Appendix J. Lactational Transfer

J.1 Introduction

Some toxic chemicals in the environment can accumulate in a woman's body and transfer to her milk during lactation. Chronic exposure to pollutants that accumulate in the mother's body can transfer a daily dose to the infant much greater than the mother's daily intake from the environment. For example, the mother's milk pathway can be responsible for about 25% of total lifetime exposure to dioxins and furans (USEPA, 2000).

Several reviews have listed numerous toxic chemical contaminants in human breast milk (Abadin et al., 1997; Liem et al., 2000; van Leeuwen and Malisch, 2002; LaKind et al., 2005; Li et al., 2009). Many of these chemical contaminants are carcinogens and/or have non-cancer health impacts on people who inhale or ingest them. Data suggest that infants during the first two years of life have greater sensitivity to many toxic chemicals compared to older children and adults (OEHHA, 2009).

Multiple chemical contaminants have been measured in breast milk or have properties that increase their likelihood of partitioning to milk during lactation. OEHHA grouped these chemicals into the following four major categories:

1) Persistent highly-lipophilic, poorly metabolized organic contaminants, such as polychlorinated biphenyls (PCBs), polychlorinated dibenzofurans (PCDFs), and polychlorinated dibenzo-p-dioxins (PCDDs), are by far the most documented group. These, by virtue of their lipophilicity, are found almost entirely in the milk fat. PCBs, methyl sulfones, and hexachlorobenzene (HCB) methyl sulfones have also been measured in the lipid phase of breast milk.

2) Lipophilic but more effectively metabolized organic contaminants such as polycyclic aromatic hydrocarbons (PAHs) occur in breast milk. The PAHs are a family of over 100 different chemicals formed during incomplete combustion of biomass (e.g. coal, oil and gas, garbage, tobacco or charbroiled meat). Some of the more common parent compounds have been measured in breast milk and research suggests that chronic exposure to PAHs produces stores in maternal fat that can transfer (carryover) to breast milk (Fürst et al., 1993; Costera et al., 2009).

3) Inorganic compounds, metals, and some organo-metallics, including the heavy metals arsenic, lead, cadmium, and mercury, have been found in breast milk. These inorganics are generally found in the aqueous phase and most are bound to proteins, small polypeptides, and free amino acids. The lipid phase may also contain some organometallics (e.g. methyl mercury) and metalloids (such as arsenic and selenium).

4) Chemicals with relatively low octanol:water partition coefficients such as phenol, benzene, halobenzenes, halophenols, some aldehydes and the more polar metabolites of PCBs, PAHs, and pesticides may occur in both the aqueous and lipid phases of breast milk.

Since this document supports risk assessments conducted under the Air Toxics Hot Spots program, we are primarily discussing Hot Spots chemicals emitted from stationary sources.

Many of these persistent chemicals are ubiquitous in the environment and are global pollutants found in low concentrations in air, water and soil. Because some of these chemicals bio-concentrate in animal fat, the primary pathway of exposure to breastfeeding mothers would be consumption of animal products such as meat, milk, and eggs. Nearby polluting facilities can be a local source of exposure and can add to the mother's body burden of contaminants from global pollution through multiple pathways.

This appendix develops lactational transfer coefficients for use in estimating the concentration of a multipathway chemical in mother's milk from an estimate of chronic incremental daily dose to the mother from local stationary sources. OEHHA derived human lactation transfer coefficients from studies that measured contaminants in human milk and daily intake from inhalation or oral routes of exposure from global pathways (e.g. air, cigarette smoke or diet) in the same or a similar human population.

Briefly, human milk transfer coefficients (Tco_{hm}) represent the transfer relationship between the chemical concentration found in milk and the mother's chronic daily dose (i.e. concentration (µg/kg-milk)/dose (µg/day) under steady state conditions. In its simplest form, the biotransfer factor is:

$$Tco_{hm} = C_m / D_t \qquad \textbf{(Eq. J-1)}$$

where:

Tco_{hm} = transfer coefficient from ingested and inhaled media (day/kg)
C_m = concentration of chemical in mother's milk (µg/kg-milk)
D_t = total maternal dose through all exposure routes (µg/day)

Equation J-2 estimates the concentration of contaminants in mother's milk by incorporating the Tco in the following way:

$$Cm = [DOSEair + DOSEwater + DOSEfood + DOSEsoil + DOSEdermal\ ] \times Tco_{hm} \times BW \qquad \textbf{(Eq. J-2)}$$

where:

BW = the body weight of the mother at age 25 (default = 70.7 kg)
DOSEair = dose to the mother through inhalation (µg/kg-BW-day)
DOSEwater = dose to the mother though drinking water ingestion (µg/kg-BW-day)

DOSEfood = dose to the mother through ingestion of food sources (µg/kg-BW-day)
DOSEsoil = dose to the mother through incidental ingestion of soil (µg/kg-BW-day)
DOSEdermal = dose to the mother through dermal exposure to contaminated soil (µg/kg-BW-day)

However, if separate biotransfer information is available for the oral and inhalation route, equation J-3 incorporates route-specific Tcos in the following way:

$$Cm = [(D\_inh \times Tco_{m\_inh}) + (D\_ing \times Tco_{m\_ing})] \times BW \quad \textbf{(Eq. J-3)}$$

where:

D_ing = the sum of DOSEfood + DOSEsoil + DOSEwater through ingestion (mg/kg-BW-day)
D_inh = the sum of DOSEair + DOSEdermal through inhalation and dermal absorption (mg/kg-BW-day)
Tcom_inh = biotransfer coefficient from inhalation to mother's milk (d/kg-milk)
Tcom_ing = biotransfer coefficient from ingestion to mother's milk (d/kg-milk)

These coefficients, applied to the mother's chronic daily dose estimated by the Hot Spots exposure model, estimate a chemical concentration in her milk (see Table J.1-1).

Table J.1-1: Default Tcos (d/kg) for Mother's Milk

Chemical/chem. group	Tco	LCL	UCL
PCDDs - oral	3.7	2.68	5.23
PCDFs - oral	1.8	1.27	2.43
Dioxin-like PCBs - oral	1.7	0.69	4.40
PAHs – inhalation	1.55	0.731	3.281
PAHs – oral	0.401	0.132	1.218
Lead - inhalation	0.064	0.056	0.074

LCL, lower 95% confidence limit of the mean Tco; UCL, upper 95% confidence limit of the mean Tco

Table J.1-1 lists the transfer coefficients for dioxins, furans, dioxin-like PCBs, PAHs and lead that OEHHA has estimated from data found in the peer-reviewed literature and reviewed in this appendix. One key factor that plays a role in the difference between oral and inhalation transfer coefficient (e.g., for PAHs) is first pass metabolism which is lacking in dermal and inhalation exposures. Thus, for simplicity, OEHHA recommends applying the transfer coefficients from inhalation to the dermal absorption pathway for lead and PAHs. For lead, we recommend using the inhalation Tco for all the other pathways of exposure to the mother. Likewise, for PCDD/Fs and dioxin-like PCBs, we recommend using the oral Tco for the other pathways of exposure to the mother in Eq. J-2.

Estimates of toxicant biotransfer to breast milk are ideally chemical-specific. Data necessary to develop a transfer model are available in the open literature for a limited number of chemicals. Therefore, for some toxicants OEHHA has modeled the transfer of a class of chemicals with similar physical-chemical properties using a single Tco when data in the open literature are lacking.

The Hot Spots exposure model can estimate long-term total dose from an individual facility or group of facilities through many pathways of contamination and routes of exposure to the mother and ultimately to her infant. In this appendix, "multipathway toxicants" refers to airborne-released chemicals that can cause exposure through pathways in addition to inhalation. The indirect exposure pathways evaluated under the Hot Spots program include incidental ingestion of contaminated soil, ingestion of contaminated home-raised meat and milk, surface drinking water, homegrown produce, angler-caught fish and skin contact with contaminated soil.

Relative to the lifetime average daily dose to the infant from other exposure pathways in the Hot Spots exposure model, the dose of some chemicals from mother's milk will be negligible. However, the mother's milk pathway may be a substantial contributor to the estimated total lifetime cancer risk for some chemicals emitted from a Hot Spots facility. Exposure from global sources is expected to make up most (almost all) of a mother's toxicant body burden for chemcials like PCDDs. Therefore, the contribution to a mother's toxicant body burden from a single Hot Spot facility is expected to be very small. Regardless of the mother's toxicant body burden from both local and global sources, the benefits of breastfeeding outweigh the risks to the infant exposed to these toxicants during breastfeeding. Breast-feeding has a number of universally accepted benefits for the infant as well as for the mother (Mukerjee, 1998).

We established transfer coefficients (Tcos) for individual congeners of PCDDs/Fs and dioxin-like PCBs, individual and summary carcinogenic PAHs and lead through equations J.1-1 through J.1-3. We used data on exposure and breast milk contamination from background (global), accidental and occupational sources, and a set of simplifying assumptions. We assume that a mother's intake and elimination rates remain constant before lactation. We also assume that changes in a woman's body due to the onset of lactation occur as a single shift in elimination rate and do not change over the lactation period. Unless a study reported the geometric mean or median, we converted arithmetic mean and standard deviation to geometric mean and GSD.

In the following sections, we describe the methods for deriving specific Tcos from measurements of human milk intake and transfer estimates from studies of populations published in the open literature. In some cases, OEHHA adjusted some measurements of human milk and contaminant intake to account for confounding factors. In such cases, OEHHA describes the method of adjustment in the text and table containing adjusted values.

J.2 Mothers' Milk Transfer Coefficients for PCDD/Fs and PCBs

Polychlorinated dibenzo-p-dioxins and furans (PCDD/Fs) are two series of almost planar tricyclic aromatic compounds with over 200 congeners, which form as impurities in the manufacture of other chemicals such as pentachlorophenol and PCBs. PCDD/Fs also form during combustion (e.g. waste incineration) and the breakdown of biomass (e.g. in sewage sludge and garden compost) (Liem et al., 2000). IARC has classified many dioxins and dioxin-like compounds as known or possible carcinogens (WHO, 1997; OEHHA, 2009). Their carcinogenic potency is related to the potency of 2,3,7,8-TCDD in a toxic equivalent (TEQ) weighting scheme (OEHHA, 2009).

The main exposure to PCDD/Fs in the general population from global sources is through the intake of food of animal origin. PCB exposure has been linked to fish consumption. For example, Jensen (1987) observed that congener distribution patterns in contaminated fish and human milk were very similar suggesting that one of the primary sources of human exposure to PCBs in the study population was ingestion of contaminated fish (Jensen, 1987).

Estimates of PCDD/F and PCB TEQ-intake from dietary sources contaminated by global sources can vary by 3 to 4-fold within some populations and by as much as 29-fold between populations (Liem et al., 2000; Focant et al., 2002). Exposure from diet can be at least an order of magnitude higher than intake from ambient air or cigarette smoking (i.e., 0.1 to 4 pg/day) (Liem et al., 2000).

J.2.1 Biotransfer of PCDD/Fs and PCBs to Human Milk

The potential health impacts from exposure to PCBs, PCDDs and PCDFs include carcinogenicity, developmental, endocrine disruption, reproductive toxicity, and neurotoxicity. These persistent, lipophilic compounds can accumulate in the fat of women, transfer to breast milk, and thus result in infant exposure. Some countries implemented measures to reduce dioxin emissions in the late 1980s (Liem et al., 2000). PCBs were banned in the late 1970's and are no longer used in commercial products. Nevertheless, following the PCB ban and efforts to reduce PCDDs, PCDFs emissions, these toxicants are still detected worldwide in human milk, although at declining levels.

The World Health Organization (WHO) has carried out a series of international studies on levels of approximately 29 dioxins and dioxin-like contaminants in breast milk. The first WHO-coordinated study took place in 1987-1988, the second round in 1992-1993 and the third round was initiated in 2000-2003. In the second round, in which concentrations of PCBs, PCDDs and PCDFs were determined in milk samples collected in 47 areas from 19 different countries, mean levels in industrialized countries ranged from 10-35 pg I-TEQ/g-milk (Liem et al., 2000).

Much lower levels (40% lower than 1993) were detected in the 3rd round (Liem et al., 1995; Liem et al., 2000; van Leeuwen and Malisch, 2002) WHO exposure study. Nevertheless, several recent investigators have continued to measure levels of dioxin-like compounds in breast milk (LaKind et al., 2004; Barr et al., 2005; Wang and

Needham, 2007; Li et al., 2009). PCBs still appear in human milk and are still much higher than the total concentrations of PCDDs and PCDFs. Several studies report pg/g-fat levels of PCDD/Fs compared to ng/g-fat levels of PCBs (100 to 1000 times higher) measured in human milk (Chao et al., 2003; Chao et al., 2004; Hedley et al., 2006; Sasamoto et al., 2006; Harden et al., 2007; Wittsiepe et al., 2007; Raab et al., 2008; Todaka et al., 2008).

Thus, nursing infants have the potential to ingest substantial doses during the breastfeeding period, relative to typical total lifetime dose of these compounds from global sources. Consequently, this pathway of exposure may supply a substantial fraction of PCDDs and PCDFs (about 25%) of the infant's total lifetime dose of these compounds (USEPA, 2000). Several studies have detected higher levels of PCBs in the sera (Schantz et al., 1994), adipose tissues (Niessen et al., 1984; Teufel et al., 1990) and bone marrow (Scheele et al., 1995) of mostly breast-fed children relative to partially breast fed infants. These studies were conducted many years after PCBs were banned and no longer used in commercial products. Some investigators have reported a 4-fold greater level of PCBs in the blood of fully breast-fed compared to partially breast-fed infants (Niessen et al., 1984).

In another study, Abraham et al (1994, 1996, 1998) measured elevated PCB concentrations in nursing infants after approximately one year of feeding (Abraham et al., 1994; Abraham et al., 1996; Abraham et al., 1998). These authors reported levels of 34 to 45 ppt (pg TEQ/g blood lipid) among breastfed infants versus 3 to 3.3 ppt blood lipid PCDD/F TEQ concentrations among formula fed infants.

Numerous studies have measured dioxins, furans and dioxin-like PCBs in mother's milk (Liem et al., 2000) The twenty nine dioxin-like PCBs listed in Table J.2-1 are recognized by OEHHA as carcinogens and have potency factors associated with them (OEHHA, 2008). Concentrations of TCDD (2,3,7,8-tetrachlorodibenzo-p-dioxin), the most toxic PCDD, are low relative to other PCDDs and more than 50% of the total PCDD content consists of Octa-CDD. Early studies found around 70% of the total Hexa-CDDs (HxCDDs) is 1,2,3,6,7,8-HxCDD, and the remainder is mainly 1,2,3,4,7,8-HxCDD and 1,2,3,7,8,9-HxCDD (USEPA, 1998). These proportions have not shifted in recent studies (Sasamoto et al., 2006; Zhao et al., 2007; Raab et al., 2008).

PeCDD (1,2,3,7,8 Penta-CDD) is always found in the emissions from waste incinerators (USEPA, 1998). Early studies indicated that the presence of 1,2,3,7,8-PeCDD with other PCDDs/PCDFs in human milk suggested that the major source of exposure came from waste incinerator emissions (Buser and Rappe, 1984; Rappe et al., 1985; Mukerjee and Cleverly, 1987). Note that these congeners are measurable in human milk currently (Sasamoto et al., 2006; Zhao et al., 2007; Raab et al., 2008).

Levels of PCDFs in human milk tend to be lower than PCDDs. However, PCDFs dominate in particulates emitted by combustion sources, including hazardous waste incinerators, and are present in higher concentrations in the atmosphere than PCDDs (USEPA, 1998). HxCDDs/HxCDFs and HpCDDs/HpCDFs are prevalent in pentachlorophenol. Incineration of wood and other products impregnated with

pentachlorophenol results in the formation of these congeners and emissions of hexa- and hepta-CDDs/CDFs. Both 1,2,3,7,8 and 2,3,4,7,8-PeCDFs have been detected in human milk, but 90% of the PeCDFs is generally 2,3,4,7,8-PeCDF. 1,2,3,4,7,8-, and 1,2,3,6,7,8- HxCDFs, 2,3,4,6,7,8-HxCDFs, and 1,2,3,4,6,7,8-HpCDF are also prevalent.

Several investigators have observed that dose, degree of chlorination, degree of lipophilicity, and molecular weight influence how much PCDD/F congener is absorbed through the lungs or gut, metabolized and transferred from blood to milk (Yakushiji, 1988; Abraham et al., 1998; Schecter et al., 1998; Kostyniak et al., 1999; Oberg et al., 2002; Wittsiepe et al., 2007).

Numerous studies have attempted to correlate exposure to individual dioxins, furans and dioxin-like PCBs from ingestion of contaminated food with levels in human biological samples such as blood and milk. Transfer from intake sources to human milk has often been estimated in the context of accidental or occupational exposures or after a substantial decline in environmental concentrations (Liem et al., 1995; Pinsky and Lorber, 1998; Liem et al., 2000; Focant et al., 2002; Furst, 2006; Milbrath et al., 2009). Steady state conditions are not reached in these studies because the half-lives of these compounds are in years and exposure changed considerably over the period evaluated in each study.

Others have attempted to model the relationship between maternal intake and concentration in mother's milk using an indicator compound such as TCDD (Smith, 1987; Lorber and Phillips, 2002). Less understood is the relationship between modeled and measured transfer estimates of individual dioxins, furans and dioxin-like PCBs. The following sections describe the sources of data and methods for deriving estimates of transfer for an array of dioxins, furans and dioxin-like PCBs that have accounted to some extent for the non-steady state condition and other confounders.

J.2.2 Oral Biotransfer

OEHHA located a series of studies conducted on the Dutch population that allows for an oral biotransfer estimate of dioxins and furans, and accounts for changing exposure conditions. In 1988, Albers et al. collected and analyzed three hundred nineteen breast milk samples from women enrolled through 28 maternity centers located throughout the Netherlands. Maternity centers were selected based on geographic distribution and degree of urbanization. Human milk samples were analyzed for 17 PCDD/F congeners and 8 PCB congeners (Albers et al., 1996).

Liem et al. (1995) took a similar approach to collect about 100 samples from first-time mothers enrolled in 1993 through maternity centers dispersed throughout The Netherlands. Based on information obtained from a questionnaire about characteristics of the study subject, investigators determined that the 1993 cohort appeared to be comparable to the cohort studied in 1988. With one exception, (1,2,3,4,7,8- HxCDD), a consistent downward trend can be seen among congeners of PCDD/Fs and PCB-118 that were analyzed during both sampling periods, (Table J.2-1).

Table J.2-1: Summary Estimates of Dioxin-like Compounds Dietary Intake during Three Periods Over 15 years, and Human Milk Levels over Five Years in the Dutch Population

Chemical/ group	TEF	1978 (diet)[a]	1984/5 (diet)[a]	1994 (diet)[a]	1988 (milk)[b]	1993 (milk)[a]
		Mean, SD	Mean, SD	Mean, SD	Mean, SD	Mean, SD
		pg/d*	pg/d*	pg/d*	pg/kg-milk	pg/kg-milk
2,3,7,8-TCDD	1	13.2, 1.32	6, 2.94	3.6, 1.26	264,14	124, 56
1,2,3,7,8-PeCDD	1	39.6, 6.73	15, 4.65	4.8, 2.26	435,185	324, 116
1,2,3,4,7,8-HxCDD	0.1	85.8, 23.17	23.4, 17.55	7.2, 5.98	328,51	344, 192
1,2,3,6,7,8-HxCDD	0.1	325.8, 45.61	89.4, 42.02	19.8, 22.77	2445,349	1484, 668
1,2,3,7,8,9-HxCDD	0.1	105, 21.0	32.4, 21.38	10.8, 9.61	395,32	276, 132
1,2,3,4,6,7,8-HpCDD	0.01	2016, 463.68	1908, 2671.2	150, 120	3242,114	1796, 984
OctaCDD	0.0001	12420, 4595	9180, 10281	1170, 749	28844,2896	11788, 6708
2,3,7,8-TCDF	0.1	106.8, 9.61	84, 31.08	21, 14.7	100,8	16, 16
1,2,3,7,8-PeCDF	0.05	24.6, 4.67	6.6, 2.71	3.6, 1.51	30,10	8, 8
2,3,4,7,8-PeCDF	0.5	178.8, 25.03	65.4, 13.73	23.4, 12.87	807,108	720, 300
1,2,3,4,7,8-HxCDF	0.1	178.8, 30.40	43.8, 9.20	27.6, 11.04	293,20	208, 92
1,2,3,6,7,8-HxCDF	0.1	54, 3.78	27, 6.21	13.8, 5.52	261,17	176, 84
1,2,3,7,8,9-HxCDF	0.1	<0.05	<0.04	<0.04	NA	NA
2,3,4,6,7,8-HxCDF	0.1	55.8, 6.70	25.2, 6.80	9, 5.76	133,19	96, 52
1,2,3,4,6,7,8-HpCDF	0.01	471, 117.75	176.4, 65.27	51.6, 22.19	523,55	240, 124
1,2,3,4,7,8,9-HpCDF	0.01	39, 4.68	7.8, 5.07	3, 1.62	NA	4, 4
OctaCDF	0.0001	466.8, 107.36	195, 78.0	69.6, 37.58	49,10	12, 12
PCB-77	0.0001	NA	NA	NA	NA	452, 872
PCB-81	0.0001	NA	NA	NA	NA	NA
PCB-126	0.1	1350, 202.5	924, 221.76	378.6, 87.08	NA	3284, 1448
PCB-169	0.01	270, 54.0	181.2, 86.98	174, 214.02	NA	2320, 988

Table J.2-1: Summary Estimates of Dioxin-like Compounds Dietary Intake during Three Periods Over 15 years, and Human Milk Levels over Five Years in the Dutch Population

Chemical/ group	TEF	1978 (diet)[a]	1984/5 (diet)[a]	1994 (diet)[a]	1988 (milk)[b]	1993 (milk)[a]
		Mean, SD	Mean, SD	Mean, SD	Mean, SD	Mean, SD
		ng/d*	ng/d*	ng/d*	ng/kg-milk	ng/kg-milk
PCB-105	0.0001	71.4, 13.57	70.2, 33.7	13.2, 5.54	NA	160, 80
PCB-114	0.0005	6.6, 0.92	11.4, 8.66	1.8, 1.35	NA	NA
PCB-118	0.0001	289.2, 43.38	247.2, 111.24	49.2, 15.25	1009,565	971.2, 456
PCB-123	0.0001	18.6, 3.91	15, 7.65	2.4, 0.89	NA	NA
PCB-156	0.0005	191.4, 63.16	27.6, 8.28	9, 2.79	NA	564, 236
PCB-157	0.0005	22.2, 6.44	4.8, 1.73	1.8, 0.72	NA	108, 48
PCB-167	0.00001	79.2, 22.18	11.4, 2.51	3.6, 1.01	NA	152, 64
PCB-189	0.0001	43.8, 13.14	2.4, 0.53	1.2, 0.31	NA	48.4, 48

[a] (Liem et al., 2000); [b] (Albers et al., 1996), NA, not available

* Conversion from g-fat to kg-milk = 0.04 g-fat/g-milk*1000g/kg; Liem et al. reported dietary intake estimates in units of mass/body weight/day. Therefore, we converted their estimates to units of mass/day by multiplying by the default 60 kg body weight used by Liem et al (Liem et al., 2000).

Liem et al. (2000) reported dietary intake for three time-periods (see Table J.2-1)(Liem et al., 2000). Dietary intake estimates were based on concentrations of PCDD/Fs and PCBs measured in composite samples of 24-hr duplicate diets in the Dutch adult population in 1978, 1984-85, and 1994 and combined with individual consumption data collected in 1987-1988 (Albers et al., 1996) (briefly summarized previously) for approximately 6000 individuals from 2200 families over a 2-day period . In a separate study, these same investigators estimated dioxin and dioxin-like compounds in human milk fat collected in the period 1992-1993 from more than 80 women (Liem et al., 1995; Liem et al., 2000).

Liem et al. (2000) observed a downward trend in estimated dietary intake of individual congeners of PCDDs PCDFs and PCBs in the Dutch population during three intervals from 1978 to 1994 (see Table J.2-1)(Liem et al., 2000). A downward trend was also seen in a study of these toxicant levels in the diet and human milk of the German population from 1983 - 2003 (Furst, 2006; Wilhelm et al., 2007). However, about half of the mono-ortho PCBs did not show a similar linear decline. This pattern is consistent with observations made by Alcock et al., (1996) who reported some evidence that the environmental load of PCDD/Fs increased in the 1960s, peaked around 1975 and then began to decline (Alcock et al., 1996).

OEHHA has derived lactational transfer coefficients for PCDD/Fs and dioxin-like PCBs from studies of exposure from global sources and by multiple pathways. The proportional contribution from various exposure pathways to total exposure from a single Hot Spots facility is likely to be quite different from that found from global sources.

However, we assume that the estimate of transfer to milk from global sources, such as that derived from the Dutch studies, reasonably represents the transfer in persons from communities near Hot Spot facilities in California.

The Hot Spots program allows for reporting emissions of individual congeners of dioxins, furans and PCBs, when emissions are speciated. It also permits reporting of emissions as total dioxins and furans or PCBs. Speciation of emissions produces a more accurate (and lower) risk estimate. This is because unspeciated emissions are assumed to be 2,3,7,8-TCDD, which has the highest potency factor among the dioxins and furans. Therefore, OEHHA has derived congener Tcos for individual PCBs and dioxins that can be used when emissions are speciated.

J.2.3 Mothers' Milk Transfer Coefficients (Tco) for PCDD/Fs and PCBs

To calculate oral Tcos, OEHHA used adjusted reference half-lives for the chemicals in adults estimated from dietary and occupational exposures. OEHHA estimated oral Tcos for these chemicals using estimates of body weight reported in Chapter 10 of this document, reference half-lives reported in Milbrath et al. (2009) and the steady-state equation developed by Smith (1987) (Smith, 1987; Milbrath et al., 2009).

Milbrath et al., (2009), in a systematic review of studies reporting half-lives in the human body, developed average human biological reference half-lives for 28 out of 29 dioxins and dioxin-like PCBs with OEHHA-recognized potency factors (see Table J-2-2) (Milbrath et al., 2009).

Each reference half-life was derived from data on occupational exposures (Flesch-Janys et al., 1996; van der Molen et al., 1996) or dietary intake of the general population (Ogura, 2004). Note that mean half-lives vary by more than 2-fold among dioxin, 5-fold among furans and more than 100-fold among PCB congeners.

Table J.2-2: Half-lives of PCDD/Fs and Dioxin-like PCB Congeners in Humans as Measured in Blood (Milbrath et al., 2009)

Chemical	N studies	Half-life range (yrs)	Mean half-life in adult (yrs)	Median half-life in adult (yrs)	Study
TCDD	10	1.5 – 15.4	7.2	6.3	a
1,2,3,7,8-PeCDD	4	3.6 – 23.1	11.2	8.5	a
1,2,3,4,7,8-HxCDD	3	1.4 – 19.8	9.8	10.9	a
1,2,3,6,7,8-HxCDD	4	2.9 – 70	13.1	12	a
1,2,3,7,8,9-HxCDD	3	2.0 – 9.2	5.1	6.8	a
1,2,3,4,6,7,8-HpCDD	4	1.6 – 16.1	4.9	3.7	a
OctaCDD	4	1.8 - 26	6.7	5.7	a
2,3,7,8-TCDF	1	0.4	2.1	0.9	b
1,2,3,7,8-PeCDF	4	0.9-7.5	3.5	1.9	b
2,3,4,7,8- PeCDF	16	1.5-36	7	4.9	b
1,2,3,4,7,8-HxCDF	14	1.5-54	6.4	4.8	a
1,2,3,6,7,8-HxCDF	6	2.1-26	7.2	6	a
2,3,4,6,7,8-HxCDF	6	1.5-19.8	2.8	3.4	b
1,2,3,4,6,7,8-HpCDF	11	2.0-7.2	3.1	3	a
1,2,3,4,7,8,9-HpCDF	1	2.1-3.2	4.6	5.2	b
OctaCDF	1	0.2	1.4	1.6	b
PCB-77	2	0.1-5.02	0.1	0.1	c
PCB-81	-	-	0.7	0.73	c
PCB-126	3	1.2-11	1.6	2.7	c
PCB-169	3	5.2-10.4	7.3	10.4	c
PCB-105	4	0.56-7.0	2.4	2.4	c
PCB-114	2	7.4-31.7	10	25	c
PCB-118	10	0.82-33.7	3.8	1.6	c
PCB-123	2	5.3-15.3	7.4	12	c
PCB-156	7	1.62-100	16	5.35	c
PCB-157	2	13-26	18	20	c
PCB-167	2	8.7-35	12	12	c
PCB-189	2	16-166.7	22	41	c

[a] (Flesch-Janys et al., 1996); [b] (van der Molen et al., 1996); [c] (Ogura, 2004)

In an initial review of the literature, Milbrath et al (2009) reviewed evidence about factors that can affect elimination rates. Personal factors such as body fat, smoking status and past lactation practices can affect body burden and elimination rates. For example, smoking has been associated with a 30% to 100% increase in elimination rates of some dioxin congeners (Flesch-Janys et al., 1996; Milbrath et al., 2009). As well, the onset of lactation sets a new elimination pathway into effect and can substantially reduce the maternal body burden of PCBs during 6 months of lactation (Niessen et al., 1984; Landrigan et al., 2002).

Half-lives derived from children would be less than that from older adults due, in part, to the effects of the growing body on estimates of blood concentrations. Models based on rat data demonstrate a linear relationship between increasing fat mass and half-life length at low body burdens, with the impact of adipose tissue on half-life becoming less important at high body burdens (Emond et al 2006). At high body burdens, dioxins are known to up-regulate the enzymes responsible for their own elimination. Human data suggest that the serum concentration of TCDD where this transition occurs is 700 pg/g and 1,000 – 3,000 pg/g for PCDFs (Kerger et al 2006, Leung et al 2005). Therefore, investigators selected a subset of data based on the following criteria:

- blood serum concentrations of PCDD/Fs were less than 700 pg /g blood lipid total toxic equivalents (TEQs) at the time of sampling
- subjects were adults
- measurements were not reported as inaccurate in later studies

Milbrath et al selected the reference values to represent a 40- to 50-year-old adult with blood dioxin concentrations in the range where fat drives the rate of elimination (i.e. at lower body burdens). In addition, Milbrath rejected half-lives longer than 25 years if the original study calculated half-lives assuming steady-state conditions.

For the retained subset, the investigators calculated the mean and range of half-lives to establish a representative set of half-lives for each congener in a moderately exposed adult (Milbrath et al., 2009). They also adjusted reference half-lives for age, body fat, smoking habits and breast-feeding status as these factors were all strong determinants of half-life in humans (Milbrath et al., 2009).

A generally accepted approach to estimating the concentration of a lipophilic chemical in milk is outlined by Smith (1987). This approach is based on average maternal daily intake, an estimate of the half-life ($t_{1/2}$) of PCDDs/PCDFs and PCBs and body weight-normalized (BW) proportionality factors. The chemical concentration in breast milk can be calculated by equation J-4:

$$Cm = (Emi)(t_{1/2})(f1)(f3)/(f2)(0.693) \quad \textbf{(Eq. J-4)}$$

Where:

Cm = chemical concentration in milk (mg/kg milk)
Emi = average daily maternal intake of contaminant (mg/kg-BW/day)
$t_{½}$ = biological half-life (days)
f1 = proportion of chemical in mother that partitions into fat (e.g. 0.8)
f2 = proportion of mother's body weight that is fat (e.g. 0.33 = kg-fat/kg-BW)
f3 = proportion of breast milk that is fat (e.g., 0.04 = kg-fat/kg-milk)

Smith's approach requires an estimate of the biological half-life of PCBs and PCDDs/PCDFs in the adult human and is restricted to poorly metabolized, lipophilic chemicals that act predominantly by partitioning into the fat component and quickly reaching equilibrium in each body tissue (including breast milk).

Because of Milbrath's approach, Tco-estimates for dioxins, furans and dioxin-like PCBs apply the following conservative assumptions regarding factors that affect elimination rates:

- lower enzyme induction based on nonsmokers with a body burden below 700 ppt in the blood
- adult age
- no recent history of breast-feeding
- body fat estimates based on older adults

Transfer coefficients (Ng, 1982) are ideally calculated from the concentration of contaminant in milk following relatively constant long-term exposure that approximates steady state conditions. Because Smith's equation is linear, it can be rearranged to solve ratio of the chemical concentration in milk to the chemical taken into the body per day, which is the transfer coefficient (Equation J-5).

$$Tco = Cm/(Cf)(I) \quad \textbf{(Eq J-5)}$$

Where:

Tco is the transfer coefficient (day/kg or day/liter)
Cm = measured chemical concentration in milk (µg/kg or mg/liter milk)
Cf = measured chemical concentration in exposure media (e.g. food) (µg/kg food)
I = reported daily intake of exposure media (kg/day of food)

The following equation (Eq-J-6) is equation Eq J-5 substituted into equation Eq J-4 and rearranged to solve for Tco.

$$Tco = (t_{1/2})(f1)(f3)/(BW)(f2)(0.693) \quad \textbf{(Eq J-6)}$$

Note that Emi in equation J-4 = (Cf)(I)/BW with units of mg/kg-BW/day. BW is the average adult body weight of the mother (kg).

Transfer coefficients (Tcos) in Table J.2-3 (column-2) combine milk data (milk concentration of PCDD/Fs and PCBs) with dietary intake estimates listed in Table J.2-1. OEHHA derived individual Tcos from data presented in (Liem et al., 1995; Albers et al., 1996; Liem et al., 2000). Because the median is a reasonable estimate of the geometric mean in skewed distributions, Tcos were derived from median half-lives listed in column-5 of Table J.2-2. Tcos range from less than one to more than ten d/kg-milk among dioxins and furan and less than two to more than 20 d/kg-milk among dioxin-like compounds.

Table J.2-3: Arithmetic Mean Transfer Coefficients (Tcos) for Individual PCDD/F and PCB Congeners Measured in Human Milk and Dietary Intake from a Dutch Population (d/kg-milk) Compared to the Median and Geometric Mean Tcos Derived from Reference Half-lives ($t_{1/2}$) and Equation J-6

Chemical/group	Tcos (GM) based on slope factors	Tco based on median reference half life (Milbrath et al 2007)	Tco based on t1/2 GM*	Tco based on t1/2 GSD	Tco based on t1/2 LCL	Tco based on t1/2 UCL
2,3,7,8-TCDD	49.62	5.36	4.02	2.76	2.14	7.53
1,2,3,7,8-PeCDD	8.76	7.24	6.53	2.16	3.07	13.90
1,2,3,4,7,8-HxCDD	0.98	9.28	5.60	3.41	1.40	22.48
1,2,3,6,7,8-HxCDD	11.02	10.21	3.27	4.20	0.80	13.32
1,2,3,7,8,9-HxCDD	4.89	5.79	3.32	1.91	1.60	6.88
1,2,3,4,6,7,8-HpCDD	2.88	3.15	1.96	2.74	0.73	5.26
OctaCDD	5.54	4.85	2.29	3.25	0.72	7.28
2,3,7,8-TCDF	3.18	0.77	1.76	1.36	0.96	3.23
1,2,3,7,8-PeCDF	3.43	1.62	1.91	2.49	0.78	4.68
2,3,4,7,8- PeCDF	2.77	4.17	1.78	4.24	0.88	3.62
1,2,3,4,7,8-HxCDF	2.16	4.09	0.99	5.29	0.41	2.38
1,2,3,6,7,8-HxCDF	7.89	5.11	2.64	3.01	1.09	6.39
1,2,3,7,8,9-HxCDF	NA	NA	NA	NA	NA	NA
2,3,4,6,7,8-HxCDF	3.18	2.89	0.55	3.18	0.22	1.39
1,2,3,4,6,7,8-HpCDF	2.40	2.55	1.82	1.63	1.36	2.44
1,2,3,4,7,8,9-HpCDF	NA	4.43	3.63	1.34	2.06	6.42
OctaCDF	0.32	1.36	0.99	2.83	0.13	7.55
PCB-77	NA	NA	0.06	6.38	0.004	0.72
PCB-81	NA	NA	0.38	1.35	0.248	0.57
PCB-126	NA	2.30	0.34	2.61	0.11	1.01
PCB-169	NA	8.85	5.60	1.27	4.28	7.32
PCB-105	NA	2.04	1.07	3.02	0.36	3.16
PCB-114	NA	2.04	2.74	3.11	0.57	13.20
PCB-118	0.01	1.36	0.55	6.17	0.18	1.70
PCB-123	NA	1.36	2.93	2.63	0.77	11.18
PCB-156	NA	4.55	3.23	7.10	0.76	13.81
PCB-157	NA	17.02	14.10	1.21	10.84	18.34
PCB-167	NA	10.21	5.93	1.76	2.70	13.00
PCB-189	NA	34.90	4.23	2.77	1.03	17.33

slope factors obtained from the longest interval between measures of diet (1978-1994) and milk (1988-1993) in the Dutch population; * GM, geometric mean, GSD, geometric standard deviation derived from natural log of three half-life values, low, high and median reported in Milbrath et al. (Milbrath et al., 2009) LCL, lower 95% confidence limit of the mean Tco; UCL, upper 95% confidence limit of the mean Tco

OEHHA evaluated the relationship between Tcos predicted by Equation J-6 (column 3) using median reference half-lives and those derived from slope factors (column 2). Briefly, slope factors were calculated by taking the difference between cross-sectional dietary intake estimates taken in 1978 and 1994 and the difference between cross-sectional human milk concentrations taken in 1988 and 1993 from the Dutch population. Most Tcos derived from reference half-lives compare reasonably well with those derived from slope factors.

In columns 4-7 of Table J.2-3 the GM, GSD and 95%CLs of transfer coefficients (Tcos) for individual dioxins and dioxin-like congeners are derived from equation J-6 and geometric distribution estimates and 95% confidence intervals of half-lives provided in (Milbrath et al., 2009).

A Random-effects model derived summary estimates shown in Table J.2-4 from individual summary estimates shown in columns 4-7 of Table J.2-3.

Table J.2-4: Tco Estimates Stratified by Dioxin, Furan and Dioxin-like PCB Congeners (mean, 95%CI from Random-effects Model)

Chemical group	N congeners	Tco	LCL	UCL
PCDDs - oral	7	3.7	2.68	5.23
PCDFs - oral	9	1.8	1.27	2.43
Dioxin-like PCBs - oral	12	1.7	0.69	4.40

LCL, lower 95% confidence limit of the mean Tco; UCL, upper 95% confidence limit of the mean Tco

OEHHA believes that a Random-effects model is appropriate because OEHHA assumes that the compounds found in exposure studies are a subgroup from a population of congeners in each subgroup (i.e., dioxins and dioxin-like compounds). Random-effects models assume there are multiple central estimates and incorporate a between-compound estimate of error as well as a within-compound estimate of error in the model. In contrast, a Fixed-effects model assumes that observations scatter about one central estimate (Kleinbaum, 1988).

J.2.4 Carryover Rate

Looking at mother's milk Tcos in terms of carryover rate suggests that accumulation of dioxins and dioxin-like compounds in the mother's body occurs but varies by more than 100-fold among individual compounds (based on Tcos derived from equation J-6).

Carryover rate, a term commonly used in the dairy literature (McLachlan et al., 1990) is defined as the daily output of dioxins and dioxin-like compounds in mother's milk (µg/day) over the daily intake of dioxins and dioxin-like compounds (µg/day). This rate is estimated by multiplying a dioxin's and dioxin-like Tco by the daily output of mother's milk. Since milk production in human mothers are about 1.0 kg/day, a dioxins and dioxin-like Tco is the carryover rate for a typical 60 kg woman.

A carryover rate > 1 would suggest that dioxins and dioxin-like compounds could accumulate in body fat and transfer to the fat in mother's milk. With an average dioxin Tco of 3.7 d/kg, 370% of the mother's average daily intake from ingested sources, transfers to mother's milk. This high transfer-value suggests that accumulation or concentrating of carcinogenic dioxins and dioxin-like compounds occur in the mother's body. Oral Tcos less than one d/kg (e.g., 1,2,3,4,7,8-HxCDF and 2,3,4,6,7,8-HxCDF) suggest that net metabolism or excretion occurs in the mother's body.

J.3 Mothers' Milk Transfer Coefficients for PAHs

The polycyclic aromatic hydrocarbons (PAHs), a family of hundreds of different chemicals, are characterized by fused multiple ring structures. These compounds are formed during incomplete combustion of organic substances (e.g. coal, oil and gas, garbage, tobacco or charbroiled meat). Thus, PAHs are ubiquitous in the environment and humans are likely to be exposed to these compounds on a daily basis. PAHs are a common pollutant emitted from Hot Spots facilities and are evaluated under the program.

Only a small number of the PAHs have undergone toxicological testing for cancer and/or noncancer health effects. PAHs with cancer potency factors are the only ones that can be evaluated for cancer risk using risk assessment. However, PAHs that lack cancer potency factors have been measured in various studies and can serve as a useful surrogate for PAHs with cancer potency factors because of their physical-chemical similarity to PAHs with cancer potency factors.

Less than 30 specific PAHs are measured consistently in biological samples or in exposure studies. For example, Table J.3-1 lists commonly detectable PAHs in food and the environment (Phillips, 1999). In one analysis, pyrene and fluoranthene together accounted for half of the measured PAH levels in the diet (Phillips, 1999). Table J.3-1 includes nine PAHs that have cancer potency factors and are recognized by OEHHA as presenting a carcinogenic risk to humans (OEHHA, 2009).

Table J.3-1: PAHs with and without Cancer Potency Factors Commonly Measured in Food (Phillips, 1999)

PAHs without Cancer Potency Factors	PAHs with Cancer Potency Factors
Benzo[ghi]perylene	Dibenz[a,h]anthracene
Fluoranthene	Indeno[1,2,3-cd]pyrene
Pyrene	Benzo[a]pyrene
Phenanthrene	Benzo[k]fluoranthene
Anthracene	Chrysene
Fluorene	Benzo[b]fluoranthene
Acenaphthylene	Benz[a]anthracene
Acenaphthene	Naphthalene
Benzo[b]naphtho[2,1-d]thiophene	Benzo[j]fluoranthene
Benzo[ghi]fluoranthene	
Cyclopenta[cd]pyrene	
Triphenylene	
Perylene	
Benzo[e]pyrene	
Dibenz[a,j]anthracene	
Anthanthrene	
Coronene	

Few investigators have attempted to correlate PAH exposure from contaminated food and ambient air with PAH concentrations in human biological samples such as the blood or mother's milk. This is likely due to insensitive limits of detection for PAHs yielding few positive measurements, possibly due to the rapid and extensive metabolism of PAHs in mammals (West and Horton, 1976; Hecht et al., 1979; Bowes and Renwick, 1986).

This extensive metabolism often results in low or immeasurable concentrations of PAHs in mother's milk and blood (e.g. (Kim et al., 2008)). Nevertheless, emissions of PAHs from stationary sources are common and the increased sensitivity of infants to carcinogens necessitates looking into development of mother's milk transfer factors (Tco) for carcinogenic PAHs.

Four studies have measured PAHs in mother's milk of smokers and non-smokers (see Table J.3-2). The 16 PAHs reported in these studies are among the most common PAHs released into the environment and found in biological samples (Phillips, 1999; Ramesh et al., 2004).

TABLE J.3-2: Measured Concentrations (µg/kg-milk) of PAHs in Human Milk

Chemical / chemical group	**Urban smokers (Italy)** n=11[a] (Zanieri et al., 2007)	**Urban non-smokers (Italy)** n=10 (Zanieri et al., 2007)	**Rural Non-smokers (Italy)** n=11 (Zanieri et al., 2007)	**Rural Non-smokers (Italy)** n=10 (Del Bubba et al., 2005)	**Non-smokers (USA)** n=12 (Kim et al., 2008)	**Unknown (Japan)** n=51 (Kishikawa et al., 2003)
PAHs with Cancer Potency Factors AM, SD						
Naphthalene	10.54, 6.08	6.83, 2.18	4.42, 1.17	4.70, 2.44	NA[d]	NA
Chrysene	0.90, 2.09	0.59, 0.94	<0.018	<0.018	--[c]	0.06, 0.08
Benzo[a] anthracene	0.98, 1.47	0.61, 0.94	0.07, 0.16	0.974, 1.82	--	0.004, 0.01
Benzo[b] fluoranthene	0.53, 1.24	0.55, 0.80	<0.019	0.560, 1.39	--	0.41, 0.26
Benzo[k] fluoranthene	0.13, 0.30	<0.018	<0.018	0.114, 0.343	--	0.01, 0.01
Benzo[a]pyrene	0.52, 0.65	<0.018	<0.018	<0.018	--	0.002, 0.003
Dibenzo[a,h] anthracene	1.33, 3.33	<0.014	<0.014	<0.014	--	0.01, 0.01
Indeno[1,2,3-c,d] pyrene	0.42, 0.94	<0.011	<0.011	<0.011	--	0.003, 0.01
Sum	15.35	8.58	4.5	6.4	--	0.5
PAHs without Cancer Potency Factors AM, SD						
Anthracene	0.16, 0.45	0.71, 1.57	0.21, 0.56	0.616, 1.58	--[c]	0.01, 0.01
Acenaphthylene	7.73, 11.95	9.09, 3.08	4.11, 3.62	6.95, 4.18	NA[d]	NA
Phenanthrene	3.67, 2.39	0.97, 0.51	0.64, 0.58	0.553, 0.493	0.49, 0.44	0.25, 0.16
Fluorene	5.13, 9.45	1.50, 1.60	0.06, 0.21	1.06, 1.70	0.13, 0.13	NA
Acenaphthene	10.55, 17.73	3.12, 1.79	1.37, 1.31	2.72, 1.69	NA	NA
Pyrene	1.03, 1.25	1.40, 3.01	0.21, 0.30	0.620, 1.64	0.05, 0.04	0.02, 0.05
Fluoranthene	2.86, 2.60	0.54, 0.76	0.53, 1.03	0.250, 0.441	0.06, 0.05	0.02, 0.03
Benzo[g,h,i] perylene	1.51, 2.24	<0.018	<0.018	<0.018	--	--
Sum	32.64	17.33	7.13	12.8	0.73	0.3

[a] group includes one rural smoker; [b]values below detection limits were treated as zero in estimates of the mean; [c] – indicates all measurements were below the detection limits; [d] not assessed; (Kishikawa et al., 2003; Del Bubba et al., 2005; Zanieri et al., 2007; Kim et al., 2008) µg, microgram; kg, kilogram; n, number of samples; AM, Arithmetic Mean; SD, Standard Deviation

In this section, we estimated Tcos for PAHs with and without cancer potency factors. Additionally, none of the PAHs has a chronic Reference Exposure Level (REL) value. PAHs without cancer potency factors (other) are included because they:

- have structures similar to carcinogenic PAHs and are thus suitable as surrogate compounds
- are frequently measured in exposure studies
- produce measurements at detectable levels

In Table J.3-2, the sum of carcinogenic PAHs in human milk of Italian women is about 2-fold lower than the sum of other PAHs.

Because of their similarities in structure, the Tcos developed from other abundant PAHs are expected to compare reasonably well with the Tcos developed for less abundant carcinogenic PAHs.

J.3.1 Inhalation Biotransfer of PAHs to Mother's Milk

Biotransfer of PAHs to breast milk via the mother's inhalation pathway must be considered separately from biotransfer of PAHs to breast milk from the mother's oral route. PAHs will show a different pattern of metabolism depending on the route of exposure because of first pass metabolism in the liver from oral exposure, different rates and patterns of metabolism in the lung, and other factors. Smoking cigarettes represents a significant source of PAHs resulting in measurable levels of PAHs in mother's milk. Therefore, OEHHA chose a study that measured PAH concentrations in breast milk in smoking women and nonsmoking women to estimate inhalation Tcos for PAHs.

Of the four studies listed in Table J.3-2, the Italian study by Zanieri et al. (2007) allowed correlation of PAH intake via chronic smoking with PAH levels found in human milk (Zanieri et al., 2007). These investigators reported individual PAH concentrations in the milk of urban smoking and nonsmoking mothers, and in rural smoking and nonsmoking mothers.

Zanieri et al (2007) had obtained self-reported smoking habits (an arithmetic average of 5.4 cigarettes smoked per day) but not the daily dose of PAHs due to smoking (Zanieri et al., 2007). Therefore, OEHHA estimated daily PAH doses using published estimates of the amounts of PAHs a smoker voluntarily consumes during smoking per cigarette from simulated cigarette smoking studies. Ding et al. (2005) measured the amount of 14 individual PAHs that would be inhaled because of smoking major U.S. cigarette brands (Table J.3-3). Two other simulated smoking studies were included that estimated the inhaled amounts of two additional PAHs not covered in the Ding study (Gmeiner et al., 1997; Forehand et al., 2000).

Table J.3-3: Summary Estimates of Polycyclic Aromatic Hydrocarbons (PAHs) Intake from Cigarettes (µg/cigarette)

PAH	Ding et al (n=5)	Ding et al (n=50)	Ding et al (n=5)	Gmeiner et al (n=3)	Forehand et al (n=4)	Pooled
With Cancer Potency Factors	1[#] AM, SD[1]	2 AM, SD	3 AM, SD	1 AM, SD	1 AM, SD	AM, SD
Naphthalene	0.3503, 0.021	0.192, 0.044	0.407, 0.187	0.236, 0.019	0.362, 0.011	0.292, 0.087
Chrysene	0.0157, 0.0003	0.0197, 0.0024	0.0314, 0.0028	0.0218, 0.0009	0.0112, 0.0003	0.015, 0.0017
Benzo[a] anthracene	0.0134, 0.0007	0.0165, 0.0015	0.0226, 0.0025	0.0132, 0.0005	0.014, 0.0004	0.015, 0.0014
Benzo[b] fluoranthene	0.0094, 0.003	0.0106, 0.0013	0.0183, 0.0024	0.0086, 0.0003	0.0112, 0.0003	0.010, 0.0012
Benzo[k] fluoranthene	0.0015, 0.00014	0.0019, 0.00029	0.0039, 0.00070	0.0015, 0.00008	NA	0.0020, 0.0004
Benzo[a]pyrene	0.0103, 0.00041	0.011, 0.00077	0.0147, 0.00118	0.0079, 0.00024	0.0076, 0.00023	0.0092, 0.00067
Dibenzo[a,h] anthracene	NA	NA	NA	0.0006, 0.00013	0.0023, 0.00021	0.0023, 0.00017
Indeno[1,2,3-c,d] pyrene	NA	NA	NA	0.0035, 0.00039	NA	0.0035, 0.00039
Without Cancer Potency Factors	1 AM, SD	2 AM, SD	3 AM, SD	1 AM, SD	1 AM, SD	AM, SD
Anthracene	0.0749, 0.0052	0.0698, 0.0084	0.074, 0.0089	0.0381, 0.0023	0.0358, 0.0011	0.043, 0.0060
Acenaphthylene	0.1169, 0.0082	0.0883, 0.0097	0.153, 0.0306	0.0504, 0.0040	NA	0.083, 0.0167
Phenanthrene	0.1348, 0.0054	0.1452, 0.0131	0.144, 0.0144	0.11, 0.0033	0.1477, 0.0044	0.134, 0.0094
Fluorene	0.2175, 0.0087	0.1563, 0.0188	0.257, 0.0257	0.119, 0.0048	0.239, 0.0048	0.184, 0.0151
Acenaphthene	0.0848, 0.0025	0.0513, 0.0072	0.088, 0.0167	0.0253, 0.0013	NA	0.062, 0.0092
Pyrene	0.0486, 0.0029	0.0495, 0.0069	0.077, 0.0231	0.0332, 0.0017	0.0321, 0.0010	0.036, 0.0109
Fluoranthene	0.0744, 0.0037	0.063, 0.0107	0.101, 0.0121	0.0462, 0.0018	0.0516, 0.0026	0.056, 0.0076
Benzo[g,h,i] perylene	NA	NA	NA	0.0025, 0.00030	0.0023, 0.00018	0.0023, 0.00025

[1]AM arithmetic mean,, SD standard deviation ; #, Experiment number listed in the study reference by the first author in row one of columns two through six in the table (Gmeiner et al., 1997; Forehand et al., 2000; Ding et al., 2005)

Based on the estimated intake of 16 measured PAHs in simulated smoking studies and the PAHs found in breast milk from long-time smoking mothers by Zanieri et al. (2007), OEHHA was able to estimate transfer coefficients (Tco) with a modified version of Equation J-1:

$$Tco_{hmi} = Cm_i/(C_{cig\_i} \times I_{cig/day} \times f_{smoke}) \quad \textbf{(Eq. J-7)}$$

where:

Cm_i = adjusted geometric average ith PAH concentration due to smoking (µg per kg milk as wet weight)

C_{cig_i} = geometric average dose of the ith PAH per cigarette (µg/cigarette averaged across experiments)

$I_{cig/day}$ = geometric average number of cigarettes smoked (4.75 cigarettes/day)

f_{smoke} = adjustment for under-reporting of smoking frequency (2)

Cm_i is the adjusted geometric average of the ith PAH in whole milk due to smoking. OEHHA obtained these estimates by converting arithmetic estimates to geometric estimates of the mean and standard deviation and subtracting the GM concentration in the milk of primarily urban nonsmokers from the GM concentration in the milk of urban smokers. This adjustment accounts for oral intake of PAHs from dietary sources and inhalation of PAHs in urban air from combustion sources other than cigarettes. Implicit in this adjustment is the assumption by OEHHA that oral intake and exposure to other airborne PAHs is similar between smokers and nonsmokers who participated in the Zanieri study.

OEHHA also included a 2-fold smoking habit adjustment-factor (f_{smoke}) in Eq. J-7 based on published data to account for the recognized tendency of smokers to under-report their smoking habits. The studies examined the accuracy of self-reported smoking habits among pregnant women and parents with small children (Marbury et al., 1993; Graham and Owen, 2003). They measured airborne nicotine in the smoker's breathing zone and obtained the number of cigarettes smoked per day by each smoker. The data presented in Figure (1) of Marbury et al suggest that mothers under-reported their smoking rate by 50% (Marbury et al., 1993).

Table J.3-4 presents the Tcos for cancer and noncancer PAHs calculated using Eq. J-7. However, Zanieri and Del Bubba did not find measurable levels of some PAHs, particularly PAHs with 5 or 6 carbon rings, in milk from nonsmokers. In these cases, the concentration representing half the limit of detection (between 0.006-0.014 µg/kg) was used as the background concentration of the PAH in mother's milk.

There are two main limitations in the data provided in Table J.3-4. For some PAHs, no individual Tco was calculated because the concentration of the individual PAH was higher in mother's milk of nonsmokers than in smokers. For example, in column two of Table J.3-4, mother's milk benzo[b]fluoranthene, pyrene and anthracene have negative concentration values.

These discrepancies could be due to the natural variation in the ability of individuals to transfer inhaled PAHs to milk, or as Zaneiri et al. suggested, a result of greater exposure to certain PAHs in some foods compared to cigarette smoke. The small sample sets (n=11 for each group of smokers and nonsmokers) in the Zanieri study are less likely to represent the true mean in the study population and magnify the large variation in this biological response.

Additional uncertainties in the use of smokers to estimate PAH transfer coefficients include that fact that lung metabolism may be different in smokers because of the much higher doses of PAHs that smokers receive relative to those only exposed in ambient pollution. Cytochrome P-450 enzymes are known to be induced when exposure is greater and therefore metabolism could be proportionately greater in smokers. In addition, at higher dose levels some enzyme systems may become saturated which could alter the pattern of metabolism.

However, smokers are the best population for estimating PAH Tcos because the inhalation dose can be separated from background inhalation and dietary exposure, and the inhalation dose from the cigarettes can be estimated. OEHHA requested raw data from the investigators for individual women in the study, but unfortunately, only the summary statistics from the published paper were available to us.

Table J.3-4: Inhalation Transfer Coefficients (Tcos) for Individual PAHs with and without Potency factors from Geometric Mean and Standard Deviation Estimates (GM, GSD) of Human Milk (Cm) and Intake from Cigarettes (Ccig) (d/kg-milk)

PAH (no. of rings)[a]	Adjusted Cm (µg/kg wet wt.)	C_{cig} (µg/cig)	Inhalation Tco[b] (d/kg)
With Cancer Potency Factors	**GM, GSD**	**GM, GSD**	**GM, GSD**
Naphthalene (2)	2.78, 1.63	0.2798, 1.34	1, 2.66
Chrysene (4)	0.04, 5.34	0.0149, 1.12	0.28, 8.11
Benzo[a]anthracene (4)	0.20, 4.31	0.0149, 1.1	1.4, 6.52
Benzo[b]fluoranthene (5)	*-0.09, 5.01*	0.0099, 1.13	NA[c]
Benzo[k]fluoranthene (5)	0.05, 2.95	0.002, 1.22	0.26, 4.6
Benzo[a]pyrene (5)	0.26, 2.29	0.0092, 1.08	2.97, 3.45
Dibenzo[a,h]anthracene (5)	0.46, 3.85	0.0023, 1.08	2.11, 5.81
Indeno[1,2,3-c,d]pyrene (6)	0.16, 3.65	0.0035, 1.12	4.81, 5.54
Without Cancer Potency Factors	**GM, GSD**	**GM, GSD**	**GM, GSD**
Anthracene (3)	*-0.22, 6.29*	0.0426, 1.15	NA
Acenaphthylene (3)	*-4.56, 2.9*	0.0814, 1.22	NA
Phenanthrene (3)	2.00, 1.94	0.0035, 1.07	1.57, 2.92
Fluorene (3)	1.31, 4.1	0.1336, 1.09	0.75, 6.19
Acenaphthene (3)	2.48, 3.26	0.0613, 1.16	4.21, 5
Pyrene (4)	0.04, 4.57	0.0345, 1.34	0.12, 7.48
Fluoranthene (4)	1.63, 3.29	0.0555, 1.14	3.06, 5.02
Benzo[g,h,i]perylene (6)	0.77, 2.72	0.0023, 1.11	35.24, 4.13

[a] no. of rings, number of rings are an indicator of lipophilicity (greater # of rings, more likely to partition to body fat); [b] Sum of each PAH found in mother's milk microgram per kilogram (µg/kg) over the sum of the daily intake (µg/day) of the same PAH x 4.75 cigarettes/day x an adjustment factor of 2; [c] NA, not available because the concentration of PAH in mother's milk of smokers was lower than the concentration in nonsmokers, so an individual Tco could be calculated

Tco values for carcinogenic PAHs in Table J.3-4 are determined for all available PAHs and included in a summary estimate (see Table J.3-7 near the end of this section).

Unlike the other PAHs with cancer potency factors, naphthalene is not considered a multipathway chemical under the Hot Spots program because it is regarded as a gas, and therefore not subject to appreciable deposition onto soil, etc. Naphthalene was included in this analysis because this PAH constitutes a large proportion of the total mass of PAHs inhaled. Among the carcinogenic PAHs in Table J.3-4, naphthalene predominates in both mainstream smoke (63% of total carcinogenic PAHs) and in mother's milk (56% of total carcinogenic PAHs). Naphthalene is also the only PAH that

is considered a gas, and therefore, its physical properties are different from other larger PAHs that are semi-volatile or exist primarily as a solid. In spite of these differences, the summary estimate did not change when naphthalene was excluded in the analysis (summary Tco = 1.55 versus 1.60).

Due to few measurable levels of carcinogenic PAHs in milk samples, there is more uncertainty in the carcinogenic PAH Tco compared to the PAH Tco for PAHs without cancer potency values. Nevertheless, summary estimates for PAH Tcos from inhaled sources differ by less than a factor of two (Tco for carcinogens, 1.2 versus Tco without cancer potency values, 2.06) suggesting that there may be no systematic difference between these two groups of chemicals. Therefore, OEHHA combined individual Tcos for PAHs from both groups into an overall inhalation Tco (see Table J.3-7 and Figure J.3-1 at the end of this section of the Appendix). In Figure J.3-1, the top seven estimates of inhalation Tcos are carcinogenic PAHs and the bottom six estimates are PAHs without cancer potency values.

The combined estimate is the summary of all 13 PAH estimates combined using a Random-effects model. OEHHA assumes that the PAHs found in exposure studies are a subgroup from a population of PAHs. Random-effects models assume there are multiple central estimates and incorporate a between-PAH estimate of error as well as a within-PAH estimate of error. In contrast, a Fixed-effects model assumes observations scatter about one central estimate (Kleinbaum, 1988).

OEHHA recommends using the inhalation Tco based on the summary estimates provided in Table J.3-7 rather than using the individual PAH Tcos values provided in Table J.3-4, to assess transfer of individual inhaled PAHs to mother's milk. There are a high number of non-detects and small sample sizes in these data. The estimation of PAH Tco values with this method might be improved with more sensitive methods for measurement of breast milk PAH content and larger study populations to better estimate biological variation and estimates of PAH transfer from air to mother's milk. Such improved data could allow for a robust determination of the Tco values for individual compounds.

The key assumption underlying the development of these Tcos is that the variability in individual PAHs Tcos is sufficiently small to justify the use of an average value for individual PAH congeners. This approach appears to be the best available given the available studies.

J.3.2 Oral Biotransfer of PAHs to Mother's Milk

Diet is the largest contributor by pathway to total PAH intake from ubiquitous background sources for the general public and other situations where airborne levels are not remarkably high (Lioy et al., 1988). In a risk assessment of a reference nonsmoking male, a mean total PAH intake of 3.12 µg/d was estimated of which dietary intake was 96.2%, air 1.6%, water 0.2% and soil 0.4% (Menzie et al., 1992; Ramesh et al., 2004). Inhalation, soil ingestion and homegrown produce pathways can be important when considering total dose from a single stationary source. PAHs

contaminate homegrown produce and soil through direct deposition. Milk and meat from home-raised animals or commercial sources would be less of a contributor because many PAHs are highly metabolized by these animals following intake from contaminated pastures and soil.

There are no studies available that relate PAH dietary intake directly to mother's milk concentrations for these compounds, although studies of PAH dietary intake have been performed in several countries. Therefore, the PAH biotransfer efficiency to mother's milk from food was calculated using PAH dietary intake data and mother's milk PAH data from separate studies. OEHHA recognizes the uncertainty in this approach but it appears to be the best currently available. Table J.3-5 shows the daily dietary intake of carcinogenic PAHs from published studies of European residents.

Regional preferences, ethnicity, and individual dietary preferences will influence the amount of PAHs ingested with food. In addition, there were differences among the intake studies in the number and type of PAHs investigated in foods. Even though dietary habits and PAH analysis methods can result in different levels of PAH intake, the total dietary intakes of PAHs in each of five studies in Table J.3-5 were generally within an order of magnitude of each other.

Table J.3-5: Summary Estimates of PAHs with and without Cancer Potency Factors Dietary Intake (µg/day)

PAH (no. of rings[a])	**Italian** Lodovici et al (1995) Adults	**Dutch** De Vos et al. (1990) [c] Adult males	**Spanish** Marti-Cid et al. (2008) Adults	**Spanish** Falco et al. (2003) Adults	**U.K.** Dennis et al. (1983) Adults
With Cancer Potency Factors	**AM[b], SD**	**AM***	**AM***	**AM, SD**	**AM***
Naphthalene (2)	NA[d]	NA	1.846	0.823, 0.056	NA
Chrysene (4)	0.84, 0.0131	0.86 – 1.53	0.204	0.564, 0.037	0.5
Benzo[a]anthracene (4)	0.47, 0.0093	0.2 – 0.36	0.139	0.310, 0.021	0.22
Benzo[b]fluoranthene (5)	0.17, 0.0101	0.31 – 0.36	0.137	0.188, 0.014	0.18
Benzo[k]fluoranthene (5)	0.06, 0.0043	0.1 – 0.14	0.086	0.094, 0.006	0.06
Benzo[a]pyrene (5)	0.13, 0.0003	0.12 – 0.29	0.083	0.113, 0.008	0.25
Dibenzo[a,h]anthracene (5)	0.01, 0.0026	NDd[e]	0.084	0.048, 0.003	0.03
Indeno[1,2,3-c,d]pyrene (6)	ND	0.08 – 0.46	0.102	0.045, 0.003	ND
Without Cancer Potency Factors	**AM, SD**	**AM***	**AM***	**AM, SD**	**AM***
Anthracene (3)	NA	0.03 – 0.64	0.428	0.088, 0.006	NA
Acenaphthylene (3)	NA	NA	0.354	0.402, 0.026	NA
Phenanthrene (3)	NA	NA	3.568	2.062, 0.150	NA
Fluorene (3)	NA	NA	0.934	0.206, 0.017	NA
Acenaphthene (3)	NA	NA	0.368	0.071, 0.005	NA
Pyrene (4)	0.19, 0.0043	NA	1.084	1.273, 0.092	1.09
Fluoranthene (4)	1.03, 0.0106	0.99 – 1.66	1.446	0.848, 0.062	0.99
Benzo[g,h,i]perylene (6)	0.20, 0.0009	0.2 – 0.36	0.112	0.214, 0.017	0.21

[a] no. of rings, number of rings are an indicator of lipophilicity (greater # of rings, more likely to partition to body fat);
[b] Arithmetic mean (AM), Standard Deviation (SD);
[c] The Dutch dietary intakes were presented as the range of lower bound values (calculated by taking values below the detection limit to be zero) to upper bound values (calculated by taking values below the detection limit to be equal to the limit)
[d] *NA,* Not available; [e] ND, Not determined;
* no measure of variance was reported (Dennis et al., 1983a; Dennis et al., 1983b; De Vos et al., 1990; Lodovici et al., 1995; Falcó et al., 2003; Martí-Cid et al., 2008)

Based on the estimated intake of the same measured PAHs in dietary studies and the PAHs found in breast milk from nonsmoking mothers (Del Bubba et al., 2005; Zanieri et al., 2007), OEHHA was able to estimate transfer coefficients (Tco) by Equation J-8, a version of Equation J-1:

$$Tco_{hmoi} = Cm_{oi} / (D_{oi}) \quad \textbf{(Eq. J-8)}$$

where:

Cm_{oi} = geometric average ith PAH concentration in mother's milk (µg per kg milk as wet weight)
D_{oi} = geometric average dose of the ith PAH per day from dietary sources (µg/day)

Cm_{oi} is the geometric average of the ith PAH in whole milk from nonsmoking, rural dwelling women. OEHHA obtained estimates of GM and GSD by pooling and converting arithmetic estimates to geometric estimates of the mean and standard deviation from two studies of nonsmoking rural-dwelling women (Del Bubba et al., 2005; Zanieri et al., 2007). D_{oi} is the geometric average of the ith PAH taken in through dietary sources. Oral PAH Tcos for both carcinogenic and noncancer PAHs are shown in Table J.3-6.

The Italian dietary study by Lodovici et al. (1995) supplied data in which OEHHA could calculate estimates of dietary intake of nine PAHs among a population living mostly in urban settings. OEHHA obtained GM and GSD estimates by converting arithmetic estimates of dietary intake reported in Lodovici et al (1995) and estimates of intake variability from Buiatti et al (1989).

These investigators estimated that the entire study population consumes about 1.9 µg of carcinogenic PAHs per day from dietary sources. Approximately 46% of the total carcinogenic PAH intake comes from cereal products, non-barbecued meat, oils and fats. Even though meat barbecued on wood charcoal has the highest PAH levels, the contribution of these barbecued foods is only about 13% of the carcinogenic PAH intake.

A limitation of the Italian dietary intake study is that the population examined was 58% men, and the study did not report any body weight adjustments. Thus, the sample population may not represent the female population sampled by Zanieri et al (2007). Other studies that have compared dietary PAH intake levels between men and women indicate that men consume slightly higher levels of PAHs than women do (5% to 15% on a µg/kg-body weight-day basis) (Falco et al 2003, Marti-Cid et al 2008), so the bias introduced by this assumption may not be significant.

Table J.3-6 presents the dietary intake and mother's milk concentrations for individual PAHs from the Italian studies. OEHHA calculated Tcos for individual PAHs common to both the studies of dietary intake and mother's milk concentration. The mother's milk concentrations for individual PAHs represents the pooled average reported in the Zanieri et al. and Del Bubba et al. studies.

Table J.3-6: Oral Transfer Coefficients (Tcos) for Individual PAHs Based on Italian Data from a Daily PAH Dietary Intake Study (Lodovici et al., 1995; Del Bubba et al., 2005; Zanieri et al., 2007) and Mother's Milk PAH Concentration Studies (Del Bubba et al., 2005; Zanieri et al., 2007).

PAH	Mother's milk PAH concentration (µg/kg-milk)	Daily PAH intake (µg/d)	Oral PAH Tco (d/kg)
With Cancer Potency Factors	GM[a], GSD[b]	GM, GSD	GM, GSD
Naphthalene	4.12, 1.41	NA[c]	NA
Chrysene	0.01, 3.36	0.49, 2.82	0.02, 4.93
Benzo[a]anthracene	0.12, 5.41	0.27, 2.82	0.44, 7.25
Benzo[b]fluoranthene	0.21, 3.61	0.1, 2.82	2.1, 5.21
Benzo[k]fluoranthene	0.055, 3.01	0.034, 2.82	1.62, 4.54
Benzo[a]pyrene	0.01, 3.36	0.076, 2.82	0.13, 4.93
Dibenzo[a,h]anthracene	0.007, 3.36	0.003, 2.82	2.33, 4.93
Indeno[1,2,3-c,d]pyrene	0.011, 3.36	NA	NA
Without Cancer Potency Factors	GM, GSD	GM, GSD	GM, GSD
Anthracene	0.13, 4.26	NA	NA
Acenaphthylene	4, 1.99	NA	NA
Phenanthrene	0.41, 2.03	NA	NA
Fluorene	0.12, 6.32	NA	NA
Acenaphthene	1.39, 2.16	NA	NA
Pyrene	0.15, 3.47	0.11, 2.82	1.35, 5.05
Fluoranthene	0.16, 3.34	0.6, 2.82	0.27, 4.91
Benzo[g,h,i]perylene	0.01, 3.37	0.116, 2.82	0.08, 4.94

[a] GM, geometric mean; [b]GSD, geometric standard deviation; [c] NA, Not available;

Oral Tcos were calculated for each individual PAH by equation J-8. The average Tco for carcinogenic and PAHs without cancer potency factors was calculated as the sum of the Tco values over the total number of PAHs evaluated. Similar Tco values are obtained for both groups of PAHs (0.46 d/kg) and 0.31 d/kg, respectively). This finding suggests that, on average, the PAHs with cancer potency factors as a whole transfer to mother's milk with about the same efficiency as some of the most common PAHs without cancer potency factors that are taken in through the diet.

Summary Tcos were calculated using a Random-effects model to pool across individual PAH-Tcos. OEHHA found no systematic difference between summary estimates stratified by PAHs with or without cancer potency factors (data not shown). Therefore, we pooled Tcos for both groups by route of intake (see Table J.3-7).

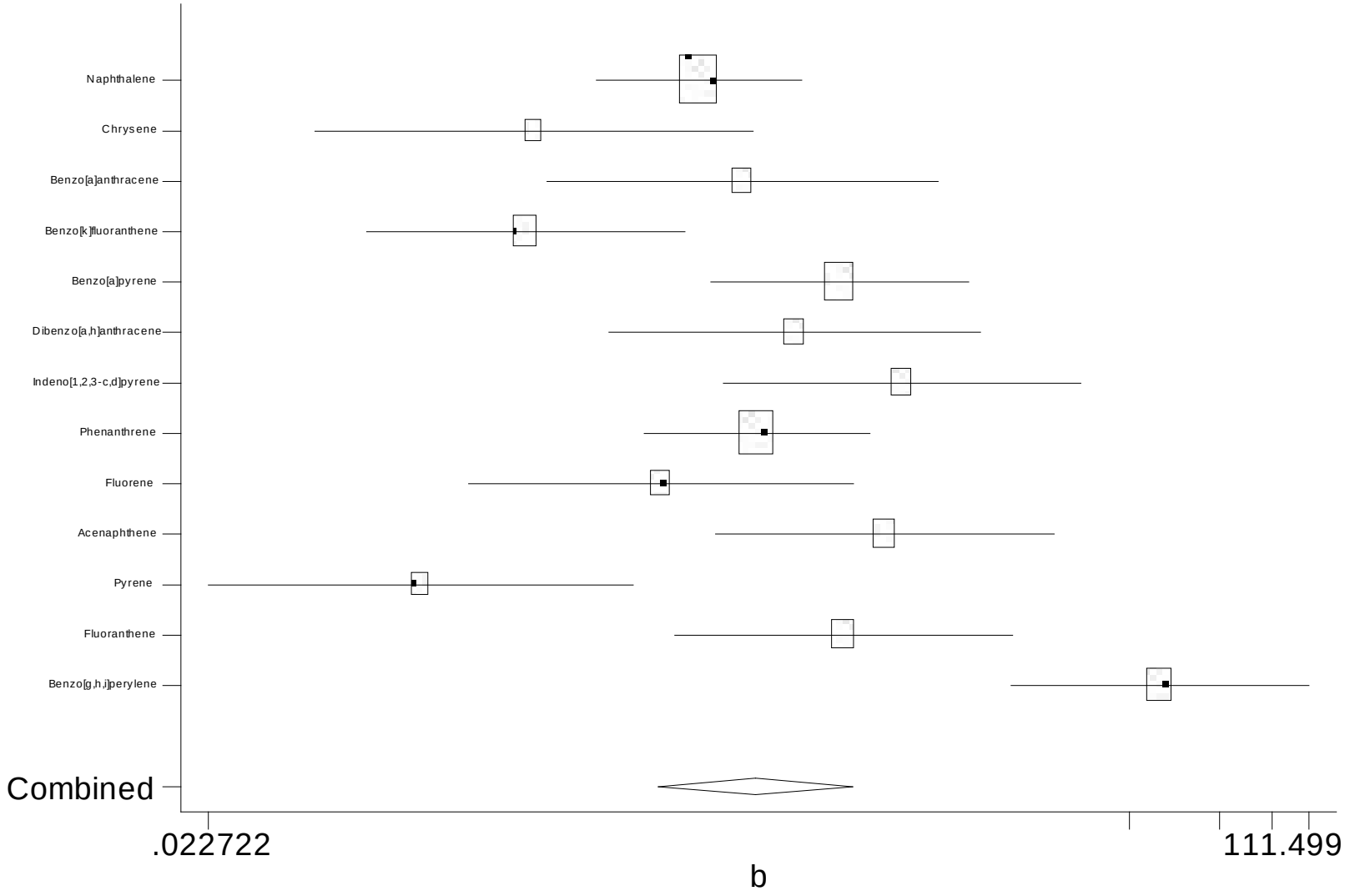
Table J.3-7: Random Effects Estimate and 95% Confidence Intervals of Tcos Stratified by Intake Route and Data Source

Tco (data source)	No. PAHs	summary estimate (random effects model)	LCL	UCL
Inhalation	13	1.55	0.731	3.281
Oral (Italian)	9	0.401	0.132	1.218

LCL, lower 95% confidence limit of the mean Tco;
UCL, upper 95% confidence limit of the mean Tco.

Similar to the inhalation Tco derivation, limitations of the oral Tco derivations include the small number of women examined for PAHs in mother's milk (n=21) and the large number of "below detection limit" results for milk concentrations, particularly for the larger PAHs with more than four rings. OEHHA assumed that the arithmetic estimates, minimum and maximum values reported by investigators represented a lognormal distribution and converted estimates from arithmetic to geometric. Nevertheless, the use of sparse data to derive an inhalation Tco and data from potentially two different study populations to generate an oral Tco – one for dietary PAH intake and another for mother's milk PAH concentrations - introduces considerable uncertainty.

Figure J.3-1: Inhalation Tcos (b, 95% CL) Based on Italian Data, (Random-effects Model)



The top seven estimates are PAHs with potency factors and bottom six estimates are PAHs without potency factors; summary of all 13 PAHs is labeled “combined” = 1.55 d/kg; b, the Tco in units of day/kg-milk

J.3.3 Comparison and Use of Inhalation and Oral PAH Tcos

Comparison of the oral and inhalation Tcos also presents a number of interesting findings. For example, comparing the averaged inhalation and oral mother's milk Tcos generated from the Italian studies for carcinogenic PAHs, the mean inhalation Tco is about four times greater than the oral Tcos based on Italian study data.

Although studies in humans are lacking, (Grova et al., 2002) showed that BaP is poorly absorbed through the gut in goats when administered orally in vegetable oil. Radiolabeled BaP fed to these animals led to 88% recovery of the radioactivity in feces, indicating little BaP reached the bloodstream where it could be taken up in mother's milk. In contrast, respiratory absorption of PAHs in particulate form through smoking is about 75% efficient (Van Rooij et al., 1994).

The following factors may have influenced the difference between oral Tco values and inhalation Tco values:

- First-pass metabolism in the liver following oral intake before reaching the blood supply of the breast versus entering systemic blood circulation prior to passage through the liver with the inhalation route (however, some PAH metabolism occurs in the lung)
- Gut assimilation of PAHs is likely to occur at a different rate than the rate of passage across the lung

Looking at mother's milk Tcos in terms of carryover rate suggests that accumulation of PAHs in the mother's body occurs more readily when inhaled versus ingested. Carryover rate, defined here as the daily output of PAHs in mother's milk (µg/day) over the daily intake of PAHs (µg/day), can be estimated by multiplying a PAH Tco by the daily output of mother's milk. Since milk production in human mothers are about 1.0 kg/day, the calculated carryover rate turns out to be the same as the PAH Tco value. A carryover rate greater than one in PAH transfer suggests that accumulation occurs in the mother's body prior to lactation.

The average inhalation Tco of 1.6 d/kg daily inhalation of a PAH mixture, indicates that 160% of the daily intake from inhaled sources transfers to mother's milk. This high transfer-value suggests that some accumulation of PAHs with cancer potency factors may occur in the mother's body before lactation begins. An average oral Tco of 0.40 d/kg for PAHs with cancer potency factors indicates 40% of the daily intake from diet transfers to mother's milk following oral intake of PAHs.

This suggests that metabolism occurs in the mother's body. The uncertainties in our Tco estimation methods could account for both of these results. If the Tco estimation is correct, the mother may be metabolizing a considerable fraction of her intake prior to partitioning into the fat stores. There could also be inefficient transfer to mother's milk for unknown reasons or metabolism following transfer of PAHs to mother's milk.

J.4 Mothers' Milk Transfer Coefficients for Inorganic Lead

Inorganic lead is naturally present on the earth's crust and may enter terrestrial and aquatic ecosystems due to the weathering of rocks. Traces of lead can not only be found in the immediate vicinity of emission sources but also are present, albeit at very low levels, in every part of the world (Castellino and Castellino, 1995).

Lead particulate matter is the primary form of lead present in the air (OEHHA 1997). Atmospheric movements may transport lead aerosol in the form of very fine particles, a long way from its place of emission. Refineries, mineral extraction industries, and smelting plants for lead and other metals are largely responsible for emitting lead-containing aerosols into the atmosphere (Castellino and Castellino, 1995) in the U.S.

Human intake of lead can occur by inhalation of airborne particles and ingestion of lead-contaminated food and water. Furthermore, people can be exposed using lead-glazed or painted cooking and eating utensils. Lead may also be ingested in foods or drinks contaminated with the metal during the industrial processes of food production or preservation (Castellino and Castellino, 1995). The potential pathways of concern with Hot Spots facilities would be inhalation, soil ingestion, and dermal absorption, home raised meat, homegrown produce, surface drinking water consumption, and breast milk consumption.

Background levels of lead in the blood of the U.S. population have declined in recent years mainly resulting from the removal of lead from gasoline and paint. Results from an NHANES study (1991 – 1994) show that the geometric mean blood lead level in the U.S. adult population (20 – 69 years of age) was about 4 µg/dL (Pirkle et al., 1994), which is over a 70% decline in blood lead from blood lead levels obtained from 1976 to 1980. The NHANES IV survey (1999- 2000) found an additional 50% reduction (1.75 µg/dL) in the U.S. adult population (CDC, 2005).

As of the date of this report, measured levels of lead at ambient air quality monitoring sites in California are very low. Lead exposure in the California population is likely to occur from sources other than Hot Spots facility emissions, such as old lead-based paint. However, no threshold has been identified for lead-induced neurotoxicity in children and therefore an evaluation of all potential routes of exposure for Hot Spots facilities is prudent. Further, there are significant lead emissions from some Hot Spots facilities.

In an effort to derive lactation transfer coefficients for inorganic lead, OEHHA drew from studies conducted on subjects exposed to lead through multiple pathways at higher levels from other areas of the world. OEHHA assumes that the transfer of lead derived from these studies serves as a reasonable surrogate for the transfer of lead from contaminated media near a Hot Spots facility in California.

J.4.1 Inorganic Lead in Human Milk

Breast milk levels of lead correlate with levels of lead in whole blood but are generally much lower (Sternowsky and Wessolowski, 1985; Castellino and Castellino, 1995; Li et al., 2000; Ettinger et al., 2004). Castellino et al (1995) reviewed 11 studies conducted between 1933 to 1989 and observed that in the vast majority of cases, the mean values of lead in breast milk vary from 0.17 to 5.6 µg/L (Castellino and Castellino, 1995).

Ursinyova and Masamova (2005) published a table of 32 human milk summary estimates from studies published between 1983 and 2001. Mean human milk levels of lead generally ranged from 0.5 to 50 µg/L (Ursinyova and Masanova, 2005). Average blood lead levels during that timeframe ranged from 24 to 460 (µg/L) (Gulson et al., 1998a).

Because lead levels in milk correlate well with whole blood, OEHHA searched for studies that reported both lead levels in milk and blood before and/or during lactation for derivation of a lactational Tco for lead. However, several investigators have questioned high results from early studies of lead in breast milk. For example, Ettinger et al (2004), Gulson (1998b) and others cautioned that high levels of lead in breast milk might be due to contamination from some past sample collection techniques (Hu et al., 1996; Newman, 1997; Gulson et al., 1998a; Smith et al., 1998; Ettinger et al., 2004). These sources of lead include the use of the following products to prepare nipples or express breast milk:

- lead acetate ointment
- lead in nipple shields
- lead in alcohol wipes from foil wrap

Gulson et al (1998a) also suggested that analytical problems, indicated by an unusually wide range in lead concentrations for the quality control standard in Parr et al (1991), warrant verification by follow-up studies (Parr et al., 1991; Gulson et al., 1998a). Gulson et al (1998a) assessed lead concentrations in maternal blood versus the concentration of lead in breast milk per concentration in maternal whole blood from studies conducted over 15 years prior to 1998. From this assessment, they suggested that milk lead levels less than about 15% of maternal blood lead levels best represent the relationship between lead in maternal blood and milk. In other words, milk lead levels that were greater than 15% of blood lead levels were suspected of being contaminated with lead during sample collection and/or assessment. Therefore, OEHHA has included only summary estimates from studies published after 1990 that did not report or show evidence of breast milk contamination.

OEHHA located eight studies that met our inclusion criteria. Table J.4-1 summarizes key attributes of the study populations.

Table J.4-1: Studies with Summary Estimates of Concurrent Maternal Blood and Milk Levels of Lead)

Study	Country	Group	Study period	Measurement	# Study subjects
(Nashashibi et al., 1999)	Greece	Residents of Athens and surrounding areas	~1999	At delivery, at onset of lactation	47
(Li et al., 2000)	China, Shanghai	Not occupationally exposed	prior to 2000	At delivery, at onset of lactation	32
(Counter et al., 2004)	Equador, Pujili	Pottery glazers	2003	Post partum	13
(Ettinger et al., 2004)	Mexico, Mexico City	Exclusive breast feeders	1994-1995	One month postpartum	88
(Ettinger et al., 2004)	Mexico, Mexico City	Partial breast feeders	1994-1995	One month postpartum	165
(Namihira et al., 1993)	Mexico, Mexico City	Reside near New Smelter	1986	postpartum	35
(Hallen et al., 1995)	Sweden	Reside in Rural areas	1990-1992	6 weeks postpartum	39
(Hallen et al., 1995)	Sweden	Reside near Smelter area	1990-1992	6 weeks postpartum	35
(Baum and Shannon, 1996)	U.S.A Camden, New Jersey	Mothers of lead poisoned infants	1996	Postpartum	2
(Gulson et al., 1998b)	Australia	Immigrants from eastern Europe	Early 1990s	At delivery and average during lactation	9

Regression analyses suggest a linear relationship between lead in maternal blood and milk among women with substantially elevated levels of lead in blood. For example, Namihira et al (1993) reported a significant linear relationship (r = 0.88) between levels of lead in blood and milk for blood lead levels in the range of 35 µg/dL -100 µg/dL from a study of 35 lactating women living in Mexico City (Namihira et al., 1993). At these levels of lead in blood, authors reported a univariate regression of 4.3% representing the average level of lead in breast milk relative to the average level of lead in blood.

A similar study of 47 lactating women conducted by Nashashibi et al also reported a significant linear relationship (r=0.77) between lead in milk and blood for blood lead levels in the range of 5 µg/dL - 25 µg/dL (Nashashibi et al., 1999). Based on a univariate regression, the average level of lead in breast milk was about 7% the average level of lead in blood. OEHHA calculated similar estimates of the milk/blood lead ratio from Li et al (2000), Counter et al (2002) and Ettinger et al (2004) (see Table J.4-2).

Table J.4-2 Concurrent Measurements of the Lead Concentration (µg/L) in Mother's Milk and Blood

Study	N	Blood AM,SD	Milk AM,SD	Blood GM,GSD	Milk GM,GSD
(Nashashibi et al., 1999)	47	149, 41.1	20,5	143.64, 1.31	19.4, 1.28
(Li et al., 2000)	119	142.5, 69.14	5.63,4.39	128.21, 1.58	4.44, 1.99
(Counter et al., 2004)	13	171, 91	4.6,5.3	150.96, 1.65	3.02, 2.51
(Ettinger et al., 2004)	88[a]	94, 48	1.4,1.1	83.72, 1.62	1.1, 2
(Ettinger et al., 2004)	165[b]	95, 43	1.5,1.2	86.55, 1.54	1.17, 2.02
(Namihira et al., 1993)	35	459, 198.8	29.94,25.75	421.19, 1.51	24.7, 1.86
(Hallen et al., 1995)	39[c]	31.4, 6.7	0.5,0.3**	30.71, 1.23	0.43, 1.74
(Hallen et al., 1995)	35[d]	31.7, 10.2	0.9,0.4***	30.18, 1.37	0.82, 1.53
(Baum and Shannon, 1996)	2	315, 35.4	5.02,0.50	313.03, 1.12	5, 1.1
(Gulson et al., 1998b)	9	29, 8	0.73,0.7	27.96, 1.31	0.53, 2.24

[a]exclusively breast fed; [b] partially breast fed; [c] rural setting; [d] near smelter; * < LOD taken as 1/2 LOD as GM and 9.9 = max, **based on LOD of 0.5 µg/L and 2 out of 39 samples above LOD; *** based on 16/35 above LOD

Li et al. (2000) stratified milk lead levels by low, medium and high blood lead levels. Their findings suggest that slightly higher transfer rates occur at low levels relative to high levels of lead in blood (Li et al., 2000). This may be due to more efficient transfer rates at lower body burdens of lead or it could result from very slight breast milk contamination during collection and/or assessment.

J.4.2 Biotransfer from Bone to Blood during Pregnancy and Lactation

Lead transferred from blood to human milk reflects both the mother's current and ongoing intake of lead exposure as well as lead mobilized due to physiological changes of pregnancy and lactation from bone stores due to past exposures. Several studies provided indications of internal transfer of lead from bone stores. Internal transfer was evident by comparing the rise in blood lead levels during lactation to blood lead levels measured prior to lactation (see Table J.4-3).

Table J.4-3: Change in Blood Lead Levels from Pregnancy (bloodpreg) to Lactation (bloodlac) (µg/L)

Study	N	Bloodpreg	Bloodlac	Bloodpreg	Bloodlac
		AM,SD	AM,SD	GM,GSD	GM,GSD
(Gulson et al., 1997)**	8	22.4, 6	32, 8.4	21.64, 1.30	30.95, 1.29
(Ettinger et al., 2004)	~86-88 excl	81, 38	94, 48	73.33, 1.56	83.72, 1.62
(Ettinger et al., 2004)	164-165 part	90, 44	95, 43	80.85, 1.59	86.55, 1.54
(Tellez-Rojo et al., 2002)	425	84, 40	93.7, 43.04	75.84, 1.57	85.15, 1.55
(Sowers et al., 2002)*	15	13.7, 7.75	17, 5.29	11.93, 1.69	16.23, 1.36
(Rothenberg et al., 2000)	311	27.59, 26.49	32.03, 21.78	22, 1.96	28, 1.68

* SD for blood lead level during lactation estimated for blood lead at 6-months from figure 2;
** bloodlact is max blood lead level during pregnancy and lactation;
excl, exclusively breastfed part, partially breastfed.

These investigators conducted longitudinal monitoring of blood samples to determine stable lead isotope profiles by mass spectrometry and chemical analyses of blood samples for total lead content over a 300-day period. Gulson et al followed Australian women (15 immigrants and 7 non-immigrants) to study the mobilization of lead from the maternal skeleton during pregnancy and lactation (Gulson et al., 1995; Gulson et al., 1997; Gulson et al., 1998a; Gulson et al., 1998b; Gulson et al., 1999; Gulson et al., 2001). Investigators measured maternal and infant blood, urine, diet, and breast milk from 21 mothers and 24 infants. The arithmetic mean and standard deviation lead concentration in breast milk were AM (SD) 0.73 (0.70) µg/kg and the geometric mean and standard deviation were GM (GSD) 0.55 (2.24) respectively. Levels ranged from 0.09 to 3.1 µg/kg.

Gulson et al (1997) provided evidence that lead in female immigrants to Australia was mobilized from skeletal stores during pregnancy, with increases in blood lead concentration of about 20% and a mean increase in skeletal lead contribution to blood lead of 31%. Authors concluded that between 45% and 70% of lead in blood comes from mobilized long-term tissue lead stores (Gulson et al., 1997).

Investigators obtained environmental samples of house dust, drinking water, urban air, gasoline, and a 6-day duplicate diet quarterly. The GM (GSD) blood lead concentration for the immigrant females on arrival in Australia (either prior to or during early pregnancy) was 3.0 µg/dL (SD 1.56) (range: 1.9 to 20 µg/dL) and for the Australian controls was 3.1 µg/dL (range: 1.9 to 4.3 µg/dL). Skeletal lead contribution to blood lead was significantly greater ($p< 0.001$) during the post pregnancy period than during the 2nd and 3rd trimesters.

The contribution of skeletal lead to blood lead during the post-pregnancy period remained constant at the increased level even though the duration of breast-feeding varied from 1 week to 6 months. The authors concluded that the increased contribution of skeletal lead both during pregnancy and in the post pregnancy period is consistent with increased bone resorption and may be associated with inadequate calcium intake.

Sowers et al (2000) followed lactating women enrolled in prenatal program located in Camden, New Jersey between 1997 and 2000 (Sowers et al., 2002). These women were part of a larger cohort of 962 women enrolled in study of calcium metabolism in pregnancy and lactation. A nested cohort of 15 women with a mean (standard deviation) age of 23.7 (5.42) years, who provided breast milk samples through 6 months postpartum or longer and were unaware of their blood lead levels, was included in the study. Blood and milk lead levels along with measures of bone loss and osteocalcin concentrations were evaluated. Authors reported the precautions taken to avoid contamination of milk samples by environmental lead.

The arithmetic mean (standard deviation) (µg/dL) of blood lead levels at delivery for 15 breast-feeding and 30 randomly selected bottle-feeding women were 1.37 (0.78) and 1.31 (1.10) respectively. Mean maternal blood lead levels rose to 1.6, (1.7) µg/dL at three and six months during lactation, respectively. Compared to bottle-feeding women, blood lead levels from breast-feeding women were consistently higher by 15 – 35% during the first six months postpartum. Authors found that breast-feeding women had greater bone loss as reflected in the bone change data and higher serum osteocalcin concentrations than bottle-feeding women.

The arithmetic mean of lead in breast milk samples (standard deviation) were 5.6 (4.2) and 5.9 (3.87) µg/L at three and six months post partum. Breast milk lead was also measured 1.5 and 12 months post partum. However, authors did not measure blood lead at 1.5 months, did not indicate how many women were still breast-feeding and did not attempt to estimate how many liters/day study subjects produced. The relative increase in blood lead levels from delivery to an active lactating period (e.g. one to 6 months) is consistent with the relative increases in blood lead found in other studies (see Table J.4-3).

Tellez-Rojo et al (2002) concluded that maternal bone lead levels are an important predictor of maternal blood lead levels over the course of lactation. In fact, bone lead from past exposures can contribute an additional 40% of the lead measured in blood during lactation (see Table J.4-3) (Tellez-Rojo et al., 2002).

Ettinger et al (2004) measured relatively high maternal blood lead levels in women exposed to lead in the air while living in Mexico City. Between January 1994 and June 1995, investigators selected 1398 women from three maternity hospitals in Mexico City for participation in a randomized control trial (Tellez-Rojo et al., 2002; Hernandez-Avila et al., 2003; Ettinger et al., 2004). From this study population, 629 women agreed to participate. Ettinger et al. (2004) examined a nested cohort of 255 women with a mean (standard deviation) age of 24 (5) years with both breast milk, maternal and infant blood lead levels at delivery and one-month post partum. The authors reported the precautions taken to avoid contamination of milk samples by environmental lead.

For breast-feeding women, the arithmetic mean (standard deviation) of blood lead level at delivery was 8.7 (4.2) and at one-month post partum was 9.4 (4.5) µg/dL. At one-month post partum, the average (standard deviation) lead level in breast milk was 1.5 (1.2) µg/L. After adjusting for parity, calcium intake, infant weight change and breastfeeding status, an increase in blood lead was associated with a 33% increase in breast milk lead.

Rothenberg et al (2000) recruited immigrant women, almost exclusively from Latin America, from outpatient clinics in South Central Los Angeles to examine bone lead contribution to blood lead. Investigators contacted subjects from June 1995 through July 1998. Three hundred eleven subjects were followed from late pregnancy to one or two months after delivery. The investigators evaluated bone lead levels after delivery and blood lead levels both pre- and post-delivery. Ages ranged from 15 to 44 years. Prenatal blood lead was lower on average GM = 2.2 µg/dL (0.4 to 38.7) than postnatal blood lead GM = 2.8 µg/dL (0.4 to 25.4). In fact, postnatal blood lead level increased by 27% relative to the prenatal blood lead level.

A questionnaire was administered including questions about present breast feeding practice (presently nursing yes/no) and past history of breast feeding (ever nursed and total months nursed). Breast milk samples were not obtained from this cohort. Tibia and calcaneus bone lead levels were associated with prenatal blood lead levels and calcaneus but not tibia lead was associated with postnatal blood lead levels (Rothenberg et al., 2000).

J.4.3 Inhalation Biotransfer of Lead to Mother's Milk

Ideally, lead transfer to human milk would include estimates of lead in ambient air and major sources of oral exposure over time along with human milk estimates from the exposed lactating population. However, few studies have attempted to correlate lead exposure from multiple pathways (e.g. oral sources such as contaminated food, water, dust and soil and inhalation sources such as ambient air) with lead concentrations in human mother's milk. This is likely due to the multiple effects of daily intake from environmental sources (Sannolo et al., 1995) and internal transfer from lead released from bone stores during pregnancy and lactation (Gulson et al., 1997).

Although exposure to lead can come from many sources, ambient air contaminated from combustion sources has been a significant source of exposure in the U.S.

population and European countries (U.S. EPA 1998). The relationship between air lead and blood lead has been studied extensively in both field studies and experimental chamber studies. OEHHA evaluated studies conducted prior to 1997 in their health risk assessment of inorganic lead under the toxic air contaminant program (OEHHA, 1997).

Briefly, in the OEHHA report, the contribution of airborne lead to blood lead levels was examined using several different methods – disaggregate, aggregate, uptake biokinetic, and physiologically based pharmaco-kinetic models (OEHHA, 1997). Findings were evaluated for linearity over a wide range of air and blood lead levels and are expected to apply to some exposure scenarios under the Hot Spots program. Most of these studies were conducted prior to 1985 when both air and blood lead levels were much higher than they are now. For example, the level of lead in the air used in chamber studies was 3.2 $\mu g/m^3$ representing low exposure and 10.9 $\mu g/m^3$ representing high exposure, while background air was typically between 7 $\mu g/m^3$ and 8 $\mu g/m^3$ in the city of Los Angeles during similar time-periods – late 1960s / early 1970s. Lead in Los Angeles air is 100-fold lower today (Ospital et al., 2008).

The relationship between air lead concentration and blood lead is not linear. Higher slopes are observed at lower air lead concentrations. However, the aggregate model was chosen because it implicitly incorporates all air-related pathways (i.e. soil, dust, water, contaminated food, etc.) and has averaged slopes estimated from a wide range of air concentrations. Using this model OEHHA estimated that an average change of 1.8 µg/dL in adult blood lead levels ($\mu g/m^3$) per $\mu g/m^3$ air lead concentration with current ambient air levels in California.

As part of our effort to estimate a lactational transfer factor for lead (Tco), we searched for studies that examined slope factors in other populations or were conducted subsequent to our 1997 report (OEHHA, 1997).

In addition to the kinetics of lead in the general adult population, recent studies have observed that - under similar exposure conditions - plasma lead rises by about 20% – 80% during lactation (Gulson et al., 1997; Gulson et al., 1998b; Gulson et al., 1999; Rothenberg et al., 2000; Tellez-Rojo et al., 2002). Findings from these and other investigations suggest that, in addition to daily environmental sources of exposure, breast milk levels of lead also reflect lead released from lead accumulated in the lactating woman's bones.

We were not able to locate studies that measured both long-term exposure to ambient air lead and lead levels in breast milk. Therefore, we calculated estimates of transfer from blood to human milk from separate study populations to combine with estimates of lead transfer from air to blood.

J.4.4 Population Transfer Coefficient (Tco) for Lead

OEHHA has derived transfer coefficients for lead using Equation J-9

$$Tco_{hma}=(Cma/C_{blood}^{+})x(C_{blood}^{+}/C_{blood})x(C_{blood}/(C_{air} \times BR))xF_{c1}\,xF_{c2} \qquad \textbf{Eq. J-9}$$

where:

Cma = geometric mean human milk lead level (µg/L-milk as wet weight)
C_{blood}^{+} = geometric mean blood lead level during lactation (µg/dL)
C_{blood} = geometric mean blood lead level during non-lactating state (µg/dL)
C_{air} = geometric mean concentration of lead in ambient air (µg/m^3)
BR = geometric mean breathing rate for adult women (14 m^3/day)
F_{c1} = conversion factor (L-milk)/(kg-milk) ~ **(**0.97**)**
F_{c2} = conversion factor (dL)/(L) = 10

Cm_a is the geometric mean human milk lead level that incorporates all (aggregated) air-related pathways of lead. C_{blood}^{+} is the geometric mean blood lead level among lactating women measured during lactation (µg/L). C_{blood} is the geometric mean blood lead level taken from the general population during a non-lactating state (µg/L). C_{air} is the geometric mean concentration of lead in the ambient air (µg/m^3) inhaled by the same population where blood lead levels were measured. BR is the geometric mean breathing rate for adult women (14 m^3/day) (see Chapter 2). F_{c1} is the inverse of the specific gravity of breast milk (1.03 g/ml)(Sergen, 2006). F_{c2} is the conversion from deciliters to liters.

J.4.4.1 Biotransfer from Blood to Milk

Three groups measured maternal blood lead before and during lactation along with lead in mother's milk (Gulson et al., 1997; Gulson et al., 1998a; Gulson et al., 1998b; Sowers et al., 2002; Ettinger et al., 2004). However, Sowers et al. reported unusually high levels of lead in breast milk relative to blood, which suggest contamination problems. It is possible that breast milk samples were contaminated by the sampling collection technique (e.g. lead in the nipple shields). However, it is also possible that a more efficient active transport mechanism at lower blood lead levels could explain higher levels of lead in breast milk relative to blood. More studies of mothers with low blood lead levels are needed to further verify the results reported by Sowers et al.

For our purposes, Gulson et al (1995, 1997, 1998a, 1998b) and Ettinger et al (2004) provide the best estimates of the change in blood lead levels before the onset of lactation, during lactation and relative to the levels of lead in breast milk (Gulson et al., 1997; Gulson et al., 1998a; Gulson et al., 1998b; Ettinger et al., 2004).

J.4.4.2 Transfer from Air to Blood

Equation J-10 describes estimation of aggregate transfer from airborne and associated sources that appears in the OEHHA 1997 report on the health effects of airborne inorganic lead (OEHHA, 1997):

Slope factor = $(C_{bloode} - C_{bloodr})/(C_{aire} - C_{airr})$ **Eq.-J-10**

$(C_{bloode} - C_{bloodr})$ is the difference between lead concentration in the blood of exposed compared to reference group and $(C_{aire} - C_{airr})$ is the difference in air lead between exposed and reference group. This simplified model assumes that the exposed and reference communities are similar in confounders such as age and smoking habits and reasonably comparable in their exposure to other sources of lead (e.g. paint).

Subsequent to OEHHA's 1997 report, Ranft et al (2008) published results from studies conducted on exposure to air pollutants among residents living near industrial sources along the rivers Rhine, Ruhr and Wupper in North Rhine-Westphalia Germany during five time-periods from 1983 to 2000. Authors reported the distribution of ambient air lead levels for each of the five time-periods (Ranft et al., 2008).

During the early years (1983 – 1991), ambient air lead levels ranged from 0.100 – 0.510 $\mu g/m^3$. Whereas, during the later years (1997 – 2000), air lead levels were much more variable - ranging from 0.025 to 0.729 $\mu g/m^3$. The 50^{th} percentile (P 50) declined by almost a factor of 20 from years 1983 to 2000. During the earliest years (1983 – 1991), P 50 declined by a factor of four from 0.465 to 0.100 $\mu g/m^3$. Based on data collected from 1991 to 2000, these investigators reported that childhood blood lead would decrease by a factor of 6.4: 95%CI (6.02 – 6.80) from the decrease in lead concentration in polluted ambient air (m^3/dL).

OEHHA calculated a similar slope factor from the study of 500, 55-yr-old women living in industrial areas of the North Rhine – Westphalia, Germany from 1985 to 1990 by Wilhelm and associates (Wilhelm et al., 2007). The investigators reported that mean blood lead levels among these women declined from 7.2 to 5.0 µg/dL. Based on ambient air levels of lead reported in Ranft et al (2008), OEHHA estimated that blood lead levels in 55-year old women would change by 6-fold per unit of change in ambient air levels of lead (µg/dL) over a similar period (GM, 6.2; 95% CI 6.1 – 6.4) (Ranft et al., 2008). This estimate is within the range of slope factors reported previously by OEHHA for the general adult population (OEHHA, 1997).

J.4.4.3 Transfer from Air and Body Stores to Milk

Tables J.4-4 and J.4-5 show the Tcos derived by combining air to blood and blood to milk transfer of inorganic lead from the available data. Table J.4-4 shows the transfer factors derived from the study of eight women who provided samples of blood before and during lactation as well as samples of milk during lactation (Gulson et al., 1998a; Gulson et al., 1998b). The geometric mean and standard deviation blood lead levels prior to lactation were low (GM 2.2 µg/dL, GSD1.3).

Table J.4-4: Transfer Coefficients (Tcos) for Inorganic Lead Measured in Human Blood and Milk (d/kg-milk) from Data Reported in (Gulson et al., 1998a; Gulson et al., 1998b) and the Change in Blood Lead with the Change in Lead Concentration Measured in Ambient Air (slope factor)

Source	Slope factor m^3/dL	Tco (d/kg milk) GM	GSD	LCL	UCL
OEHHA	1.8	0.024	3.19	0.009	0.061
Willhelm/Ranft	6.2	0.08	3.19	0.031	0.203

LCL, lower 95% confidence limit of the mean Tco; UCL, upper 95% confidence limit of the mean Tco

Table J.4-5 shows the transfer factors derived from the study of 253 women who provided samples of blood prior-to and during lactation as well as samples of milk during lactation (Ettinger et al., 2004).

Table J.4-5: Biotransfer Coefficients (Tcos) for Inorganic Lead Measured in Human Blood and Milk (d/kg-milk) from Data Reported in (Ettinger et al., 2004) and the Change in Blood Lead with the Change in Lead Concentration Measured in Ambient Air (slope factor)

Source	Slope factor m^3/dL	Tco (d/kg milk) GM	GSD	LCL	UCL
OEHHA	1.8	0.019	3.00	0.017	0.022
Willhelm/Ranft	6.2	0.064	3.00	0.056	0.074

LCL, lower 95% confidence limit of the mean Tco; UCL, upper 95% confidence limit of the mean Tco

Compared to Gulson et al (1998), the geometric mean, blood lead levels prior to lactation observed by Ettinger et al (2004) were about 4-fold higher (7.3 and 8.0 for exclusive and partial lactators, respectively)(Gulson et al., 1998b; Ettinger et al., 2004). However, the transfer factors derived from residents of Mexico and immigrants to Australia differ by less than a factor of two.

J.4.5 Study Limitations, Influencing Factors and Uncertainty (inorganic compounds)

Our Tco estimate for lead has not considered the influence of maternal age, parity, length of lactation, and body weight on concentration of lead in milk.

J.5 Summary and Recommendations

This appendix develops lactational transfer coefficients for use in estimating the concentration of a multipathway chemical in mother's milk from an estimate of chronic incremental daily dose to the mother from local stationary sources. OEHHA derived human lactational transfer coefficients from studies that measured contaminants in human milk and daily intake from inhalation or oral exposure (e.g. air, cigarette smoke or diet) in the same or a similar human population. These coefficients can be applied to the mother's chronic daily dose estimated by the Hot Spots exposure model to estimate a chemical concentration in her milk.

We established transfer coefficients (Tcos) for individual congeners and WHO-TEQ summary PCDDs/Fs and dioxin-like-PCBs, individual and summary carcinogenic PAHs, and lead through equations J-1-3, data on exposure and breast milk contamination from background (global), accidental and occupational sources, and a set of simplifying assumptions. We assume that a mother's intake and elimination is constant before lactation. We also assume that changes in a woman's body due to the onset of lactation occur as a single shift in elimination rate over the lactation period. In some cases, OEHHA adjusted some measurements of human milk and contaminant intake to account for confounding factors. In such cases, OEHHA describes the method of adjustment in the text and table containing adjusted values.

We described the methods for deriving specific Tcos from measurements of human milk, intake and transfer estimates from studies of populations exposed to general global sources of pollutants. Although the proportional contribution from various exposure pathways to total exposure from a single Hot Spots facility is likely to be quite different from exposure found with global sources, we believe Tcos in this appendix have been derived from data that serve as reasonable surrogates of transfer from Hot Spot facility exposures.

J.5.1 Dioxins and Furans

Personal factors such as body fat, smoking status and past lactation practices can affect body burden and elimination rates. For example, smoking has been associated with a 30% to 100% increase in elimination rates of some dioxin congeners (Milbrath et al. 2009, Flesch-Janys et al. 1996). As well, the onset of lactation sets a new elimination pathway into effect and can substantially reduce the maternal body burden of PCBs during 6 months of lactation (Niessen et al.1984, Landrigan et al. 2002).

Therefore, OEHHA incorporated conservative assumptions regarding these factors into our model (i.e. reference half-lives based on body burden below 700 ppt in the blood, adult age, nonsmoker, no recent prior breast-feeding period and percent body fat of older adults) in addition to accounting for the substantial variability between individual congeners of PCDDs, PCDFs and dioxin-like PCBs.

To calculate oral Tcos, OEHHA used adjusted reference half-lives for the chemicals in the adult human body derived from dietary and occupational exposures. OEHHA

estimated oral Tcos for these chemicals from estimates of body weight reported in Chapter 10 of this document, the steady-state equation developed by Smith (1987) and reference half-lives reported in Milbrath et al (2009). Milbrath et al (2009) adjusted reference half-lives for age, body fat, smoking habits and breast-feeding status as these factors were all strong determinants of half-life in humans.

A carryover rate > 1 would suggest that dioxins and dioxin-like compounds could accumulate in body fat and transfer to the fat in mother's milk. An average dioxin Tco of 3.7 d/kg indicates that 370% of the daily intake from ingested sources transfers to mother's milk. This high transfer-value suggests that some accumulation of carcinogenic dioxins and dioxin-like compounds occurs in the mother's body. For individual congeners, an oral Tco less than one (e.g. 1,2,3,4,7,8-HxCDF and 2,3,4,6,7,8-HxCDF) suggests that some metabolism occurs in the mother's body.

J.5.2 PAHs

Based on the estimated intake of 16 measured PAHs in simulated smoking studies and the PAHs found in breast milk from long-time smoking mothers (Zanieri et al. 2007), OEHHA was able to estimate transfer coefficients (Tco) with a modified version of Equation J-1.

The key assumption underlying the development of these Tcos is that the variability in an individual PAHs Tcos is sufficiently small to justify the use of an average value for individual PAH congeners. This approach appears to be the best available given the available studies.

OEHHA calculated oral Tcos for each individual PAH by Equation J-8. The average Tco for carcinogenic and PAHs without cancer potency factors was calculated as the sum of the Tco values over the total number of PAHs evaluated. Similar Tco values are obtained for both groups of PAHs (0.46 d/kg) and 0.31 d/kg, respectively). This finding suggests that, on average, the PAHs with cancer potency factors as a whole transfer to mother's milk with about the same efficiency as some of the most common PAHs without cancer potency factors that are taken in through the diet. Therefore, summary Tcos were calculated by pooling across individual PAH-Tcos from both groups (see Table J.3-7).

J.5.3 Inorganic Lead

In an effort to derive lactational transfer coefficients for inorganic lead, OEHHA has drawn from studies conducted on subjects exposed to lead through multiple pathways at higher levels from other areas of the world. OEHHA assumes that the transfer of lead derived from these studies serves as a reasonable surrogate for the transfer of lead from contaminated media near a Hot Spots facility in California.

We were not able to locate studies that measured both long-term exposure to ambient air lead and lead levels in breast milk. Therefore, we calculated estimates of transfer from blood to human milk from separate study populations to combine with estimates of lead transfer from air to blood.

For our purposes, Gulson et al (1995, 1997, 1998a, 1998b) and Ettinger et al (2004) provide the best estimates of the change in blood lead levels due to the onset of lactation as well as during lactation relative to the levels of lead in breast milk.

Based on ambient air levels of lead reported in Ranft et al (2008), OEHHA estimated that blood lead levels in 55-year old women would change by 6-fold per unit of change in ambient air levels of lead (µg/dL) over a similar period (GM, 6.2; 95% CL 6.1 – 6.4).

Compared to Gulson et al (1998), the geometric mean blood lead levels prior to lactation observed by Ettinger et al (2004) were about 4-fold higher (7.3 and 8.0 for exclusive and partial lactators, respectively) (Gulson et al., 1998b; Ettinger et al., 2004).

The transfer factors derived from residents of Mexico and immigrants to Australia differ by less than a factor of two. However, our Tco estimate for lead has not considered the influence of maternal age, parity, length of lactation, and body weight on concentration of lead in milk.

J.5.4 Recommendations

OEHHA recommends using the Tcos based on the summary estimates provided in Table J.1-1 rather than the individual compound Tcos provided in Tables J.2-3, J.3-4, and J.3-6 to assess transfer of compounds to mother's milk. Tcos of individual compound are less robust that summary Tcos listed in Table J.1-1 because in some cases they have derived from data containing a high number of non-detects and small sample sizes. Additional studies might improve the estimation of individual Tco values, especially studies that incorporate more sensitive methods for analyzing breast milk PAH content and larger study populations to better estimate biological variation and estimates of PAH transfer from air to mother's milk. Such improved data could allow for a robust determination of the Tco values for individual compounds (see Table J.1-1).

Table J.1-1: Default Tcos (d/kg) for Mother's Milk

Chemical/chem. group	Tco	LCL	UCL
PCDDs - oral	3.7	2.68	5.23
PCDFs - oral	1.8	1.27	2.43
Dioxin-like PCBs - oral	1.7	0.69	4.40
PAHs – inhalation	1.55	0.731	3.281
PAHs – oral	0.401	0.132	1.218
Lead - inhalation	0.064	0.056	0.074

LCL, lower 95% confidence interval of the mean Tco; UCL, upper 95% confidence interval of the mean Tco

When calculating cancer risk from speciated PCDD/Fs, dioxin-like PCBs and PAHs, assume that the ratios of congeners measured in the emissions are preserved when transferred from the mother's body to breast milk. OEHHA recommends a single Tco for each chemical group (e.g. PCDDs oral). Risk assessors can apply TEQs to the

infant dose after applying the Tco for a chemical group to each congener in the group to calculate infant cancer risk for the mother's milk pathway.

The mother's exposure from multiple pathways should be included in estimating the concentration of contaminant in mother's milk. One key factor that plays a role in the difference between oral and inhalation transfer coefficient (e.g., for PAHs) is first pass metabolism which is lacking in dermal and inhalation exposures. Thus, for simplicity, OEHHA recommends applying the transfer coefficients from inhalation to the dermal absorption pathway for lead and PAHs. For lead, we recommend using the inhalation Tco for all the other pathways of exposure to the mother. Likewise for PCDD/Fs and dioxin-like PCBs, we recommend using the oral Tco for the other pathways of exposure to the mother in Eq. J-2.

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