Other media, including vegetation, agricultural products, or human blood were not sampled.

Schecter and Papke (1998) examined CDD/CDFs and PCBs 77, 126, and 169 in blood sampled from 10 residents living near a PCB manufacturing facility in Alabama in 1997, and compared these concentrations to a pooled sample from a control group representing 100 adults. The results showed that, for the 10 residents, total lipid-based CDD/CDF concentrations ranged from 825 ppt to 6,422 ppt. The corresponding total CDD/CDF concentrations from the pooled control sample was 1,112 ppt. Total PCB concentrations ranged from 240 ppt to 5,216 ppt for the 10 nearby residents, compared to 1,112 ppt for the pooled control sample. PCB-77 was only detected in the blood of 5 of the 10 residents, ranging from 41 ppt to 713 ppt. PCB-126 concentrations ranged from 104 ppt to 4,050 ppt in residents, compared to 48 ppt found in the control sample. PCB-169 concentrations ranged from 136 ppt to 2,807 ppt for the 10 residents, compared to 35 ppt for the control sample. In terms of TEQ, the total I-TEQ_D and I-TEQ_F concentrations ranged from 16.3 ppt to 38.9 ppt, and from 6.7 ppt to 131 ppt, respectively, compared with 18.5 ppt and 8.3 ppt from the control blood. TEQ_P-WHO_{94}s ranged from 34 ppt to 360 ppt compared to 32 ppt for the control blood.

There were also studies conducted in Asia to address localized impacts. Luksemburg et al. (1997) reported, in a preliminary study, that high levels of CDD/CDFs were observed in soil and sediment samples collected inside and outside a sodium pentachlorophenate plant in Tianjin, China. The plant is situated in a wetland with rivers emptying into the nearby Pacific Ocean and close to several large housing developments. Human hair samples collected from barber shops in the housing developments near the plant were also collected and CDD/CDFs were detected in these samples. The I-TEQ_{DF} concentrations in soil ranged from 15 ppt at a site upstream of the plant to 740,000 ppt within the plant, and was 1,800 to 2,200 ppt at sites outside the plant. The I-TEQ_{DF} concentrations in sediment ranged from 150 ppt at a site 50 km away from the site to 110,000 ppt in a drainage canal located just southwest of the plant. Hair samples contained I-TEQ_{DF} concentrations ranging from 12 to 120 ppt. According to Luksemburg et al. (1997), "the isomer profiles of all the samples were consistent with the

pentachlorophenol sources." However, it should be noted that no background information on the test subjects (time of residence, health records, etc.) were collected in this study.

The major findings and conclusions based on this review of localized sources include:

- Localized impacts, meaning elevated concentrations of CDD/CDFs above background, have been found in the vicinity of some CDD/CDF sources.

- Localized impacts appear to be limited to an area within 5 km of an incinerator source, perhaps only within 2 to 3 km of the source, and in some cases, only within a few hundred meters of the source. One study noted elevations in grass, cow's milk, and human blood on a farm located 2 km from an incinerator presumed to be emitting high amounts of CDD/CDFs. Not all of the studies described in the literature discussed distance from the source, as the surveyed areas were simply identified as "industrial."

- Several studies continued environmental samplings after efforts were made to reduce emissions or after the sources were shut down. In these cases, reductions in CDD/CDF concentrations were noted for various media including, cow's milk, vegetation, and air. As discussed below, vegetation has been found to respond rapidly to reductions in air concentrations, and the time to reach steady state in cow's milk given a steady input of CDD/CDFs is also relatively short. In other cases, such as in the accumulation of CDD/CDFs in soils or in body fat, the benefits may not be as immediate. Soil and body fat are reservoirs in which the residence time of these compounds are measured on the order of years.

The available data reviewed above suggest that measurable impacts near incinerators only occur if the incinerator emits very high amounts of dioxins, in contrast to emissions that are known to be within regulatory limits. However, two key descriptors here, including "measurable impacts" and "very high amounts of emissions" cannot be rigorously defined. The data suggest that "measurable" impacts can be defined as

elevations in dioxin concentrations in environmental or biotic media on the order of 5-10 times higher than typical background. "Very high amounts" of releases is less well defined. The Columbus incinerator is the only incinerator reviewed above for which emission data were available, and the stack test of 1992 showed emissions that were about 200 times higher than the 1995 proposed regulatory limit for solid waste incinerators of 30 ng of total dioxins per m^3. By comparison of environmental media sampling, one could surmise that the metals reclamation plant in Tyrol, Austria, and the incinerators in the Derbyshire area of Central England, if not others noted above, were also emitting unusually high amounts of dioxins.

Also, it is important to understand that elevations in air, soil, vegetation, and animal products do not automatically translate to higher exposure levels. This document (and several other efforts worldwide) have concluded that the bulk of exposure to dioxins occurs via the diet, and specifically animal fats. Higher exposure to an individual would only result if an individual subsisted on animal food products from animals raised near incinerators (meaning also that the animal's diet was comprised of vegetation grown where the animal is raised), and perhaps only incinerators emitting high amounts of dioxins. As described above, there are limited human tissue data for individuals where localized environmental contamination has been demonstrated. In one study in Austria of a farming family consuming home-grown milk near the metals reclamation plant, both the milk and the blood of the family were shown to have elevated levels of dioxins. In the vicinity of a municipal solid waste incinerator in Japan where CDD/CDF and PCB concentrations in soil were elevated, nearby residents also had elevated blood levels of CDD/CDF/PCBs. In the U.S., there have been no studies to evaluate the prevalence of subsistence behavior near sources, in general, and near high emitting incinerators, in particular. Even if there is a sparsity of subsistence behaviors near sources in the U.S., it is reasonable to assume that animal fats produced near high emitting incinerators would likely have elevated CDD/CDF levels and be consumed. If incinerators are meeting regulation limits, they would not be high emitters, and the likelihood of localized impacts would be small.

In addition to the localized contamination resulting from incinerator emissions, as described above, there have been several incidents involving contamination of commercial food supplies from natural and accidental sources in various parts of the world. For

example, ball clay was found to be the source of elevated CDD/CDF levels in animal food products in the United States (Ferrario et al., 2000). Ball clay from a mine in Mississippi, which was used as an anti-caking agent in soy-based animal feeds, was found to be the source of contamination after poultry and catfish samples collected in the same region of the United States were found to have concentrations of CDD/CDFs that were significantly elevated above background concentrations. The incident, which occurred in 1998, involved less than 5 percent of the national poultry production. Subsequently, the use of ball clay in animal feeds was discontinued. In Germany, dairy products were found to be contaminated in 1998 (Malisch, 1998). The concentration of CDD/CDFs in milk was 1.38 pg I-TEQ_{DF}/g fat (N = 43) in 1998, compared to 0.62 pg I-TEQ_{DF}/g fat (N = 76) in 1997. After intense investigation, contaminated citrus pulp obtained from Brazil, which was used as a feed ingredient for dairy cows in certain regions of Germany in 1998, was found to be the source of contamination of the food supply. In 1999, similar contamination of the commercial food supply occurred in Belgium when 500 tons of animal feed was inadvertently contaminated with approximately 50 kg of PCBs and 1 g of dioxins in transformer oil (Van Larebeke et al., 2001). The feed was delivered to poultry farms (and to a lesser extent rabbit, cow, and pig breeding facilities), primarily in Belgium. This contaminated feed represented a "limited percentage" of the feed produced in Belgium, but was delivered to hundreds of farms in the country. The mean TEQ_{DFP}-WHO_{94} concentrations were 170 pg/g fat in poultry, 2.3 pg/g fat in eggs, and 2,320 pg/g fat in animal feed. Once discovered, animal products with excessive levels were destroyed, including approximately 2 million chickens.

5.5. CIGARETTE SMOKERS

As discussed in Volume 1, cigarette smoking has been found to be a source of CDD/CDFs. As a result, individuals who smoke cigarettes, and nonsmokers who are exposed to second-hand smoke, may experience higher levels of exposure to dioxin-like compounds than the general population. Matsueda et al. (1994) reported that the mean I-TEQ_{DF} content of a pack of U.S. cigarettes was 8.6 pg. This estimate is based on analytical data from seven brands of U.S. cigarettes. Assuming that a pack of cigarettes contains 20 cigarettes, the I-TEQ_{DF} content of a single cigarette would be 0.43 pg. This value represents about half of the I-TEQ_{DF} value reported for a mainstream cigarette smoke from a Swedish brand of cigarettes (Löfroth and Zebühr, 1992) and is about five times higher than the I-TEQ_{DF} level in mainstream smoke from German cigarettes (Ball et al., 1990). The daily intake of CDD/CDFs by smokers can be estimated by multiplying the CDD/CDF content of a single cigarette by the mean number of cigarettes smoked per day by current smokers. According to U.S. EPA (1992), 25.5 percent of the adult U.S. population were smokers in 1990. The average daily number of cigarettes smoked by this population was 19.1. Thus, mean CDD/CDF exposures via cigarette smoking are estimated to be 8.2 pg I-TEQ_{DF}/day for smokers. This level of exposure represents over 10 percent of the average daily background dose of CDD/CDFs from soil, air, water, and foods, as described in Chapter 4. The use of data on the total I-TEQ_{DF} content of a cigarette from Matsueda et al. (1994) results in uncertainties as to the estimate of exposure to smokers because the approach assumes that all of the dioxin in the unburned cigarette is inhaled. It is likely that some of the dioxins are released with the sidestream smoke rather than being inhaled. It is also possible that dioxins are destroyed and/or formed during the combustion process. Thus, it is unclear if these factors would lead to a net increase or decrease in the amount of dioxins inhaled. However, as described above, the I-TEQ_{DF} value reported by Matsueda et al. (1994) is less than that in mainstream (i.e., inhaled) smoke reported by Löfroth and Zebühr (1992) and greater than that of Ball et al. (1990) and provides the best estimate of CDD/CDFs in cigarettes to which smokers may be exposed.

Nonsmokers may also be exposed to CDD/CDFs from environmental tobacco smoke. Although the data on the frequency, magnitude, and duration of exposure to environmental tobacco smoke are limited, an idea of the magnitude of exposure to

CDD/CDFs can be gained by assuming that nonsmokers receive a fraction of the CDD/CDF TEQ received by smokers. Based on data for nicotine, the dose to nonsmokers exposed to environmental tobacco smoke is estimated to be 0.1 to 0.7 percent that of smokers (U.S. EPA, 1992). For 4-aminobiphenyl, nonsmokers exposed to environmental tobacco smoke were estimated to receive a dose that was 10 to 20 percent that of smokers (U.S. EPA, 1992). Assuming that nonsmokers receive 0.1 to 20 percent of the dose of CDD/CDFs from second-hand smoke that smokers receive, the estimated daily dose of CDD/CDFs for nonsmokers would range from 0.008 pg I-TEQ_{DF}/day to 1.6 pg I-TEQ_{DF}/day. It should be noted, however, that individual exposure to sidestream smoke is highly variable, depending on a person's proximity to smokers, how often they are near smokers, and the ventilation rate in these areas.

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Table 5-1. Concentrations of CDDs, CDFs, and Dioxin-Like PCBs in Blood (lipid based) of a Breast-Fed and a Formula-Fed Infant at the Age of 11 and 25 Months

Compound (conc. in pg/g fat)	Age (Months)			
	Breast-Fed Infant		Formula-Fed Infant	
	11	25	11	25
2,3,7,8-T4CDF	<2.7*	<2.5	<3.0	<2.5
2,3,7,8-T4CDD	3.7	4.1	<1.0	<1.0
1,2,3,7,8-P5CDF	<1.2	n.d. (1.4)	<1.2	n.d. (2.5)
2,3,4,7,8-P5CDF	23.1	29.7	1.5	<2.5
1,2,3,7,8-P5CDD	11.1	15.2	<1.0	n.d. (1.8)
1,2,3,4,7,8H6CDF	9.8	12.2	<2.2	<2.5
1,2,3,6,7,8-H6CDF	8.1	10.2	<1.0	<2.5
2,3,4,6,7,8-H6CDF	<3.4	<3.0	<2.3	<2.5
1,2,3,4,7,8-H6CDD	7.8	9.1	n.d (1.1)	n.d. (2.8)
1,2,3,6,7,8-H6CDD	43.0	51.7	2.5	<5.4
1,2,3,7,8,9-H6CDD	7.1	8.1	n.d. (1.2)	<4.5
1,2,3,4,6,7,8-H7CDF	13.1	n.a.	<5.8	<6.0
1,2,3,4,6,7,8-H7CDD	24.3	29.7	8.8	<10.0
OCDF	<5.0	n.a.	<5.0	n.a.
OCDD	148.7	204.0	79.3	70.0
TEQ_{DF}-WHO_{98} (<LD=0.5*LD)	29.2	36.8	2.4	2.3
PCB 77	23 (m)	20 (m)	26 (m)	20 (m)
PCB 126	287	n.a.	24	n.a.
PCB 169	270	183	7	11
TEQ_{P}-WHO_{98}	31.4	1.8	7	0.1

* for values reported as "<" a value (2.7, e.g.), ½ the concentration was used for TEQ calculations.
n.a. = not analyzed
n.d. = not detected (limit of detection)
(m) = maximum value, due to possible contribution of a contaminant

Source: Abraham et al. (1995).

Table 5-2. Concentrations of CDDs and CDFs in Adipose Tissue (lipid based) of Stillborn, Formula-Fed, and Breast-Fed Infants

Compound (conc. in pg/g fat)	Stillborn (n = 3)	Formula-Fed (n = 8)	Breast-Fed (n = 9)
2,3,7,8-TCDD	1.6	0.4	1.7
1,2,3,7,8-PCDD	3.4	1.1	4.9
1,2,3,4,7,8-HxCDD	2.5	1.0	4.0
1,2,3,6,7,8-HxCDD	8.8	4.0	19.9
1,2,3,7,8,9-HxCDD	1.3	0.7	3.7
1,2,3,4,6,7,8-HpCDD	12.9	5.0	25.2
OCDD	51.2	29.1	91.6
2,3,7,8-TCDF	1.4	1.9	1.1
1,2,3,7,8,-PCDF	0.2	1.0	0.5
2,3,4,7,8-PCDF	9.2	3.1	10.6
1,2,3,4,7,8-HxCDF	3.7	1.7	3.5
1,2,3,6,7,8-HxCDF	2.4	1.0	2.8
2,3,4,6,7,8-HxCDF	1.0	0.2	1.1
1,2,3,7,8,9-HxCDF	0.1	0.1	0.1
1,2,3,4,6,7,8-HpCDF	3.6	1.6	3.8
1,2,3,4,7,8,9-HpCDF	0.4	0.1	0.1
OCDF	2.1	1.8	1.6
TEQ_{DF}-WHO_{98}	11.9	4.3	15.9

Note: Average congener concentrations calculated assuming non-detects equal to ½ detection limit.

Source: Kreuzer et al. (1997).

Table 5-3. Parameters Used for Modeling the Impact of Nursing on Body Burden and Body Lipid Concentrations of TEQs from Infancy to Adulthood

Time After Birth	TEQ_{DFP}-WHO_{98} Concentration in Breast Milk Fat (pg/g)	Body Weight (kg)	Lipid Fraction	Half-life (yrs)	Administered Dose of Dioxin TEQ_{DFP}- WHO_{98}, pg/day[a]				
					Formula Only	6-week BF	6 Months BF	1 Year BF	2 Year BF
At birth	25	3.3	0.14	0.40	50	800	800	800	800
1 month	22.9	4.3	0.16	0.50	50	733	733	733	733
2 months	20.8	4.6	0.18	0.60	50	667 / 50	667	667	667
3 months	18.8	6.0	0.20	0.70	50	50	600	600	600
4 months	16.7	6.7	0.22	0.75	50	50	533	533	533
5 months	14.6	7.4	0.23	0.80	50	50	467	467	467
6 months	12.5	7.9	0.25	1.00	50	50	400	400	400
7 months	11.5	8.4	0.25	1.00	50	50	50	367	367
8 months	10.4	8.8	0.24	1.05	50	50	50	333	333
9 months	9.4	9.2	0.24	1.08	50	50	50	300	300
10 months	8.3	9.4	0.23	1.10	50	50	50	267	267
11 months	7.3	9.8	0.23	1.12	50	50	50	233	233
1 year	6.3	11.3	0.23	1.14	50	50	50	200	200
2 years	--	13.3	0.20	1.39	50	50	50	50	200
5 years	--	19.7	0.15	2.12	54	54	54	54	54
11 years	--	41.1	0.15	3.60	65	65	65	65	65
18 years	--	65.1	0.13	5.33	66	66	66	66	66
34 years	--	71.5	0.21	7.70	66	66	66	66	66
55 years	--	73.8	0.27	9.76	66	66	66	66	66

a Dose = TEQ_{DFP}-WHO_{98} concentration in milk fat (pg/g) x lipid fraction in milk (0.04) x ingestion rate of milk (800 g/day).

Table 5-4. Model Validation Data and Results (all concentrations in ppt TEQ_{DF}-WHO_{98} lipid basis)

Description	Observed Data				Model Predictions	
	Milk TEQ_{DF}-WHO_{98}/month	Milk TEQ_{DF}-WHO_{98}/month	Child TEQ_{DF}-WHO_{98}/month	Weeks Breast-Fed	Child TEQ_{DF}-WHO_{98} @ Selected k(t)*	Child TEQ_{DF}-WHO_{98} @ Long k(t)
1st Mother, 1st child	23.5 / 2	14.0 / 11	34.7 / 11	26	34	51
1st Mother, 2nd child	13.7 / 2	12.7 / 5	11.9 / 11	29	27	39
2nd Mother, 1st child	26.5 / 2	15.2 / 11	44.2 / 12	30	36	56
2nd Mother, 2nd child	18.3 / 2	13.1 / 6	18.8 / 12	32	27	41
3rd Mother, only child	13.7 / 2	NA	5.0 / 13	7	10	16
4th Mother, only child	12.7 / 2	13.0 / 6	26.5 / 12	30	21	32
Average, pg/g TEQ_{DF}-WHO_{98}			23.5		26	39

* Predicted child TEQ_{DF}-WHO_{98} at the time of measurement (between 11 and 13 months) using the more rapid dissipation rate, k(t), selected for this model in comparison to the slower k(t) (longer half-life of 7 years) shown in the last column.

Table 5-5. Results of PK Modeling for Formula Feeding and 4 Breast Feeding Scenarios

Description of Model Output	Formula	6-wk BF	6-mo BF	1-yr BF	2-yr BF
Peak concentration, pg TEQ_{DFP}-WHO_{98}/g lipid	13.0	34.1	44.3	44.3	44.3
Time after birth of peak	9 yr	6 wk	9 wk	9 wk	9 wk
AUC[1] after 1 year	2,168	5,989	12,129	13,645	13,645
AUC after 10 years	39,433	46,516	62,696	73,183	86,370
AUC after 70 years	27,5419	282,654	299,304	310,210	324,202
AUC (bf) / AUC (formula)[2] - 1 yr	---	2.8	5.6	6.3	6.3
AUC (bf) / AUC (formula) - 10 yr	---	1.2	1.6	1.9	2.2
AUC (bf) / AUC (formula) - 70 yr	---	1.03	1.09	1.13	1.18

[1] AUC = measure of accumulated exposure defined as, "area under the curve", equal to lipid-concentration, ppt TEQ_{DFP}-WHO_{98} * days. For example, a lifetime at 10 ppt TEQ_{DFP}-WHO_{98} lipid would yield an AUC of 10 ppt TEQ_{DFP}-WHO_{98} * 70 years * 365 d/yr = 255,500 ppt TEQ_{DFP}-WHO_{98}-day.

[2] AUC (bf) / AUC (formula) = ratio comparing the accumulated exposure difference between the breast-feeding scenario and the formula. A result of 6.0 means that the accumulated exposure for the breast-feeding scenario being evaluated is 6 times more than a formula only scenario.

Table 5-6. Sensitivity Analysis Testing of PK Model for Breast-Milk Impacts[3]

Description of Model Output	6-mo baseline	Dissipation Tests		Dose Tests		Extremes	
		Sc #1	Sc #2	Sc #3	Sc #4	Sc #5	Sc #6
Peak concentration, pg TEQ_{DFP}-WHO_{98}/g lipid	44.3	49.8	44.3	48.1	28.5	54.0	28.5
Time after birth of peak	9 wk	9 wk	9 wk	9 wk	9 wk	10 wk	9 wk
AUC[1] (sa) / AUC (6-mo)[2] - 1 yr	—	1.3	1.0	1.2	0.6	1.6	0.6
AUC (sa) / AUC (6-mo) - 10 yr	---	2.2	0.8	1.1	0.8	2.6	0.7
AUC (sa) / AUC (6-mo) - 70 yr	---	1.4	0.7	1.03	0.96	1.5	0.6

[1] AUC = measure of accumulated exposure defined as, "area under the curve", equal to lipid-concentration, ppt TEQ_{DFP}-WHO_{98} * days. For example, a lifetime at 10 ppt TEQ_{DFP}-WHO_{98} lipid would yield an AUC of 10 ppt TEQ_{DFP}-WHO_{98} * 70 years * 365 d/yr = 255,500 ppt TEQ_{DFP}-WHO_{98}-day.

[2] AUC (sa) / AUC (6-mo) = ratio comparing the accumulated exposure difference between the sensitivity analysis scenario and the 6-month breast-feeding baseline scenario. A result of 6.0 means that the accumulated exposure for the sensitivity analysis scenario being evaluated is 6 times more than the 6-month baseline scenario.

[3] Scenario definitions:

Sc #1: Use of the Pinsky and Lorber (1998) lipid-based function for dissipation rate

Sc #2: Use of the Kreuzer, et al. (1997) modeled dissipation rate

Sc #3: Assumption of mother's milk concentration not declining from 25 ppt TEQ_{DFP}-WHO_{98} lipid

Sc #4: Assumption of mother's milk concentration beginning at 15 ppt TEQ_{DFP}-WHO_{98}, declining to 7.5 ppt TEQ_{DFP}-WHO_{98} after 6 months.

Sc #5: Use of Pinsky and Lorber (1998) lipid-based function for dissipation rate and the assumption of mother's milk concentration not declining from 25 ppt TEQ_{DFP}-WHO_{98} lipid.

Sc #6: Use of Kreuzer, et al. (1997) modeled dissipation rate and the assumption of the mother's milk concentration beginning at 15 ppt TEQ_{DFP}-WHO_{98}, declining to 7.5 ppt TEQ_{DFP}-WHO_{98} after 6 months.

Table 5-7. Estimated CDD/CDF/PCB Exposures for Adult Subsistence Fishermen

Media	Conc. TEQ_{DFP}-WHO_{98}[a]	Contact Rate[b]	Daily Intake (pg/kg-day)[c]
Soil ingestion	11.6 ppt[e]	50 mg/day	8.2×10^{-3}
Soil dermal contact	11.6 ppt	12 g/day[f]	1.9×10^{-3}
Freshwater fish ingestion	2.2 ppt[g]	59 to 170 g/day	$1.9 \text{ to } 5.3 \times 10^{+0}$
Marine fish ingestion	0.51 ppt[g]	12.5 g/day	9.1×10^{-2}
Inhalation	0.12 pg/m^3	13.3 m^3/day	2.3×10^{-2}
Water ingestion	0.00056 ppq	1.4 L/day	1.1×10^{-5}
Milk ingestion	0.027 ppt	175 g/day	6.8×10^{-2}
Dairy ingestion	0.18 ppt	55 g/day	1.4×10^{-1}
Vegetable fat ingestion	0.093 ppt[e]	17 g/day	2.2×10^{-2}
	Total		$2.2 \text{ to } 5.7 \times 10^{+0}$ [d]

[a] Values from Table 3-64.

[b] Values for adult soil ingestion, inhalation, water ingestion, and subsistence fish ingestion from Exposure Factors Handbook (U.S. EPA, 1997). Contact rates for milk, dairy, and vegetable fats are based on data from USDA (1995).

[c] Daily intake (mg/kg-day) = [Contact rate (g/day; m^3/day; L/day; mg/day) x Conc. TEQ x Unit Conversion (soil unit conversion = 10^{-3}, all other media no unit conversion needed)/Body Weight (kg)] or Contact rate (g/kg-day) x Conc. TEQ x Unit Conversion.

[d] Approximately equivalent to 77 to 186 pg/day, assuming an adult body weight of 70 kg.

[e] Calculated by setting nondetects to zero.

[f] Calculated as the surface area of the body that contacts the soil (5,700 cm^2/day) x the rate that soil adheres to the skin (0.07 mg/cm^2) x the fraction of CDD/CDFs absorbed through the skin (0.03); exposure factors based on recommendations in U.S. EPA (1999) for an adult resident, which assumes that the lower legs, forearms, hands, and head are exposed to the soil.

[g] This concentration is a species-specific ingestion-weighted average value.

Table 5-8. Levels of Different PCB Congeners in Blood Samples from Three Groups of Men with Different Fish Consumption Habits

Congener (UIPAC)	Fish Intake					
	None		Moderate		High	
	Plasma (n = 9)	Lipid (n = 8)	Plasma (n = 14)	Lipid (n = 7	Plasma (n = 14)	Lipid (n = 11)
Non-ortho-PCBs						
77 (pg/g)[a]	0.04 (0.01-0.09)	15 (3-38)	0.1[b] (9.03-0.2)	41[b] (26-62)	0.2[b,c] (0.1-0.5)	50[b] (15-140)
126 (pg/g)	0.73 (0.3-1.2)	220 (100-450)	1.05 (0.6-2.4)	400[b] (210-650)	2.8[b,c] (1.2-4.9)	790[b,c] (380-1400)
169 (pg/g)	0.65 (1.3-1.5)	200 (100-340)	0.86 (0.4-1.7)	250 (170-360)	1.80[b,c] (0.3-3.6)	570[b,c] (210-1200)
Mono-ortho-PCBs						
105 (ng/g)	0.02 (0-0.03)	5 (0-13)	0.04 (0.02-0.07)	14[b] (9-20)	0.14[b,c] (0.04-0.3)	39[b,c] (18-77)
118 (ng/g)	0.12 (0.05-0.21)	41 (17-92)	0.21 (0.12-0.43)	76 (45-120)	0.58[b,c] (0.21-1.00)	160[b,c] (84-300)
156 (ng/g)[d]	0.13 (0.05-0.34)	40 (19-68)	0.14 (0.07-0.28)	44 (30-64)	0.3[b,c] (0.05-0.7)	90[b,c] (36-180)
157 (ng/g)[d]	0.02 (0.01-0.05	6.6 (2.8-11)	0.02 (0.01-0.05)	7.8 (5.4-11)	0.06[b,c] (0.01-0.14)	18[b,c] (7.4-39)
Di-ortho- and other PCBs						
180 (ng/g)[e]	1	400	1	400	2	600

Notes: Means and ranges indicated on plasma and lipid basis.

[a] Near the detection limit.
[b] $p < .05$, compared with group "none."
[c] $p < .05$, compared with group "moderate."
[d] Quantified, using single-response factors.
[e] CB-180 quantified from two fractions, concentrations thus estimated.

Source: Asplund et al. (1994).

Table 5-9. Mean TEQ Levels in Pooled Serum Samples

	$I\text{-}TEQ_{DF}$ (ppt, lipid basis)	$TEQ_P\text{-}WHO_{94}$ (ppt, lipid basis)
Cornwall		
Sports Fishers		
<38 years, lower	20.8	--
higher	22.2	3.6
38 years, lower	28.4	3.1
higher	31.4	9.5
> 50 years, higher	33.5	17.3
Nonfish Eaters		
<38 years	24.7	2.6
38-50 years	29.8	6.8
>50 years	36.8	9.7
Mississauga		
Sports Fishers		
<38 years	32.4	--
38-50 years	40.1	--
>50 years	41.2	--
Nonfish Eaters		
<38 years	34.0	--
38-50 years	29.1	--
>50 years	34.3	--

Source: Adapted from Cole et al. (1995).

Table 5-10. Mean CDD/CDF Levels in Serum of Consumers of Great Lakes Sport Fish (ppt, lipid adjusted)

	All Sport Fish Consumer Subjects (ppt) (n = 31)[a]	Lake Michigan Participants (ppt) (n = 9)	Lake Huron Participants (ppt) (n-11)	Lake Erie Participants (ppt) (n = 11)	Comparison Group[a] (ppt) (n = 70)
CDD Congeners					
2,3,7,8-TCDD	5.6	4.7	10.5	4.9	2.8
1,2,3,7,8-PeCDD	10.4	9.8	16	5.8	5.5
1,2,3,4,7,8-HxCDD	8.4	11.4	8.4	5.5	9.0
1,2,3,6,7,8-HxCDD	126	120	142	115	70.8
1,2,3,7,8,9-HxCDD	7.0	8.7	5.5	5.8	8.4
1,2,3,4,6,7,8-HpCDD	134	144	153	95.9	124
1,2,3,4,6,7,9-HpCDD		ND	ND		4.4
OCDD	777	783	918	623	971
Total	1,062	1,087	1,258	844	1,188
Total I-TEQ_D	27.5	25.8	36	20.7	15.5
CDF Congeners					
2,3,7,8-TeCDF	2.2	2.4	2.1		2.1
1,2,3,7,8-PeCDF	2.0	ND	1.7	ND	1.6
2,3,4,7,8-PeCDF	17.7	20.4	22.8	10.4	5.5
1,2,3,4,7,8-HxCDF	12.7	11.6	16.0	10.2	8.0
1,2,3,6,7,8-HxCDF	9.0	8.0	10.5	7.7	5.3
1,2,3,7,8,9-HxCDF	ND	ND	ND	ND	1.8
2,3,4,6,7,8-HxCDF	5.1	6.0	4.8	8.0	3.8
1,2,3,4,6,7,8-HpCDF	20.0	22.1	22.9	15.2	21.3
1,2,3,4,7,8,9-HpCDF	ND	ND	ND	ND	NA
OCDF		ND		ND	6.9
Total	58.2	70.8	79.3	48.3	87.3
Total I-TEQ_F	11.9	13.2	14.8	7.8	4.9

a One individual was excluded from the data summary due to unusually high occupational/environmental exposures.

b Comparison group is from a 1991 unpublished NCEH/CDC data set of a Jacksonville, Arkansas, population of 70 individuals.

Source: Anderson et al. (1998).

Table 5-11. Mean PCB Levels in Serum of Consumers of Great Lakes Sport Fish (ppt, lipid adjusted)

	All Sport Fish Consumer Subjects[a] (ppt) (n = 31)	Lake Michigan Participants (ppt) (n = 9)	Lake Huron Participants (ppt) (n-11)	Lake Erie Participants (ppt) (n = 11)	Comparison Group[b] (ppt) (n = 70)
Coplanar PCB Congeners					
77	14.6	16.5	14.2	13.3	12.6
81	13.5	17.4	13.2		8.6
126	148	261	187	28	18.4
169	80.8	113	84.2	48.4	17.9
Coplanar PCB Total	228	340	282	75.4	57.4
$I\text{-}TEQ_P\text{-}WHO_{94}$	17.4	26	23	4.8	1.8
Congener-Specific PCBs					
28	0.08	0.08	0.1	0.08	ND
52	0.01	ND	0.01	ND	ND
56	0.02	0.06	ND	ND	ND
58	0.04	0.08	0.04	0.01	ND
74	0.3	0.6	0.4	0.2	0.009
99	0.4	0.7	0.5	0.1	ND
101	ND	0.01	ND	ND	ND
1.5	0.1	0.2	0.1	0.02	0.4
118	0.4	0.8	0.5	0.08	0.03
130	0.1	0.2	0.1	0.02	NA
138	0.8	1.3	0.8	0.4	0.4
146	0.2	0.3	0.2	0.04	ND
153	1.1	1.7	1.1	0.6	0.4
156	0.02	0.04	0.02	ND	NA
157	0.1	0.2	0.1	0.08	NA
187	0.03	0.07	0.03	ND	ND
170	0.1	0.2	0.2	0.07	ND
172	0.02	0.05	0.03	ND	ND
177	0.04	0.09	0.06	ND	ND
178	0.07	0.13	0.08	0.03	ND
180	0.4	0.8	0.4	0.2	0.4
183	0.1	0.2	0.1	0.03	ND
187	0.3	0.4	0.3	0.08	0.04
189	ND	ND	ND	ND	NA
193	0.03	0.08	0.02	ND	NA
194	0.09	0.1	0.1	0.05	0.004
195	0.04	0.07	0.06	ND	ND
201	0.2	0.3	0.2	0.09	0.04
203/196	0.09	0.2	0.11	0.03	0.007
206	0.07	0.08	0.08	0.04	ND
209	0.02	0.03	0.04	ND	NA
Total	5.2	8.6	5.7	2.2	1.2

a One individual was excluded from the data summary due to unusually high occupational/environmental exposures.
b Comparison group from a 1996 unpublished data set of 41 non-Great Lake sport fish consumers analyzed by the Wisconsin State Laboratory of Hygiene.

Source: Anderson et al. (1998).

Table 5.12. Average PCB and CDD/F TEQ-WHO_{98} Concentrations (all concentrations in pg/g whole weight)

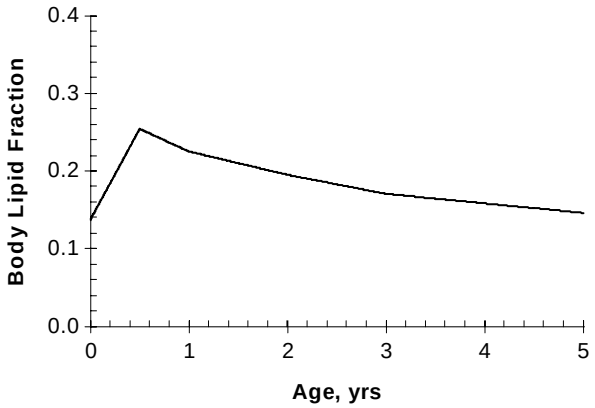
Main Water Body	Location	Species	$TEQ_P WHO_{98}$	TEQ_{DF}-WHO_{98}	TEQ_{DPF}-WHO_{98}
Lake Superior	Black Bay	Lake Trout (5)	9.4	0.68	14
	Jackfish Bay	Lake Trout (5)	13	5.3	2.5
	Peninsula Harbour	Lake Trout (5)	9.5	2.8	3.3
	Algoma Area	Lake Trout (5)	83	23	3.7
	Algoma-Agawa Bay	L. Whitefish (5)	4.5	5.4	0.83
	Goulais Bay	L. Whitefish (5)	4.1	1.8	2.3
Lake Huron	Manitoulin Island	L. Whitefish (5)	1.4	0	>1.4
	Nottawassaga River	Chinook (5)	14	0.94	15
	Nottawasaga River	Rainbow Trout (5)	6.9	0	>6.9
	Tobermory	L. Trout (5)	21	3.5	5.9
	Oliphant/Fishing Is.	L. Trout (5)	12	0.75	17
	Oliphant/Fishing Is.	L. Whitefish (5)	4.4	2.7	1.7
	Bruce Cty	Carp (5)	31	2.1	14
	Grand Bend	L. Trout (5)	22	0.76	29
Lake Erie	Western Basin	Ch. Catfish (5)	55	8.1	6.8
Niagara River	Niagara River Bar	Lake Trout (5)	79	22	3.5
	Niagara River Bar	Chinook (5)	52	12	4.4
	Niagara River Bar	Brown Trout (5)	21	4.6	4.5
	Niagara River	White Perch (5)	6.2	3.2	1.9
	Niagara River	Rainbow Trout (5)	22	4.8	4.6
	Niagara River	White Bass (4)	1.6	0	>1.6
Lake Ontario	Welland River	Carp (5)	11	0.13	86
	Hamilton Harbour	Carp (5)	25	1.9	13
	Hamilton Harbour	Ch. Catfish (5)	58	6.7	8.7
	Bronte Creek	Brown Trout (5)	56	8.3	6.7
	Port Credit	Lake Trout (4)	72	19	3.8
	Credit River	Brown Trout (5)	41	10	4.1
	Credit River	Chinook (5)	39	8.7	4.5
	Don River	White Sucker (5)	16	4.4	3.6
	Whitby Harbour	Carp (5)	27	40	0.66
	Whitby/Pickering	Chinook (5)	29	6.8	4.3
	Cobourg	L. Trout (5)	67	26	2.6
	Trent River	Chinook (5)	182	59	3.1
	Trent River - 4	L. Whitefish (5)	52	5.8	9.0
	Upper Bay of Quinte	Whitefish (5)	8.7	7.0	1.2
	L. Bay of Quinte	L. Trout (5)	110	29	3.8
	Cataraqui River	Carp (5)	57	4.7	12
Northern Areas	Mattagami River	White Sucker (5)	21	0	>21
	Cochrane	White Sucker (5)	21	0	>21

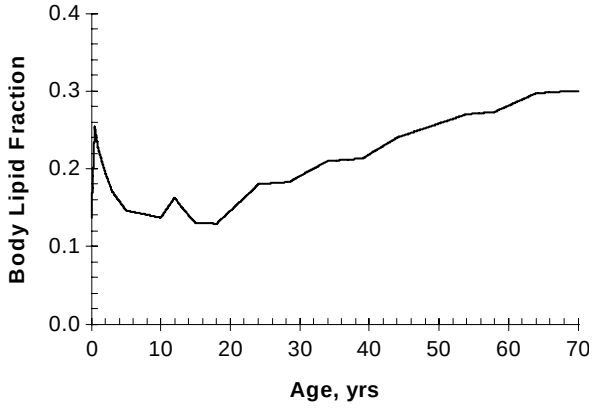
Source: Kolic et al. (2000).

Table 5-13. Comparison Between Mean PCB Levels in Fish-eating Populations and Controls

PCBs	Fishermen		Controls	
	Mean Concentration (ppt, lipid basis)	TEQ_P-WHO_{94} (ppt, lipid basis)	Mean Concentration (ppt, lipid basis)	TEQ_P-WHO_{94} (ppt, lipid basis)
126	1540	154	48	4.8
169	1010	10.1	29	0.29
118	568	56.8	25.4	2.54
170	539	53.9	27.7	2.77
180	1776	17.76	48.2	0.48
TOTAL TEQ_P-WHO_{94}	--	292.6	--	10.9

Source: Adapted from Dewailly et al. (1994).


Body Lipid Fraction
0.4
0.3
0.2
0.1
0.0
0
1
2
3
4
5
Age, yrs


Body Lipid Fraction
0.4
0.3
0.2
0.1
0.0
0
10
20
30
40
50
60
70
Age, yrs

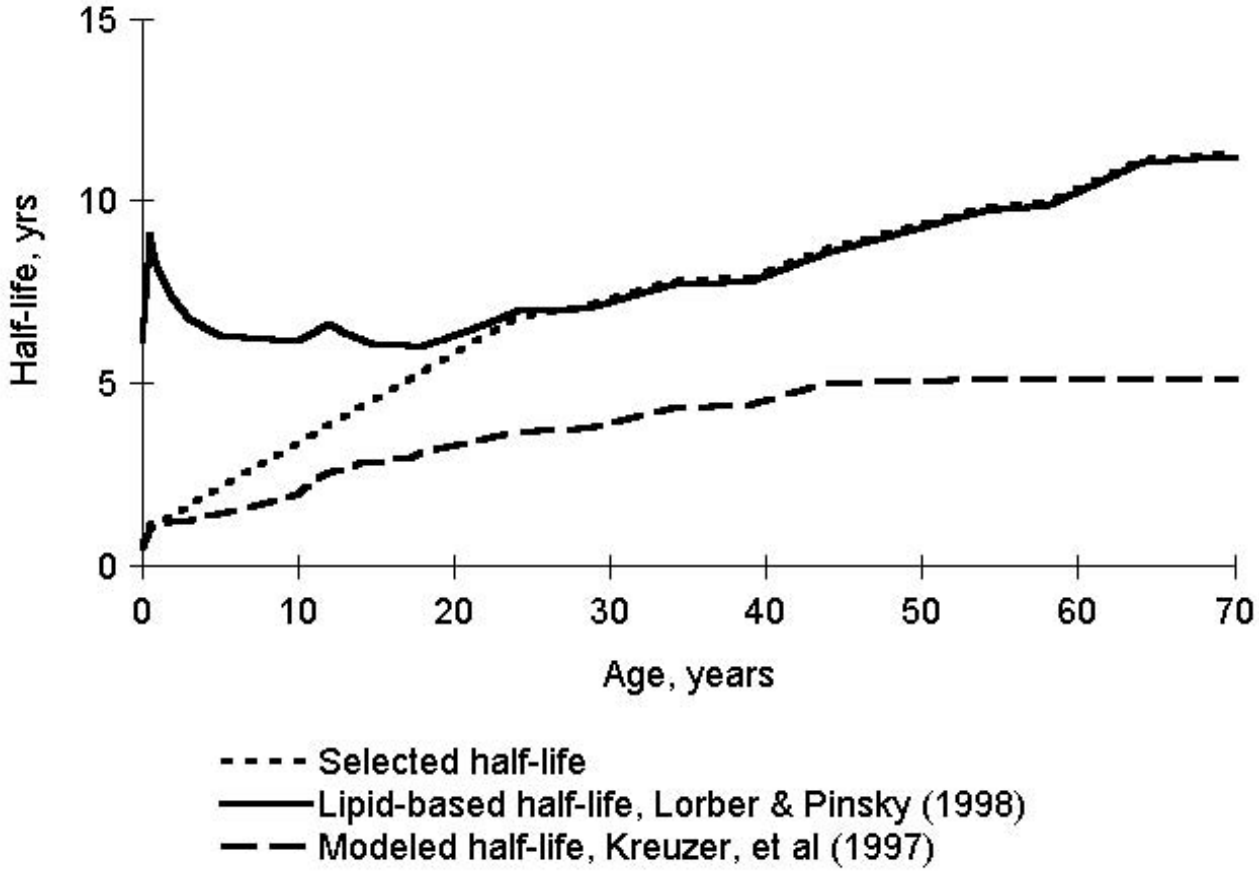
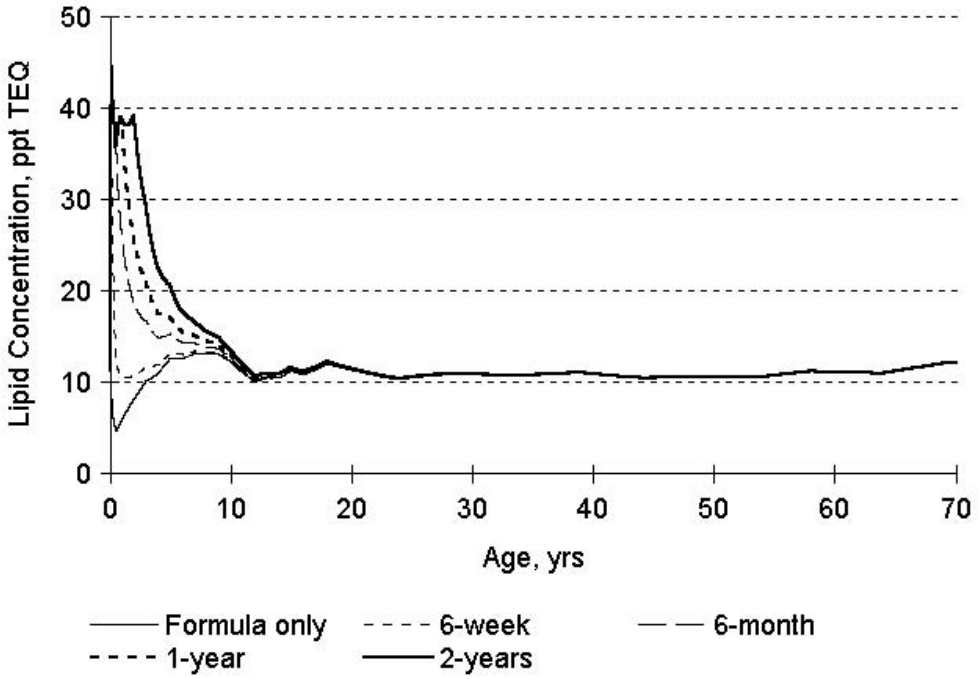


Figure 5-2. Comparison of the selected half-life of TEQs in the body with two options that were available in the literature for 2,3,7,8-TCDD.

(A)



(B)

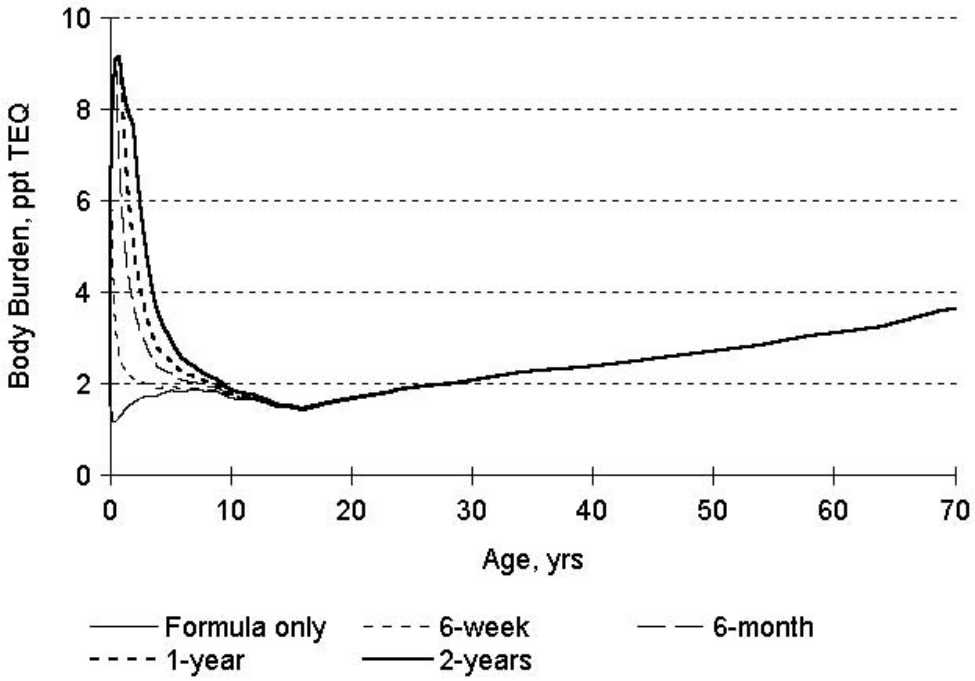
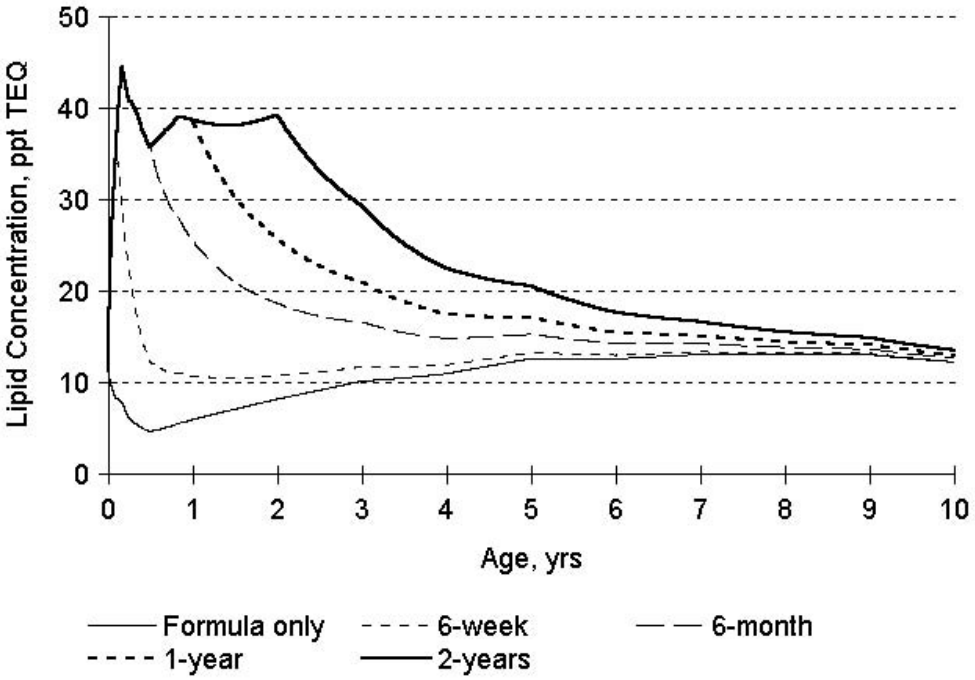


Figure 5-3. Demonstration of the model for evaluating impacts on lipid concentrations (A) and body burdens (B) of infants resulting from various nursing scenarios during a lifetime.

(A)



(B)

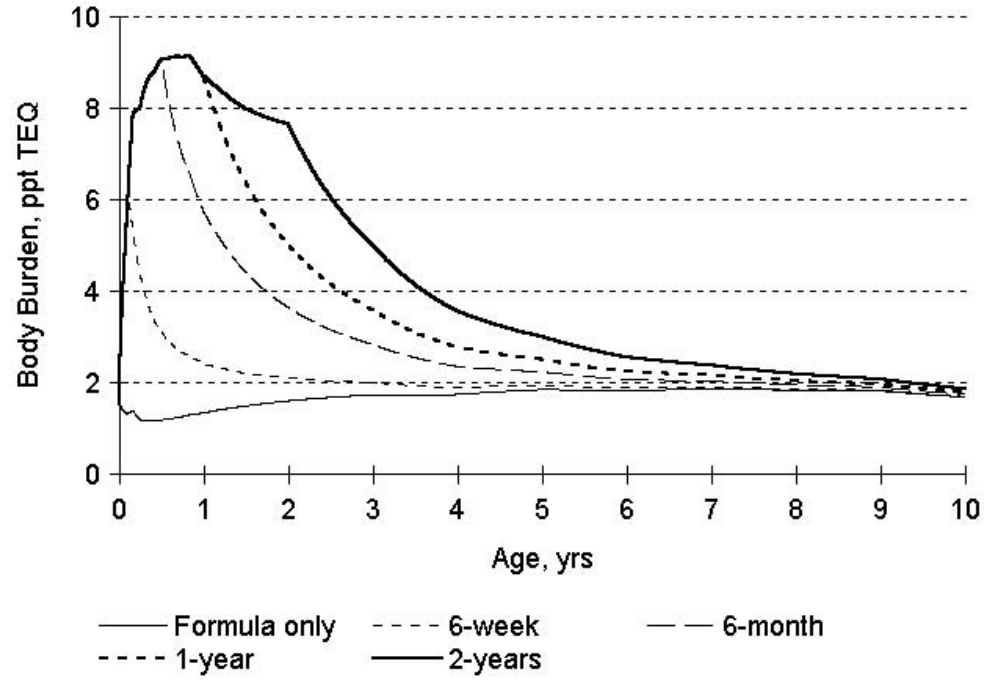
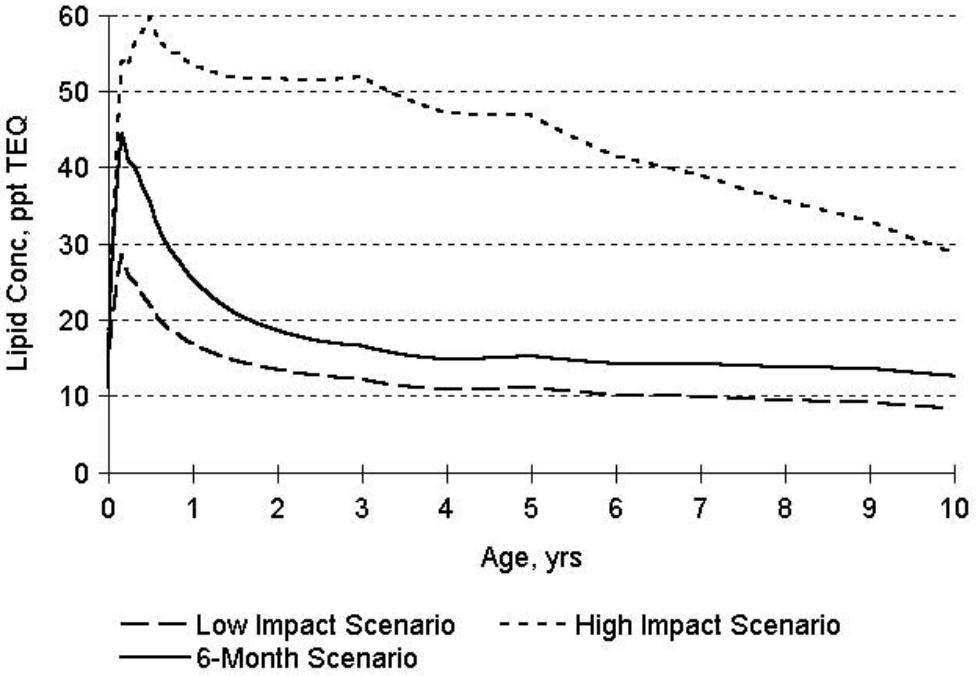


Figure 5-4. Demonstration of the model for evaluating impacts on lipid concentrations (A) and body burdens (B) of infants resulting from various nursing scenarios during the first 10 years of life.

(A)



(B)

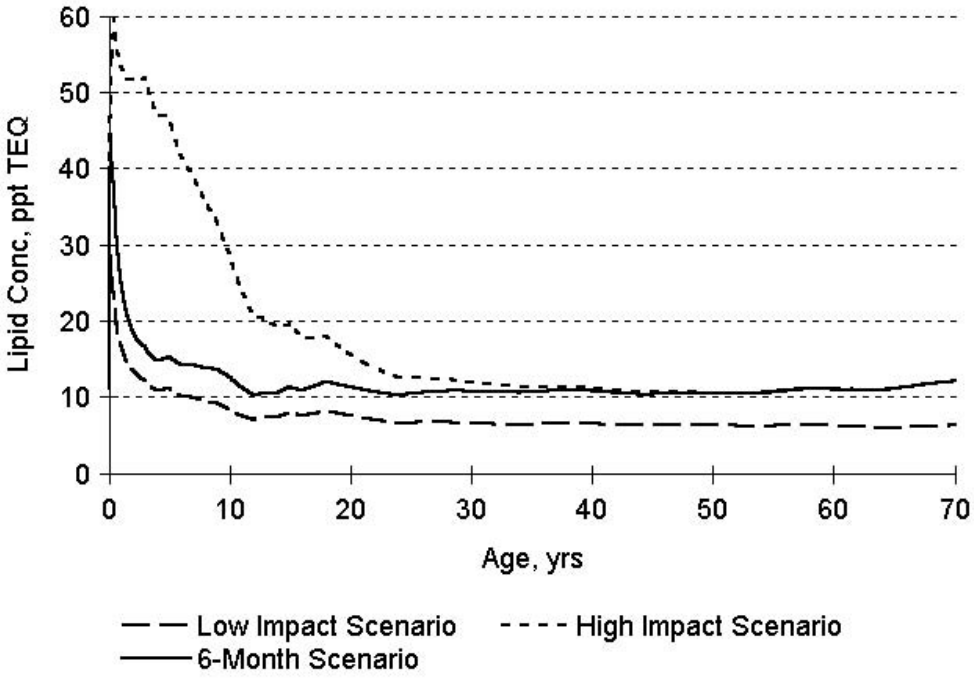


Figure 5-5. Results of sensitivity analysis showing the difference when making modeling assumptions that lead to a high impact to the infant (high impact scenario) and to a low impact to the infant (low impact scenario) as compared to the baseline scenario for a 6-month breast-feeding scenario (6-month scenario).