PREDICTED CONCENTRATIONS OF POLYCHLORINATED DIBENZO-P-DIOXINS AND FURANS IN FAT TISSUE DUE TO CHLOROPHENATE EXPOSURE IN B.C. SAWMILLS

by

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Abstract

Chlorophenols were used to prevent sapstain fungal growth on lumber in sawmills located in Canada, the United States Scandinavia, and elsewhere, from the 1940s to the late 1980s. Elevated levels of chlorophenols have been measured in the urine of sawmill workers particularly those with dermal exposure. Since polychlorinated dibenzodioxins (PCDDs) and furans (PCDFs) are contaminants created in the manufacture of chlorophenols, it is expected that sawmill workers were exposed. PCDD/Fs have half-lives on the order of years and accumulate in adipose tissue. Biological monitoring is not easily carried out due to its invasive nature and cost, consequently little information exists on PCDD/F levels in sawmill workers.

In a cohort of Canadian sawmill workers assembled for a cancer incidence and mortality study, we estimated the adipose tissue concentrations of PCDD/F compounds, using a single-compartment pharmacokinetic model. Estimates of dermal and inhalation exposure to chlorophenols throughout the working lives of the sawmill workers were combined with PCDD/F contamination levels, half-lives, and absorption efficiencies to estimate tissue concentrations. Each variable in the model was assigned a distribution based on literature-reported data, as well as information about the sawmill cohort. The predicted distributions of PCDD/F concentrations were then estimated using 5,000-run Monte Carlo analyses. Predicted median adipose tissue concentrations of all dioxins and tetra- and penta-chlorinated furans among the sawmill workers were similar to background levels in unexposed residents of the same region, though about 10 to 30% of sawmill workers were estimated to have elevated levels of these congeners. Median levels of hexa-, hepta-, and octa-chlorinated furans were predicted to be 2 to 15 times background levels. Sensitivity analyses indicate that the

variability of the model predictions was most influenced by estimates of PCDD/F skin absorption efficiency, duration of employment at the sawmill, and levels of PCDD/F in the chlorophenols.

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1.0 Introduction

1.1 Purpose of Study

British Columbia (B.C.) sawmill workers have had elevated body burdens of chlorophenates due to the use of these compounds as antisapstain fungicides from the early 1940s to the late 1980s. Polychlorinated dibenzo-p-dioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs) are created during the production of chlorophenates and their contamination levels have been consistently reported in chlorophenate products. It is hypothesized that sawmill workers have been exposed to PCDD/F compounds concomitantly with exposure to chlorophenates throughout the history of chlorophenate use in B.C. sawmills.

Exposure to chlorophenate compounds is determined by measurement of metabolites in urine. In contrast to chlorophenates, PCDD/F compounds have a long half-life and accumulate in the adipose tissue of humans rather than being quickly metabolized and excreted. Biological monitoring of exposure to PCDD/F compounds is invasive and expensive due to the low levels of detection needed, and very few reports of biological sampling for this occupationally exposed group exists to date.

The purpose of this investigation was to estimate the concentration of PCDD/Fs in the fat tissue due to chlorophenate exposure in a cohort of B.C. sawmill workers. Data collected on this cohort as well as literature based data were used in a pharmacokinetic model to predict PCDD/F concentrations. Specific aims of the study included:

- development of a pharmacokinetic model which is appropriate for PCDD/F compounds and the sawmill exposure scenario,
- finding cohort- and literature-based data to be used as inputs into the model,

- describing the input variables and assigning each variable an appropriate distribution,
- using Monte Carlo analysis to calculate predicted PCDD/F concentrations in the fat tissue due to chlorophenate exposure in sawmills, and
- comparing predicted concentrations of PCDD/Fs due to chlorophenate exposure to levels found in the literature for unexposed and exposed populations, as well as to measured PCDD/F levels found in sawmill workers.

This introduction will provide an overview of PCDD/F compounds, including their physicochemical properties, toxicity and sources. As PCDD/F exposure is concomitant with chlorophenate use, the overview is followed by an examination of the history of chlorophenate use in B.C. sawmills, including a review of the job types associated with chlorophenate exposure as well as an examination of dermal versus inhalation exposure to chlorophenates in sawmills. A cursory review of pharmacokinetic principles is then followed by a description of the pharmacokinetic properties of PCDD/F compounds.

1.2 General Overview of Polychlorinated Dibenzodioxins and Furans

1.2.1 Structure and Physical Properties

In order to illustrate the similarities as well as the range of differences within the group of PCDD/F compounds, it is essential to first examine their chemical structures. Physicochemical properties of the compounds were compiled for use in various aspects of the model and are reviewed here to provide insight into the behaviour of these compounds.

1.2.1.1 Structure

PCDD/Fs are tricyclic aromatic hydrocarbons consisting of two benzene rings connected by a

third oxygenated ring. The middle ring contains a single oxygen atom in PCDF compounds and two oxygen atoms in the case of PCDDs. The basic structures are shown in Figure 1.1. These compounds comprise part of a wider group of halogenated aromatic chemicals all of which have similar biological effects. Members of this group include polychlorinated biphenyls (PCBs), diphenyl ethers, naphthalenes as well as brominated compounds with similar structures (Safe 1990,1992; Hanberg et al., 1990).

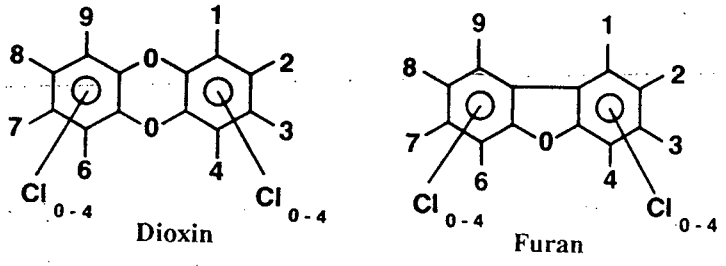

Figure 1.1 - Chemical Structure of PCDD/F Compounds

PCDD and PCDF molecules have up to eight chlorine atoms attached at any of eight specific locations on the molecule. The numbering system outlined in Figure 1 serves to identify specific isomers. There are 75 congeners of PCDDs and 135 congeners of PCDFs. A congener is defined by the United States Environmental Protection Agency (USEPA) as "any one particular member of the same chemical family" (USEPA, 1989). The abbreviated synonyms associated with each congener is outlined in Table 1.1.

Table 1.1: Synonyms Associated with Congeners

Congener Names	**Synonym**
Tetrachlorinated Dioxins and Furans	TCDD/TCDF
Pentachlorinated Dioxins and Furans	PeCDD/PeCDF
Hexachlorinated Dioxins and Furans	HxCDD/HxCDF
Heptachlorinated Dioxins and Furans	HpCDD/HpCDF
Octachlorinated Dioxins and Furans	OCDD/OCDF

Within each group possessing the same number of halogen atoms, the specific compounds are known as isomers, each of which are named according to the location of the halogen(s) on the molecule, for example there are 22 isomers within the group of TCDDs. The number and location of the chlorine atoms plays a significant role in determining the chemical and physical properties as well as the toxicity of each congener.

1.2.1.2 Physical Properties

The molecule 2,3,7,8-TCDD has been recognized as the most toxic and thus the most extensively studied of the PCDD/F compounds. A limited amount of research has been carried out in determining the physical and chemical properties of other PCDD and PCDF compounds. Properties such as molecular weights, melting and boiling points, vapour pressures, solubilities in water and octanol/water partition coefficients play a large role in determining the fate of these compounds in the environment.

1.2.1.2.1 Molecular Weights

The molecular weights of the compounds range between 306 for a TCDF isomer and 460 for OCDD. The molecular weight of each congener is listed in the Table A of Appendix I.

1.2.1.2.2 Melting/Boiling Points

The range of melting points for PCDD/F congeners has been reported to be approximately 180°C to 320°C. This range of melting points not only applies to the entire group of congeners but has also been reported between isomers, with 1,2,3,7-TCDD having a melting point of 172°C (Freisen et al., 1985) while 2,3,7,8-TCDD has been reported with a melting point in the range of 320-325°C (Merck Index, 1989). Table B, Appendix I lists the melting

points reported for the congeners.

The range of boiling points for the PCDD/F congeners is between 419°C for 1,2,3,4-TCDD (Rordorf, 1989) and 537°C for OCDF (Rordorf, 1989). The boiling points are listed in Table C of Appendix I.

1.2.1.2.3 Vapour Pressures

Very few measured vapour pressure values are available in the literature for the PCDDs and PCDFs. Results which have been reported have either been experimentally derived by methods such as gas chromatography capillary column retention time data, or have been calculated. The range of values for PCDD/F congeners is shown in Table D, Appendix I.

It has been previously noted that the volatility generally tends to decrease with the increasing number of chlorine atoms on the PCDD/F molecule (Rappe et al., 1982). This trend may be identified in Table D, however it is not strong due to the wide range of values identified for each group of isomers. The range of estimates for the vapour pressures within all PCDDs spans seven orders of magnitude, while estimates for PCDFs cover five orders of magnitude. Despite this large range of possible values, all reported values represent what are generally considered to be very low vapour pressures.

1.2.1.2.4 Solubility in Water

Again relatively few measured water solubility values are available in the literature for all PCDD/F compounds. Some reported values are listed in Table E, Appendix I.

Friesen et al., (1985, 1990) used two methods to measure the water solubilities of PCDDs and PCDFs. A High Performance Liquid Chromatography (HPLC) generator column in 1985 was used on a series of chlorinated dioxins. In 1990, a gas chromatography/mass spectrometry detection generator column was used to measure the aqueous solubilities of the furans. Other values of water solubility were cited in a compilation of physicochemical properties of PCDD/Fs by Mackay (1992), however, only those values which were consistently cited were included in Table E. Experimentally derived values were also favoured over calculated values. This decision was reinforced by the USEPA's (1994) attempt to estimate the water solubility of compounds utilizing the log transformation of the octanol/water partition coefficient as described in Lyman et al. (1982). This method did not yield satisfactory results when compared with experimentally derived values, differing by up to two orders of magnitude. Generally, compounds with water solubilities in the ranges of those reported in Table E are considered to have very poor solubility in water.

1.2.1.2.5 Octanol/Water Partition Coefficients

The octanol/water partition coefficient is often used in modelling the environmental fate of organic chemicals. As the values for the log octanol/water partition coefficient increases, the compound is more likely to be attracted to animal or human fat tissues and have a lower water solubility. These compounds also have a tendency to accumulate in soils and aquatic sediments. The reported ranges of log octanol/water partition coefficients of PCDD/Fs are listed in Table F, Appendix I.

The range of reported octanol/water partition coefficients for PCDDs covers over eight orders of magnitude, while PCDF values span approximately three orders of magnitude. There is a

general trend of increasing log octanol/water partition coefficients with increasing chlorine substitution.

Log octanol/water partition coefficients such as those reported in Table F indicate that these substances tend to adsorb strongly to organic components in the soil and may bioconcentrate in those organisms exposed to the compounds. This has been demonstrated in the case of PCDD/Fs with their high affinity for sediments and potential for accumulating in fish, birds, animals and humans.

1.2.2 Toxicity

1.2.2.1 Mechanism

PCDD/F congeners have similar chemical structures, but it is apparent that the number and location of the chlorine atoms on the molecules play a significant role in determining the compound's physicochemical properties. However, PCDD/F compounds generally do elicit similar toxic effects thought to be caused by a common mechanism.

A key step in this mechanism is binding to the cytoplasmic receptor protein, the Ah receptor (Poland and Knutson, 1982; Goldstein and Safe, 1989; Ahlborg et al. 1992). Once this binding occurs, a shedding and binding of cofactors takes place which allows the complex to move into the nucleus. In the nucleus, the complex will influence the rate of transcription of specific messenger RNAs which in turn changes the rate of synthesis of associated proteins.

Proteins induced by the Ah receptor include cytochromes P450IA1 and P450IA2, also known as CYP1A1 and CYP1A2 (Durrin et al., 1987; Jones et al., 1985, 1986; Neal et al., 1982;

Neal, 1985). These cytochromes oxidize foreign substances allowing for their further metabolic degradation, thereby reducing their biological effect (Nebert and Jensen, 1979; Nebert and Gonzalez, 1987). The PCDD/Fs are active in inducing the two cytochromes, but are not easily oxidized due to the presence of their halogen atoms. The persistence of attachment to the receptor by PCDD/Fs, especially 2,3,7,8-TCDD, renders the receptor ineffective to respond to other foreign substances (Webster and Commoner, 1994).

The Ah receptor has been reported to not only induce the two cytochromes, but also to regulate the expression of certain genes (Sutter and Greenlee, 1992). Interference by PCDD/Fs may therefore result in the disturbance of hormone regulation, growth factors and other molecular messengers that control growth (Webster and Commoner, 1994).

The relative affinity of PCDD/F compounds to the Ah receptor is governed by the number and placement of the chlorine atoms around the molecule. The planar 2,3,7,8-TCDD has demonstrated the greatest affinity with the receptor. 2,3,7,8-TCDD is generally acknowledged as the most toxic of the PCDD/F congeners, which implies that toxicity appears to be directly correlated with goodness of fit to the Ah receptor. Other PCDD/F molecules bind to the Ah receptor with different degrees of affinity, resulting in correlated toxic responses. The differing levels of toxic responses have resulted in "Toxicity Equivalency Factor" or TEFs.

1.2.2.2 Toxicity Equivalency Factors

All congeners exhibit a similar mechanism of action and similar toxic responses, however some PCDD/Fs require higher doses to elicit these responses. Originally, when measuring PCDD/F levels in the environment, it was difficult to estimate the relative toxicity of the

sample. Grant (1977) suggested a method of interpreting mixtures of PCDD/F in which the potency of each congener defined by a toxicity equivalency factor (TEF) that expresses its toxicity relative to 2,3,7,8-TCDD, which was assigned a TEF value of 1.0. Of 210 dioxins and furans, only those congeners with chlorines in the 2,3,7,8 positions (a total of seventeen) contribute significantly to toxicity, the remaining 193 congeners have TEF values of zero.

As the TEF system developed, many different schemes existed throughout the world. In order to facilitate international communication between scientists and regulatory agencies, the Committee on the Challenges of Modern Society (CCMS), a North Atlantic Treaty Organization (NATO) agency created a working group to consolidate all schemes into one. The Exposure and Hazard Assessment Working Group of the Pilot Study on International Information Exchange on Dioxins and Related Compounds developed what is known as the "International Toxicity Equivalency Factor" (I-TEF) scheme for estimating the risk of mixtures of dioxins and furans in the environment (CCMS, 1988). The I-TEF scheme has been adopted by Canada, Denmark, Germany, Italy, the Netherlands, Norway, the United Kingdom and the United States (Health and Welfare Canada, 1990). The I-TEFs (CCMS, 1988) are listed in Table 1.2.

Table 1.2: International Toxicity Equivalency Factors (CCMS, 1988)

Congener	Equivalency Factor
2,3,7,8-TCDD	1
1,2,3,7,8-PeCDD	0.5
1,2,3,4,7,8-HxCDD 1,2,3,7,8,9-HxCDD 1,2,3,6,7,8-HxCDD	0.1
1,2,3,4,6,7,8-HpCDD	0.01
OCDD	0.001
2,3,7,8-TCDF	0.1

Congener	Equivalency Factor
2,3,4,7,8-PeCDF	0.5
1,2,3,7,8-PeCDF	0.05
1,2,3,4,7,8-HxCDF 1,2,3,7,8,9-HxCDF 1,2,3,6,7,8-HxCDF 2,3,4,6,7,8-HxCDF	0.1
1,2,3,4,6,7,8-HpCDF 1,2,3,4,7,8,9-HpCDF	0.01
OCDF	0.001

The I-TEFs have been universally recognized as being of an interim nature and are subject to modification as the data on the relative bioavailability and pharmacokinetics of the congeners grows (Kutz,1990). CCMS has acknowledged that the preferred method of assessing risk from mixtures of PCDD/Fs would be to utilize a short-term assay that could measure toxicity directly, however until this is possible, I-TEFs are considered appropriate (Barnes, 1991).

Concerns have been raised regarding the use of I-TEFs even as an interim measure in environmental risk assessments. McLachlan (1993a) has outlined four uses of toxicity equivalents which include: comparison of PCDD/F levels in the same matrix; comparison of risk associated from levels of PCDD/F in the same matrix; legislation; and the calculation of the transfer of PCDD/Fs from one matrix to another. McLachlan postulates that the use of TEFs for these purposes results in erroneous conclusions on the toxicity of environmental samples. A main point of contention for McLachlan is based on the principle that TEFs are decided based on the toxicity of the congener in the tissue, however, the factors are applied to the concentrations of congeners in the environment. These factors, therefore, do not account for transfer rates of the congeners through the various matrices, which may differ by more than an order of magnitude (McLachlan, 1993a).

McLachlan (1993), has suggested a new system which is based on "exposure toxicity equivalents" (ETEs) which are based on the same principle as TEFs, however the congener specific transfer rates from matrix to matrix are included in the ETE factor derivation. This system is obviously more complex than the I-TEF system, however, rough calculations have demonstrated that this method yields significantly different results than the TEF system, once the exposure routes and associated transfer rates for each congener are taken into account. The main obstacle in implementing this system is a lack of data on the environmental behaviour of specific PCDD/F congeners (McLachlan, 1993).

1.2.2.3 General Toxicity

1.2.2.3.1 Animal Data

Symptoms from toxic exposure to 2,3,7,8-TCDD in laboratory animals include listlessness, loss of body weight, atrophy of the thymus, hair loss/epidermal changes, liver damage, immunotoxicity, birth defects, reduced fertility and cancer (Poland and Knutson, 1982; Silbergeld and Gasiewicz, 1989). However, a marked interspecies variability has been noted in the pathology and LD_{50} of 2,3,7,8-TCDD (Neal et al., 1982). The range of single lethal oral dose ranges from 0.6 ug/kg body weight for guinea pigs to 5051 ug/kg body weight for hamsters (OME, 1985).

Other congeners of dioxins and furans, specifically those with 2,3,7,8-substitution, have produced similar toxic effects in most species although these congeners are generally found to be less toxic than 2,3,7,8-TCDD. Differences in the toxicity of the isomers within a homologous group have also been noted (McConnell et al., 1978). LD_{50} values have been estimated for congeners other than TCDD in several species such as the guinea pig, mouse

and Sprague-Dawley (S.D.) rat and are compared in Table 1.3 (McConnell et al., 1978; Schwetz et al., 1973).

Table 1.3: LD_{50} Values for Specific PCDD Congeners in the Guinea Pig, Mouse and Sprague-Dawley Rat

Congener	LD_{50} - Guinea Pig (ug/kg body weight)	LD_{50} - Mouse (ug/kg body weight)	LD_{50} - S.D. Rat (ug/kg body weight)
1,2,3,4,7,8-HxCDD	73	825	NA
1,2,3,6,7,8-HxCDD	70-100	1250	NA
1,2,3,7,8,9-HxCDD	60-100	>1440	NA
1,2,3,4,6,7,8-HpCDD	>600	NA	NA
OCDD	NA	NA	>1,000,000

Table 1.3 demonstrates that the guinea pig is the most susceptible species to the PCDD congeners. It may also be noted that the dose required to induce toxicity increases with increasing chlorination of the congener.

1.2.2.3.2 Human Data

Some signs of toxicity which are common to humans, non-human primates and hairless mice include chloracne, dermal hyperkeratinosis and edema (NRCC, 1981).

A common element in human exposure to PCDD/F compounds is that it never occurs in isolation, but involves exposure to other compounds as well. This factor makes it difficult to attribute symptoms solely to the PCDD/F compounds, however, some signs and symptoms have been attributed to PCDD/Fs.

Numerous industrial accidents involving the manufacture of chlorinated phenols or phenoxy herbicides have resulted in populations exposed to short-term high level doses of PCDD/Fs. The rate, route and length of exposure differs in the reports, however, some common effects

have been noted. Skin lesions, mainly chloracne, are one of the most common symptoms of exposure to PCDD/F compounds, along with hyperpigmentation, thickening of the skin, hair loss and hirsutism. Liver, kidney and gastrointestinal disturbances include fluctuations in serum levels of liver enzymes, enlarged liver, porphyria cutanea tarda, and abnormal liver function tests. Respiratory and cardiac disorders have also been reported as well as hypothyroidism and hypercholesterolemia. Various neurological and psychological anomalies associated with exposure include listlessness, sleep disturbances, nausea, headaches, sexual dysfunction, depression and lack of appetite (Bleiberg et al.,1964; May, 1973; Oliver, 1975; IARC, 1978; WHO, 1989).

PCDF exposure to large populations has been documented on at least two occasions. In both the Yusho (in 1968) and Yu-Cheng (1978) incidents, rice oil contaminated by polychlorinated biphenyls (PCBs) containing low levels of PCDFs resulted in exposure to a mixture of PCDF compounds. The symptoms reported from both rice oil incidents were similar, including: chloracne; rough texture of the skin on hands and feet; blackening of nails; dark discolouration of gums and skin; eye secretion; swelling of the eyelid; sweating of the palms (Kuratsure et al., 1972; Rogan et al., 1988). Most of these effects subsided over a 10-year period with some symptoms such as nail pigmentation and skin cysts being more persistent. Rogan et al.(1988) noted that children exposed in the womb in the Yu-Cheng poisoning incident often died soon after birth, and had reduced size, abnormal gums, skin, nails, teeth and lungs.

Epidemiological studies attempting to draw conclusions regarding PCDD/F exposure and physiological effects usually have inherent limitations due to the long latency periods of many

of the effects such as cancer and the subtle effects of other outcomes. If the more subtle outcomes are not pursued specifically, they may be missed in an epidemiological study. Exposure misclassification was also a major limitation before blood and tissue sampling were available. Exposure was usually assumed by presence in a contaminated area which, if misclassification was taking place, may have biased studies toward a null result.

1.2.2.4 Carcinogenicity

Various studies designed to demonstrate the carcinogenic properties of 2,3,7,8-TCDD in experimental animals have been positive in both sexes and in several species, however, questions remain concerning the carcinogenic mechanism and how this applies to human exposure at low doses (OME, 1985; USEPA, 1985; IARC, 1987).

1.2.2.4.1 Animal Data

TCDD has been demonstrated to be a multisite carcinogen with the main sites for development of tumours and carcinomas being the liver, thyroid, lung, tongue, hard palate and nose of rats and mice following long-term exposure (OME, 1985; USEPA, 1985; IARC, 1987).

Congeners other than TCDD have also been shown to possess carcinogenic properties in laboratory animals. A mixture of 1,2,3,6,7,8- and 1,2,3,7,8,9-HxCDD administered orally to female rats and mice was found to produce an increase in hepatocellular carcinoma and adenoma as well as an increase in neoplastic nodules (NCI, 1980). Inconclusive results were found in male mice. Percutaneous application of HxCDD resulted in a statistically insignificant increase in skin fibrosarcoma (NCI(a), 1980). The Ames test was carried out

with OCDD, but no significant increase in point mutations was noted (Seiler, 1973).

1.2.2.4.2 Human Data

Human epidemiological evidence linking exposure to PCDD/F mixtures and cancer has been mixed. Most studies are hindered by limitations such as co-exposures, inadequate measurement of exposure resulting in exposure misclassification as well as long latency periods for disease development.

Significant increases in soft-tissue sarcoma have been found in several studies of workers exposed to TCDD-contaminated phenoxyacetic acid herbicides in agricultural sectors based in Sweden (Hardell, 1977; Hardell and Sandstrom, 1979; Eriksson et al., 1981; Hardell and Eriksson, 1988). Eriksson et al. (1990) have also suggested that higher chlorinated PCDD congeners may be carcinogenic. Some aspects of the earlier studies have been criticized for the possibility of bias from differential exposure misclassification between cases and controls (Bond et al., 1989; Colton, 1986), however, the later studies have been redesigned to reflect these criticisms.

No association between soft tissue sarcoma or non-Hodgkin's lymphomas and exposure to phenoxy acid or chlorophenols was found by Woods et al. (1987) in a study conducted on workers in Washington State. Other studies of workers exposed to phenoxy herbicides or chlorophenols have also demonstrated little or no increases in soft tissue lymphoma or malignant lymphoma (Olsson and Brandt, 1988; Wingren et al., 1990). In a retrospective cohort study of almost 24,000 sawmill workers in BC, Hertzman et al., (1995) found no association between soft tissue sarcoma, nasal cancer and lung cancer and chlorophenate

exposure. In this study, an increased risk of non-Hodgkins lymphoma with increasing chlorophenate exposure was noted. In nested case control studies of workers exposed to phenoxy herbicides, chlorophenols and dioxins, Kogevinas et al. (1995) found a higher risk of soft tissue sarcoma in workers with substantial exposure to phenoxy herbicides, but relatively weak evidence of increased risk of non-Hodgkin's lymphoma.

Increased mortality from all cancers as well as cancers of the lung and the haematopoietic system were reported in the highest exposed subgroups in cohorts occupationally exposed to TCDD in Boehringer and BASF plants which suffered process upsets while manufacturing trichlorophenol (Manz et al., 1991; Zober et al., 1990). Fingerhut et al. (1991) reported a study of over 5000 workers thought to be exposed to TCDD, with blood serum samples to validate exposure estimates, in which a statistically significant increase in lung cancer and all cancers combined was reported.

Other studies on populations exposed during a process upset in 1949 at a Monsanto facility in Nitro, West Virginia have reported no significant increases in cancer (Zack and Suskind, 1980; Zack and Gaffey, 1983; Suskind and Hertzberg, 1984). Some of these studies have been reexamined and have been reported to contain serious flaws including exposure misclassification (Hay and Silbergeld, 1985).

As a result of the conflicting human epidemiological results, IARC (1987) has rated 2,3,7,8-TCDD as a probable human carcinogen, citing what the organization considers to be sufficient evidence in animals and inadequate evidence in humans. It is hoped that new technology such as the ability to measure PCDD/F in tissues such as blood, will aid in

exposure classification of future epidemiological studies, giving more convincing results.

1.2.2.5 Non-Carcinogenic Effects

1.2.2.5.1 Animal Data

2,3,7,8-TCDD has demonstrated teratogenic properties in several strains of mice, with cleft palates, kidney anomalies and hydronephrosis being prevalent (Smith et al., 1976; OME, 1985; Couture et al., 1990). Murray et al. (1979) noted reproductive as well as developmental effects with rats exposed to PCDD/Fs. Rats receiving 0.01 or 0.1 ug TCDD/kg/day were noted to experience changes in fertility, litter size, gestational survival, postnatal survival and postnatal body weight. A no adverse effects level on reproduction was reported at 0.001 ug TCDD/kg/day.

A mixture of HxCDD isomers administered orally to Sprague Dawley rats produced fetotoxic effects which were essentially identical to TCDD (Schwetz et al., 1973). OCDD, however, was found not be teratogenic in rats at doses up to 500 ug/kg while mild fetotoxic effects were observed at 100 ug/kg (Schwetz et al., 1973).

Most 2,3,7,8-substituted PCDD/Fs have demonstrated effects such as suppression of both cell- and humeral-mediated immune responses in mammals (OME, 1985).

1.2.2.5.2 Human Data

The EPA reassessment (USEPA, 1994) has to this point reaffirmed the view that PCDD/Fs are probable human carcinogens, but it has also noted that noncancer health effects are greater than previously thought. These effects include disruption of the endocrine and immune

systems, as well as reproductive and teratogenic effects in humans.

Research on reproductive effects has predominantly been based on paternal exposures to PCDD/Fs. Effects attributed to exposure to TCDD include loss of libido (WHO, 1989) and reduced testosterone and/or elevated luteinizing hormone (Egeland et al., 1992; USEPA, 1992).

Other epidemiological studies examining reproductive effects of 2,3,7,8-TCDD exposure, found no significant increases in stillbirths, spontaneous abortions or major defects reported in cohorts occupationally exposed at the Dow Chemical Midland and Monsanto Nitro sites (Townsend et al., 1982; Moses et al., 1984). In an exposed cohort in Seveso, the incidence of birth defects were monitored since 1977 with an increased incidence of spina bifida and haemangioma, however numbers were too small for statistical analysis (Silbergeld et al., 1987). Aschengrau and Monson (1990) found a increased risk of a Vietnam veteran fathering an infant with one or more major malformations compared to non-Vietnam veterans. Another study carried out on Vietnam veterans found no increased risk of birth defects (Center for Disease Control, 1988).

Developmental effects noted in children of exposed women in Yu- Cheng include smaller size, abnormalities of the gums, nails, skin, teeth and lungs and delayed psychomotor development (Rogan et al., 1988; Rogan, 1989)

1.2.2.6 Threshold or Non-Threshold Response to PCDD/Fs

PCDD/F compounds have created considerable debate about whether or not a threshold of

exposure exists prior to a response. The presence or absence of a threshold is the main assumption behind regulatory bodies setting "acceptable" doses. The range of "acceptable" daily doses of 2,3,7,8-TCDD set by various regulatory agencies is shown in Table 1.4 (Webster and Commoner, 1994).

Table 1.4: Acceptable Daily Doses of 2,3,7,8-TCDD

Organization	Level (pg/kg/day)*
USEPA	0.006
California	0.007
Centres for Disease Control	0.03
U.S. Food and Drug Administration	0.06
National Research Council of Canada	0.07
Germany	1-10
Netherlands	4
Canada and Ontario	10
World Health Organization	10
Washington State Dept. of Health	20-80

*Sources: USEPA (1988), except Washington State Dept. of Health (Marien et al., 1991) and World Health Organization. Summary Report: Consultation on Tolerable Daily Intake from Food of PCDD's and PCDF's, Regional Bureau for Europe (1991).

As shown in Table 1.4, "acceptable" daily doses span several orders of magnitude. High values, in the range of 10 to 80 pg/kg per day, were calculated based on the threshold theory. This assumes that there is a low dose of TCDD at which there is no response due to the fact that a certain number of receptors must be occupied before effects may occur. Using this assumption, no-observed-adverse-effects-levels in animals and safety factors are be used to estimate human intakes which are assumed not induce adverse effects. This also assumes that PCDD/Fs are non-genotoxic carcinogens.

The low acceptable doses, such as those for California or the USEPA, are based on the assumption that there is no threshold for cancerous response following exposure to

2,3,7,8-TCDD. The USEPA's acceptable dose of 0.006 pg/kg/day is consistent with an upper-bound lifetime cancer risk of one in a million, and assumes that the probability of cancer is directly proportional to dose even at low doses. This is based on a classic model for receptors in which the biological response is proportional to exposure down to a dose of zero.

1.2.3 Sources of PCDD/Fs (Historical and Present)

PCDD/Fs are not produced intentionally (except for research purposes), but are unwanted by-products of other reactions or processes. PCDD/F compounds are usually found in the environment in complex mixtures and may be produced by one or more of four categories of sources: chemical, combustion, natural and industrial (Health and Welfare Canada, 1990).

1.2.3.1 Chemical Sources

2,3,7,8-TCDD was first identified in 1957 as a contaminant formed during the production of 2,4,5-trichlorophenol (Kimmig & Schultz, 1957; Hay, 1982). TCDD is also found as a contaminant of 1,2,4,5-tetrachlorobenzene and hexachlorobenzene.

Higher chlorinated PCDD/Fs are formed during the production of chlorophenol products such as pentachlorophenol (PCP) and tetrachlorophenol (TCP) used in wood preservation and protection. In 1981, these products were considered to be the largest potential sources of PCDD/Fs in the Canadian Environment (NRCC, 1981), however by 1990, their potential as a source had been greatly reduced (Health and Welfare Canada, 1990). The role of pentachlorophenol and tetrachlorophenol in PCDD/F exposure will be examined in further detail in Section 1.3.

None of these contaminated products are currently manufactured in Canada and their use, for the most part, has decreased considerably during the 1980s as shown in Table 1.5.

Table 1.5: Canadian Sales of Dioxin-Contaminated Chemicals (Tonnes) in 1980 and 1987*

Product	1980+	1987
Pentachlorophenol	2300	1340
Sodium Pentachlorophenate and Tetrachlorophenate	1200	402
2,4,5-Trichlorophenol	50	0
2,4-Dichlorophenol	3800	4546
Hexachlorophene	7	7

* From: Health and Welfare Canada, 1990
+ Approximate Values for 1978 to 1981 (NRCC, 1981)

PCBs comprise the most significant source of furans. In 1985, a total of 75 kgs of furans were estimated to be contained in PCBs either in storage or in use in Canada (Sheffield, 1985).

1.2.3.2 Combustion Sources

PCDD/Fs were first detected in incinerator emissions in 1977 (Olie et al., 1977). Since that time, these unwanted emissions have been found to be produced when chlorine-containing products such as chemical waste, hospital waste (Lindner et al., 1990) and sewage sludge (Fiedler et al., 1990) are burned. Throughout the 1980s and 1990s, municipal incinerators were thought to be the largest combustion source of PCDD/F emissions in Canada and elsewhere (Czuczwa and Hites, 1984; Rappe, 1984; Sheffield, 1985; Health and Welfare Canada, 1991). There is considerable variation in the measured level of each isomer in fly ash from incinerators resulting from differences in design, operating conditions, and material that is incinerated (Tiernan et al, 1983; Rappe, 1984).

Other combustion processes which have been found to emit PCDD/Fs include copper smelting and electrical arcing furnaces (Rappe et al., 1986). Combustion of hydrocarbons and chlorinated additives in automobile engines have also been found to produce significant amounts of PCDD/F compounds (Ballschmiter et al, 1986). Cigarette smoke has also been recognized as a source of a mixture of PCDD/F compounds (Muto and Takizawa, 1989).

1.2.3.3 Natural Sources

Low levels of PCDD/F in soil sediments ranging in age from 300 to 1000 years are thought to be the result of forest fires and volcanoes. It appears that these are composed primarily of the more highly chlorinated PCDD/F compounds (Jansson et al., 1987). However, the role of non-industrial sources is not considered to be significant given that pre-industrial soil samples and ancient eskimo tissue yielded only trace amounts of the compounds (Hagenmaier et al., 1986; Schecter et al., 1988).

1.2.3.4 Industrial Sources

During the bleaching process in a pulp and paper mill, PCDD/Fs may be formed from the chlorine and the aromatics contained in the lignin of the wood (Fiedler et al, 1990; Hrutfiord and Negri, 1992). This unintentional production and release of PCDD/F compounds in effluent was confirmed when high concentrations of TCDD and other PCDD/F compounds were found in fish downstream from mills (USEPA, 1987; VanStrum and Merrell, 1987; Amendola et al., 1989; USEPA, 1990).

In 1990, Environment Canada estimated that approximately 100-150 grams/year of 2,3,7,8-TCDD and 2000-3000 grams/year of 2,3,7,8-TCDF are released, based on the total

number of mills, estimated bleached pulp production and estimated effluent discharge (Health and Welfare Canada, 1990).

1.3 Chlorophenates in Sawmills

Sawmill worker exposure to PCDD/F compounds has not been measured directly. However, contamination levels of PCDD/F in chlorophenates have been reported and chlorophenate exposure measurements in sawmill workers have been carried out. In this study, PCDD/F exposure was estimated from previously collected chlorophenate data. Chlorophenate use in sawmills will be examined in the following section to provide some background into the type and route of exposures. Lists and descriptions of jobs associated with chlorophenate exposure will also be examined.

1.3.1 History of Use

Pentachlorophenol and tetrachlorophenol and their more soluble sodium salts have predominately been used either for wood preservation or wood protection. Wood preservation has primarily been carried out using pressure or thermal treatment with pentachlorophenol to preserve wood products such as hydro poles or railway ties. Wood protection, on the other hand, is mainly for short-term protection of wood from fungi prior to reaching customers. Various wood protection processes have been carried out at sawmills in northwest North America and in Scandinavia.

In B.C. sawmills during the 1940s, sodium pentachlorophenate (NaPCP) in powder or pellet form was mixed with water. By the mid 1960s sodium tetrachlorophenate (NaTCP) solutions, along with relatively smaller amounts of pentachlorophenate, were introduced predominately

because of their increased water solubility. Variations of these products have been used until the end of the 1980s (between 1987-1990), when B.C. sawmills responded to concerns regarding health and environmental effects of chlorophenates and their contaminants. At this time, most mills changed to other fungicides such as borax, copper-8- quinolinolate (Copper 8), 2-thiocyanomethyl-thiobenzthiazole (TCMTB) and didecyldimethyl ammonium chloride (DDAC).

Many process changes have taken place throughout the history of wood treatment with fungicides. The techniques used to apply chlorophenate solutions may be divided into two categories: (1) treating bundles of lumber; or (2) treating each piece of lumber individually. The method of treatment often determined the type of exposure and the number of workers exposed. For example, if the fungicide was applied to the lumber as a bundle, the treatment area was usually placed at the end of the process flow, following grading or planing. However, if individual treatment was used, the treatment area could occur anywhere in the sawmill, and often was placed prior to grading and sorting.

Techniques for treating bundled lumber often utilized diptanks. One of the earliest forms of treatment involved using a crane diptank, in which a bundle of lumber was dipped into tanks of chlorophenate solution. Variations on treating bundled lumber included the drive-through diptank, the forklift diptank and the elevator diptank. The drive-through diptank utilized carrier trucks which picked up bundles and drove through the tanks. The other diptanks utilized either forklifts or automated elevators or a combination of the two to transport, raise and lower the bundles of lumber.

Early methods of treating individual pieces of lumber included hand spraying or dipping. Beginning in the 1950s, a trough diptank dipped individual pieces of lumber, however, this process often left lumber dripping and resulted in high exposures for those working downstream of the treatment area. Sprayboxes were introduced in the 1940s. These were later adapted to leave little fluid carryover on the lumber by increasing the speed of the lumber through the spraybox, using high-pressure, small-aperture nozzles, and a fine mist spray. Another adaption of the spraybox occurred in the late 1970s when many high pressure nozzles were used in a large spraybox which accommodated the lumber side-by-side, known as a crosschain spraybox. The nozzles associated with these systems proved to require extensive maintenance.

A carwash spraybox was another variation of the spraybox theme, which treated bundled lumber. This system utilized large nozzles which were not susceptible to clogging but resulted in fluid carryover as the bundle was flooded with solution.

There were general trends in the use of the various technologies throughout the history of anti-sapstain use in B.C. sawmills, however, many of the older systems of treatment remained in some mills for extended periods of time. Even as late as the 1980s, a mixture of techniques of lumber treatment existed in sawmills throughout British Columbia (See Table 1.6).

Table 1.6: Number and Type of Treatment Units in B.C. Sawmills in the 1980s (McDonald, 1989)

TYPE OF UNIT	NUMBER OF UNITS			
	1982	1985	1988 (March)	1988 (October)
DIP TANKS				
Drive-In	12	5	3	3*
Fork-Lift	11	9	{ {30	{ {24
Elevator	15	16		{
Sorting-Chain	6	4	5	
TOTAL	**45**	**35**	**38**	**27**
SPRAY UNITS				
Hand (incl. watering cans)	{ {5	{ {6	5	5
Carwash			4	4
Linear	55	78	82	70
X-Chain	0	4	21	22
TOTAL	**60**	**88**	**112**	**101**

1.3.2 Exposures Associated with Job Categories in the Sawmill

The processes used for treatment of the lumber are likely to have had a significant impact on the exposure of the workers in the sawmill. In mills with diptanks, exposure was somewhat restricted to those workers in the immediate dipping area. Mills that utilized sprayboxes for treatment often resulted in more widespread exposure, especially if the box was located prior to grading or pulling. Early sprayboxes were also not well enclosed and resulted in some overspray thus further increasing potential exposure.

In 1988, the total estimated workforce in the British Columbia wood products industry was 28,500 with about 1260 (4.4%) having potential exposure to anti-sapstain treatment solutions (Price Waterhouse, 1989). Six job categories have been be identified as having a high potential for chlorophenate exposure in B.C. sawmills (McDonald, 1989). These include:

(1) Grader: Often must handle every piece of lumber, which may lead to high exposure levels if placed after spraybox in process flow.

(2) Chain Puller: Pulls lumber from chains and manually stacks into bundles. High exposure may result if downstream of treatment system thus handling wet lumber.

(3) Stacker: Operates mechanical stackers after sorting. They must handle treated wood periodically if it becomes tangled.

(4) Maintenance: May have exposure due to maintenance of spray boxes and delivery systems.

(5) Mix Room: Duties include cleaning filters, checking dilution ratios and clean-up.

(6) Fork-lift and carrier drivers: If diptank is the method of treatment these workers are often exposed by splashing through holes in cab floor and by touching contaminated railing during dismounting.

Generally, studies in sawmills both in North America and Scandinavia have found that those workers with direct dermal contact to treated wood have had the highest urinary chlorophenate levels.

Embree et al. (1984) found the highest urinary chlorophenate concentrations in pullers, grade deck sorters, graders and stencilmen in a B.C. sawmill. In Washington state, Kleinman et al., (1986) also found that those workers handling wet, treated wood daily, such as graders and pullers had higher urinary concentrations than those workers who were "potentially heavily exposed" on a periodic basis, such as maintenance workers. In 1985, a study done by B.C. Research for Health and Welfare Canada (1986) found the highest urinary chlorophenate concentrations in a drive-in diptank carrier driver, with graders and manual chain pullers recording the second highest levels. Stacker operator and mix room attendants were next,

with maintenance and yard workers lowest in the exposure ranking.

Finnish studies have found similar results. Kauppinen and Lindroos (1985) found loaders, who draw wet boards from the transporter following chlorophenate treatment by trough-dipping, reported the highest exposure levels. Lindroos et al. (1987) reported that loaders had the highest urinary chlorophenate levels followed by those involved in trimming, grading, longitudinal packing as well as those involved in preparation of treatment solution.

Personal protective equipment was not prevalent in the B.C. sawmill workforce until the 1980s. Since 1983, more highly exposed workers have worn protective clothing including gloves, aprons, boots, respirators, goggles and face-shields, depending on the job. Graders and chain-pullers generally have worn waist-high leather aprons with plastic lining, some have bibs for additional chest protection.

1.3.3 Dermal Versus Inhalation Exposure to Chlorophenates in Sawmills

Most exposure studies on chlorophenates in sawmills have been carried out in the 1980s, thus making it difficult to extrapolate exposures associated with previous processes, work practices and formulations.

Total chlorophenate exposure is generally measured in the urine, which accounts for all routes of exposure including inhalation, ingestion and skin absorption. The Biological Exposure Index - Threshold Limit Value for pentachlorophenol in urine is 2 mg/L which is estimated to represent a similar body burden as exposure to the airborne time-weighted average limit of 0.5 mg/m^3 (ACGIH, 5th edition).

Workers with dermal exposure to chlorophenate solutions have consistently reported higher urinary concentrations of chlorophenols than those workers with inhalation exposure only. These results have been found in sawmills on the Northwest coast of North America (Kalman and Horstman, 1983; Embree et al., 1984; Kleinman et al., 1986; Fenske et al., 1987) as well as in Finland (Kauppinen and Lindroos, 1985; Lindroos et al., 1987). B.C. Research (1986) calculated that approximately 13% of the urine concentration is derived from the inhalation route, with a range of 70 to 100% of urinary chlorophenols resulting from dermal exposure. This result was further reinforced by Lindroos et al. (1987) and Fenske et al. (1987) both of whom estimated approximately 90% or more of the urinary chlorophenol level may be due to dermal exposure in heavily exposed workers.

1.4 Pharmacokinetics

1.4.1 Empirical Versus Physiologically-Based Models

Pharmacokinetics refers to the study of the absorption, distribution, metabolism and elimination of chemicals from intact organisms (Gibaldi and Perrier, 1975). The kinetic behaviour of the chemical through the organism is described by a set of equations. These models may be either one of two types: empirical or physiologically-based.

Physiologically-based pharmacokinetic (PBPK) models are composed of a series of distinct compartments representing either individual organs or tissue groups connected by arterial and venous blood flow. Grouping of tissues varies with the chemical and is based on specific biochemical, physiological and anatomical properties. However, if grouping or division of tissues take place, the physiological parameters must describe these compartments based on known anatomical and physiological data for the group of tissues, for example total blood

flow to those specific tissues must be accounted for. These models rely primarily on known physiologic parameters including: blood flow rates, cardiac output, alveolar ventilation rates, tissue volumes and partition coefficients for the chemical in question. Each tissue compartment then is described by a mass balance differential equation based on the chemical's kinetic behaviour.

In PBPK models the parameters (physiological, physicochemical and biochemical) are predetermined based on physiological and anatomical data. Because the exact value for each parameter is not known, inherent uncertainty exists for each parameter included in the model. Each of these uncertainties leads to overall uncertainty on the predictions of the resulting tissue dose. The range of possible tissue dose estimates is further widened due to individual variability in the range of values for each parameter. The appropriateness of the structure of the model, the number and validity of parameters and the individual variability must all be taken into account when deciding what type of model is appropriate.

The empirical model is not based on real physiologic or anatomical parameters, but is constructed based on kinetic data which determines the model structure and rate constants. The compartments in these models therefore do not correspond to an actual tissue groups, but are regions in which the chemical is assumed to be uniformly distributed. The compartment model is mathematically described using differential equations.

Woodruff et al. (1992) carried out a comparison study of physiologically-based and empirically-based compartmental models of benzene pharmacokinetics. They concluded that, in some cases, the empirical-based studies are advised due to the fact that they have fewer

parameters and are easier to fit. Variability in resulting tissue dose prediction depends primarily on two factors: the quantity and type of data and the number of parameters in the model. In the PBPK model, although the parameters are based on physiological information, there remains a large opportunity for variability due to the large number of parameters. The limited available input data and the large variability in the estimates of physiological parameters for PCDD/Fs indicated that a simplified empirical model would be most appropriate for this study. The model developed for this study will be described in Section 2.

1.4.2 Pharmacokinetics of PCDD/F Compounds: Absorption, Distribution, Metabolism and Elimination

1.4.2.1 Absorption

The absorption of PCDD/F compounds through the various routes is dose- and congener-specific, and is also dependent upon the vehicle in which the compound was administered. In the case of sawmill workers, the occupational exposures of interest are via the skin and respiratory tract.

1.4.2.1.1 Dermal

Dermal penetration of PCDD/F compounds in rat skin in vivo has been shown to be age- and dose-dependent (Banks et al., 1990). Of all the congeners tested, 2,3,7,8-TCDF demonstrated the highest absorption efficiency, with 48% of the applied dose absorbed, while approximately 41% of 2,3,7,8-TCDD was absorbed through rat skin following 120 hours (Banks and Birnbaum, 1991). In the Rhesus monkey, approximately 6 hours following exposure, less than 1% of the administered dose had been absorbed (Brewster et al., 1988). Poiger and Schlatter (1980) demonstrated that the vehicle plays a large role in determining the dermal

uptake of PCDD/F compounds, with an ethanol solution enhancing uptake and activated charcoal virtually prohibiting uptake.

In vitro tests have also been carried out with PCDD/F compounds in various vehicles on human cadaver and porcine skin (Weber et al., 1991, 1992; Weber, 1993). These studies have reported percent absorbed over specific time periods and with as well as without the stratum corneum. Specific results are discussed later in the paper.

The human cadaver and porcine absorption results have been used to estimate the percent absorption in the human. Studies have indicated that skin absorption in rats is rather high and not considered to be a good model for human skin, while that of pigs usually approaches skin absorption in humans (Wester and Maibach, 1985; Wester and Noonan, 1980).

1.4.2.1.2 Respiratory

Nessel et al. (1990) demonstrated that inhalation absorption does take place by observing significant systemic effects in rats following intratracheal instillation of 2,3,7,8-TCDD. However, few studies have been carried out on the absorption efficiency of PCDD/F congeners in the respiratory tract. Diliberto et al., (1992), did observe that the transpulmonary absorption of TCDD was 92% in rats following intratracheal instillation, whereas the oral absorption was 85%. The authors suggested that inhalation absorption may be similar to oral absorption.

As respiratory absorption is considered to be similar to gastrointestinal (GI) absorption, studies on GI absorption will be briefly examined. Some studies have demonstrated that

2,3,7,8-TCDD in an oily vehicle is relatively well absorbed by the gastrointestinal tract, with 50-80% of an oral dose shown to be absorbed in rats, mice, hamsters and guinea pigs (Piper et al., 1973; Rose et al., 1976; ; Allen et al., 1975; Curtis et al., 1990; Olson et al., 1980; Nolan et al., 1979). Poiger and Schlatter (1986) reported that 88.5% of orally administered 2,3,7,8-TCDD in corn oil was absorbed by a human subject. This suggests that GI absorption in the human may be comparable to the rodent species examined.

2,3,7,8-TCDF was shown to have an oral absorption efficiency of approximately 90% when administered to rats and guinea pigs (Birnbaum et al., 1980; Decad et al, 1981). 2,3,7,8-substituted pentachlorinated congeners also reported high absorption efficiencies, in the range of 70 to 85% (Brewster and Birnbaum, 1987; Kamimura et al., 1988).

It has been noted that the molecular size and solubility of the congener plays a large role in determining how easily they are absorbed by the GI tract. Higher chlorinated PCDD/F compounds appear to be less well absorbed. McLachlan et al. (1990) found gastrointestinal absorption to be related to molecular size after administration to a lactating cow, with absorption ranging from 80% in TCDD/F compounds to 20 to 40% for OCDD and OCDF compounds. OCDD was also found to be poorly absorbed (absorption efficiencies between 2 and 15%) in rats and hamsters (Birnbaum and Couture, 1988; VandenBerg et al., 1986; Norback et al., 1975).

1.4.2.2 Distribution

1.4.2.2.1 In Blood and Lymph

Following absorption from the gastrointestinal tract, 2,3,7,8-TCDD administered to rats was

found predominantly in the lymphatic system, with 90% of the absorbed dose being transported by chylomicrons (Lakshmanan et al., 1986).

When partitioning of PCDD/Fs in human whole blood was examined, it was noted that the majority of 2,3,7,8-TCDD was bound to lipoproteins (approximately 80%), 15% was associated with protein (primarily serum albumin), and less than 10% was associated with red blood cells (Patterson et al., 1989; Henderson and Patterson, 1988). The affinity to lipoproteins appears to decrease with increasing chlorination of the congeners, with only about 45% of OCDD congeners being bound to lipoproteins (Patterson et al., 1989; Schecter et al., 1990). The fraction not bound to the lipoproteins appeared to bind to other proteins. In summary, upon absorption, these compounds bind to chylomicrons, lipoproteins and other serum proteins then partition into cellular membranes and tissues either through passive diffusion or by a cellular membrane receptor.

In 1987, Patterson et al. (1987) developed a method of analysis for 2,3,7,8-TCDD in human serum. Following this development, human serum and adipose tissue 2,3,7,8-TCDD levels have been compared and were found to be highly correlated when adjusted for lipid content (Henderson and Patterson, 1988; Patterson et al., 1988; Kahn et al., 1988; Patterson et al., 1989; Schecter et al., 1990).

Schecter et al., (1990a), however, noted that the plasma to adipose tissue ratio (on a lipid basis) increased with increasing chlorine substitution in the congeners. For example, 2,3,7,8-substituted TCDD/F and PeCDD/F had plasma lipid/adipose tissue ratios of around 1.0, while OCDD demonstrated a ratio of approximately 2. Similar results in the comparison

of plasma-lipid and adipose tissue were also obtained by other researchers (Kahn et al, 1988; Gochfeld et al, 1989; Needham et al, 1989; Schecter et al, 1990). Schecter (1991) later noted that this did not to apply to whole blood in which PCDD/F congeners are found in the same concentrations as in adipose tissue, on a lipid basis.

1.4.2.2.2 In Tissue

The liver and adipose tissue are the major storage sites of PCDDs and PCDFs for most species. In all mammalian species studied, the 2,3,7,8-substituted congeners are preferentially retained in the body tissue (Abraham et al., 1989; Ahlborg et al., 1990; Kuroki, et al., 1980; VandenBerg et al., 1983).

The distribution of PCDD/Fs is species- and congener-specific. Rats, mice and hamsters tend to accumulate significantly more 2,3,7,8-TCDD in the liver as opposed to the adipose tissue (Allen et al., 1975; Lakshmanan et al., 1986; Piper et al., 1973; Vinopal and Casida, 1973; Rose et al., 1976). Similar tissue ratios were reported for PCDFs (Birnbaum et al, 1980; Kuroki et al, 1980; Morita and Oishi, 1977; Nagayama et al, 1980). Others have reported an increasing liver/adipose tissue ratio for penta- and hexachlorinated congeners (VandenBerg et al., 1986; 1989).

The distribution of congeners is also time-dependent as tissues such as the liver metabolize the congeners more rapidly than the adipose tissue thus affecting the liver/adipose tissue ratio. Although guinea pigs appear to have a tissue distribution of 2,3,7,8-TCDD similar to other rodent species, the metabolism by the liver is much slower (Gasiewicz and Neal, 1979; Olson, 1986).

Some have suggested that the distribution of PCDD/F compounds is dose dependent with increasing liver/adipose tissue ratios found in rats when higher doses were administered (Abraham et al., 1988; Poiger et al, 1989; Kedderis et al., 1991; Curtis et al., 1990; Poland et al., 1989; Leung et al, 1990; Shen and Olson, 1987). Other studies have not noted a dose-dependent tissue distribution of 2,3,7,8-TCDD in rats (Rose et al., 1976; Tritscher et al., 1992), however, at this point the majority of evidence suggests dose-dependent tissue distribution.

In primates, the liver plays a less significant role in tissue distribution. The adipose tissue is the major storage site (VanMiller et al., 1976; Birnbaum et al., 1981). Poiger and Schlatter (1986) found approximately 90% of absorbed 2,3,7,8-TCDD to be sequestered in the fat of a human following ingestion. Few comparisons have been done on the liver to adipose tissue ratio of PCDD/F compounds in humans but some of the available results are discussed. Leung et al. (1990a) found the liver concentration of 2,3,7,8-TCDD to be one tenth that of the adipose tissue on a wet-weight basis but approximately the same on a lipid basis in 26 individuals examined.

Equivalent levels of PCDD/Fs in the liver and adipose tissue on a lipid basis were not observed in other studies. Ryan et al. (1985) examined PCDD/F levels in tissues of two deceased individuals from upstate New York. The adipose tissue demonstrated the highest concentration of PCDD/Fs of all tissues. When calculated on a lipid basis, the liver concentration of PCDDs was from two to four times greater than the adipose tissue. These results may have been confounded due to the fact that one of the individuals had a diseased liver. However, Ryan et al. postulated that factors other than lipophilicity may draw the

congeners to the liver. Thoma et al. (1989, 1990) found the liver/adipose tissue ratio (on a lipid basis) to vary depending on chlorination of the congener when tissues of 28 German individuals were examined. A general trend demonstrated increasing liver/adipose tissue ratio with increasing chlorination (ranging from 2.05 ratio for TCDD to 11.83 for OCDD). This was observed with both PCDD and PCDF congeners. It is important to note that considerable variation in the liver to adipose tissue concentration ratio has been reported, sometimes up to an order of magnitude between individuals (Olson, 1994) which makes it difficult to extract meaningful conclusions from the few results reported.

1.4.2.3 Metabolism

It appears that similar paths of metabolism exist in most animals, however the rates at which the metabolism takes place varies from species to species (Health and Welfare Canada, 1990). Rats have the fastest rates of metabolism for 2,3,7,8-TCDD, followed by mice, monkeys and finally guinea pigs (elimination rates are discussed in the next section 1.5.4). Several metabolites of 2,3,7,8-TCDD have been identified in rats and dogs including: 1-hydroxy-2,3,7,8-TCDD; 8-hydroxy-2,3,7-TriCDD; 2-hydroxy-1,3,7,8-TCDD; 3,7,8-trichloro-3-hydroxydibenzo-p-dioxin and 1,2-dichloro-4,5-hydroxybenzene (Sawahata et al., 1982; Poiger et al., 1982).

The radio-labelled compounds found remaining in tissues is usually the parent compound which suggests that the metabolites are readily excreted. Metabolism of 2,3,7,8-TCDD, therefore, is generally recognized as a detoxification process (Mason and Safe, 1986; Weber et al., 1982).

Limited information is available on the metabolism of other 2,3,7,8-substituted congeners, although three phenolic metabolites were found from PeCDD in the rat (Wacker et al., 1986). It is assumed that other 2,3,7,8-substituted congeners, except OCDD, would be metabolized in a similar fashion. OCDD was found not to be readily broken down into metabolites by the rat (Birnbaum and Couture, 1988). It is thought that the fully chlorinated molecule limits oxygenation.

Metabolism is required for urinary and biliary elimination, however, direct intestinal excretion of parent compound is another major route of elimination which is not regulated by metabolism.

2,3,7,8-TCDD metabolites have not yet been identified in humans, however, a self-dosing experiment carried out by Wendling et al. (1990) suggests humans are capable of metabolizing this congener.

1.4.2.4 Elimination

Elimination of PCDD/F in laboratory animals is congener- and species-specific. In most species, 2,3,7,8-TCDD excretion occurs primarily through the feces, with relatively minor amounts of metabolites found in the urine (Piper et al., 1973; Allen et al., 1975; Olson, 1986; Rose et al., 1976; Gasiewicz and Neal, 1979; Pohjanvirta et al., 1990). The elimination half-lives for 2,3,7,8- TCDD in several species are recorded in Table 1.7.

Table 1.7: Elimination Half-Lives of 2,3,7,8-TCDD in Various Species[+]

Species	Elimination Half-Life (days)	Reference
Rat	17	Piper et al. (1973)
	21	Allen et al. (1975)
	22	Pohjanvirts et al. (1990)
	31	Rose et al. (1976)
	17-31	Health and Welfare Canada (1990)
Mouse	11	Gasiewicz et al. (1983)
	13	Gasiewicz et al. (1983)
	24	Gasiewicz et al. (1983)
	9.6-24.4	Health and Welfare Canada (1990)
Hamster	10.8	Olson et al. (1980)
	15	Olson et al. (1980)
	12-15	Health and Welfare Canada (1990)
Guinea Pig	30	Gasiewicz et al. (1983)
	94	Olson (1986)
	22-94	Health and Welfare Canada (1990)
Beef Cattle	115	Jensen et al. (1981)
Monkey	73	Neubert et al. (1990)
	391	Bouwam et al. (1989)

[+] Adapted from Schlatter, 1991

2,3,7,8-TCDF has been found to have a shorter elimination half-life in the rat than 2,3,7,8-TCDD due to the more rapid metabolism (Birnbaum et al., 1980).

It is difficult to utilize these results to extrapolate to humans as large doses are often administered in laboratory settings which may cause toxicity or enzyme induction.

In humans a half-live of 2120 days (5.8 years) was estimated over a period of 125 days for 2,3,7,8-TCDD following a single oral dose administration (Poiger and Schlatter, 1986). When the elimination of the TCDD in the individual was examined over a six-year period, the elimination half-live was estimated to be 9.7 years (Schlatter, 1991). Studies carried out on Ranch Hand personnel exposed to 2,3,7,8-TCDD examined the difference in serum levels in 1982 and 1987 and estimated a half-life of approximately 7 years (Pirkle et al., 1989). Wolfe et al. (1994) re-examined the half-lives in two serum samples of these veterans and others in

an expanded cohort, taking into account changes in half-life estimation with increasing body fat, redistribution of fat stores and age considerations. The half-life of 2,3,7,8-TCDD was estimated at 11.3 years with a confidence interval of 10.0 to 14.1 years.

Estimated half-lives for other congeners range from 0.8 to 50 years. Studies which estimate half-lives performed on a small number of individuals or on examination of as few as two time points should be viewed with caution (Philips, 1989). The estimates also assume a simple, single-compartment, first-order elimination process.

Examination of elimination of PCDF compounds from the body have primarily been carried out on those exposed during the Yusho and Yu-Cheng rice oil poisonings. Estimated half-lives of 2-3 years resulted from the Yu-Cheng population, while Yusho subjects demonstrated longer, more variable half-lives (Ryan and Masuda, 1991). It appears that the faster elimination is the result of higher exposure levels. The elimination half-lives for each congener will be examined in Section 2.

2.0 Model Description

This section is divided into two parts: model development and model inputs. The model development section outlines the pharmacokinetic principles and equations which constitute the model. The model input section dissects each input variable and provides a detailed description of the data. The model input section also describes the Monte Carlo and sensitivity analyses which were carried out on the data.

2.1 Model Development

As noted in section 1.4.1, an empirically-based pharmacokinetic model was considered to be appropriate due to limited input data and potential variability of parameters required for a physiologically-based pharmacokinetic model. A one-compartment model was considered to be an accurate description of PCDD/F compounds in humans due to their relatively rapid distribution to the fat tissue. A single compartment model with a first order elimination process was also assumed by the authors of several other studies of PCDD/Fs, including a self-dosing kinetic study (Poiger and Schlatter, 1986; Leung et al., 1988; Schecter and Ryan, 1988; Schecter et al., 1990b; Wolfe et al., 1994). Subsequent to a discussion of these factors with John Kim, research assistant, Department of Pharmacokinetics and Pharmaceutics at U.B.C., the one-compartment model was considered to be a suitable choice by the author.

2.1.1 Single Compartment Model

A single compartment model assumes that chemical concentrations throughout the body are in rapid equilibrium during the period of exposure. This does not mean concentrations are equal in all tissues, but rather that the compound's distribution is a rapid process. Thus, in the

single-compartment model, the compound is assumed to be evenly distributed in the compartment of a given volume.

Processes such as input and elimination are usually either zero-order or first-order reactions. In zero-order reactions, the rate of change in concentration is a constant. In first-order reactions, the rate of change is proportional to the concentration of compound to which the body is exposed. Most physiological processes such as diffusion, carrier-mediated uptake, metabolism and excretion are first-order reactions at low concentrations (Renwick, 1994).

A black box may be used to conceptualize the model, as shown in Figure 2.1.

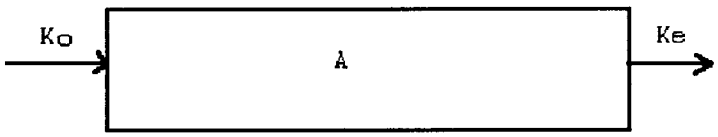

Figure 2.1 - Black Box Portrayal of the Pharmacokinetic Model

In Figure 2.1, K_o represents a zero-order input constant into the compartment. Elimination, represented by K_e, the elimination rate constant, is a first-order process and is dependent upon the amount of compound in the compartment, A. The chemical is assumed to be dissolved and evenly distributed within the compartment. With these assumptions, the following equation results:

$$\frac{dA}{dt} = K_o - K_e * A \qquad (2.1)$$

Where:

dA/dt = change in the amount of compound in the body with respect to time
K_o = constant input rate
K_e = first order elimination rate constant
A = amount of compound in the body

In the above equation, the initial input period will yield a small amount of compound in the body. As the amount of compound in the body increases, the product of K_e*A (rate of output) will also increase. The rate of output will continue to increase until it eventually equals the rate of input, at which point steady state is achieved (Welling, 1986).

Integration of the above equation yields:

$$A = \frac{K_o}{K_e} * (1 - e^{-(K_e * t)}) \qquad (2.2)$$

Equation 2.2 yields an estimate of the total amount of compound in the body. In traditional pharmacokinetics, this equation would often be divided by an apparent volume of distribution (V_d) to yield an estimate of the concentration of compound in the plasma. In this study, the main site of interest is the adipose tissue, where PCDD/F compounds have been found to concentrate (See Section 1.4.2.2.2).

When the zero order infusion of compound into the compartment stops, the elimination will continue from the compartment in a first-order fashion. In concentration terms this is expressed in equation 2.3:

$$C_{t+T} = C_t * e^{-(K_e * T)} \qquad (2.3)$$

Where:

$C_{(t+T)}$ = concentration after infusion time (t) and post infusion time (T)
C_t = concentration after total infusion time
T = post infusion time (no input)
K_e = elimination rate constant

Taking into account the above factors, a resulting equation is created to calculate the concentration of PCDD/F compounds in adipose tissue following exposure in the workplace. Assumptions include: a single-compartment model with a first order elimination rate constant, a zero order input constant and all PCDD/F compounds concentrating in the adipose tissue. The equation also accounts for elimination of PCDD/F when no exposure is taking place. This is displayed in Equation 2.4.

$$C_f = \frac{K_o}{K_e} * \frac{(1 - e^{-(K_e * t_e)})}{M_f} * (e^{-(K_e(t_w - t_e))}) \qquad (2.4)$$

Where:

C_f = Concentration of PCDD/F in fat tissue (pg/g)
K_o = Input Constant of PCDD/F compounds (pg/wk)
K_e = Elimination Rate Constant of PCDD/Fs (wk^{-1})
M_f = Mass of fat tissue (g)
t_e = Total time exposed to chlorophenates (wks)
t_w = Duration of working life at sawmill (wks)

2.2 Model Inputs

2.2.1 K_o:Input Constant (pg/wk)

This variable is in units of mass/time and represents the constant rate of uptake of PCDD/F compounds via relevant routes of entry into the body for the chlorophenate exposure scenario, in this case, the dermal and respiratory routes. Background exposure due to dietary intake was not included as an input variable in the model. The input rate is assumed to be a zero-order process as the amount of PCDD/F exposure is not a finite quantity which is depleted as it is absorbed into the body, but is constantly replenished due to continuous exposure.

The two components of the K_o variable (dermal and respiratory) are added to give a total input constant of PCDD/F compounds in units of pg/week, as demonstrated in equation 2.5.

$$K_o = DAbs(pg/week) + IAbs(pg/week) \qquad (2.5)$$

Where:
DAbs = Dermal Absorption of each PCDD/F congener (pg/wk)
IAbs = Inhalation Absorption of each PCDD/F congener (pg/wk)

While attempting to quantify the input constant of PCDD/Fs via the dermal route of exposure, it became apparent through literature searches that direct measurements of dermal exposure to PCDD/Fs in sawmill workers did not exist. An alternative to direct dermal measurements was pursued by estimating PCDD/F exposure using measurements of dermal chlorophenate exposure in sawmill workers.

Following scientific and government literature searches, two studies were found which carried out direct dermal chlorophenate exposure measurements, Fenske et al. (1987) and BC Research (1986). Each of these studies utilized a different technique for dermal exposure assessment. In the Fenske et al. (1987) study, fluorescent tracer technique and video imaging analysis was used to determine the rate of dermal exposure to tetrachlorophenate on 7 pullers during one day of sampling in a sawmill located in Washington State. In the BC Research (1986) study, a total of 20 patches were placed at various locations on three workers: a grader, a chain puller and a carrier driver, during one day of sampling at a BC sawmill. The patches were removed at the end of the working day and analyzed for total PCP/TCP content.

Obtaining data for the inhalation component of K_o proved to be equally difficult. Again, due to lack of direct air concentration measurements of PCDD/F compounds in sawmills, input

values were estimated from chlorophenate air concentration measurements. Several reports of measured air concentrations of chlorophenates in sawmills were compiled (Arsenault, 1976; Klienman et al., 1986; Levin et al., 1976; BC Research, 1986; McDonald, 1989; Kauppinen and Lindroos, 1985).

The chlorophenate exposure estimates were multiplied by measured levels of contamination with PCDD/Fs to yield an estimate of PCDD/F exposure via either the dermal or respiratory route. These values were then multiplied by an absorption efficiency appropriate to each congener and each route of entry to produce an input constant in pg/wk, as demonstrated in equations 2.6 and 2.7:

$$DAbs(pg/wk) = [TCPExp * Contam . * AE] + [PCPExp * Contam . * AE] \quad (2.6)$$

Where:

TCPexp	=	TCP Exposure via the dermal route (ug/wk)
PCPExp	=	PCP Exposure via the dermal route (ug/wk)
Contam	=	Contamination of TCP or PCP with PCDD/F congeners (pg/ug)
AE	=	Absorption Efficiency of the Dermal route (%)

Equation 2.7 is essentially the same as 2.6 but deals with TCP and PCP exposure due to inhalation, as well as the absorption efficiency of the inhalation route.

$$IAbs(pg/wk) = [TCPExp * Contam. * AE] + [PCPExp * Contam. * AE] \quad (2.7)$$

Where:

TCPexp	=	TCP Exposure via the inhalation route (ug/wk)
PCPExp	=	PCP Exposure via the inhalation route (ug/wk)
Contam	=	Contamination of TCP or PCP with PCDD/F congeners (pg/ug)
AE	=	Absorption Efficiency of the Inhalation route (%)

Equation 2.7 assumes that the TCP and PCP is in aerosol form and that measured contamination levels of PCDD/F in TCP/PCP solutions would apply to the aerosol droplets. A second assumption of PCDD/F vapour is examined later in the inhalation section.

The variables in equations 2.6 and 2.7 will be examined separately in the following sections.

2.2.1.1 Dermal Component of K_o: "DAbs" (pg/wk)

As noted earlier, the dermal component of K_o is comprised of exposure to TCP/PCP (ug/wk), contamination of TCP/PCP with PCDD/F compounds (pg/ug), and absorption efficiency of the dermal route of exposure for the various congeners.

2.2.1.1.1 Dermal Exposure to TCP/PCP: "TCP/PCP Exp" (ug/wk)

Two sources of data have been used to estimate dermal exposure to chlorophenates. The first source is an investigation carried out by BC Research (1986) of chlorophenate use and exposure in B.C. sawmills for Health and Welfare Canada. This study was carried out at a sawmill in B.C. where a total of 20 dermal patches were worn for one day by three workers: grader, chain puller and carrier driver. The patches were placed at various locations on their bodies where exposure was expected to occur, and were worn next to the skin, on the first layer of clothing, or on outer layers of clothing.

The other main source of dermal exposure to chlorophenates in sawmills is Fenske et al. (1987). This study was carried out in a planer mill located in Washington State, in which the relative importance of dermal versus inhalation exposure to chlorophenates was quantitatively estimated using a fluorescent tracer and video imaging system. During the one day of

sampling, measurable exposure levels were found on seven pullers in the hand and forearm region. The exposure levels were translated into exposure rates on an hourly basis.

In both studies, personal protective equipment was worn. In the BC Research study, samples were taken underneath clothing as well as on the outside of clothing. In the Fenske study, only chlorophenates reaching the skin beneath clothing was monitored.

Total dermal exposure to chlorophenates data obtained in the BC Research study was extrapolated from the patch results by multiplying by an estimated area of the body region where the patch was located (arms, chest/back and legs). This process was performed on both the TCP and PCP patch results. The Fenske study detected TCP exposure in the arm region only. This result was combined with the BC Research TCP arm results to yield an average TCP arm exposure estimate.

The total body "TCP Exp" variable calculation is illustrated in equation 2.8.

$$TCPExp = [ArmExp.*ArmArea + FenskeExp(Arm)]/2 \; (Chest/BackExp.*Chest/BackArea) + (LegExp*LegArea) \qquad (2.8)$$

Where:

Arm Exp	=	TCP arm patch results by BC Research (ug/cm^2*day)
Arm Area	=	Arm surface area (cm^2)
Fenske Exp	=	TCP arm exposure results by Fenske (ug/day)
Chest/Back Exp	=	TCP chest/back patch results by BC Research (ug/cm^2*day)
Chest/Back Area	=	Chest/back surface area (cm^2)
Leg Exp	=	TCP leg exposure results by BC Research (ug/cm^2*day)
Leg Area	=	Leg surface area (cm^2)

The "PCP Exp" variable is calculated in a similar fashion, however there is no Fenske exposure value for PCP. The equation is illustrated below:

$$PCPExp = (ArmExp. * ArmArea) + (Chest / Back Exp. * Chest / Back Area) + (Leg Exp * Leg Area) \quad (2.9)$$

Where:

Arm Exp	=	PCP arm patch results by BC Research (ug/cm^2*day)
Arm Area	=	Arm surface area (cm^2)
Chest/Back Exp	=	PCP chest/back patch results by BC Research (ug/cm^2*day)
Chest/Back Area	=	Chest/back surface area (cm^2)
Leg Exp	=	PCP leg exposure results by BC Research (ug/cm^2*day)
Leg Area	=	Leg surface area (cm^2)

2.2.1.1.1.1 BC Research TCP/PCP Arm Patch Results: "Arm Exp" (ug/cm^2*day)

The measurements on the three workers were taken during an average work shift, with patches placed next to skin, on outer clothing as well as on intermediate layers (on shirt under jacket). The patches were placed on areas thought to be most susceptible to exposure including the forearms, chest and legs of the graders and chain pullers, and forearms, back and legs (including the ankle) of the carrier driver. In estimating total dermal exposure to chlorophenates, the full range of patch results was used, representing chlorophenate permeating the clothing as well as a worst case exposure estimate assuming no clothing worn (estimated from the patches placed on the outermost layers of clothing).

The results obtained by BC Research were reported in terms of mass of TCP and PCP collected on the patches. These results were then converted from ug/patch over a work shift into units of ug/cm^2*day. Each patch area measured 25 cm^2. The results were also kept separate in terms of arm, chest and leg exposure estimates. The results for the arm patches are found in the following tables.

Table 2.1: Measured TCP Arm Exposure (BC Research, 1986)

Worker	Location of Patch	ug/patch*day	ug/cm^2*day
Grader	Inside Forearm; On skin, under shirt and jacket	0.66	0.026
	Inside Forearm; On padded jacket	2.83	0.11
Chain Puller	Inside Forearm; Under shirt and sweater	2.25	0.09
	Inside Forearm; On sweater	6.33	0.25
Carrier Driver	Outer Forearm; On skin, under shirt and sweater	1.86	0.074
	Outside upper arm; On sweater	7.20	0.29
	Outside upper arm; On sweater	4.41	0.18
		Mean	0.15
		Standard Deviation	0.10

Table 2.2: Measured PCP Arm Exposure (BC Research, 1986)

Worker	Location of Patch	ug/patch*day	ug/cm^2*day
Grader	Inside Forearm; On skin, under shirt and jacket	0.24	0.010
	Inside Forearm; On padded jacket	2.06	0.082
Chain Puller	Inside Forearm; Under shirt and sweater	1.09	0.044
	Inside Forearm; On sweater	3.26	0.130
Carrier Driver	Outer Forearm; On skin, under shirt and sweater	0.74	0.030
	Outside upper arm; On sweater	1.56	0.062
	Outside upper arm; On sweater	1.84	0.074
		Mean	0.062
		Standard Deviation	0.039

The TCP and PCP exposure estimates were assumed to follow a lognormal distribution. The arithmetic mean and standard deviation were used as inputs into the Monte Carlo analysis to create a lognormal distribution. This would cover the full range of possible exposure values to chlorophenates through dermal exposure on the arms, in unit of ug/cm^2*day.

2.2.1.1.1.2 Arm Surface Area Estimates (cm^2)

To estimate dermal arm exposure, the patch results obtained by BC Research were assumed to be representative of exposure to the entire arm. The dermal exposure estimates to chlorophenates were converted to units of ug/day by multiplying by a distribution of possible areas of the arm.

Various reports exist which estimate the surface area of the upper extremities and are outlined in Table 2.3.

Table 2.3: Surface Areas of the Arm

Body Region	Surface Area (cm^2)	Reference
Entire Arm	3287	Martin et al., 1984
	3402	ICRP, 1975
	3190	USEPA, 1986
Upper Arms	1430	USEPA, 1986
	1320	Davis, 1980
Forearms	1210	Davis, 1980
	1208	WHO, 1980
	1286	Franklin et al., 1981
	1140	USEPA, 1986
Hands	820	Davis, 1980
	808	WHO, 1980
	1075	Franklin et al., 1981
	840	USEPA, 1986

The forearm and hands have been consistently reported as being areas of high exposure in graders, chainmen and pullers (McDonald, 1989; Fenske et al., 1987; Klienman et al., 1986). The distribution of the arm surface area variable was allowed to reflect probable historic exposure before the use of personal protective equipment. The forearm areas above were used to calculate a mean of 1200 cm^2 and a standard deviation of 560. In a lognormal distribution the potential area covers a range from zero to a maximum of approximately 3400 cm^2, representing total arm exposure.

2.2.1.1.1.3 TCP Arm Exposure Results (Fenske): "Fenske Exp" (ug/day)

Fenske et al. (1987) utilized fluorescent tracer with a video imaging system to estimate dermal exposure to sodium tetrachlorophenate in a planer mill. Measurements were only carried out on pullers. During an eight-hour workday, measurable amounts of

tetrachlorophenates were found only on the hands and forearms. The exposure estimates of the 7 pullers were expressed in terms of a mean exposure rate of 178.0 ug/hr with a standard deviation of 42.2. This exposure estimate to chlorophenates was assumed to be lognormally distributed.

To estimate total dermal exposure to chlorophenates on the arms, the average of the two sources of dermal data was used. The distribution of values from BC Research and from Fenske were added and divided by two to result in the arm component of the dermal exposure value for the input rate constant.

2.2.1.1.1.4 BC Research TCP/PCP Chest/Back Patch Results: "Chest/Back Exp" (ug/cm^2*day)

Patches were placed on various areas of the chest on the graders and chain pullers, and on the back of the carrier driver. All patch results were combined to estimate a mean and standard deviation of potential chest exposure to chlorophenates. The TCP and PCP exposure estimates are recorded separately in the following tables.

Table 2.4: Measured TCP Chest/Back Exposure (BC Research, 1986)

Worker	Location of Patch	ug/patch*day	ug/cm^2*day
Grader	Lower Left; On shirt, under jacket	0.73	0.029
	Lower Right; On jacket	17.3	0.692
Chain Puller	Lower Left; On shirt, under sweater	1.35	0.054
	Lower Right; On sweater	33.9	1.36
Carrier Driver	Top Right; On sweater	4.33	0.173
	Lower Left; On sweater	5.40	0.216
		Mean	0.42
		Standard Deviation	0.52

Table 2.5: Measured PCP Chest/Back Exposure (BC Research, 1986)

Worker	Location of Patch	ug/patch*day	ug/cm²*day
Grader	Lower Left; On shirt, under jacket Lower Right; On jacket	0.20 10.4	0.008 0.416
Chain Puller	Lower Left; On shirt, under sweater Lower Right; On sweater	0.47 15.4	0.019 0.616
Carrier Driver	Top Right; On sweater Lower Left; On sweater	1.03 1.22	0.041 0.049
		Mean	0.192
		Standard Deviation	0.260

The mean and standard deviation of the TCP and PCP exposure estimates used to create a lognormal distribution.

2.2.1.1.1.5 Chest/Back Surface Area Estimates (cm^2)

As in the arm area exposure estimates, the chest patches were assumed to represent average exposure over much of the torso. The exposure estimates to chlorophenates were converted to units of ug/day by multiplying by a distribution of potential chest/back areas.

Measurements for the surface area of the trunk have the following results:

Table 2.6: Surface Areas of the Back/Chest

Body Region	Surface Area (cm^2)	Reference
Torso	4888	Martin et al., 1984
Torso	6067	ICRP, 1975
Torso	5690	USEPA, 1986
Back	3550	Davis, 1980
Chest & Stomach	3550	Davis, 1980
Back	1536	Franklin et al., 1981
Chest	1536	Franklin et al., 1981

The measurements of the torso were divided by 2 to represent the chest and back separately and all estimates were further divided reduced by 2 to represent a reasonable potential

average exposure area in the chest or back of sawmill workers. This resulted in a mean of approximately 1090 cm^2. When lognormally distributed, with a standard deviation of 500, potential values include very low exposures as well as exposures close to what is assumed to be an upper limit at 2500 cm^2.

2.2.1.1.1.6 BC Research TCP/PCP Leg Patch Results: "Leg Exp" (ug/cm^2*day)

Patches were placed on the legs, both above and below the knee of the grader and chain puller, as well as on the thigh, below the knee and on the ankle of the carrier driver. The patch results from these areas were combined to estimate a mean and standard deviation of potential leg exposure to chlorophenates. The TCP and PCP exposure estimates are recorded separately.

Table 2.7: Measured TCP Leg Exposure (BC Research, 1986)

Worker	Location of Patch	ug/patch*day	ug/cm^2*day
Grader	Above Knee; On pant leg	5.73	0.229
	Below Knee; On pant leg	2.56	0.102
Chain Puller	Below Knee; On pant leg below apron	27.7	1.11
	Below Knee; On pant leg below apron	8.33	0.333
Carrier Driver	Front of Thigh; On pant leg	12.3	0.492
	Below Knee; On pant leg	31.6	1.26
	Ankle, outside; On pant leg	56.1	2.24
		Mean	0.823
		Standard Deviation	0.764

Table 2.8: Measured PCP Leg Exposure (BC Research, 1986)

Worker	Location of Patch	ug/patch*day	ug/cm²*day
Grader	Above Knee; On pant leg Below Knee; On pant leg	2.14 0.67	0.0856 0.027
Chain Puller	Below Knee; On pant leg below apron Below Knee; On pant leg below apron	13.4 5.26	0.536 0.210
Carrier Driver	Front of Thigh; On pant leg Below Knee; On pant leg Ankle, outside; On pant leg	4.57 20.9 25.5	0.183 0.836 1.02
		Mean	0.414
		Standard Deviation	0.390

The arithmetic means and standard deviations for the leg exposure estimates were used in lognormal distributions in the Monte Carlo analysis.

2.2.1.1.1.7 Leg Surface Area Estimates (cm^2)

Measurements for the surface area of the lower extremities have yielded the results displayed in table 2.9.

Table 2.9: Surface Areas of the Legs

Body Region	Surface Area (cm^2)	Reference
Thigh	2250	Davis, 1980
	3725	Franklin et al., 1981
	3477	WHO, 1980
	1980	USEPA, 1986
Lower Legs	2380	Davis, 1980
	2592	Franklin et al., 1981
	2322	WHO, 1980
	2070	USEPA, 1986

It was assumed that most exposure, especially in pullers and graders, would be on the frontal area of the legs. It was also assumed that most exposure may have historically taken place on the thighs, before the use of aprons, or on the lower legs following the introduction of aprons. A mean of 1300 cm^2 was calculated from halving all the leg surface area estimates.

A standard deviation of 500 was chosen to cover potentially exposed surface areas ranging from zero to an upper limit of 2500 cm^2.

2.2.1.1.2 Contamination of TCP or PCP with PCDD/F Congeners: "Contam." (pg/ug)

Various studies have been carried out which have measured the amount of PCDD/F contamination in several PCP and TCP solutions. The results from these studies have been compiled in the following tables. The mean and standard deviation of the contamination level of each congener has been calculated for TCP and PCP respectively. The means and standard deviations were used to create a lognormal distribution.

Table 2.10: Contamination of 2,3,4,6-TCP and Technical Grade TCP by PCDD/F Congeners

2,3,4,6-TCP & Technical Grade TCP					
Congener	Levels of Contam. (pg/ug)	Country of Origin of TCP	Author	Mean (pg/ug)	Standard Deviation
TCDD	0.05 0.4 0.7	Sweden Finland Finland	Rappe et al., 1979 Rappe et al., 1978 Rappe et al., 1978	0.38	0.33
PeCDD	0.05 3.5 5.2	Sweden Finland Finland	Rappe et al., 1979 Rappe et al., 1978 Rappe et al., 1978	2.9	2.6
HxCDD	0.5 4.1 5.3 9.5 14 15	Sweden USA Finland Finland USA USA	Firestone, 1972 Firestone, 1972 Rappe et al., 1978 Rappe et al., 1978 Firestone, 1972 Firestone, 1972	8.1	5.8
HpCDD	2.1 5.1 5.6 10	Finland USA Finland Sweden	Rappe et al., 1978 Firestone, 1972 Rappe et al., 1978 Rappe et al., 1979	5.7	3.3
OCDD	0.2 0.3 0.7 2	USA Finland Finland Sweden	Firestone, 1972 Rappe et al., 1978 Rappe et al., 1978 Rappe et al., 1979	0.80	0.83
TCDF	0.25 0.5 0.5 10	Sweden Sweden Finland Finland	Rappe et al., 1978a Rappe et al., 1979 Rappe et al., 1982 Rappe et al., 1978	2.8	4.8
PeCDF	10 10 10 10	Sweden Finland Sweden Finland	Rappe et al., 1979 Rappe et al., 1982 Rappe et al., 1978a Rappe et al., 1978	10	**

2,3,4,6-TCP & Technical Grade TCP					
Congener	Levels of Contam. (pg/ug)	Country of Origin of TCP	Author	Mean (pg/ug)	Standard Deviation
HxCDF	60 70 70 70	Finland Sweden Finland Sweden	Rappe et al., 1978 Rappe et al., 1979 Rappe et al., 1982 Rappe et al., 1978a	68	5.0
HpCDF	60 70 70 70	Finland Sweden Finland Sweden	Rappe et al., 1978 Rappe et al., 1979 Rappe et al., 1982 Rappe et al., 1978a	68	5.0
OCDF	10 10 10 10	Finland Sweden Finland Sweden	Rappe et al., 1978 Rappe et al., 1979 Rappe et al., 1982 Rappe et al., 1978a	10	**

Table 2.11: Contamination of PCP by PCDD/F Congeners

Technical Grade PCP					
Congener	Levels of Contam. (pg/ug)	Country of Origin of PCP	Author	Mean (pg/ug)	Standard Deviation
TCDD	0.027 0.05 0.052 0.06 0.08 0.12 0.16 0.23 0.25	Germany Switzerland Germany Switzerland Switzerland Switzerland Switzerland Switzerland Switzerland	Hagenmaier & Brunner, 1987 Buser & Bosshardt, 1976 Hagenmaier & Brunner, 1987 Buser & Bosshardt, 1976 Buser & Bosshardt, 1976 Buser & Bosshardt, 1976 Buser & Bosshardt, 1976 Buser & Bosshardt, 1976 Buser & Bosshardt, 1976	0.11	0.08
PeCDD	0.015 0.015 0.03 0.03 0.03 0.03 0.03 0.031 0.08 0.213	Switzerland Switzerland Switzerland Switzerland Switzerland Switzerland Switzerland Germany Switzerland Germany	Buser & Bosshardt, 1976 Buser & Bosshardt, 1976 Buser & Bosshardt, 1976 Buser & Bosshardt, 1976 Buser & Bosshardt, 1976 Buser & Bosshardt, 1976 Buser & Bosshardt, 1976 Hagenmaier & Brunner, 1987 Buser & Bosshardt, 1976 Hagenmaier & Brunner, 1987	0.05	0.06

Technical Grade PCP					
Congener	Levels of Contam. (pg/ug)	Country of Origin of PCP	Author	Mean (pg/ug)	Standard Deviation
HxCDD	0.015	Switzerland	Buser & Bosshardt, 1976	4.6	6.6
	0.015	Switzerland	Buser & Bosshardt, 1976		
	0.015	Switzerland	Buser & Bosshardt, 1976		
	0.1	USA	Health & Safety Exec., 1982		
	0.23	Germany	Hagenmaier & Brunner, 1987		
	0.25	Switzerland	Buser & Bosshardt, 1976		
	0.4	Switzerland	Buser & Bosshardt, 1976		
	0.5	USA	Health & Safety Exec., 1982		
	1.2	USA	Health & Safety Exec., 1982		
	1.55	Canada	Miles et al., 1985		
	1.6	USA	Health & Safety Exec., 1982		
	1.76	Canada	Miles et al., 1985		
	2.2	Canada	Miles et al., 1985		
	3.4	Switzerland	Buser & Bosshardt, 1976		
	3.4	Switzerland	Buser & Bosshardt, 1976		
	3.9	Germany	Hagenmaier & Brunner, 1987		
	14	USA	IARC, 1986		
	14.8	Canada	Miles et al., 1985		
	15.4	Canada	Miles et al., 1985		
	16.3	Canada	Miles et al., 1985		
	20	USA	IARC, 1986		
HpCDD	0.3	Switzerland	Buser & Bosshardt, 1976	9.6	13.1
	0.3	Switzerland	Buser & Bosshardt, 1976		
	0.3	Switzerland	Buser & Bosshardt, 1976		
	0.4	Switzerland	Buser & Bosshardt, 1976		
	1.3	USA	IARC, 1986		
	2.8	Switzerland	Buser & Bosshardt, 1976		
	4.2	Switzerland	Buser & Bosshardt, 1976		
	5.4	USA	IARC, 1986		
	5.8	Germany	Hagenmaier & Brunner, 1987		
	9.1	USA	IARC, 1986		
	10	USA	IARC, 1986		
	18.5	Germany	Hagenmaier & Brunner, 1987		
	36	Switzerland	Buser & Bosshardt, 1976		
	40	Switzerland	Buser & Bosshardt, 1976		
OCDD	1.2	Switzerland	Buser & Bosshardt, 1976	37.1	47
	1.2	Switzerland	Buser & Bosshardt, 1976		
	1.5	Switzerland	Buser & Bosshardt, 1976		
	1.5	Switzerland	Buser & Bosshardt, 1976		
	3.3	USA	IARC, 1986		
	3.8	USA	IARC, 1986		
	5.1	Switzerland	Buser & Bosshardt, 1976		
	11	Switzerland	Buser & Bosshardt, 1976		
	21	Sweden	Jensen & Renberg, 1972		
	32.4	Germany	Hagenmaier & Brunner, 1987		
	41.6	Germany	Hagenmaier & Brunner, 1987		
	50	Sweden	Jensen & Renberg, 1972		
	50	Sweden	Jensen & Renberg, 1972		
	105	Switzerland	Buser & Bosshardt, 1976		
	115	Switzerland	Buser & Bosshardt, 1976		
	150	Sweden	Jensen & Renberg, 1972		

Technical Grade PCP

Congener	Levels of Contam. (pg/ug)	Country of Origin of PCP	Author	Mean (pg/ug)	Standard Deviation
TCDF	0.01	Switzerland	Buser & Bosshardt, 1976	0.10	0.27
	0.01	Switzerland	Buser & Bosshardt, 1976		
	0.01	Switzerland	Buser & Bosshardt, 1976		
	0.01	Switzerland	Buser & Bosshardt, 1976		
	0.01	Switzerland	Buser & Bosshardt, 1976		
	0.01	Switzerland	Buser & Bosshardt, 1976		
	0.012	Germany	Hagenmaier & Brunner, 1987		
	0.02	Switzerland	Buser & Bosshardt, 1976		
	0.02	Switzerland	Buser & Bosshardt, 1976		
	0.082	Germany	Hagenmaier & Brunner, 1987		
	0.9	Sweden	Rappe et al., 1978		
PeCDF	0.015	Switzerland	Buser & Bosshardt, 1976	0.41	1.2
	0.015	Switzerland	Buser & Bosshardt, 1976		
	0.027	Germany	Hagenmaier & Brunner, 1987		
	0.03	Switzerland	Buser & Bosshardt, 1976		
	0.03	Switzerland	Buser & Bosshardt, 1976		
	0.03	Switzerland	Buser & Bosshardt, 1976		
	0.05	Switzerland	Buser & Bosshardt, 1976		
	0.08	Switzerland	Buser & Bosshardt, 1976		
	0.13	Switzerland	Buser & Bosshardt, 1976		
	0.137	Germany	Hagenmaier & Brunner, 1987		
	4	Sweden	Rappe et al., 1978		
HxCDF	0.09	Germany	Hagenmaier & Brunner, 1987	5.8	9.6
	0.1	Switzerland	Buser & Bosshardt, 1976		
	0.2	Switzerland	Buser & Bosshardt, 1976		
	0.7	Switzerland	Buser & Bosshardt, 1976		
	0.75	Switzerland	Buser & Bosshardt, 1976		
	1.2	Switzerland	Buser & Bosshardt, 1976		
	3.0	Germany	Hagenmaier & Brunner, 1987		
	4.1	Switzerland	Buser & Bosshardt, 1976		
	11	Switzerland	Buser & Bosshardt, 1976		
	11	Switzerland	Buser & Bosshardt, 1976		
	32	Sweden	Rappe et al., 1978		
HpCDF	0.86	Germany	Hagenmaier & Brunner, 1987	22.8	37
	1.0	Switzerland	Buser & Bosshardt, 1976		
	1.2	Switzerland	Buser & Bosshardt, 1976		
	1.3	Switzerland	Buser & Bosshardt, 1976		
	2.3	Switzerland	Buser & Bosshardt, 1976		
	3.6	Switzerland	Buser & Bosshardt, 1976		
	13	Switzerland	Buser & Bosshardt, 1976		
	13.2	Germany	Hagenmaier & Brunner, 1987		
	44	Switzerland	Buser & Bosshardt, 1976		
	50	Switzerland	Buser & Bosshardt, 1976		
	120	Sweden	Rappe et al., 1978		
OCDF	2.1	Switzerland	Buser & Bosshardt, 1976	22.6	38
	2.5	Switzerland	Buser & Bosshardt, 1976		
	3.0	Switzerland	Buser & Bosshardt, 1976		
	3.9	Switzerland	Buser & Bosshardt, 1976		
	4.1	Switzerland	Buser & Bosshardt, 1976		
	4.25	Germany	Hagenmaier & Brunner, 1987		
	8.6	Switzerland	Buser & Bosshardt, 1976		
	24	Switzerland	Buser & Bosshardt, 1976		
	29	Switzerland	Buser & Bosshardt, 1976		
	37.2	Germany	Hagenmaier & Brunner, 1987		
	130	Sweden	Rappe et al., 1978		

2.2.1.1.3 Efficiency of Dermal Absorption of PCDD/F Congeners: "AE" (%)

The percentage of skin absorption was primarily estimated from studies examining 2,3,7,8-TCDD penetration through human cadaver skin and porcine skin which has been noted to closely resemble that of humans (Wester and Maibach, 1985; Wester and Noonan, 1980). The stratum corneum is generally accepted to be the main barrier to penetration of most molecules into the body. Penetration into the stratum corneum as well as into the epidermis were included in the compiled results. Measurements in which the stratum corneum was removed were also included as this was thought to accurately depict a standard working condition, in which the skin may be damaged. The results were compiled into the following table which includes results using various vehicles and exposure periods, but were separated into tables of: penetration into the stratum corneum, and penetration into the epidermis.

Table 2.12: % Penetration of TCDD into the Stratum Corneum

% Penetration into the S.C.	Skin Type	Exposure Period	Vehicle	Author
44.7	Human cadaver	30 min	Acetone	Weber et al., 1991
26.8	Human cadaver	100 min	Acetone	Weber et al., 1991
24.9	Human cadaver	300 min	Acetone	Weber et al., 1991
21.8	Human cadaver	1000 min	Acetone	Weber et al., 1991
6.15	Human cadaver	30 min	Mineral Oil	Weber et al., 1991
6.05	Human cadaver	100 min	Mineral Oil	Weber et al., 1991
5.14	Human cadaver	300 min	Mineral Oil	Weber et al., 1991
9.97	Human cadaver	1000 min	Mineral Oil	Weber et al., 1991
43.7	Human cadaver	100 min	Acetone	Weber et al., 1992

Table 2.13: % Penetration of TCDD into the Epidermis

% Penetration into the Epi.	Skin Type	Exposure Period	Vehicle	S.C. Intact	Author
1.80	Human cadaver	30 min	Acetone	Yes	Weber et al., 1991
45.1	Human cadaver	30 min	Acetone	No	Weber et al., 1991
0.42	Human cadaver	100 min	Acetone	Yes	Weber et al., 1991
43.3	Human cadaver	100 min	Acetone	No	Weber et al., 1991

% Penetration into the Epi.	Skin Type	Exposure Period	Vehicle	S.C. Intact	Author
4.07	Human cadaver	300 min	Acetone	Yes	Weber et al., 1991
24.6	Human cadaver	300 min	Acetone	No	Weber et al., 1991
15.7	Human cadaver	1000 min	Acetone	Yes	Weber et al., 1991
62.5	Human cadaver	1000 min	Acetone	No	Weber et al., 1991
0.34	Human cadaver	30 min	Mineral Oil	Yes	Weber et al., 1991
1.73	Human cadaver	30 min	Mineral Oil	No	Weber et al., 1991
1.09	Human cadaver	100 min	Mineral Oil	Yes	Weber et al., 1991
3.72	Human cadaver	100 min	Mineral Oil	No	Weber et al., 1991
0.76	Human cadaver	300 min	Mineral Oil	Yes	Weber et al., 1991
3.93	Human cadaver	300 min	Mineral Oil	No	Weber et al., 1991
3.43	Human cadaver	1000 min	Mineral Oil	Yes	Weber et al., 1991
6.63	Human cadaver	1000 min	Mineral Oil	No	Weber et al., 1991
4.06	Human cadaver	100 min	Acetone	Yes	Weber et al., 1992
37.5	Human cadaver	100 min	Acetone	No	Weber et al., 1992
2.4	Porcine skin	1000 min	Mineral Oil	Yes	Weber, 1993
8	Porcine skin	1000 min	Acetone	No	Weber, 1993

The percentage penetration into the stratum corneum and epidermis were combined to cover a wider range of possibilities which resulted in a mean of 15.8% and a standard deviation of 17.8. These were set as lognormally distributed in the Monte Carlo analysis.

2.2.1.2 Inhalation Component of K_o: "IAbs" (pg/wk)

As shown in Equation 2.7, the inhalation component is calculated in a similar fashion to the dermal component, the only differences being that TCP and PCP exposure is via the air and the absorption efficiency is different for the respiratory route. This variable assumes that TCP and PCP measured air concentrations are in aerosol form and the PCDD/F congeners are found in equal concentration in the aerosol droplets as in the spray or dip solutions. An alternative assumption was that the measured air concentrations of PCP and TCP were in vapour form. In this case, the vapour concentration of PCDD/F would not be directly

calculated from their contamination of the chlorophenates. Using the vapour assumption, separate calculations were carried out to estimate vapour concentrations of PCDD/F using Raoult's Law.

Air concentration measurements of chlorophenates were collected using impingers and bubblers. It was assumed that neither the aerosol nor the vapour assumption could be dismissed simply on the basis of sampling device, therefore both assumptions were examined.

2.2.1.2.1 Assuming PCDD/F is in PCP/TCP Aerosol Droplets

2.2.1.2.1.1 Inhalation Exposure to TCP/PCP: "TCP/PCP Exp" (ug/wk)

The variables representing TCP inhalation exposure (TCP Exp) and PCP inhalation exposure (PCP Exp) may be further expanded upon. Each is comprised of two components: the air concentration of either TCP or PCP in units of ug/m^3 and the inhalation rate in m^3/hr. These values are then multiplied by 40 hours/week to represent a typical exposure time of a working week. These are demonstrated in the following equation:

$$TCP/PCPExp(ug/wk) = TCP/PCPAirConc.(ug/m^3) * InhalationRate(m^3/hr) * 40hrs/wk \qquad (2.10)$$

The two variables found in equation 2.10 (TCP/PCP Air Concentrations and Inhalation Rate) will be examined in the following sections.

2.2.1.2.1.1.1 TCP/PCP Air Concentrations (ug/m^3)

Various studies have recorded air concentrations of TCP, PCP or total chlorophenates in sawmills, both in North America and Scandinavia. These results have been compiled in the

following tables. The first two tables list results of measurements of PCP and TCP air concentrations, respectively. When total chlorophenates in air were reported, the ratio of TCP to PCP was assumed to be 2:1. This ratio was consistently found by BC Research (1986) when examining the contents of the six solutions (including both spray and dip tank solutions) in three B.C. sawmills.

Table 2.14: Measured Air Concentrations of PCP

PCP in air (ug/m^3)	Location	Author
19	Dipping Area	Arsenault, 1976
6	Spray Area	Arsenault, 1976

Table 2.15: Measured Air Concentrations of TCP

TCP in air (ug/m^3)	Location	Author
8	Ave. of Grading and Pulling Station (U.S.)	Klienman et al., 1986
3.3	Near washing fountain	Klienman et al., 1986
6.2 (Feb.) 10.0 (June)	Near off-loaders	Klienman et al., 1986
0.8	On loaders near dock	Klienman et al., 1986
1.6 (Feb.) 9.8 (June)	Near hula sawyer	Klienman et al., 1986
3.6	Grading area	Klienman et al., 1986
4.8 (Feb.) 12.2 (June) 10.8 (June)	Behind graders	Klienman et al., 1986
3.7 (Feb.)	Near stamper	Klienman et al., 1986
9.7 (June) 7.0 (June)	Midway down chain line	Klienman et al., 1986
10.6 (Feb.) 4.4 (June)	Near end of chain line	Klienman et al., 1986
1.6	Trimming area	Levin et al., 1976
0.1	Grading area	Levin et al., 1976

Table 2.16: Measured Air Concentrations of Total Chlorophenates: TCP and PCP Levels Estimated

Tot. Chloro. (ug/m^3)	TCP in air (ug/m^3)	PCP in air (ug/m^3)	Location	Author
70 70	46.7 46.7	23.3 23.3	Dip tank carrier cab	BC Research, 1986
10 10	6.7 6.7	3.3 3.3	Trimming area	BC Research, 1986
10 10	6.7 6.7	3.3 3.3	Grading station	BC Research, 1986
20 30	13.3 20	6.7 10	Mixing room	BC Research, 1986
20 20	13.3 13.3	6.7 6.7	Grading station - lumber enters	BC Research, 1986
20 20	13.3 13.3	6.7 6.7	Grading station - lumber leaves	BC Research, 1986
10 20	6.7 13.3	3.3 6.7	Chain - lumber leaves	BC Research, 1986
5 5	3.3 3.3	1.7 1.7	Planermill endloading area	BC Research, 1986
10 10	6.7 6.7	3.3 3.3	Planermill grading area	BC Research, 1986
80 120	53.3 80	26.7 40	Near sawmill spray boxes	BC Research, 1986
50 60	33.3 40	16.7 20	Sawmill grading area	BC Research, 1986
10 10 20 20 60 60	6.7 6.7 13.3 13.3 40 40	3.3 3.3 6.7 6.7 20 20	Grader	McDonald, 1989
10 20	6.7 13.3	3.3 6.7	Chain Puller	McDonald, 1989
5	3.3	1.7	Stacker	McDonald, 1989
24	16	8	Outdoor vat-dipping	Kauppinen and Lindroos, 1985
66	44	22	Prep. of treatment solution	Kauppinen and Lindroos, 1985
64	42.7	21.3	Indoor vat dipping	Kauppinen and Lindroos, 1985
24	16	8	Spraying of bundles	Kauppinen and Lindroos, 1985
55	36.7	18.3	Trough dipping/loading bridge	Kauppinen and Lindroos, 1985
75	50	25	Machine stacking	Kauppinen and Lindroos, 1985

A distribution of possible air concentrations was created for TCP and PCP. The mean and standard deviation for PCP air concentration, calculated from PCP values and the PCP estimate from total chlorophenates were 10.9 ug/m^3 and 9.27 respectively. The mean and standard deviation of TCP were 16.5 ug/m^3 and 17.2 respectively.

2.2.1.2.1.1.2 Inhalation Rate (m^3/hr)

According to Reference Man (ICRP, 1975), the range of breathing rates for the average adult man may be as follows:

Resting:	0.36 m^3/hr (based on 12 breaths/min)
Light Activity:	1.2 m^3/hr (based on 16 breaths/min)
Heavy Work:	2.6 m^3/hr (based on 21 breaths/min)
Maximal (Exercise):	6.7 m^3/hr (based on 40 breaths/min)

In the Monte Carlo analysis, a triangular distribution, in which fixed minimum, maximum and likeliest values were chosen, was assumed for this variable. The likeliest rate for an average sawmill worker in a position of puller or grader was assumed to fall directly between the light activity and heavy work at 1.9 m^3/hr. The minimum value chosen to be between the resting and light activity level (0.78 m^3/hr) and the maximum value was between the heavy work rate and a maximum breathing rate (4.7 m^3/hr).

2.2.1.2.1.2 Efficiency of Inhalation Absorption of PCDD/F Congeners: AE (%)

As noted in section 1.4.2.1.2, few studies have been carried out on the absorption efficiency of PCDD/F congeners in the respiratory tract, except for those of Diliberto et al., (1992) and Nessel et al. (1990) who suggested that inhalation absorption is comparable to oral absorption.

In the model, it was assumed that reported oral absorption efficiencies would be used to estimate the percentage inhalation absorption. Ranges of percentages absorbed in the gastrointestinal tract have been reported for tetra and penta congeners, with similar absorption efficiencies resulting. The only higher chlorinated congener found to be studied was OCDD where much lower percentages absorbed were reported. From these results, it was assumed that OCDD/F absorption efficiencies are significantly lower and were kept separate in calculating a distribution of possible values.

Absorption efficiencies of near 100% have been reported in nursing infants (McLachlan, 1993; Jödicke et al., 1992). These data were not included as it was assumed that the nature of the vehicle played a significant role in these high absorptions. The results used combine rat, guinea pig and human data and are found in the following table:

Table 2.17: Gastrointestinal Absorption Efficiencies of PCDD/F Congeners (excluding OCDD) in Various Species

Congener	Species	Dose (ug/kg)	% Absorbed	Author
TCDD	Sprague-Dawley Rat	50	70	Piper et al., 1973
TCDD	Sprague-Dawley Rat	1.0	84	Rose et al., 1976
TCDD	Hartley Guinea Pig	1.45	50	Nolan et al., 1979
TCDD	Golden Syrian Hamster	650	74	Olson et al., 1980
TCDD	Human	0.001	87	Poiger & Schlatter, 1986
TCDF	Fischer 344 Rat	30.6 306	90 90	Birnbaum et al., 1980
TCDF	Hartley Guinea Pig	6	90	Decad et al., 1981
PeCDF	Fischer 344 Rat	34 170 340	70 70 70	Brewster & Birnbaum, 1987

The mean and standard deviation used in the inhalation absorption efficiency for these congeners were 77% and 12.6 respectively. This was used to produce a normal distribution

in the Monte Carlo analysis, however a limit of 100% absorption was specified in the analysis.

Table 2.18: Gastrointestinal Absorption Efficiency of OCDD

Congener	Species	Dose (ug/kg)	% Absorbed	Author
OCDD	Fischer 344 Rat	50 500 500 5000	12 15 2 5	Birnbaum & Couture, 1988

The mean and standard deviation used to estimate inhalation absorption for OCDD/F congeners were 8.5% and 6.0 respectively. This was used in a lognormal distribution as the low values could not go below a value of zero.

2.2.1.2.1.3 Contamination of TCP or PCP with PCDD/F Congeners: "Contam." (pg/ug)

The values are the same as used in the dermal component. See Section 2.2.1.1.2

2.2.1.2.2 Assuming PCDD/F is in Vapour Form

If the measured air concentration of PCP and TCP are assumed to be in vapour form, then the vapour air concentration of PCDD/F's in the solution must be calculated separately to estimate exposure. While not estimating PCDD/F exposure from TCP/PCP values, other aspects of the exposure estimate are similar, therefore an equation similar to a combination of equations 2.7 and 2.10 may be used. This calculation does require fewer steps as the PCDD/F exposure is not being estimated from TCP/PCP levels. The equation is demonstrated below:

$$IAbs\ (pg/wk) = [PCDD/FExp(pg/m^3) * InhalationRate(m^3/hr) * 40hrs/wk * AE] \quad (2.11)$$

The variables: inhalation rate and AE (absorption efficiency) are the same as in sections 2.2.1.2.1.1.2 and 2.2.1.2.1.2 respectively. Only the PCDD/F exposure estimate will be discussed below.

2.2.1.2.2.1 Vapour Concentrations of PCDD/Fs (pg/m^3)

It was assumed that the ideal gas law applied to this mixture of gases, as the concentrations of gases mixing with air were generally very low. It was assumed that Raoult's Law applied to calculate the vapour pressure of this mixture. Henry's Law, a special case of Raoult's Law, applies to a substance with low solubility and high vapour pressure and was thought to not be appropriate for PCDD/F compounds in this situation. Limited data existed on Henry's Law constants for these compounds, another factor in favour of choosing Raoult's Law.

Raoult's Law assumes an ideal solution exists in which plotting the vapour pressure of each component versus its molar fraction would yield a straight line over the range of mole fractions. Raoult's Law is stated in the following equation:

$$P_i = X_i * VP_i \qquad (2.12)$$

Where:
P_i = Partial Pressure of component "i"
X_i = Molar fraction of component "i" in the mixture
VP_i = Vapour pressure of component "i" in the mixture

Measurements of PCP and TCP concentrations in spray box, dip tank and mixing tank solutions from three B.C. sawmills were carried out by BC Research (1986). Two methods were used to estimate the P_i value for each congener. Originally, maximum and minimum values of TCP and PCP reported in the solutions were combined with maximum and

minimum values of PCDD/F contamination to estimate the possible molar fraction for each congener in the solutions. This value was then multiplied by the maximum and minimum reported vapour pressures for each congener to yield a range of P_i values. A mean and standard deviation was calculated from this range and inputted into the model.

A second method used distributions for each variable in a Monte Carlo analysis to yield a mean and standard deviation of P_i estimates. The distributions for the percentage of TCP/PCP in the sawmill solutions, contamination levels of PCDD/F and vapour pressures for each congener were defined and the calculations yielded a distribution of potential vapour concentrations for each congener. The mean and standard deviation of estimated vapour concentrations for each congener is listed in Table 2.19. Results using this alternative method were inputted into the model and found not to affect the output of the model.

Table 2.19: Estimated Vapour Concentration of PCDD/F's using Raoult's Law

Congener	Type of Estimate	Calculated P_i Values (pg/m^3)	
		Mean	Standard Deviation
TCDD	Distribution	4.61×10^{-6}	6.68×10^{-6}
	High-Low Est.	1.83×10^{-6}	4.15×10^{-6}
PeCDD	Distribution	1.02×10^{-6}	1.33×10^{-6}
	High-Low Est.	8.82×10^{-8}	1.95×10^{-7}
HxCDD	Distribution	1.54×10^{-5}	1.86×10^{-5}
	High-Low Est.	1.61×10^{-6}	3.94×10^{-6}
HpCDD	Distribution	3.89×10^{-6}	4.20×10^{-6}
	High-Low Est.	5.48×10^{-7}	1.28×10^{-6}
OCDD	Distribution	8.71×10^{-5}	1.62×10^{-4}
	High-Low Est.	3.27×10^{-5}	8.18×10^{-5}
TCDF	Distribution	9.74×10^{-5}	1.60×10^{-4}
	High-Low Est.	2.03×10^{-5}	4.79×10^{-5}
PeCDF	Distribution	7.02×10^{-5}	7.45×10^{-5}
	High-Low Est.	7.40×10^{-6}	1.15×10^{-5}

Congener	Type of Estimate	Calculated P_i Values (pg/m^3)	
		Mean	Standard Deviation
HxCDF	Distribution	1.14×10^{-4}	1.33×10^{-4}
	High-Low Est.	1.68×10^{-5}	2.64×10^{-5}
HpCDF	Distribution	5.65×10^{-5}	5.65×10^{-5}
	High-Low Est.	5.82×10^{-6}	1.03×10^{-5}
OCDF	Distribution	2.37×10^{-6}	2.56×10^{-6}
	High-Low Est.	2.78×10^{-7}	6.10×10^{-7}

The mean and standard deviation value of PCDD/F vapour exposure (pg/m^3) for each congener was assumed to follow a lognormal distribution. When inputted into equation 2.11, these values comprised the inhalation component of K_o, assuming the PCDD/F is found in vapour form.

2.2.2 K_e: Elimination Rate Constants of PCDD/Fs (wk^{-1})

The elimination rate constant may be calculated from the elimination half-life ($T_{1/2}$) of a compound. The elimination half-life is the time taken for the amount of compound in the organism to decrease by one-half and is in units of time. This may then be translated into the elimination rate constant which describes the fractional loss of a compound from the body, in units of $time^{-1}$.

The elimination rate constant is calculated using the following equation:

$$K_e = \frac{0.693}{T_{1/2}} \qquad (2.5)$$

Table 2.20: Reported Half-Lives for PCDD/Fs

Congener	t1/2 Values (Years)	Exposure Incident	Number of Individuals	Sample	Time Period Between First and Last Analysis	No. of Points	Reference
TCDD	4.4	Calculated based on PBPK	NA	NA	NA	NA	Webster & Connett, 1991
	5.8	Male Volunteer	1	Faecal excretion	125 days	28	Poiger & Schlatter, 1986
	6.7	Calculated based on PBPK	NA	NA	NA	NA	Kissel & Robarge, 1988
	7.1	Vietnam Veterans	36	Serum	5 years	2	Pirkle et al., 1989
	5-8						Boddington et al., 1990
	5-10						Schecter & Ryan, 1991
	8	Assumption used in model	NA	NA	NA	NA	Sullivan et al., 1991
	9.7	Male Volunteer	1	Adipose tissue	6 years	5	Schlatter, 1991
	11.3	Vietnam Veterans	337	Serum	5 years	2	Wolfe et al., 1994
PeCDD	5	Calc. based on daily intake estimates and body burden	NA	NA	NA	NA	Schlatter, 1991
HxCDD	3.5	PCP in wood of home	1	Adipose tissue	28 months	2	Gorski et al., 1984
	15	Calc. intake vs. body burden	NA	NA	NA	NA	Schlatter, 1991
HpCDD	3.2	PCP in wood of home	1	Adipose tissue	28 months	2	Gorski et al., 1984
	25	Calc. intake vs. body burden	NA	NA	NA	NA	Schlatter, 1991
OCDD	5.7	PCP in wood of home	1	Adipose tissue	28 months	2	Gorski et al., 1984
	50	Calc. intake vs. body burden	NA	NA	NA	NA	Schlatter,1991
TCDF	5-12 days	Monkey PBPK	NA	NA	NA	NA	King et al., 1983
	1.3	Calc. intake vs. body burden	NA	NA	NA	NA	Schlatter, 1991
PeCDF	1.7	Yu-Cheng	2	Blood	5.6 years	1.7	Ryan et al., 1990
	2-3	Yu-Cheng	3	Blood	9 years	5-6	Ryan & Masuda, 1991
	4.5	Worker exp. to PCB	1	Blood/Adipose comb.	6 years	7	Schecter et al., 1990
	> 5	Yusho	9	Blood	7 years	3-5	Ryan & Masuda, 1991
	6.3	Calc. intake vs. body burden	NA	NA	NA	NA	Schlatter, 1991
HxCDF	2-3	Yu-Cheng	3	Blood	9 years	5-6	Ryan & Masuda, 1991
	2.4	Yu-Cheng	2	Blood	5.6 years	3	Ryan et al., 1990
	4.0	Worker exp. to PCB	1	Blood/Adipose comb.	6 years	7	Schecter et al., 1990
	4.9	Worker exp. to PCB	1	Blood/Adipose comb.	6 years	7	Schecter et al., 1990
	> 5	Yusho	9	Blood	7 years	3-5	Ryan & Masuda, 1991
HpCDF	<1.7	PCP in wood of home	1	Adipose tissue	28 months	2	Gorski et al., 1984
	2.4	Yu-Cheng	2	Blood	5.6 years	3	Ryan et al., 1990
	2-3	Yu-Cheng	3	Blood	9 years	5-6	Ryan & Masuda, 1991
	6.8	Worker exp. to PCB	1	Blood/Adipose comb.	6 years	7	Schecter et al., 1990
OCDF	1.8	PCP in wood of home	1	Adipose tissue	28 months	2	Gorski et al., 1984

The reported half lives for all congeners were compiled and are listed in table 2.20. The reported half-lives were then converted to units of weeks rather than years to correspond with the units of the other variables in equation 2.4, and were reported in terms of elimination rate constants in Table 2.21.

Table 2.21: Mean and Standard Deviation of Elimination Rate Constants

Congener	Reported Half-Life (Years)	Half-Life (Weeks)	Elimination Rate Constant ($Week^{-1}$)	Mean	Standard Deviation
TCDD	4.4	228.8	0.00303	1.92×10^{-3}	5.40×10^{-4}
	5.8	301.6	0.00230		
	6.7	348.4	0.00199		
	7.1	369.2	0.00188		
	6.5*	338.0	0.00205		
	7.5*	390.0	0.00178		
	8.0	416.0	0.00167		
	9.7	504.4	0.00137		
	11.3	587.6	0.00118		
PeCDD	5.0	260.0	0.00267	2.67×10^{-3}	5.40×10^{-4} **
HxCDD	3.5	182.0	0.00381	6.35×10^{-3}	3.59×10^{-3}
	15.0	780.0	0.00888		
HpCDD	3.2	166.4	0.00416	2.35×10^{-3}	2.57×10^{-3}
	25	1300	0.00053		
OCDD	5.7	296.4	0.00234	1.31×10^{-3}	1.46×10^{-3}
	50	2600	0.00027		
TCDF	1.3	67.6	0.01025	1.03×10^{-2}	5.40×10^{-4}
PeCDF	1.7	88.4	0.00784	4.18×10^{-3}	2.39×10^{-3}
	2.5*	130.0	0.00533		
	4.5	234.0	0.00296		
	5.0	260.0	0.00266		
	6.3	327.6	0.00212		
HxCDF	2.5*	130.0	0.00533	3.92×10^{-3}	1.41×10^{-3}
	2.4	124.8	0.00555		
	4	208.0	0.00333		
	4.9	254.8	0.00272		
	5	260.0	0.00267		
HpCDF	1.7	88.4	0.00784	5.17×10^{-3}	2.42×10^{-3}
	2.4	124.8	0.00555		
	2.5*	130.0	0.00533		
	6.8	353.6	0.00196		
OCDF	1.8	93.6	0.00740	7.40×10^{-3}	5.40×10^{-4} **

Notes: * When a range was given, the middle value was chosen
** If no standard deviation was able to be calculated, the standard deviation of TCDD was used.

The half-lives of each congener were assumed to be lognormally distributed. A lognormal distribution was chosen to avoid any values within the distribution being negative.

2.2.3 M_f: Mass of Fat Tissue (g)

The mass of fat tissue in an average sawmill worker was divided into two components: the average adult male mass and the percent of fat tissue. These were multiplied to yield M_f as shown in the following equation:

$$M_f(g) = AdultMaleMass(g) * PercentLipidTissue(\%) \quad (2.11)$$

Distributions of possible values were created for each of the variables, as described in the following sections.

2.2.3.1 Adult Male Mass (g)

Several compilations of male mass have been carried out. The average measurements were combined with age specific masses, to cover a wide range of possible values. The values are listed in the table below:

Table 2.22: Weight Values for an Average Male

Age Category	Weight (kg)	Author
17-19 yrs	73.1	Durnin and Womersley, 1973
20-29 yrs	70.1	
30-39 yrs	79.8	
40-49 yrs	76.9	
50-72 yrs	80.4	
20-24 yrs	75.1	Documenta Geigy, 1970 (For Males of between 5'10"-6'2" in height)
25-29 yrs	78.1	
30-39 yrs	80.1	
40-49 yrs	82.9	
50-59 yrs	83.7	
19-65 yrs	78.4	Pheasant, 1986
Mean	78.1	
Standard Deviation	4.1	

These results from Pheasant (1986) and Documenta Geigy (1970) generally reflect the mass of adult males in North America. The data from Durnin and Womersley (1973) was based on mainly sedentary middle-class men in Great Britain, however a variety of body types were included in the analysis.

These results were converted to units of grams, giving a mean of 78100g and a standard deviation of 4100. It was assumed that these values would be distributed normally in the Monte Carlo analysis.

2.2.3.2 Percentage of Fat Content in Body (%)

For a sawmill workforce, this parameter should reflect a range of possible values of adipose tissue mass for the adult male. As with the mass measurements, the Durnin and Womersley (1973) measurements were not from a randomly selected population, but do represent all varieties of body types. It is important to note that variations in both these parameters occur with changes in age.

Table 2.23: Percent Fat in Average Adult Male

Age Category	Percentage Fat (%)	Author
20.3 yrs	11.1	ICRP, 1974
49.0 yrs	21.3	
50.5 yrs	25.8	
70.0 yrs	30.5	
20-29 yrs	15	Durnin & Womersley, 1973
30-39 yrs	23	
40-49 yrs	25	
50-72 yrs	28	
15-69 yrs	18	Documenta Geigy, 1970
Mean	22.0	
Standard Deviation	6.3	

The mean and the standard deviation were used in a lognormal distribution. It was assumed that a lognormal distribution was most appropriate to avoid unnaturally low fat estimates.

2.2.4 t_w : Duration of Working Life at Sawmill (wks)

The duration of working life at sawmill is used in the model to represent the total elimination period of PCDD/F compound, taking into account both exposure period and periods in which no exposure takes place. Since it represents total elimination time, it is calculated assuming a 24-hour day and seven day week, the potential time in which the PCDD/F compounds may be eliminated from the body.

The total amount of time spent working at a sawmill was based on an actual cohort of 23,829 sawmill workers compiled by Hertzman et al. (1995), involving 11 chlorophenate using sawmills located in B.C. In order to qualify for the cohort, the subject must have worked at least one year in one of the study mills between January 1, 1950 and December 31, 1985. A total of 260 days constituted a working year. The mean of the total time worked resulting from this cohort was 2538.03 days (excluding weekends) with a standard deviation of 2503.08. The mean and standard deviation were divided by 5 working days/wk to change to a weekly basis to yield a mean of 507.6 wks with a standard deviation of 500.62. This was distributed lognormally.

2.2.5 t_e : Total Time Exposed to Chlorophenates (wks)

The total time exposed represents the period of input of PCDD/F into the model. It was assumed to be continuous over an 8-hour working day, five days per week.

The total time exposed to chlorophenates was estimated in the same cohort of 23,829 workers in terms of "exposure hours per year". Exposure assessment for the cohort was carried out by 10 to 20 experienced workers familiar with various points in the history of chlorophenate use in the mills including: changes in application technology, changes in formulation and in location of application of the chlorophenates. These workers independently rated all job titles for each exposure period. The job titles were then assigned average estimates of duration (hrs/day) and frequency (days/week) of chlorophenate exposure. These scores were then combined with each subject's work history to yield a total time exposed to chlorophenate estimate (Hertzman et al., 1995). The resulting mean of exposure estimates is 6773.63 hours with a standard deviation of 2503.081.

These values were divided by 40 hrs/wk to yield a mean of 169.34 wks and a standard deviation of 209.32. This was distributed lognormally in the Monte Carlo analysis.

2.2.6 Probability and Sensitivity Analysis

Analysis of the variability in a model may be carried out by two main approaches: using single point values or using a probabilistic approach known as the Monte Carlo technique. Monte Carlo analysis uses a distribution of possible values for each variable rather than single points. In order to examine uncertainty and variability within the model, a programme called "Crystal Ball" (Decisioneering Inc., Denver, Colorado) which utilized Monte Carlo analysis was chosen.

Crystal Ball works in conjunction with a spreadsheet to assign each variable a type of probability distribution (eg. normal or lognormal) and appropriate descriptions of the

distribution (eg. mean, standard deviation). When the programme is running, a number from each variable cell is randomly chosen which conforms the particular distribution defined for that cell, the output is then calculated with these numbers and the result is added to a forecast graph which grows with each trial as this process is repeated. The forecast chart produced demonstrates the probability of each outcome and may be accompanied by a sensitivity analysis.

The program was set to run for 5000 iterations using a Latin Hypercube sampling technique, which divides each probability distribution into intervals of equal probability. A value is then generated for each interval according to the interval's probability distribution. This form of sampling is more precise as it samples the entire range of distribution values in a more consistent manner (Crystal Ball, 1993).

The sensitivity analysis identifies the key variables in the model by displaying them in a sensitivity chart which ranks the variables based on their influence on the forecast cell. Spearman rank correlation coefficients also describe the degree to which the assumptions and forecasts change together.

3.0 Results - Predicted Concentrations of PCDD/Fs in Fat Tissue due to Chlorophenate Exposure in Sawmills (pg/g)

3.1 Median Results

PCDD/F concentrations in the fat tissue of sawmill workers were calculated separately for each congener using the model. The aerosol and vapour assumptions were also kept separate, resulting in a total of twenty reports. The output report consists of descriptive statistics for the simulation, a forecast chart, percentile information in 10% increments, a sensitivity chart as well as a description of any pertinent variables. The full reports for the aerosol and vapour assumptions are found in Appendices II and III respectively. Some of the more pertinent results from the output reports have been extracted and are displayed in this section.

The reports are the results of up to a maximum of 5000 iterations using the Monte Carlo technique. However, in order to exclude extreme outliers, the results in this section are based on model output within 2.6 standard deviations of the mean.

The median, mean and standard deviation of the predicted fat concentration of PCDD/F in sawmill workers are displayed in Tables 3.1 and 3.2 for each congener and each assumption (aerosol and vapour).

The frequency distribution of the predicted PCDD/F concentrations for all congeners was lognormal with highly positive skew. Due to some extremely high possible concentration values calculated as outputs, some means were much larger than the median values. Due to the skew in the distribution, the medians were chosen as indicators of central tendency.

Table 3.1: Median, Mean and Standard Deviation of Predicted PCDD/F Concentrations in Fat Tissue due to Occupational Exposure to Chlorophenates in Sawmills: Aerosol Assumption

Congener	Median (pg/g)	Mean (pg/g)	Standard Deviation
TCDD	2.4	5.2	8.2
PeCDD	11	29	55
HxCDD	18	210	7,000
HpCDD	62	140	230
OCDD	44	140	280
TCDF	0.83	8,000	440,000
PeCDF	32	95	290
HxCDF	260	800	7,400
HpCDF	200	580	1,500
OCDF	9.8	170	4,500

Table 3.2: Median, Mean and Standard Deviation of Predicted PCDD/F Concentrations in Fat Tissue due to Occupational Exposure to Chlorophenates in Sawmills: Vapour Assumption

Congener	Median (pg/g)	Mean (pg/g)	Standard Deviation
TCDD	1.1	3.6	13
PeCDD	5.1	15	27
HxCDD	7.6	1,600	69,000
HpCDD	24	65	110
OCDD	37	170	750
TCDF	0.36	38	1,700
PeCDF	15	59	240
HxCDF	110	250,000	14,000,000
HpCDF	90	9,500	350,000
OCDF	8.5	67	760

The highest median PCDD/F fat concentrations in sawmill workers were predicted for the hexa- and hepta- chlorinated furan congeners. These congeners were consistently reported as having the highest contamination values in the 2,3,4,6-tetrachlorophenate compounds listed in Table 2.10. Hepta- and octachlorinated dioxins recorded the next highest predicted fat concentrations in sawmill workers.

Overall, the aerosol assumption reported fat concentrations approximately twice that of the vapour assumption. This, however, does not include the octa-congeners. Results from the octachlorinated dioxin and furan congeners were similar for both aerosol and vapour assumptions.

The mean values were consistently higher than the medians, demonstrating the positively skewed distribution of the predicted fat concentrations. The high means and standard deviations also demonstrate the potential for extremely large values being calculated by the model.

3.2 Percentile Results

Although the median was used to describe the central tendency of the predicted PCDD/F concentrations, it was also of interest to examine the upper limit of possible concentrations for each congener. Results were compiled for the 5th, 10th, 30th, 50th (median), 70th, 90th and 95th percentile values in the following tables, with aerosol and vapour results displayed separately. The comprehensive list of values for each percentile range are found in Appendices II and III.

Table 3.3: 5, 10, 30, 50, 70, 90 and 95 Percentiles of Predicted PCDD/F Concentrations in Fat Tissue due to Chlorophenate Exposure in Sawmills: Aerosol Assumption (pg/g)

Congener	5%	10%	30%	50%	70%	90%	95%
TCDD	0.28	0.46	1.2	2.4	4.6	13	20
PeCDD	0.87	1.7	5.3	11	23	72	110
HxCDD	0.07	0.53	6.7	18	43	140	260
HpCDD	4.0	8.4	29	62	120	340	550
OCDD	3.0	5.9	20	44	100	350	630
TCDF	0.0	0.0	0.18	0.83	2.7	14	30
PeCDF	0.86	3.1	14	32	70	210	340

Congener	5%	10%	30%	50%	70%	90%	95%
HxCDF	12	34	120	260	500	1,300	2,200
HpCDF	2.6	13	89	200	440	1,300	2,200
OCDF	0.05	0.34	3.6	9.8	26	95	180

Table 3.4: 5, 10, 30, 50, 70, 90 and 95 Percentiles of Predicted PCDD/F Concentrations in Fat Tissue due to Chlorophenate Exposure in Sawmills: Vapour Assumption (pg/g)

Congener	5%	10%	30%	50%	70%	90%	95%
TCDD	0.09	0.15	0.49	1.1	2.5	7.4	13
PeCDD	0.34	0.63	2.3	5.1	12	40	67
HxCDD	0.03	0.26	2.5	7.6	20	71	140
HpCDD	1.3	2.7	11	24	54	170	280
OCDD	1.9	3.7	14	37	85	320	630
TCDF	0.0	0.0	0.08	0.36	1.3	7.3	18
PeCDF	0.33	1.2	5.9	15	35	120	220
HxCDF	4.4	12	50	110	240	800	1,400
HpCDF	1.4	6.1	36	91	210	680	1,200
OCDF	0.04	0.24	2.6	8.5	23	89	170

3.3 Sensitivity Analysis

The sensitivity charts indicate which variables in the model have the most influence on the output by displaying the variables in a bar chart. The complete results from the sensitivity analysis for each congener are found in Appendices IV and V, representing aerosol and vapour assumptions respectively.

Results from the top four factors in each sensitivity analysis have been compiled in the following tables for comparison purposes. The variables are accompanied by their respective correlation coefficients which are descriptions of the degree to which the variable and the output change together.

Table 3.5: Top Four Variables Listed in Sensitivity Analyses with Correlation Coefficient: Aerosol Assumption

Congener	#1: Sensitivity	Coef.	#2: Sensitivity	Coef.	#3: Sensitivity	Coef.	#4: Sensitivity	Coef.
TCDD	TCP Contamination	+.44	Time Exposed	+.41	Skin Absorption	+.33	Percentage Fat	-.24
PeCDD	TCP Contamination	+.49	Skin Absorption	+.33	Time Exposed	+.32	Inhalation Exposure	+.22
HxCDD	Elim. Rate Constant	-.45	Time Worked	-.37	TCP Contamination	+.27	Skin Absorption	+.24
HpCDD	Elim. Rate Constant	-.42	Time Exposed	+.40	Skin Absorption	+.30	PCP Contamination	+.26
OCDD	PCP Contamination	+.51	Time Exposed	+.44	Skin Absorption	+.42	Elim. Rate Constant	-.24
TCDF	Time Worked	-.63	TCP Contamination	+.40	Skin Absorption	+.20	Time Exposed	-.17
PeCDF	Elim. Rate Constant	-.38	Skin Absorption	+.28	TCP Contamination	+.28	Inhalation Exposure	+.23
HxCDF	Skin Absorption	+.33	Elim. Rate Constant	-.30	Time Worked	-.24	Inhalation Exposure	+.23
HpCDF	Elim. Rate Constant	-.39	Time Worked	-.31	Skin Absorption	+.29	Inhalation Exposure	+.21
OCDF	Time Worked	-.54	Skin Absorption	+.37	PCP Contamination	+.18	Percentage Fat	-.15

Table 3.6: Top Four Variables Listed in Sensitivity Analyses with Correlation Coefficients: Vapour Assumption

Congener	#1: Sensitivity	Coef.	#2: Sensitivity	Coef.	#3: Sensitivity	Coef.	#4: Sensitivity	Coef.
TCDD	Skin Absorption	+.58	TCP Contamination	+.42	Time Exposed	+.37	Percentage Fat	-.21
PeCDD	Skin Absorption	+.45	TCP Contamination	+.26	Time Exposed	+.26	TCP Leg Exposure	+.18
HxCDD	Elim. Rate Constant	-.42	Skin Absorption	+.41	Time Worked	-.36	TCP Contamination	+.25
HpCDD	Skin Absorption	+.54	Time Exposed	+.35	Elim. Rate Constant	-.35	TCP Contamination	+.22
OCDD	Skin Absorption	+.49	PCP Contamination	+.46	Time Exposed	+.41	PCP Leg Exposure	+.24
TCDF	Time Worked	-.61	TCP Contamination	+.38	Skin Absorption	+.31	Time Exposed	-.17
PeCDF	Skin Absorption	+.49	Elim. Rate Constant	-.35	TCP Contamination	+.26	Time Worked	-.19
HxCDF	Skin Absorption	+.54	Elim. Rate Constant	-.26	Time Worked	-.23	Time Exposed	+.17
HpCDF	Skin Absorption	-.48	Elim. Rate Constant	-.35	Time Worked	-.30	Percentage Fat	-.17
OCDF	Time Worked	-.54	Skin Absorption	+.40	PCP Contamination	+.16	TCP Contamination	+.14

4.0 Discussion

4.1 Predicted Concentrations of PCDD/Fs in Fat Tissue due to Chlorophenate Exposure in Sawmills Compared to Concentrations Found in the General Population

The general population is not totally unexposed to PCDD/Fs. As noted in Section 1, there are many sources of PCDD/Fs in industrial societies and when absorbed these lipophilic compounds tend to bioconcentrate in organisms. The compounds then pass through the food chain, to make ingestion of contaminated food, especially meat, fish and dairy products, the primary source of background exposure (Fürst et al., 1990; Davies, 1988; Henry et al., 1992). PCDD/Fs in adipose or blood tissue have been measured in various populations and results from several studies have been compiled in Table 4.1. The studies included in Table 4.1 were chosen because the PCDD/F concentrations were obtained from "unexposed" individuals from the general population and were reported in terms of pg/g lipid.

The populations included in Table 4.1 may be briefly described. Teschke et al. (1992) measured the concentrations of PCDD/Fs in the adipose tissue of 41 British Columbians scheduled for elective abdominal surgery. The population sampled was weighted to reflect the age and sex distribution of the population. Ryan et al. (1985) analyzed human adipose tissue from the abdominal region. The 46 samples originated from all geographic regions of Canada and were obtained from individuals who had died accidentally in 1976, including all ages and both sexes. The 10 samples from Ontario specifically were collected from older patients who had died in Ontario hospitals in 1980 from such causes as heart disease, stroke, and cancer. The 6 samples reported from the USA by Ryan et al. (1985) consisted of biopsy and autopsy fat taken in 1983-84 from New York State residents in the course of normal medical procedures. The U.S. data collected by Schecter et al., (1990) was from a pool of

whole blood from 100 adult blood bank volunteers from New York State. Adipose tissue samples from USA (n=15), Germany (n=4), Japan and China were obtained from patients undergoing general surgery. German general population data compiled by Papke et al. (1994) was based on blood samples collected in 1989 (n=70) and 1992 (n=102) from people with no exposure other than food consumption. The 85 whole blood samples compiled by Schecter et al. (1990) were from the former West Germany in which all subjects were adults, 75% male with an average age of 37 years. In summary, it appears that only the Teschke et al (1992) study attempted to sample a representative portion of the actual population, in terms of sex and age. Although the studies in Table 4.1 did not examine populations with similar characteristics to this study population (sawmill workers), it provides a broad range of background data with which to compare the predicted PCDD/F concentrations in sawmill workers.

The median predicted PCDD/F concentrations in sawmill workers due to chlorophenate exposure only, not taking into account background exposure, were compared with the data in Table 4.1. Using the model results, it appears that the median predicted PCDD/F levels for most congeners fall within a normal "unexposed" range. The exceptions to this result are the hexa- and hepta- chlorinated furans. The median predicted fat concentrations due to chlorophenate exposure for these congeners using both the vapour and aerosol assumptions fall well above the highest reported levels in the general population in which the maximum measurements for HxCDF and HpCDF reported are 69 and 39.4 pg/g (lipid) respectively. This compares to the predicted sawmill workers' medians of 110 and 90 pg/g (lipid), using the lower vapour assumption.

The general population data were also compared to the specific percentile predictions of the model. HpCDF and HxCDF appear to either reach the upper range or be above the upper range of background values (depending on either aerosol or vapour assumptions) at approximately the 30th percentile of predicted PCDD/F concentration levels.

For those congeners whose median values were below that of the general population ranges, the 70th, 90th and 95th percentiles of predicted PCDD/F fat concentrations were examined. At the 70th percentile, OCDF was above the highest values reported in the population background levels for both the aerosol and vapour assumptions. PeCDD and PeCDF 70th percentile predicted concentrations were near the upper range of the background concentrations using the aerosol assumption, however were within a normal range using the vapour assumption.

The 90th percentile estimates of sawmill worker concentrations for HxCDF and HpCDF were extremely high, at levels of approximately 1300 pg/g, assuming aerosol exposure, while the vapour assumption resulted in levels of 800 pg/g (HxCDF) and 680 pg/g (HpCDF) being estimated. PeCDD and PeCDF results at the 90th percentile for both the vapour and aerosol assumptions were above the upper range of general population values with these predicted concentrations being between 2 to 4 times that of background. The aerosol assumption predictions for HpCDD and TCDF also reported 90th percentile values above the upper limit of levels reported in the general population, however the vapour assumption results were within the ranges reported in Table 4.1.

Table 4.1: PCDD/F Levels Measured in the General Population (pg/g lipid)

Country/ Region	BC	Eastern Ontario	Canada	U.S.A.		Germany				Japan	China	N. Vietnam	Range
No. of Subjects	n=41*	n=10	n=46	n=6	n=100	n=70*	n=102*	n=85	n=4	n=6	n=7	n=26	
Tissue	Adipose	Adipose	Adipose	Adipose	Whole Blood	Whole Blood	Whole Blood	Whole Blood	Adipose	Adipose	Adipose	Adipose	
TCDD	3.8	10.0	6.2	6.4	5.2	2.7	3.2	3.6	5.1	6.6	nd	0.6	nd - 10.0
PeCDD	13	13.2	10.4	9.7	21.0	6.6	13.0	14.0	21.5	13	8.1	1.0	1.0 -21.5
HxCDD	159	90.5	79.6	57.8	112	34.2	71.8	81.1	109	86	18	6.5	6.5 - 159
HpCDD	109	116	137	95.2	187	40.3	80.0	93.8	153	69	32	23.2	23.2 - 187
OCDD	421	611	796	585	1174	360	549	596	653	1360	189	44.8	44.8 - 1360
TCDF	1.7	--	--	--	3.1	1.9	2.0	2.5	3.9	3.1	11	5.6	1.6 - 11
PeCDF	8.6	18.4	16.8	14.7	15.8	14.2	33.4	36.8	70.8	13	17	na	6.8 - 70.8
HxCDF	21	17.3	17.3	28.7	32.6	16.8	29.5	31.6	37.6	69	25	8.9	8.9 - 69
HpCDF	14	39.4	32.7	16.4	36.0	12.9	22.0	21.8	23.3	7.1	nd	6.5	nd - 39.4
OCDF	2.9	--	--	--	4.2	3.4	3.1	5.5	4.2	nd	nd	nd	nd - 5.5
Reference	Teschke et al., 1992	Ryan et al., 1985	Ryan et al., 1985	Ryan et al., 1985	Schecter et al, 1990	Papke et al., 1994	Papke et al., 1994	Schecter et al. 1990	Schecter1 991	Ryan et al., 1987	Ryan et al., 1987	Schecter, 1991	

* The geometric mean or median, rather than the mean, of the data was used

At the 95th percentile, the predicted concentrations for all congeners except OCDD were above the upper range of the background population, using the aerosol assumption. Under the vapour assumption, the predicted 95th percentile concentrations for TCDD, HxCDD and OCDD only were within the normal range of reported background concentrations. The 95th percentiles for HpCDF and HxCDF (aerosol) were approximately 60 and 30 times that of the highest reported background concentration reported in Table 4.1.

4.2 Estimated Concentrations of PCDD/Fs due to Chlorophenate Exposure in Sawmills Compared to Exposed Populations

As noted in Section 1, exposures to PCDD/Fs rarely occur in isolation but instead are usually the result of exposure to other compounds. Pesticides such as 2,4,5-trichlorophenol and 2,4-dichlorophenol have been found to be contaminated primarily with 2,3,7,8-TCDD (Rappe et al., 1982). As demonstrated in contamination tables presented earlier, other chlorophenols such as TCP and PCP are more likely to be contaminated with the higher chlorinated PCDD/F congeners. PCBs generally are more highly contaminated with PCDFs than PCDDs (Vos et al. 1970).

Measured levels of PCDD/Fs in occupationally or accidentally exposed individuals were compiled in Table 4.2. When examining Table 4.2, it is important to note the type of exposures in conjunction with the levels of PCDD/F congeners reported. The exposures included in the table will be outlined briefly. Workers at a German chemical plant were exposed to compounds including lindane, chlorophenols and 2,4,5-trichlorophenol (2,4,5-T) which may result in exposure to several different PCDD/F congeners. The chemical workers in a plant in Missouri were exposed primarily to 2,4,5-T, therefore, 2,3,7,8-TCDD is expected

to be found in higher concentrations than the other congeners. Vietnam veterans and the general population of south Vietnam were potentially exposed to Agent Orange between 1962 and 1971 and were expected to have elevated levels of 2,3,7,8-TCDD as opposed to the other PCDD/F congeners. Following a PCB fire in New York state, soot analysis revealed that PCDFs were predominant with markedly lesser amounts of PCDDs. The effect of PCB contamination predominantly with PCDF compounds is also expected in populations exposed to PCB-contaminated rice oil. The final exposures outlined in Table 4.2 are to PCP and NaPCP compounds. These populations were expected to report relative concentrations of PCDD/Fs in tissue which reflect PCDD/F contamination of PCP (Table 2.11).

In Table 4.2, Vietnam veterans exposed to Agent Orange and pesticide sprayers in China exposed to NaPCP demonstrated levels of all PCDD/F congeners within the range of background levels listed in Table 4.1. The general population of South Vietnam and chemical plant workers exposed to 2,4,5-T demonstrated elevated TCDD levels compared to the background levels reported in Table 4.1. All other congeners were within normal ranges.

Workers exposed to chlorophenols in a German chemical plant demonstrated potentially extremely high levels of PCDDs, well above background. The upper levels of PeCDFs, HxCDFs and HpCDFs reported in these chemical workers were very close to the 90th percentile predicted in sawmill workers.

Table 4.2: PCDD/F Levels Measured in Exposed Populations (pg/g lipid)

Exposure	Chlorophenols, 2,4,5-T	2,4,5-T	Agent Orange	Agent Orange	PCB Fire	PCB Fire	PCB Poisoning	PCP Poisoning	NaPCP
Industry	Chemical Plant	Chemical Plant	Vietnam Veterans	General Population	Cleanup Activities	Cleanup Activities	Rice Oil	Chemical Plant	Pesticide Spraying
Region	Germany	Missouri	USA	South Vietnam	New York	New York	Yusho	U.S.A.	China
Tissue	Adipose	Adipose	Adipose	Adipose	Adipose	Adipose	Adipose	Adipose	Blood
Levels	Range (n=45)	Mean (n=4)	Geo. Mean (n=20)	Mean (n=41)	3.5 yrs (n=1)	Mean (n=4)	Mean (n=2)	n=1	Mean (n=26)
TCDD	7.5 - 2815	390	4.8	15.7	15	--	na	33	3.0
PeCDD	15 - 756	14.7	7.2	7.7	19	--	34	70	7.2
HxCDD	69 - 12,016	129.9	62.8	47.9	168	--	71	1,124	33.9
HpCDD	30 - 5,150	125	71.6	101	257	--	na	17,870	24.1
OCDD	378 - 19,865	624	398	642	1081	--	273	128,915	1148
TCDF	1 - 6	1.3	1.4	8.8	5	13.7 - 43.5	4	nd	1.5
PeCDF	18 - 241	4.3	6.1	na	54	nd - 88.1	2,132	50	2.4
HxCDF	14 - 1,790	10.3	10.0	24.7	113	nd - 308	2,926	672	20.0
HpCDF	8 - 1,184	31.5	14.8	23	32	12.5 - 46.4	324	10,850	4.9
OCDF	1 -14	--	1.0	nd	--	--	na	15,350	5.2
Reference	Beck et al., 1989	Patterson et al., 1989a	Schecter et al., 1990a	Schecter, 1991	Schecter & Ryan, 1989	Schecter, 1994	Ryan et al., 1987	Ryan et al., 1987	Schecter, 1994

Individuals exposed to PCBs during a cleanup operation also reported upper ranges of TCDF, PeCDF, HxCDF and HpCDF levels above the normal population range, but similar to the 70th percentile estimated values for sawmill workers. The exposures at Yusho and the PCP poisoning incident reported extremely high tissue concentrations of PCDD/Fs, far above the upper estimates of concentrations in sawmill workers.

Comparison of estimated concentration levels in sawmill workers with other occupationally or accidentally exposed populations suggests that the levels of PCDD/Fs estimated in sawmill workers may be within a reasonable range of others occupationally or accidentally exposed to PCDD/Fs.

4.3 Predicted Concentrations of PCDD/Fs in Fat Tissue due to Chlorophenate Exposure in Sawmills Compared to Other Sawmill Worker Populations

Very few measurements of PCDD/F levels in sawmill workers have been reported. Rappe et al. (1982) determined blood plasma levels of PCDD/Fs in four sawmill workers in Finland and Teschke et al. (1992) reported levels of PCDD/Fs in the adipose tissue of two individuals with a history of working in sawmills.

In the Rappe et al. (1982) study, 2,3,4,6-TCP was being used as the antisapstain fungicide, with PCDFs being recognized as the major contaminant in the formulation. Blood sampling was performed after six months of non-exposure, then repeated after one month of exposure to chlorophenol. The results obtained by Rappe et al. (1982) are found in Table 4.3. These

results were originally listed in units of pg/g blood plasma, however, in this study, the values were recalculated in order to estimate the concentration in units of pg/g lipid, for comparison purposes. The percentage of total lipid in plasma depends on such factors as food intake, physical exercise and genetic construction, however lipid levels have been estimated to be approximately 0.7% of total plasma (ICRP, 1975). Both the reported and recalculated results are included in Table 4.3. These estimates of PCDD/F in units of pg/g lipid are acknowledged as being extremely rough.

While examining PCDD/F levels in the general population of B.C., Teschke et al. (1992) noted two individuals who reported having worked in sawmills. The levels of PCDD/Fs (pg/g lipid) for the two individuals are also included in Table 4.3. Individual #1 worked from 1979 to 1980 as a sawmill worker. Individual #2 worked from 1939 to 1955 as a labourer in a coastal sawmill which began using chlorophenates in 1947.

The Rappe et al. (1982) data demonstrated very high detection limits when converted to units pg/g lipid in Table 4.3. A general trend, however, is apparent in the Rappe et al. (1982) data, with HpCDF registering the highest concentrations of all congeners in the blood plasma. The next highest congener found in plasma is OCDD. The relatively high HpCDF result is consistent with values predicted by the model developed in this study, however, an inconsistency does appear to exist between the model predictions and the Rappe et al. (1982) data with respect to HxCDF concentrations. The model predicts HxCDF levels to be elevated, however, this is not demonstrated in the Rappe et al. (1982) data.

Table 4.3: PCDD/F levels Measured in Sawmill Workers

Congener	Time Sampled	Loader 1		Loader 2		Cleaner		Packade		Control		B.C. Sawmill Worker #1	B.C. Sawmill Worker #2
		pg/g blood	pg/g lipid	pg/g blood	pg/g lipid	pg/g blood	pg/g lipid	pg/g blood	pg/g lipid	pg/g blood	pg/g lipid	pg/g lipid (adipose tissue)	pg/g lipid (adipose tissue)
TCDD	6 mths after latest exposure	--	--	--	--	--	--	--	--	--	--	<0.51	6.2
	After one month of exposure	--	--	--	--	--	--	--	--				
PeCDD	6 mths after latest exposure	--	--	--	--	--	--	--	--	<1	<140	8.2	<1.2
	After one month of exposure	<1	<140	<1	<140	<1	<140	2	290				
HxCDD	6 mths after latest exposure	<3	<430	3	430	<3	<430	<3	<430	<1	<140	95	384
	After one month of exposure	<1	<140	<1	<140	<1	<140	<1	<140				
HpCDD	6 mths after latest exposure	<2	<290	10	1430	2	290	<2	<290	<1	<140	57	281
	After one month of exposure	<1	<140	<1	<140	8	1140	<1	<140				
OCDD	6 mths after latest exposure	5	710	18	2570	5	710	<3	<430	3	430	392	906
	After one month of exposure	7	1000	3	430	22	3140	4	570				
TCDF	6 mths after latest exposure	--	--	--	--	--	--	--	--	--	--	1.6	3.0
	After one month of exposure	--	--	--	--	--	--	--	--				
PeCDF	6 mths after latest exposure	--	--	--	--	--	--	--	--	<1	<140	5.2	26
	After one month of exposure	<1	<140	1	140	5	710	<1	<140				
HxCDF	6 mths after latest exposure	<3	<430	<3	<430	<3	<430	<3	<430	<1	<140	12	65
	After one month of exposure	<1	<140	<1	<140	<1	<140	<1	<140				
HpCDF	6 mths after latest exposure	40	5710	18	2570	30	4290	7	1000	3	430	nd	nd
	After one month of exposure	22	3140	17	2430	17	2430	12	1710				
OCDF	6 mths after latest exposure	<3	<430	<3	<430	<3	<430	<3	<430	<2	<290	4.0	<7.8
	After one month of exposure	<2	<290	<2	<290	<2	<290	<2	<290				
Reference	Rappe et al. (1982)											Teschke et al. (1992)	

The results obtained by Rappe et al. (1982) should be viewed with caution as they were obtained from two days of sampling on only four exposed individuals. Information is lacking on the exposure histories of the individuals, as well as information concerning the sawmill itself. The analyses were also performed on the blood plasma which, as noted in the Introduction, may not have a 1:1 ratio with adipose tissue on a lipid basis. Schecter et al. (1990a) had noted that the plasma to adipose tissue levels ratio (on a lipid basis) increased with increasing chlorine substitution, for example congeners such a OCDD were found to have a plasma lipid to adipose tissue ratio of 2. Schecter (1991) noted that this was not found with whole blood. This factor suggests that values for the hepta and octa congeners in Table 4.3 may be overestimates if compared to adipose tissue since a 1:1 ratio was assumed.

In the data reported by Teschke et al. (1992), the PCDD/F levels found in worker #1 are within the ranges of background levels reported in Table 4.1. This result is not surprising as the individual reported working in a sawmill for only one year and it is not known whether the mill used chlorophenates. Worker #2, however, reported levels of HxCDD and HpCDD above the reported background levels and levels of HxCDF very close to the upper levels of reported background concentrations. Elevated levels of HxCDD and HpCDD are in contrast to the elevated HxCDF and HpCDF concentrations predicted by the model. Potential explanations for higher levels of HxCDD and HpCDD reported in this individual may be due to the fact that the period worked in a sawmill was from 1939 to 1955, with chlorophenates being introduced in 1947. During this period PCP was the primary fungicide used, and as demonstrated in Tables 2.10 and 2.11, PCP solutions demonstrate higher levels of PCDD and

lower levels of PCDF contamination than TCP. No strong conclusions may be drawn from this data as it is one sample from one individual with relatively little information concerning specific work history and exposures. Further differences in results may be due to the fact that the predicted concentrations of PCDD/Fs by the model do not include background dietary exposure, whereas this route of exposure would have been included in the data found in Table 4.3

4.4 Sensitivity Analysis

Each variable of the model was examined to identify potential areas of uncertainty which would affect the output. The variables were examined in their order of importance as identified by the sensitivity analysis.

4.4.1 Skin Absorption

The variable which plays the most significant role as defined in the sensitivity analysis is skin absorption. Skin absorption was highlighted as the primary variable for seven of the ten congeners under the vapour assumption and was within the top three of the remaining congeners assuming vapour exposure. Using the aerosol assumption, skin absorption is listed within the top four variables of all congeners.

Factors governing absorption of chemicals by the skin may be divided into physicochemical characteristics and exposure factors (Gerrity and Henry, 1990). Physicochemical characteristics governing absorption include the molecular size, molecular weight, partition

coefficient, reactivity, solubility and volatility, whereas exposure factors include the concentration of chemical, contact duration, dosing pattern, dosing vehicle, frequency of exposure and occlusion. Various methods of calculating the rate or amount of PCDD/F congeners absorbed by the skin were examined throughout the course of this study, including models of skin permeation, in vivo animal results as well as in vitro human results.

Several models have been developed to estimate the rate of skin permeation based upon Fick's first law of diffusion (Berner and Cooper, 1987; Guy and Potts, 1993; Cleek and Bunge, 1993; Morimoto et al., 1994). These models estimate the flux of the compound across the stratum corneum using the molecular weight of the compound and the octanol-water partition coefficient. To ascertain the validity of the models for PCDD/F compounds, permeation rates of TCDD were calculated using the models and compared with experimental values using human skin in vitro (Weber et al., 1991). The model estimates were found to be as much as three orders of magnitude greater than results obtained by Weber et al. (1991). Due to this difference, the models were considered inappropriate for estimating flux of PCDD/F compounds. Reasons for the large difference between model predictions and in vitro data were attributed to the fact that the coefficients used in the models were developed from experimental data collected by Flynn et al.(1990), representing over 90 compounds with log octanol-water partition coefficients ranging from -3 to 6. The extremely high log octanol-water partition coefficients for PCDD/F compounds (see Table F, Appendix I) make the coefficients in the models unsuitable for PCDD/F flux prediction.

When the model estimates proved inappropriate for estimating dermal absorption, in vitro and in vivo experimental results with various species were combined and examined. Upon examination of the data, it appeared that skin permeation estimates based on rodent studies were significantly different than the human-based data. This observation was reinforced by Rahman et al. (1992) who found that the hairless mouse recorded a four-fold higher permeation rate of TCDD compared to human skin in vitro and thus concluded that hairless mouse skin is not a suitable model for human skin TCDD permeation. This factor was incorporated into the decision to use only human and porcine in vitro data to estimate skin absorption in this study.

Several assumptions accompanied the decision to use in vitro human and porcine experimental results to predict PCDD/F skin absorption. Porcine skin was assumed to be similar to human as reported by Meyer (1986). Human cadaver skin in vitro was also assumed to be representative of skin absorption in occupational circumstances. Weber (1993) demonstrated that viable versus non-viable skin did not produce a significant difference between rates of permeation, and metabolism in the skin is unlikely due to a slow rate of biotransformation of PCDD/F compounds.

Many of the in vitro experiments were performed on skin from the thigh and back region, which lead to an assumption that skin from this region was not significantly different from the skin exposed in the sawmill. However, the site of application has been demonstrated to have an effect on the extent of absorption (Maibach et al., 1971). It is possible that the use

of thigh and back skin may have overestimated absorption for regions such as the palm which reported slightly lower absorption (Maibach et al., 1971). If more exposure takes place on areas with high absorption, such as the face and scrotal areas, back and thigh estimates may underestimate absorption.

Further sources of uncertainty include assuming that the in vitro experimental results using 2,3,7,8-TCDD would appropriately represent all PCDD/F congeners. As mentioned earlier, physicochemical properties such as molecular weight, octanol water partition coefficient and solubility play significant roles governing absorption. The wide range of physicochemical values in PCDD/F compounds displayed in the tables of Appendix I suggest that each congener may, in fact, have quite different absorption characteristics. Comparative in vivo studies on rats have found that TCDF demonstrated significantly greater absorption than TCDD and two PeCDF congeners (Brewster et al., 1989).

Permeation of dioxins/furans across the epidermis is highly dependent on the formulation applied to the skin (Poiger and Schlatter, 1980). In the data used to estimate skin absorption, either mineral oil or acetone was used as a vehicle. Mineral oil has been shown to produce a much slower rate of penetration because it competes with the lipophilic components of the stratum corneum (Weber et al., 1991). The acetone vehicle evaporates quickly upon application and is used to simulate exposure to PCDD/F in the form of dust. In the case of the sawmill workers, the effect of water and chlorophenates as vehicles was not known,

therefore both the acetone and mineral oil vehicles were used in order to provide a broad range when estimating dermal absorption.

A further area of uncertainty in estimating skin absorption of PCDD/Fs is deciding at what point the PCDD/F compounds are considered to be "absorbed". The stratum corneum is generally considered to be the rate-limiting step for most hydrophilic compounds (Guy and Hadgraft, 1989), however, for highly lipophilic compounds such as PCDD/Fs, the epidermis has been suggested as the rate limiting step (Nemanic and Elias, 1980). Jackson et al. (1993) contend that the stratum corneum is in fact the crucial barrier and the rate-limiting step may be defined as either: (i) into and through the stratum corneum, or (ii) diffusion out of the stratum corneum and into the epidermis. In estimating dermal absorption, the amount of TCDD recovered in the stratum corneum and the epidermis were included to encompass the full range of potential absorption values. Amounts recovered in the epidermis with the stratum corneum removed were also included to represent dermal absorption in which damage to the stratum corneum may have taken place due to the nature of the work being performed by the sawmill employees.

It is apparent that many areas of uncertainty exist within the variable of skin absorption. As outlined in the sensitivity analysis, this variable plays a key role in determining the output of the model, and therefore inaccurate assumptions may have significant effects on the resulting predictions.

4.4.2 Elimination Rate Constant

The elimination rate constant has been identified as a significant variable in the sensitivity analysis, appearing within the top four variables of over half the congeners.

Generally, to estimate half-lives for compounds, numerous observations of concentration are noted over a period of time. The results of the observations are then graphed with the natural log of concentration versus time. Linear regression is then carried out to determine the slope of the line which corresponds to the elimination rate constant.

For compounds such as PCDD/Fs, body burden data is very intrusive and difficult to collect. For these reasons, estimates of the biological half-lives, and thus the elimination rate constants, of these compounds have often been made on the basis of only two measurements. Congeners which have had their half-lives estimated based on only two measurements include: TCDD (Wolfe et al., 1994; Pirkle et al., 1989); HxCDD, HpCDD, OCDD, HpCDF and OCDF (Gorski et al., 1984).

The measurement of concentration within the organism at any point in time involves a degree of analytical error. If the half-life or elimination rate constant is based on only two points, any inaccuracy could cause a large error in half-life estimates. Phillips (1989) demonstrated that as the time interval decreases between two measurements, the effect of analytical error increases on the variability of the half-life estimate increases. Phillips cautions that care should be taken interpreting half-life estimates based on two measurements at a short interval,

however, as the interval size increases the estimates may be adequate. Phillips notes that the assumption of no further exposure after the first concentration measurement may bias the half-life estimate upward for compounds such as PCDDs/Fs for which there is generally a continuous background exposure. If the initial measured concentration is high, then background exposure will have a negligible effect on the half-life estimate. However, if the initial concentration is in the range of normal background levels and a steady-state is maintained, then extremely high half-life estimates may result.

Phillips' (1989) results suggest that the Gorski et al. (1984) estimates for HxCDD, HpCDD, OCDD, HpCDF and OCDF should be approached with caution as they are based on one individual with a low chronic exposure to PCP found in preserved wood used in the construction of an apartment. The measurements were also taken within a 28-month interval, a relatively short time given the potential half-lives of the congeners.

Pirkle et al. (1989) and Wolfe et al. (1994) both based their half-life estimates for TCDD on two serum measurements taken over a 5-year interval. These estimates are based on a larger number of individuals sampled than Gorski et al., with 36 included in Pirkle et al. (1989) and 337 individuals included in Wolfe et al.(1994). Results from Poiger and Schlatter (1986) on the half-life of 2,3,7,8-TCDD following self-dosing involved 28 measurement points, however, these measurements were taken over a total time interval of 125 days, a relatively brief time considering the possible half-life of TCDD. When data from fat analyses for the same individual were carried out at five points over 2182 days, a significantly different half-

life estimate for 2,3,7,8-TCDD resulted (Schlatter, 1991). Further uncertainty is recognized in both the Poiger and Schlatter (1986) and Schlatter (1991) estimates because the measurements are from only one subject.

Other estimates of half-lives, including PeCDD, HxCDD, HpCDD, OCDD, TCDF and PeCDF, also possess a large amount of uncertainty because they are calculated values (Schlatter, 1991). Schlatter compared daily intake to the body burden relative to TCDD by estimating the intake of congeners relative to TCDD from their concentration in animal fat, while the relative body burden was represented by concentrations in breast milk.

Many of the half-life estimates for PCDFs possess less uncertainty. Estimates generated by Ryan et al. (1990) and Ryan and Masuda (1991) involved several individuals who were highly exposed during rice oil poisoning incidents. There were often more than two samples taken over an interval of between 2 and 9 years. Other estimates for PCDFs were taken from one individual exposed during a PCB cleanup operation. The estimates also involved a series of samples over up to six years (Schecter et al., 1990b).

Overall, the estimates of PCDD/F half-lives should be viewed with caution. The estimated half-lives of higher chlorinated dioxins have the highest risk of being inaccurate while higher chlorinated furans may be approached with somewhat more confidence.

4.4.3 TCP Contamination

TCP Contamination was one of the top four most influential variables on the predicted PCDD/F concentration in fat tissue using both the vapour and aerosol assumptions. The compilation 2,3,4,6-TCP contamination with dioxin compounds was from both Scandinavian and North American products, however the contamination data for PCDFs is based solely on Scandinavian products. The contamination levels reported by Firestone on the North American products were similar to those found in Scandinavian products, therefore, it was assumed that it is appropriate to include the Scandinavian data in the compilation. Other levels of dioxin contamination in North American chlorophenate products were reported by Singh (1987), however these levels represent products which were composed of both PCP and TCP; the compilation of PCP and TCP was accounted for elsewhere in the model, therefore these measurements were omitted.

There is a degree of uncertainty involved in determining the extent to which the levels of contamination measured in the late 1970s represent the formulations historically used in the sawmill industry. Since there had been no changes in the chlorophenol manufacturing process for the products used in the BC sawmill industry it was assumed that the levels of contamination remained constant during the period of their use in B.C. (Teschke et al., 1994).

As with any measurements, there is also a degree of uncertainty due to analytical error. However the results from all studies were relatively consistent, therefore this is likely to be low.

A point of concern regarding the TCP contamination data, arises from the lack of data arising from different sources, particularly for PCDFs. It appears that the high contamination values for HxCDF and HpCDF have played significant roles in making these congeners prominent in the predicted output values, however, the contamination estimates have originated from the same author (Rappe).

4.4.4 PCP Contamination

PCP contamination played a less significant role than TCP contamination in the sensitivity analysis, however, it was in the top four variables for OCDD and OCDF congeners in both the aerosol and vapour assumptions as well as being significant for HpCDD using the aerosol assumption.

Many reports have been compiled which list the contamination levels of PCP with dioxins and furans. The majority of the reports are based on results for Scandinavian or European products. The contamination levels recorded for Canadian and American products do fall within a similar range, therefore all results were included. Both technical PCP and NaPCP products were included in the overall contamination estimate. Given the considerable number and variety of PCP contamination reports, this variable considered to be relatively accurate.

Relative proportions of TCP and PCP in treatment solutions were estimated based on data collected in the 1980s. The application of this data to historic exposures is questionable

especially for the period prior to the introduction of TCP, when the formulations were primarily composed of PCP.

4.4.5 Duration of Employment/Time Exposed

The time of exposure and duration of employment in BC sawmills are correlated variables and came from the same source, therefore they will be examined together. Each of these variables were demonstrated in the sensitivity analysis to play relatively significant roles in determination of the predicted PCDD/F concentrations, using both the aerosol and vapour assumptions. It is important to note that the sensitivity calculation may be inaccurate for correlated variables. If an important variable is correlated with an unimportant one, the unimportant variable may be erroneously listed as one with high sensitivity (Crystal Ball, 1993). It is therefore difficult to distinguish if both variables are equally important, or if one is being portrayed as more sensitive due to the correlation.

The duration of working life in a sawmill was based on actual data collected from almost 24,000 sawmill workers in the province of B.C. The requirements for entry into the cohort excluded those working under a full year and those who did not work at a time when chlorophenates were being used. These restrictions excluded temporary or transient workers.

The total time exposed to chlorophenates was based on exposure estimates by worker raters. The validity and reliability of the worker estimates of exposure were compared to urinary levels of chlorophenates as well as to industrial hygienist ratings (Hertzman et al., 1988;

Teschke et al., 1989). The results of both studies suggest that the worker ratings were an effective form of estimating retrospective exposures.

An aspect of the time component which should be noted is that weekends were added to the total time worked component. The weekends were additional elimination periods during which no exposure was assumed to take place. The total time exposed included only exposure time at work.

Both the duration of time worked in a B.C. sawmill and time exposed variables are considered to be relatively accurate as they are based on actual data collected from the B.C. sawmill cohort, numbering over 23,000.

4.4.6 TCP/PCP Inhalation Exposure

The TCP/PCP inhalation exposure variables were only used for the aerosol assumption. TCP inhalation exposure was found in the top four factors of the sensitivity analysis of three congeners, PeCDD, PeCDF, HxCDF and HpCDF. PCP inhalation exposure was a relatively insignificant factor in the predicted PCDD/F concentration estimates for most congeners.

The basis of this variable is the assumption that the measured concentration of TCP, PCP or total chlorophenates in the air was in the form of an aerosol rather than vapour. Given this assumption, the aerosol droplets are then assumed to contain the same concentration of PCDD/Fs as that found in TCP and PCP spray and mix solutions.

The TCP/PCP air concentrations used in the analyses include results from sawmills in Scandinavia, northwest United States and British Columbia. This compilation covers several application techniques, various locations as well as seasonal variations. It is important to note that all but one set of measurements were taken during the 1980s, with Levin et al. (1976) being the exception. It was assumed that historical air concentrations would not be significantly different. All total chlorophenate air concentrations were also assumed to have relative ratios of PCP, TCP and H_2O similar to that found in three B.C. sawmills by BC Research (1986).

Generally, the TCP/PCP air concentration data appears to be somewhat reliable, with a relatively large number of results and a range of treatment systems represented (spraying and dipping). The lack of historic air concentration data does raise questions concerning how accurately the reported air concentrations reflect exposures prior to the 1980s.

A major flaw in this variable may result from the assumption of aerosol droplets containing equal amounts of PCDD/F as is measured in solution. PCDD/Fs are described in the Introduction of having low water solubility, therefore, it is possible that when water is added to PCP/TCP, PCDD/Fs will collect in sludge below the liquid formulation as noted by Levin et al. (1976).

4.4.7 Percentage Fat/Mass of Adult Male

As with the duration of working life in sawmill/time exposed variables, these variables were correlated and will be discussed together. In the sensitivity analysis, the percentage fat variable was consistently found to have more of an effect on output than adult male mass. This suggests that the importance of the male mass variable may be artificially inflated due to the correlation with percentage fat.

The possible values of percentage fat was distributed lognormally rather than normally in the Monte Carlo analysis to avoid abnormally low fat levels being used in the analysis. These percentages represent the entire content of fat or lipids in the body.

The sources of both the percentage fat and mass in adult males were generally North American or British populations. Some studies made efforts to represent the target population in age and size (ICRP, Pheasant, and Documenta Geigy). However, Durnin and Womersley (1973) however did not attempt a random sample of the population and reported having a preponderance of sedentary, middle-class individuals although a variety of body types were represented. The ethnicity of the study sawmill population was mainly white, with a small proportion workers of Chinese and East Indian origin.

The distributions of percentage fat and body mass produced from the literature data are considered to be relatively close reflections of the population included in the cohort.

4.4.8 TCP/PCP Patch Data

The TCP and PCP patch data have been shown by the sensitivity charts to have a moderate effect on the output. Of all patch results, TCP leg exposure was usually the most outstanding, except for OCDD (aerosol and vapour) in which PCP leg exposure was primary. The uncertainties involved in all the TCP and PCP patch results will be examined together.

The dermal patch results used in the analyses were assumed to represent deposition of TCP or PCP over the body region where the patch was located. The patch results were then extrapolated to the surface area of the body region to estimate total dermal exposure. This assumption has been questioned by Fenske et al., (1985) who demonstrated that the distribution of pesticide compounds was not uniform over a given anatomical region, but was highly dependent on the work or activity being performed. Nonuniform pesticide deposition across body regions has also been demonstrated with other studies utilizing the patch technique (Wolfe et al., 1967; Wojeck et al., 1981). In dermal exposure assessment, it is generally more common to have a "hot spot" thus extrapolation from the patch may underestimate exposure if it does not represent a high exposure spot, or else may overestimate exposure if the patch were located at the spot of highest exposure (Fenske et al., 1985).

All patch results used in the BC Research (1986) study were used in the exposure estimate. It was assumed that the patches worn on the outside of clothing would represent the higher possible exposures, which may have taken place prior to the introduction of personal protective equipment such as gloves and aprons. The leg exposure estimates which

demonstrated the most significant effects on the output, were all based on patches worn outside clothing, which may have overestimated exposure. It is traditionally assumed, using the patch technique, that clothing penetration does not occur or does not contribute significantly to total exposure. However, Fenske et al. (1985) used fluorescent tracer data to demonstrate that this assumption may be inappropriate. The assumption of full penetration through clothing used in the analysis is therefore accompanied by a large degree of uncertainty and potential variability.

The patch results used in this study were taken from three individuals performing very different tasks. The sampling was performed during one shift, at one mill. Estimating exposure to air components generally involves variation of exposure over time and between workers (Rappaport, 1992). In addition to this, variability in dermal exposure estimates may also be a result of individual work practices and hygienic behaviour. It is therefore to be expected that both within- and between-person variability of dermal exposure estimates would be greater than that of corresponding respiratory exposures (Fenske, 1993). It is recognized that the patch results used in this model may not represent the true variability of dermal exposure in the sawmill workforce. These variables were not of primary importance in the sensitivity analysis, but this may in part be a result of the limited variability in the empirical data used.

In summary, there are enormous sources of variability in this data. The patch sampling technique itself incorporates assumptions which have been proven to be erroneous in other

studies. The sampling was performed on few individuals during one shift and does not begin to examine the potential within- and between-person variability in the exposure estimates. The results also do not reflect the influence of factors such as: personal hygiene, use of personal protective equipment, type of antisapstain treatment system used, as well as potential differences in historic exposures. This data also does not reflect the different exposures associated with different duties.

4.4.9 Fenske Arm Exposure Estimates

Fenske et al. (1987) estimated dermal exposure using a fluorescent tracer with a computer-based video imaging system. As with the McDonald data, measurements were performed on one day only, therefore any day-to-day variability was not accounted for. The sampling was carried out on seven pullers and two graders, however the exposure estimates were restricted to pullers only. The study was also limited to one mill.

The basis of video imaging technique involves scanning the skin surface with a camera which digitizes the light intensity of the fluorescent tracer found on the skin. Accurate estimates of chemical on the skin requires two calibration factors: (1) an accurate description of the relationship between the light intensity detected and the amount of fluorescent material and (2) the ability of the fluorescent tracer to accurately reflect the disposition of the chemical of interest (Fenske et al., 1986). Fenske et al. (1986a) noted that the fluorescent tracer and the compound of interest may differ in their ability to penetrate fabric, since penetration may be dependent on particle size, solubility or other chemical properties.

Other limitations which may be noted with the fluorescent tracer-video imaging technique include: (1) the tracer requires the introduction of a foreign substance into the production system; (2) the relative transfer of the tracer and the chemical of interest must be demonstrated during field investigations; and (3) additional quality assurance steps may be required during field studies, including range-finding and the evaluation of potential tracer degradation due to sunlight (Fenske, 1993).

When video imaging analysis was carried out on the seven pullers, exposure was only noted on the forearms and hands. It is possible that the fluorescent tracer technique underestimated exposure because of a high detection limit which may have left a substantial amount of dermal exposure undetected (Fenske et al., 1987). Underestimates of exposure may have also been caused by the clothing or fabrics worn by the workers, which limited the effectiveness of the fluorescent tracer.

It appears that the Fenske dermal exposure data suffer from similar shortfalls as the McDonald data. Few individuals were sampled during only one shift at one mill. These circumstances raise many questions concerning the validity of the measurements obtained. The effects of factors such as: different treatment systems, personal hygiene, personal protective equipment, as well as historic exposures were not able to be revealed in this data.

4.4.10 Surface Areas

The mean surface area for the arms used in the analysis corresponded to the area of the forearms. Various studies have demonstrated that the hands and forearms are the most exposed areas in workers such as pullers and graders. Fluorescent tracer used by BC Research (1987) demonstrated gross contamination of the front and back of gloves and mitts in graders and chainmen. Fenske et al. (1987) also reported exposure to the hands despite constant use of chemical resistant gloves, using the fluorescent tracer techniques. Fenske also reported that forearm exposure was related to worker activity, with graders not experiencing measurable exposure in the forearms, while all pullers examined were exposed in this region. Klienman et al. (1986) also reported observations of contaminated forearms of hula sawyers (and chain pullers) in a Washington sawmill. The distribution of arm surface area used in the analysis was thought to reflect potential exposed areas for more recent exposures above glove cuffs, etc., as well as to attempt to estimate historic exposures prior to personal protective equipment use in which the majority of surface area of the hands would be exposed as well as part of the forearms.

The mean exposed surface area of the chest was estimated at approximately one-half the frontal area. It has been noted that with pullers, the area from waist to mid-chest can be heavily contaminated (Forest Industry Health Research Program, 1989).

It was assumed in the analysis that mean exposed surface area of the legs would be based on the frontal area. The fact that graders and pullers began to wear waist-high leather aprons as

personal protective equipment emphasized that historically, the upper frontal thigh was probably an area of high exposure. The leg patch results obtained by BC Research (1986) also suggests that even wearing aprons, exposure may take place on uncovered areas on the lower legs.

The surface areas may best reflect potential exposure areas for sawmill workers such as pullers, rather than carrier drivers or other chlorophenate-exposed workers. With this in mind, the surface areas are felt to describe potentially exposed areas relatively accurately, however, the general applicability of these areas may be questioned.

4.4.11 Inhalation Rate

The inhalation rate variable had a moderate effect on the most predicted PCDD/F concentrations under the aerosol assumption, with the exceptions of OCDD and OCDF where it had little if any effect. Using the vapour assumption, inhalation rate had virtually no effect on output. The ranges of breathing rates for the average adult man were obtained from Reference Man (ICRP, 1975). The triangular distribution used in the analysis identified minimum, maximum and likeliest values which were assumed to apply in the situation of a sawmill worker.

4.4.12 Inhalation Absorption

Inhalation absorption had relatively little effect on the predicted PCDD/F concentrations based on the sensitivity analysis. Therefore, the assumption of a respiratory absorption efficiency

similar to a gastrointestinal absorption efficiency is not considered to be a significant point of uncertainty.

4.4.13 Vapour Inhalation

The vapour concentrations calculated for each of the congeners under the vapour assumption had virtually no effect on the output. It was assumed that the PCDD/Fs in the chlorophenate mixture would follow Raoult's Law and act as ideal gases. This assumption may be erroneous as the concentrations of the PCDD/Fs in the chlorophenate mixture were extremely small, and Henry's Law is considered more appropriate for dilute solutions in non-ideal situations. Henry's Law was not originally used in this situation as it generally applies to a substance with high vapour pressure, such as a gas dissolved in a liquid. In addition, very little information was available on Henry's Law constants for PCDD/F compounds. The results of potential vapour concentrations were surprising given the extremely low vapour pressures outlined in Table D, Appendix I.

Both impingers and bubblers were used as techniques for sampling air concentrations of chlorophenates therefore neither the aerosol nor vapour assumption could be easily dismissed. Other attempts were made to determine whether airborne chlorophenates were likely to be from aerosol or vapour. The potential vapour concentrations of TCP and PCP were calculated using Raoult's Law for the vapour pressures of mixtures of solvents above a liquid. Using reported vapour pressures for PCP and TCP and basing the molar fraction on the concentration of PCP, TCP and H_2O in spray and dip solutions from three mills reported by

BC Research (1986), the calculated partial pressures were compared to the measured air concentrations in Tables 2.14, 2.15 and 2.16. The calculated vapour concentrations were within the range of the measured concentrations, therefore the possibility that the airborne TCP/PCP concentrations were in vapour form could not be ruled out. It should be noted that there was a great deal of uncertainty in the calculation of the partial pressures of TCP and PCP above the mixture. It was assumed that the chlorophenate mixture followed Raoult's law and the vapours acted as ideal gases. It is also assumed that concentration measurements taken by BC Research are representative of the formulations used in the mills where air measurements were taken. Finally, the vapour pressures used in the calculations were for TCP and PCP compounds rather than for their sodium salts which would have been more appropriate. Given these uncertainties, it could not be determined with certainty whether or not the measured air concentrations of PCP and TCP were aerosol or vapour. For this reason, both assumptions were examined.

Overall, there is considerable potential variability in the calculations of both TCP/PCP vapour concentrations and PCDD/F vapour concentrations. However, given the uncertainty, a maximum predicted PCDD/F vapour concentration is still expected to be quite low and thus did not have a significant effect on the predicted PCDD/F concentration.

4.5 Model Uncertainty

As noted by William and Leggett (1984), the best way to gain understanding of the inaccuracy and uncertainty in a predictive model is to compare actual data with model

predictions in a formal statistical analysis. In this model, direct comparisons are not possible. However, the evaluation of uncertainty of each variable used in the model is thought to help to outline general model uncertainty.

Probability-based techniques such as the Monte Carlo analysis allows for consideration of a range of probable values for variables rather than point estimates which provide no quantitative information regarding uncertainty. The Monte Carlo approach has been heralded as one of the most important advances in exposure assessment of the past 20 years (Copeland et al., 1993). Although the distributions used to characterize the data may also result in inaccuracy in the model output, Copeland et al. (1993) have noted that the impact of imprecise distributions has minimal impact on the output. To ensure that additional iterations would not alter results, 5000 iterations were used in this analysis as recommended in McKone and Bogen (1991). Uncertainty in the output of the model used in this study would be reduced through further information on the distribution of the variables, especially those demonstrated in the sensitivity analyses as having significant effects on the output.

4.6 Conclusions

In summary, the model predictions suggest that HxCDF and HpCDF concentrations in the fat tissue due to chlorophenate exposure in sawmills were in the range of 4 to 5 times normal background levels. Elevated levels of HxCDF and HpCDF begin around the 30th percentile of predicted concentrations. OCDF, PeCDD and PeCDF demonstrate elevated concentrations at higher percentiles of predicted concentrations, while most congeners were estimated to

have above normal levels for only those sawmill workers estimated to be extremely highly exposed (90th percentile and above).

The sensitivity analysis identified skin absorption, the elimination rate constant, TCP/PCP contamination and duration of time worked/time exposed as the primary variables determining the predicted PCDD/F fat concentrations. The input parameters of estimated dermal TCP and PCP exposure also played an important role. These variables formed a basic input into the model and, as outlined in the Discussion, possess a great deal of uncertainty. Given this uncertainty as well as that of the other variables and their associated assumptions (examined in the Discussion), it is reasonable to assume that the output of this model suffers from the same uncertainty. However, given these qualifiers, this model may serve to demonstrate general trends associated with PCDD/F exposure in a sawmill, such as only subsets of the sawmill population appear to have PCDD/F levels above background, except for higher levels of Hx- and HpCDFs.

The model requires further validation, ideally from measurement of PCDD/Fs in the tissue of B.C. sawmill workers. PCDD/F concentration measurements should be accompanied by a detailed exposure history. The model could also be expanded to include background exposure to PCDD/F due to diet as an input variable, however this could also result in increasing uncertainty. A possibility for further work may be to improve the model by quantifying PCDD/F exposure using urinary chlorophenate levels rather than dermal and inhalation

exposure data. Urinary chlorophenate levels has been regularly collected and also reflect an actual absorbed dose of chlorophenates.

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APPENDIX I

PCDD/F PHYSICOCHEMICAL CONSTANTS

Table A: Molecular Weights of PCDD/F Congeners

Congener	Molecular Weight
TCDD	322.0
PeCDD	356.4
HxCDD	391.0
HpCDD	425.2
OCDD	460.0
TCDF	306.0
PeCDF	340.4
HxCDF	374.9
HpCDF	409.3
OCDF	443.8

Table B: Melting Points of PCDD/F Congeners

Isomer	Melting Point (°C)	References
TCDD		
1,2,3,4-	190	Poland & Yang, 1972
1,2,3,7-	172	Friesen et al., 1985
1,3,6,8-	219	Pohland & Yang, 1972
2,3,7,8-	303-306	Pohland & Yang, 1972
	"	Crummett & Stehl, 1973
	"	Branson et al, 1985
	320-325	Merck Index, 1989
PeCDD		
1,2,3,4,7-	195	Pohland & Yang, 1972
	188	Friesen & Webster, 1990
HxCDD		
1,2,3,4,7,8-	273	Pohland & Yang, 1972
HpCDD		
1,2,3,4,7,8-	265	Shiu et al, 1988
OCDD	330	Pohland & Yang, 1972
	322	Shiu et al, 1987
TCDF		
2,3,7,8-	227	Gray et al, 1976
	219	Kuroki et al, 1984

Isomer	Melting Point (°C)	References
PeCDF		
2,3,4,7,8-	196	Kuroki et al, 1984
	"	Rordorf, 1989
HxCDF		
1,2,3,4,7,8-	225.5	Kuroki et al, 1984
HpCDF		
1,2,3,4,6,7,8-	236-237	Kuroki et al, 1984
1,2,3,4,7,8,9-	221-223	Kuroki et al, 1984
OCDF	330	Doucette, 1985
	258-260	Rordorf, 1986, 1989

Table C: Boiling Points of PCDD/F Congeners

Isomer	Boiling Point (°C)	References
TCDD		
1,2,3,4-	419	Rordorf, 1987, 1989
1,2,3,7-	438.3	Rordorf, 1987, 1989
1,3,6,8-	438.3	Rordorf, 1987, 1989
2,3,7,8-	421.2	Schroy et al, 1985a
	446.5	Rordorf, 1986, 1987, 1989
PeCDD		
1,2,3,4,7-	464.7	Rordorf, 1987,1989
HxCDD		
1,2,3,4,7,8-	487.7	Rordorf, 1987, 1989
HpCDD		
1,2,3,4,7,8-	507.2	Rordorf, 1987, 1989
OCDD	510	Rordorf, 1987, 1989
TCDF		
2,3,7,8-	438.3	Rordorf, 1987, 1989
PeCDF		
2,3,4,7,8-	464.7	Rordorf, 1989
HxCDF		
1,2,3,4,7,8-	487.7	Rordorf, 1989
HpCDF		
1,2,3,4,6,7,8-	507.2	Rordorf, 1989
1,2,3,4,7,8,9-	"	Rordorf, 1989
OCDF	510	Rordorf, 1986
	537	Rordorf, 1989

Table D:PCDD/F Ranges of Vapour Pressures (mm Hg)- Experimental and Calculated

Congener	Vapour Pressure Range (mm Hg)	References
TCDD	7.4×10^{-10} - 4.03×10^{-6}	Eitzer & Hites, 1988 Eitzer & Hites, 1988
PeCDD	4.35×10^{-10} - 7.52×10^{-9}	Eitzer & Hites, 1988 Rordorf et al., 1986, 1990
HxCDD	3.84×10^{-11} - 2.9×10^{-8}	Rordorf, 1985 a, b., 1987, 1989 Eitzer & Hites, 1988
HpCDD	5.62×10^{-10} - 7.71×10^{-9}	Eitzer & Hites, 1988 Eitzer & Hites, 1988
OCDD	8.25×10^{-13} - 1.35×10^{-7}	Eitzer & Hites, 1988 Dobbs & Cull, 1982
TCDF	8.96×10^{-9} - 9.2×10^{-7}	Eitzer & Hites, 1988 Eitzer & Hites, 1988
PeCDF	4.28×10^{-9} - 1.63×10^{-7}	Eitzer & Hites, 1988 Eitzer & Hites, 1988
HxCDF	6.69×10^{-10} - 6.1×10^{-8}	Rordorf et al., 1990 Eitzer & Hites, 1988
HpCDF	3.53×10^{-11} - 1.45×10^{-8}	Eitzer & Hites, 1988 Eitzer & Hites, 1989
OCDF	3.75×10^{-12} - 7.6×10^{-9}	Eitzer & Hites, 1988 Etizer & Hites, 1989

Table E:PCDD/F values for Water Solubility (mg/L)

Congener	Water Solubility (mg/L)	References
TCDD		
1,2,3,4-	4.7×10^{-4}	Doucette & Andren, 1988
1,2,3,7-	4.2×10^{-4}	Friesen et al., 1985
1,3,6,8-	3.2×10^{-4}	Friesen et al., 1985
2,3,7,8-	2.0×10^{-4}	Crummett & Stehl, 1973
	1.93×10^{-5}	Marple et al., 1986
	7.91×10^{-6}	Adams & Blaine, 1986
PeCDD		
1,2,3,4,7-	1.2×10^{-4}	Friesen et al, 1985
HxCDD		
1,2,3,4,7,8-	4.4×10^{-6}	Friesen et al., 1985

Congener	Water Solubility (mg/L)	References
HpCDD 1,2,3,4,6,7,8-	2.4×10^{-6}	Friesen et al., 1985
OCDD	4.0×10^{-7} 7.4×10^{-8}	Friesen et al., 1985 Doucette & Andren, 1988
TCDF 2,3,7,8-	4.2×10^{-4}	Friesen et al., 1990
PeCDF 2,3,4,7,8-	2.4×10^{-4}	Friesen et al., 1990
HxCDF 1,2,3,4,7,8-	8.25×10^{-6}	Friesen et al., 1990
HpCDF 1,2,3,4,6,7,8-	1.35×10^{-6}	Friesen et al., 1990
OCDF	1.16×10^{-6}	Friesen et al., 1990

Table F:PCDD/F Ranges of Log Octanol/Water Partition Coefficients

Congener	Range Log Octanol/Water Partition Coefficient	References
TCDD	5.5 - 8.93	Shiu et al., 1988 Sarna et al., 1984
PeCDD	7.44 - 10.05	Burkhard & Kuehl, 1986 Sarna et al., 1984
HxCDD	7.79 - 10.89	Burkhard & Kuehl, 1986 Sarna et al., 1984
HpCDD	7.92 - 11.98	Sijm et al., 1989 Sarna et al., 1984
OCDD	7.53 - 13.08	Doucette & Andren, 1988 Sarna et al., 1984
TCDF	5.82 - 6.53	Burkhard & Kuehl, 1986 Sijm et al., 1989
PeCDF	6.79 - 6.92	Sijm et al., 1989 Sijm et al., 1989
HxCDF	7.70	Broman et al., 1991
HpCDF	7.92	Sijm et al., 1989
OCDF	6.90 - 8.78	Broman et al., 1991 Burkhard & Kuehl (1986)

APPENDIX II

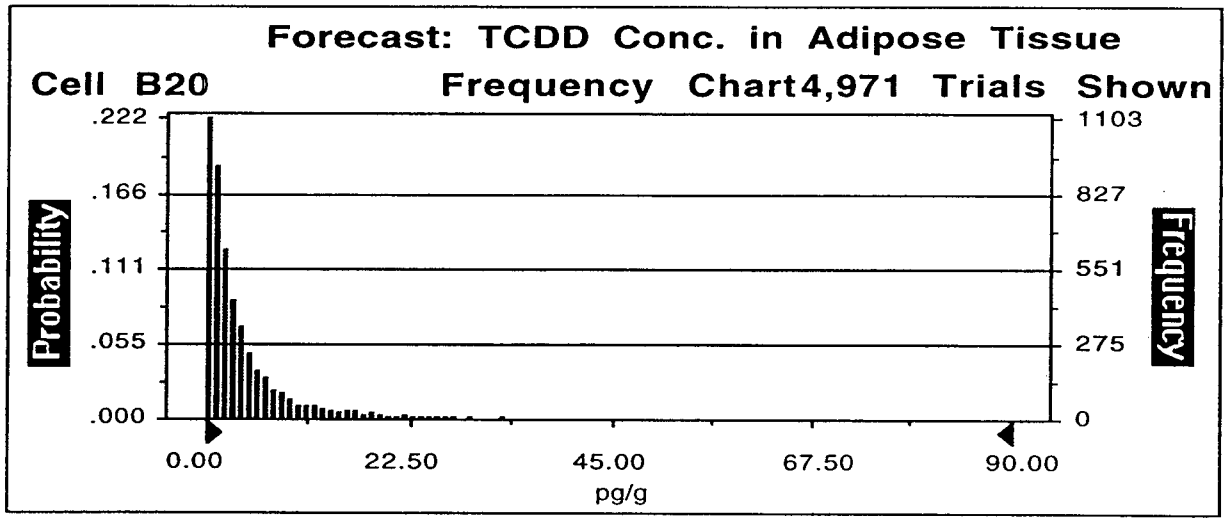
MODEL OUTPUT REPORTS: AEROSOL ASSUMPTION

Forecast: TCDD Conc. in Adipose Tissue **Cell: B20**

Summary:

Display Range is from 0.00 to 90.00 pg/g
Entire Range is from 0.00 to 1,284.30 pg/g
After 5,000 Trials, the Std. Error of the Mean is 0.40

Statistics for Display Range:	Value
Trials	4971
Mean	5.20
Median	2.41
Mode	---
Standard Deviation	8.18
Variance	66.90
Skewness	3.96
Kurtosis	24.67
Coeff. of Variability	1.57
Range Minimum	0.00
Range Maximum	90.00
Range Width	90.00
Mean Std. Error	0.12



Forecast: TCDD Conc. in Adipose Tissue (cont'd) **Cell: B20**

Percentiles for Display Range:

Percentile	pg/g
0%	0.00
10%	0.46
20%	0.81
30%	1.21
40%	1.77
50%	2.41
60%	3.35
70%	4.62
80%	6.95
90%	12.81
100%	85.31

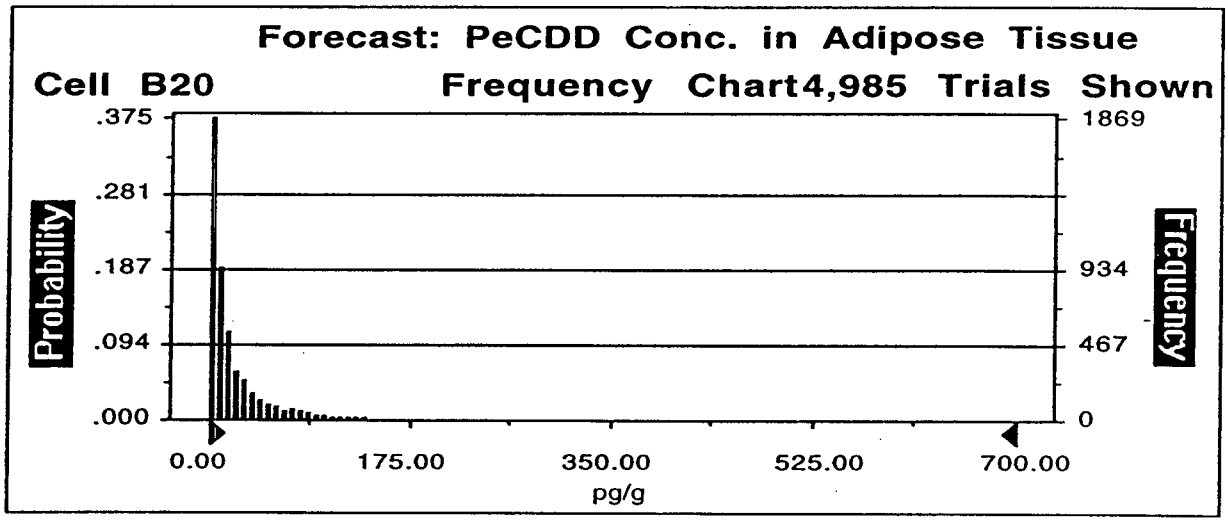
End of Forecast

Forecast: PeCDD Conc. in Adipose Tissue **Cell: B20**

Summary:

Display Range is from 0.00 to 700.00 pg/g
Entire Range is from 0.00 to 14,347.22 pg/g
After 5,000 Trials, the Std. Error of the Mean is 3.36

Statistics for Display Range:	Value
Trials	4985
Mean	28.73
Median	11.07
Mode	---
Standard Deviation	54.87
Variance	3,010.54
Skewness	5.37
Kurtosis	43.40
Coeff. of Variability	1.91
Range Minimum	0.00
Range Maximum	700.00
Range Width	700.00
Mean Std. Error	0.78



Forecast: PeCDD Conc. in Adipose Tissue (cont'd) **Cell: B20**

Percentiles for Display Range:

Percentile	pg/g
0%	0.00
10%	1.69
20%	3.26
30%	5.25
40%	7.73
50%	11.07
60%	15.54
70%	23.22
80%	36.96
90%	71.51
100%	660.36

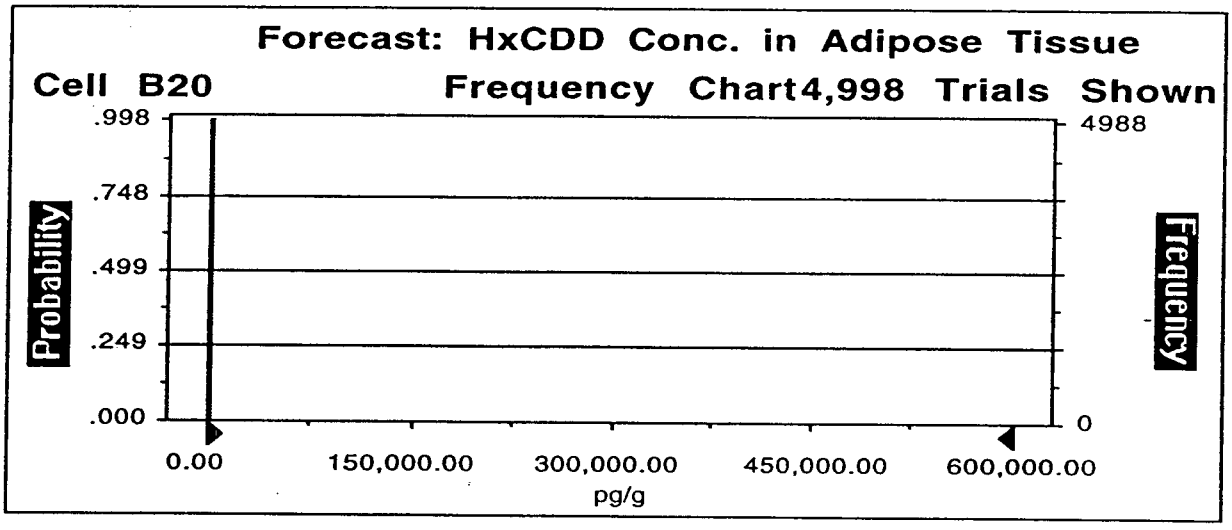
End of Forecast

Forecast: HxCDD Conc. in Adipose Tissue **Cell: B20**

Summary:

Display Range is from 0.00 to 600,000.00 pg/g
Entire Range is from 0.00 to 14,814,784.62 pg/g
After 5,000 Trials, the Std. Error of the Mean is 3,007.17

Statistics for Display Range:	Value
Trials	4998
Mean	208.31
Median	18.12
Mode	---
Standard Deviation	6,992.97
Variance	48,901,695.91
Skewness	66.98
Kurtosis	4,626.03
Coeff. of Variability	33.57
Range Minimum	0.00
Range Maximum	600,000.00
Range Width	600,000.00
Mean Std. Error	98.92



Forecast: HxCDD Conc. in Adipose Tissue (cont'd) **Cell: B20**

Percentiles for Display Range:

Percentile	pg/g
0%	0.00
10%	0.53
20%	3.05
30%	6.69
40%	11.21
50%	18.12
60%	27.10
70%	42.84
80%	72.59
90%	141.97
100%	485,047.72

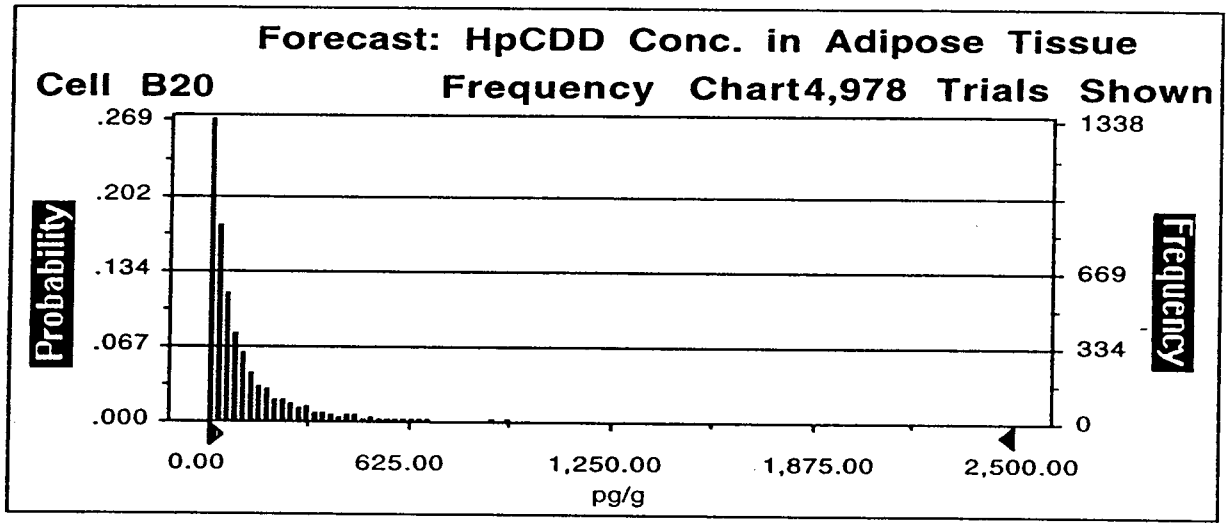
End of Forecast

Forecast: HpCDD Conc. in Adipose Tissue **Cell: B20**

Summary:

Display Range is from 0.00 to 2,500.00 pg/g
Entire Range is from 0.00 to 50,989.77 pg/g
After 5,000 Trials, the Std. Error of the Mean is 11.46

Statistics for Display Range:	Value
Trials	4978
Mean	141.06
Median	61.64
Mode	---
Standard Deviation	232.35
Variance	53,986.20
Skewness	3.95
Kurtosis	23.51
Coeff. of Variability	1.65
Range Minimum	0.00
Range Maximum	2,500.00
Range Width	2,500.00
Mean Std. Error	3.29



Forecast: HpCDD Conc. in Adipose Tissue (cont'd) **Cell: B20**

Percentiles for Display Range:

Percentile	pg/g
0%	0.00
10%	8.42
20%	17.84
30%	29.03
40%	42.41
50%	61.64
60%	86.92
70%	124.92
80%	194.58
90%	338.82
100%	2,230.55

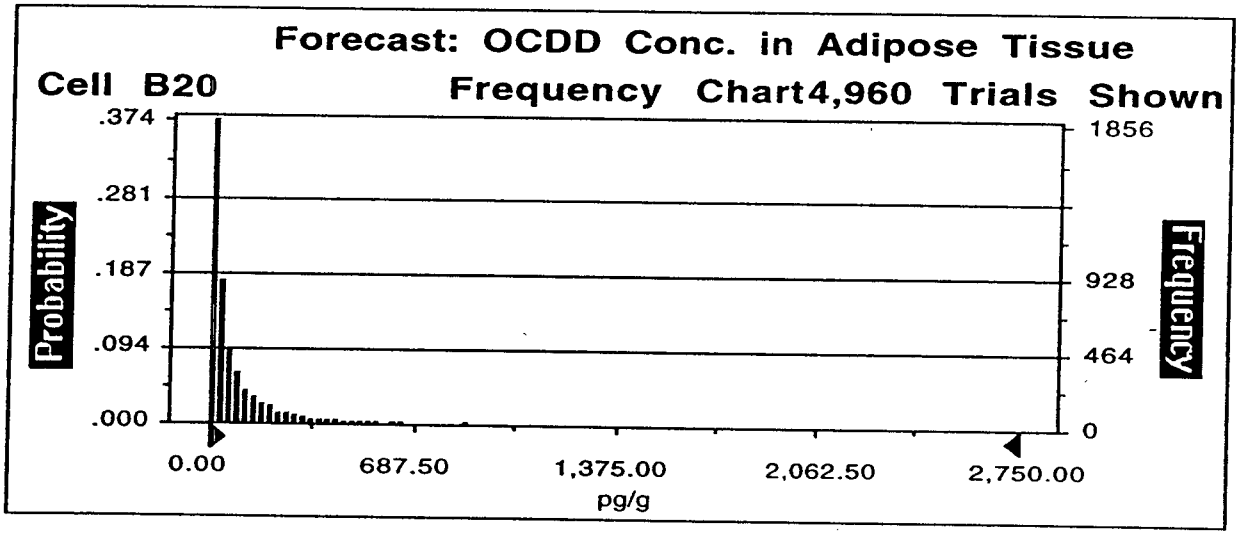
End of Forecast

Forecast: OCDD Conc. in Adipose Tissue **Cell: B20**

Summary:

Display Range is from 0.00 to 2,750.00 pg/g
Entire Range is from 0.00 to 36,063.40 pg/g
After 5,000 Trials, the Std. Error of the Mean is 12.57

Statistics for Display Range:	Value
Trials	4960
Mean	142.20
Median	44.24
Mode	---
Standard Deviation	282.97
Variance	80,069.33
Skewness	4.41
Kurtosis	27.42
Coeff. of Variability	1.99
Range Minimum	0.00
Range Maximum	2,750.00
Range Width	2,750.00
Mean Std. Error	4.02



Forecast: OCDD Conc. in Adipose Tissue (cont'd) **Cell: B20**

Percentiles for Display Range:

Percentile	pg/g
0%	0.00
10%	5.85
20%	11.96
30%	19.93
40%	30.37
50%	44.24
60%	66.63
70%	104.66
80%	173.82
90%	350.99
100%	2,656.27

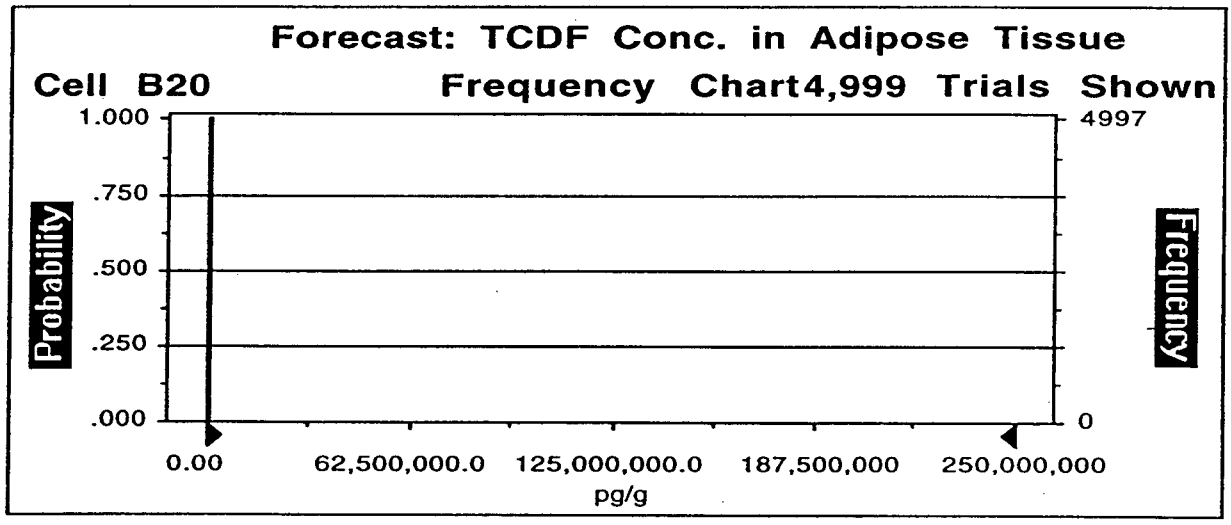
End of Forecast

Forecast: TCDF Conc. in Adipose Tissue **Cell: B20**

Summary:

Display Range is from 0.00 to 250,000,000.00 pg/g
Entire Range is from 0.00 to 6,377,881,330.37 pg/g
After 5,000 Trials, the Std. Error of the Mean is 1,275,589.93

Statistics for Display Range:	Value
Trials	4999
Mean	8,014.72
Median	0.83
Mode	---
Standard Deviation	441,363.88
Variance	1.95E+11
Skewness	62.21
Kurtosis	4,054.29
Coeff. of Variability	55.07
Range Minimum	0.00
Range Maximum	250,000,000.00
Range Width	250,000,000.00
Mean Std. Error	6,242.45



Forecast: TCDF Conc. in Adipose Tissue (cont'd) **Cell: B20**

Percentiles for Display Range:

Percentile	pg/g
0%	0.00
10%	0.00
20%	0.05
30%	0.18
40%	0.42
50%	0.83
60%	1.47
70%	2.74
80%	5.25
90%	13.62
100%	29,520,916.99

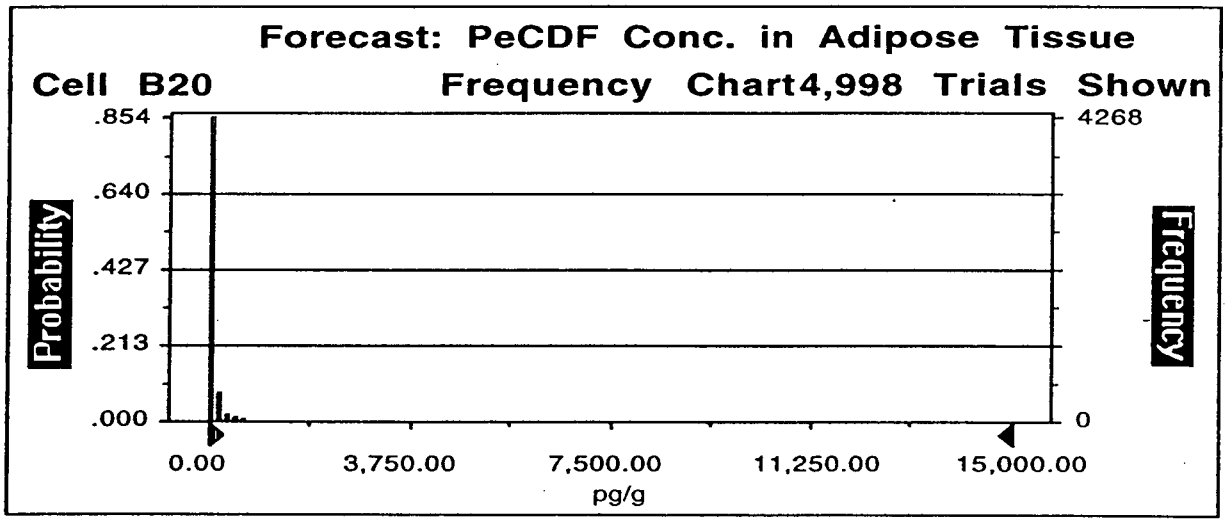
End of Forecast

Forecast: PeCDF Conc. in Adipose Tissue **Cell: B20**

Summary:

Display Range is from 0.00 to 15,000.00 pg/g
Entire Range is from 0.00 to 368,337.71 pg/g
After 5,000 Trials, the Std. Error of the Mean is 74.56

Statistics for Display Range:	Value
Trials	4998
Mean	94.61
Median	31.99
Mode	---
Standard Deviation	286.17
Variance	81,895.02
Skewness	17.82
Kurtosis	507.23
Coeff. of Variability	3.02
Range Minimum	0.00
Range Maximum	15,000.00
Range Width	15,000.00
Mean Std. Error	4.05



Forecast: PeCDF Conc. in Adipose Tissue (cont'd) **Cell: B20**

Percentiles for Display Range:

Percentile	pg/g
0%	0.00
10%	3.14
20%	8.43
30%	14.48
40%	21.77
50%	31.99
60%	47.66
70%	69.79
80%	111.29
90%	209.61
100%	10,705.08

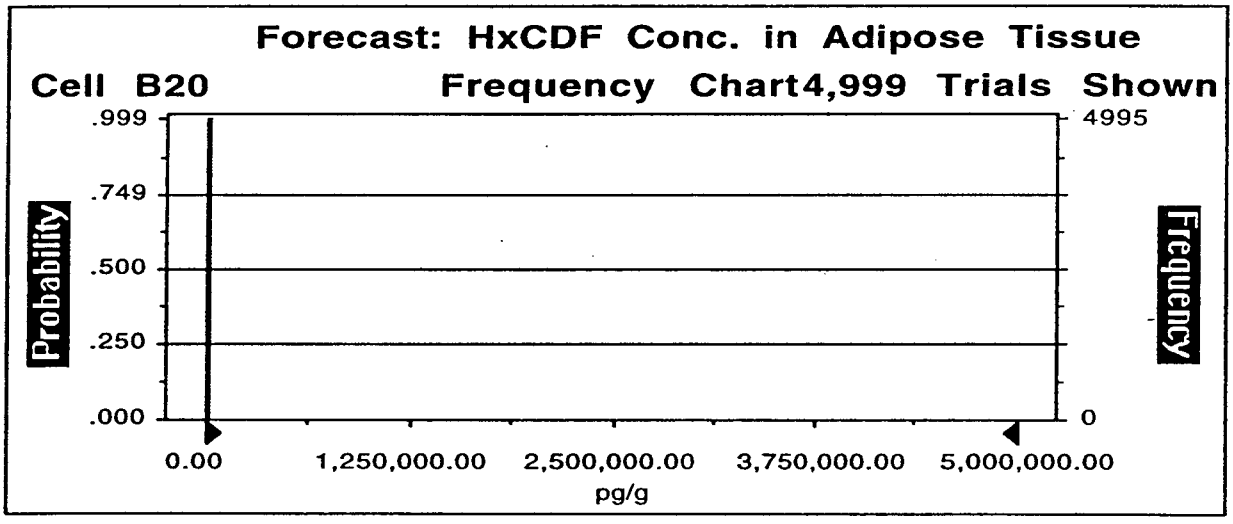
End of Forecast

Forecast: HxCDF Conc. in Adipose Tissue **Cell: B20**

Summary:

Display Range is from 0.00 to 5,000,000.00 pg/g
Entire Range is from 0.00 to 129,666,076.62 pg/g
After 5,000 Trials, the Std. Error of the Mean is 25,933.27

Statistics for Display Range:	Value
Trials	4999
Mean	797.11
Median	260.07
Mode	---
Standard Deviation	7,368.94
Variance	54,301,265.91
Skewness	54.61
Kurtosis	3,401.41
Coeff. of Variability	9.24
Range Minimum	0.00
Range Maximum	5,000,000.00
Range Width	5,000,000.00
Mean Std. Error	104.22



Forecast: HxCDF Conc. in Adipose Tissue (cont'd) **Cell: B20**

Percentiles for Display Range:

Percentile	pg/g
0%	0.00
10%	33.84
20%	76.73
30%	121.35
40%	181.07
50%	260.07
60%	354.64
70%	497.80
80%	751.95
90%	1,333.08
100%	472,950.21

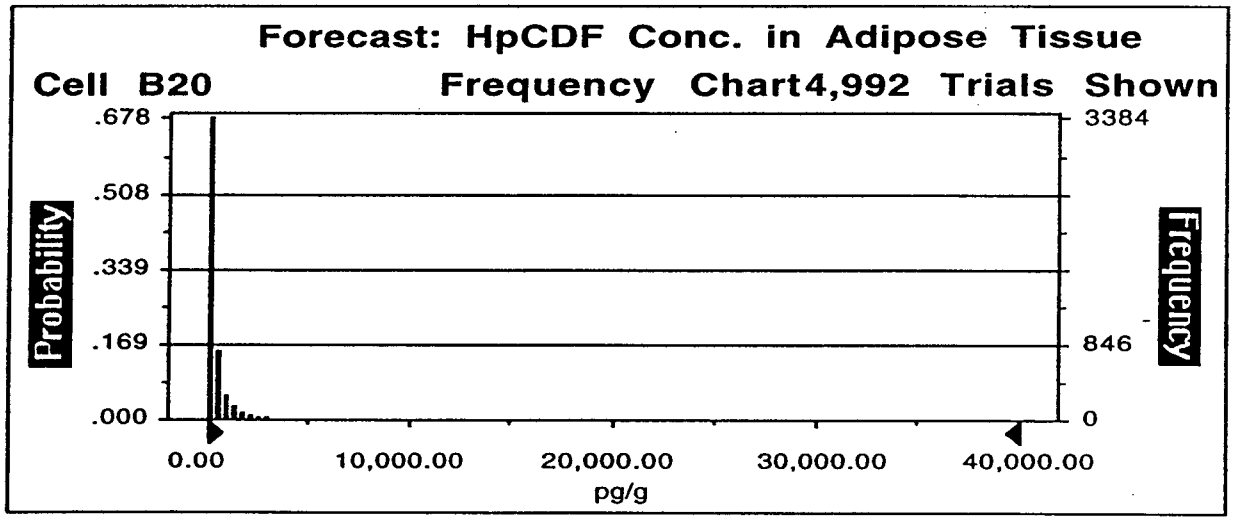
End of Forecast

Forecast: HpCDF Conc. in Adipose Tissue **Cell: B20**

Summary:

Display Range is from 0.00 to 40,000.00 pg/g
Entire Range is from 0.00 to 840,590.35 pg/g
After 5,000 Trials, the Std. Error of the Mean is 185.31

Statistics for Display Range:	Value
Trials	4992
Mean	579.31
Median	202.50
Mode	---
Standard Deviation	1,544.89
Variance	2,386,699.89
Skewness	11.17
Kurtosis	190.65
Coeff. of Variability	2.67
Range Minimum	0.00
Range Maximum	40,000.00
Range Width	40,000.00
Mean Std. Error	21.87



Forecast: HpCDF Conc. in Adipose Tissue (cont'd) **Cell: B20**

Percentiles for Display Range:

Percentile	pg/g
0%	0.00
10%	13.16
20%	48.32
30%	89.14
40%	139.08
50%	202.50
60%	298.86
70%	439.20
80%	663.85
90%	1,252.91
100%	39,834.03

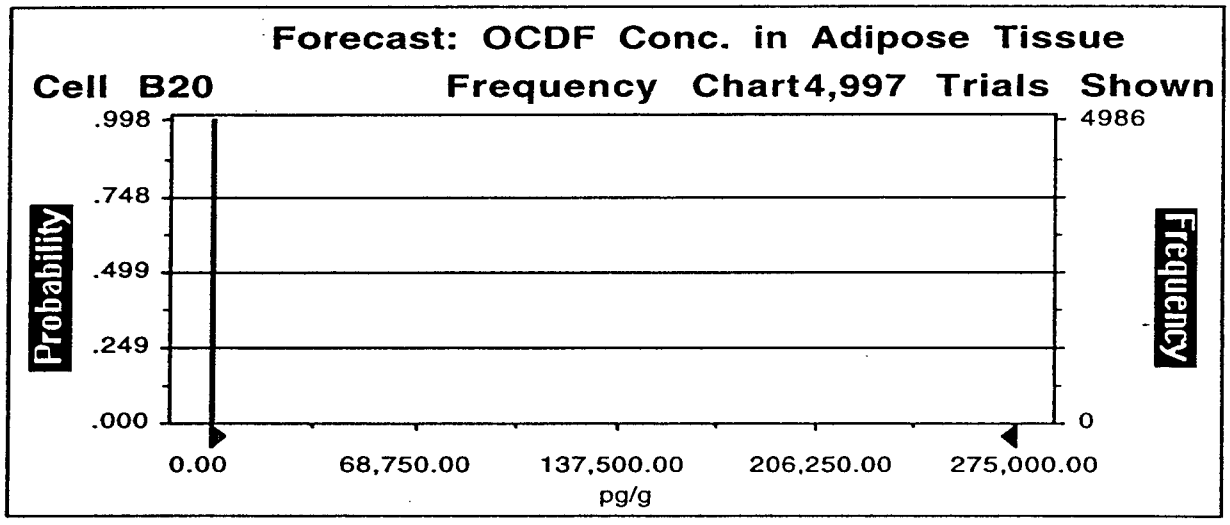
End of Forecast

Forecast: OCDF Conc. in Adipose Tissue **Cell: B20**

Summary:

Display Range is from 0.00 to 275,000.00 pg/g
Entire Range is from 0.00 to 6,933,232.81 pg/g
After 5,000 Trials, the Std. Error of the Mean is 1,419.14

Statistics for Display Range:	Value
Trials	4997
Mean	173.92
Median	9.82
Mode	---
Standard Deviation	4,487.39
Variance	20,136,655.15
Skewness	40.27
Kurtosis	1,659.58
Coeff. of Variability	25.80
Range Minimum	0.00
Range Maximum	275,000.00
Range Width	275,000.00
Mean Std. Error	63.48



Forecast: OCDF Conc. in Adipose Tissue (cont'd) **Cell: B20**

Percentiles for Display Range:

Percentile	pg/g
0%	0.00
10%	0.34
20%	1.57
30%	3.60
40%	6.13
50%	9.82
60%	15.61
70%	26.06
80%	46.01
90%	94.63
100%	201,505.79

End of Forecast

APPENDIX III

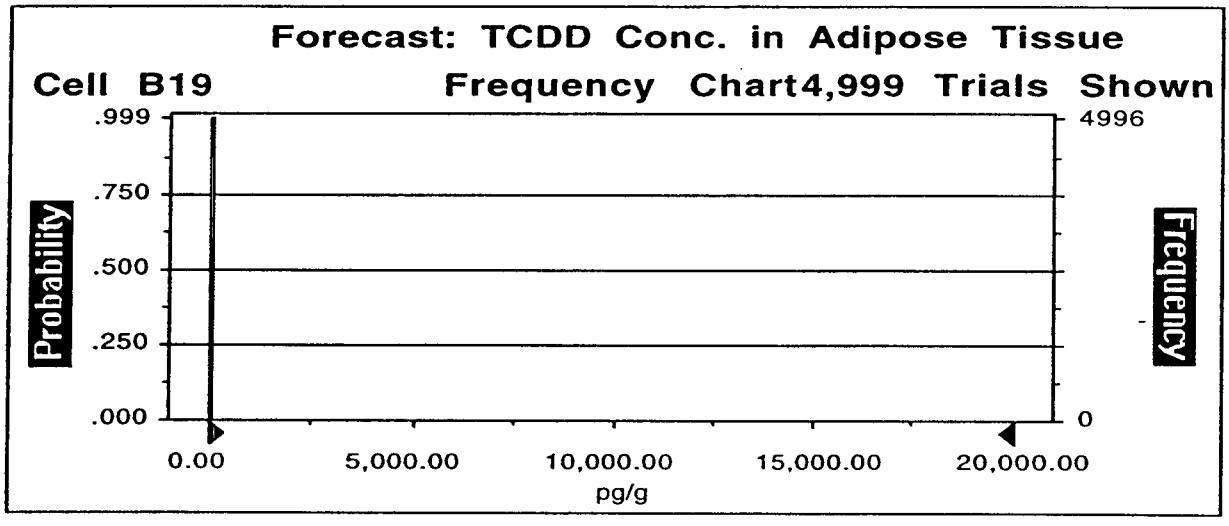
MODEL OUTPUT REPORTS: VAPOUR ASSUMPTION

Forecast: TCDD Conc. in Adipose Tissue **Cell: B19**

Summary:

Display Range is from 0.00 to 20,000.00 pg/g
Entire Range is from 0.00 to 532,105.35 pg/g
After 5,000 Trials, the Std. Error of the Mean is 106.42

Statistics for Display Range:	Value
Trials	4999
Mean	3.61
Median	1.10
Mode	---
Standard Deviation	12.62
Variance	159.38
Skewness	21.74
Kurtosis	756.99
Coeff. of Variability	3.50
Range Minimum	0.00
Range Maximum	20,000.00
Range Width	20,000.00
Mean Std. Error	0.18



Forecast: TCDD Conc. in Adipose Tissue (cont'd) **Cell: B19**

Percentiles for Display Range:

Percentile	pg/g
0%	0.00
10%	0.15
20%	0.30
30%	0.49
40%	0.75
50%	1.10
60%	1.61
70%	2.49
80%	3.91
90%	7.42
100%	542.70

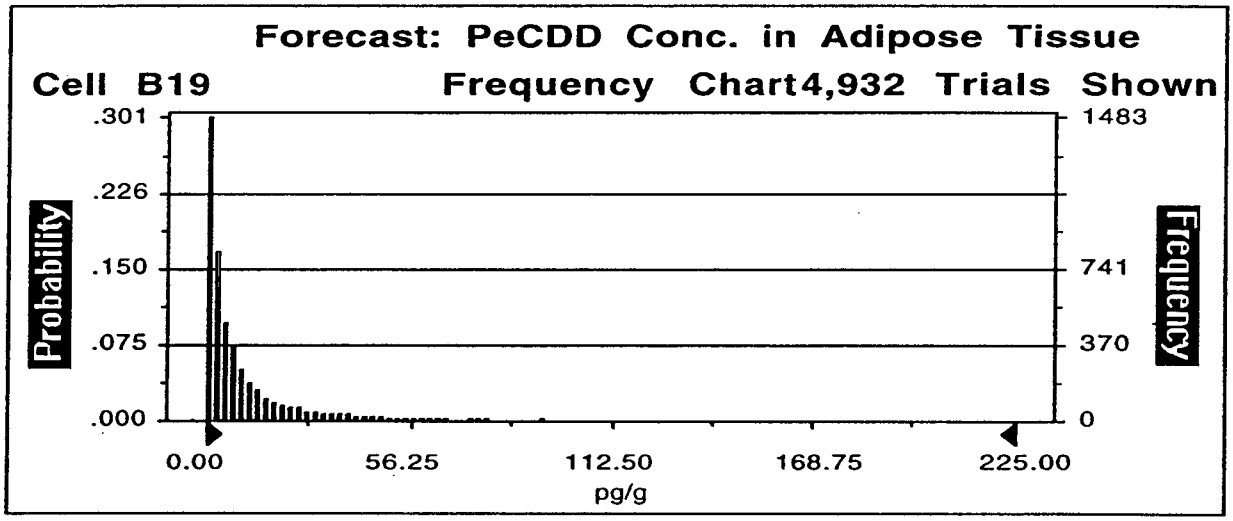
End of Forecast

Forecast: PeCDD Conc. in Adipose Tissue **Cell: B19**

Summary:

Display Range is from 0.00 to 225.00 pg/g
Entire Range is from 0.00 to 1,959.60 pg/g
After 5,000 Trials, the Std. Error of the Mean is 1.06

Statistics for Display Range:	Value
Trials	4932
Mean	15.16
Median	5.12
Mode	---
Standard Deviation	27.26
Variance	743.09
Skewness	3.64
Kurtosis	19.05
Coeff. of Variability	1.80
Range Minimum	0.00
Range Maximum	225.00
Range Width	225.00
Mean Std. Error	0.39



Forecast: PeCDD Conc. in Adipose Tissue (cont'd) **Cell: B19**

Percentiles for Display Range:

Percentile	pg/g
0%	0.00
10%	0.63
20%	1.32
30%	2.25
40%	3.54
50%	5.12
60%	7.72
70%	11.68
80%	19.63
90%	40.28
100%	220.88

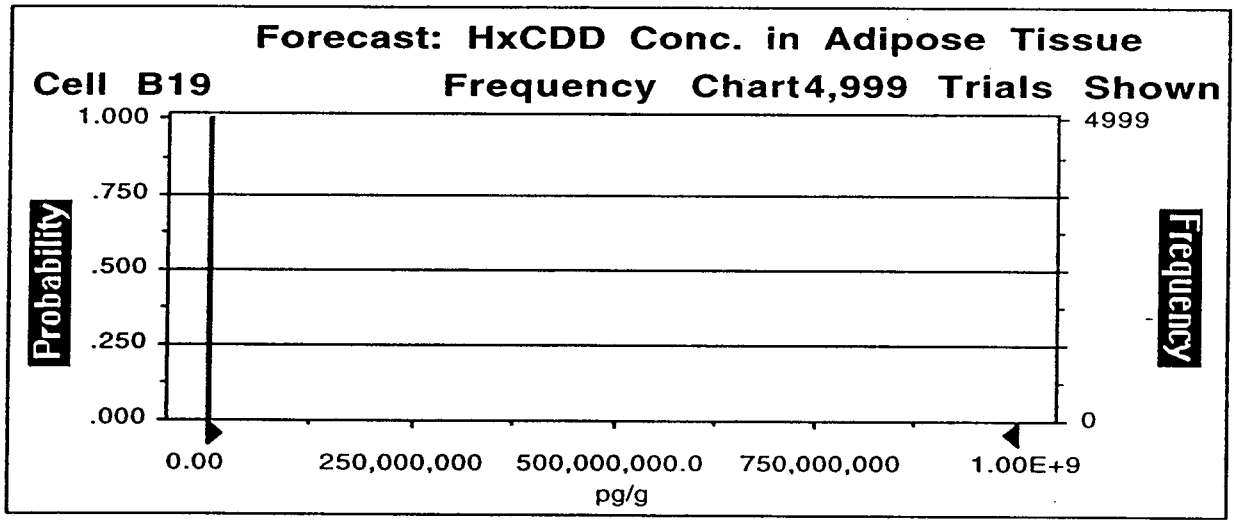
End of Forecast

Forecast: HxCDD Conc. in Adipose Tissue **Cell: B19**

Summary:

Display Range is from 0.00 to 1,000,000,000.00 pg/g
Entire Range is from 0.00 to 26,702,500,810.07 pg/g
After 5,000 Trials, the Std. Error of the Mean is 5,340,500.04

Statistics for Display Range:	Value
Trials	4999
Mean	1,063.87
Median	7.64
Mode	---
Standard Deviation	68,864.93
Variance	4,742,378,764.71
Skewness	70.52
Kurtosis	4,981.34
Coeff. of Variability	64.73
Range Minimum	0.00
Range Maximum	1,000,000,000.00
Range Width	1,000,000,000.00
Mean Std. Error	973.99



Forecast: HxCDD Conc. in Adipose Tissue (cont'd) **Cell: B19**

Percentiles for Display Range:

Percentile	pg/g
0%	0.00
10%	0.26
20%	1.15
30%	2.54
40%	4.66
50%	7.64
60%	12.42
70%	19.84
80%	34.63
90%	70.59
100%	4,865,755.36

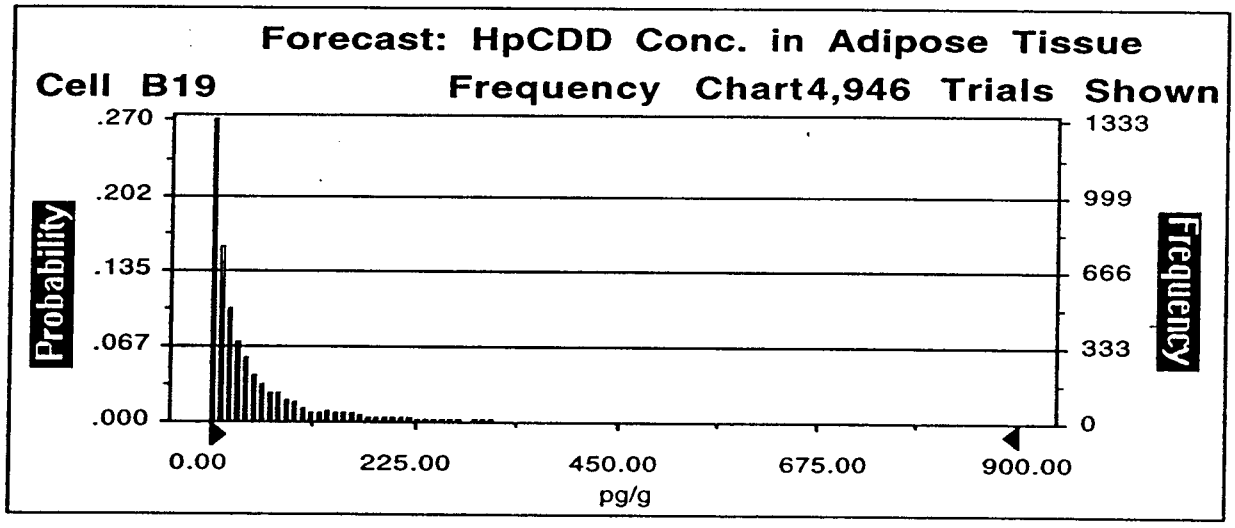
End of Forecast

Forecast: HpCDD Conc. in Adipose Tissue **Cell: B19**

Summary:

Display Range is from 0.00 to 900.00 pg/g
Entire Range is from 0.00 to 11,061.28 pg/g
After 5,000 Trials, the Std. Error of the Mean is 3.89

Statistics for Display Range:	Value
Trials	4946
Mean	65.03
Median	23.89
Mode	---
Standard Deviation	111.81
Variance	12,500.76
Skewness	3.54
Kurtosis	18.36
Coeff. of Variability	1.72
Range Minimum	0.00
Range Maximum	900.00
Range Width	900.00
Mean Std. Error	1.59



Forecast: HpCDD Conc. in Adipose Tissue (cont'd) **Cell: B19**

Percentiles for Display Range:

Percentile	pg/g
0%	0.00
10%	2.68
20%	6.11
30%	10.52
40%	16.21
50%	23.89
60%	36.10
70%	53.81
80%	85.96
90%	169.28
100%	886.33

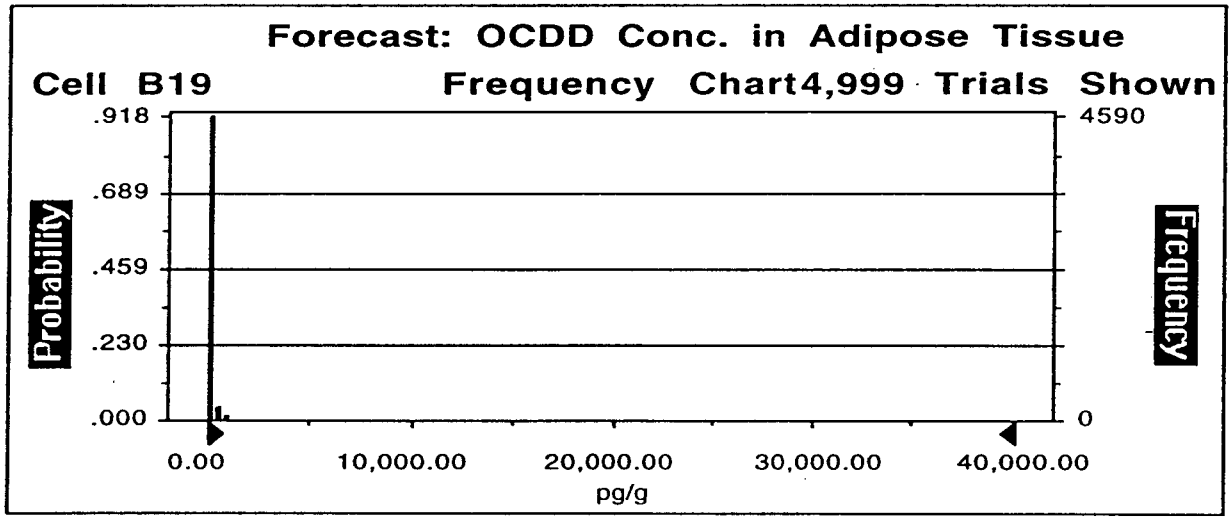
End of Forecast

Forecast: OCDD Conc. in Adipose Tissue **Cell: B19**

Summary:

Display Range is from 0.00 to 40,000.00 pg/g
Entire Range is from 0.00 to 989,341.62 pg/g
After 5,000 Trials, the Std. Error of the Mean is 198.12

Statistics for Display Range:	Value
Trials	4999
Mean	167.98
Median	37.22
Mode	---
Standard Deviation	747.64
Variance	558,963.36
Skewness	24.64
Kurtosis	941.28
Coeff. of Variability	4.45
Range Minimum	0.00
Range Maximum	40,000.00
Range Width	40,000.00
Mean Std. Error	10.57



Forecast: OCDD Conc. in Adipose Tissue (cont'd) **Cell: B19**

Percentiles for Display Range:

Percentile	pg/g
0%	0.00
10%	3.69
20%	8.15
30%	13.89
40%	22.90
50%	37.22
60%	56.74
70%	84.80
80%	148.45
90%	323.54
100%	34,158.39

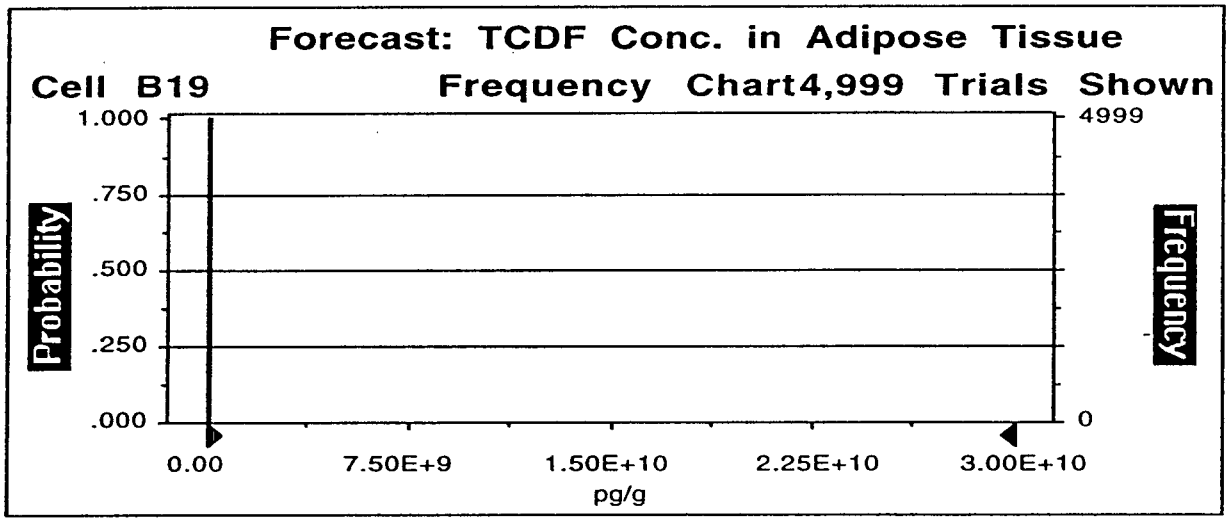
End of Forecast

Forecast: TCDF Conc. in Adipose Tissue **Cell: B19**

Summary:

Display Range is from 0.00 to 30,000,000,000.00 pg/g
Entire Range is from 0.00 to 768,238,348,988.76 pg/g
After 5,000 Trials, the Std. Error of the Mean is 153,647,669.79

Statistics for Display Range:	Value
Trials	4999
Mean	37.73
Median	0.36
Mode	---
Standard Deviation	1,676.34
Variance	2,810,109.80
Skewness	66.75
Kurtosis	4,601.85
Coeff. of Variability	44.42
Range Minimum	0.00
Range Maximum	30,000,000,000.00
Range Width	30,000,000,000.00
Mean Std. Error	23.71



Forecast: TCDF Conc. in Adipose Tissue (cont'd) **Cell: B19**

Percentiles for Display Range:

Percentile	pg/g
0%	0.00
10%	0.00
20%	0.02
30%	0.08
40%	0.18
50%	0.36
60%	0.67
70%	1.33
80%	2.84
90%	7.33
100%	116,113.88

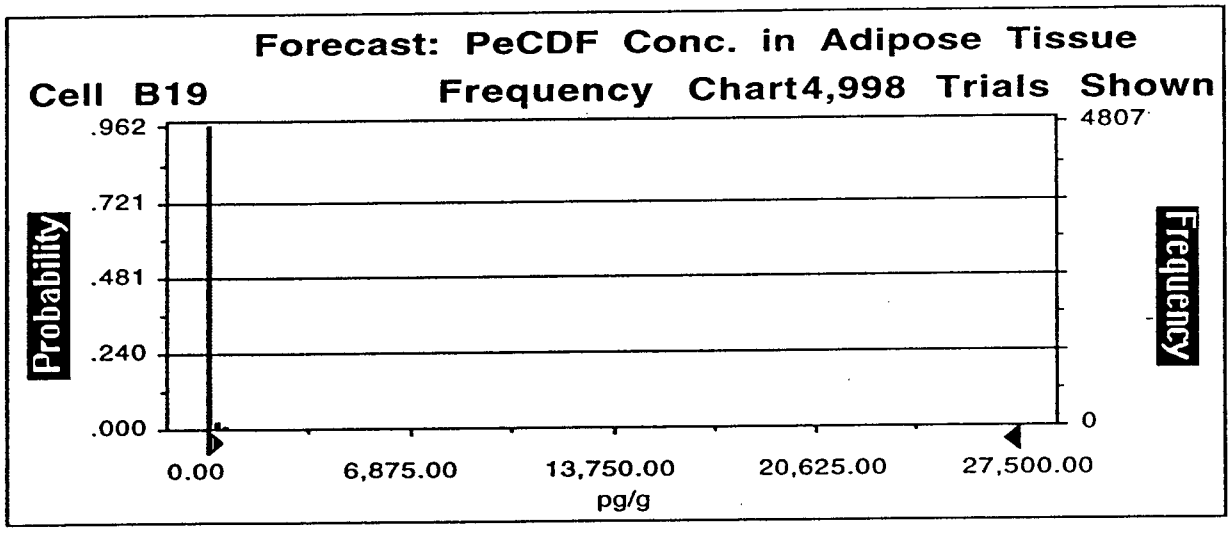
End of Forecast

Forecast: PeCDF Conc. in Adipose Tissue **Cell: B19**

Summary:

Display Range is from 0.00 to 27,500.00 pg/g
Entire Range is from 0.00 to 651,518.38 pg/g
After 5,000 Trials, the Std. Error of the Mean is 139.90

Statistics for Display Range:	Value
Trials	4998
Mean	58.62
Median	14.82
Mode	---
Standard Deviation	244.16
Variance	59,611.92
Skewness	27.16
Kurtosis	1,059.59
Coeff. of Variability	4.17
Range Minimum	0.00
Range Maximum	27,500.00
Range Width	27,500.00
Mean Std. Error	3.45



Forecast: PeCDF Conc. in Adipose Tissue (cont'd) **Cell: B19**

Percentiles for Display Range:

Percentile	pg/g
0%	0.00
10%	1.15
20%	3.18
30%	5.85
40%	9.68
50%	14.82
60%	22.99
70%	35.07
80%	58.33
90%	124.90
100%	11,167.67

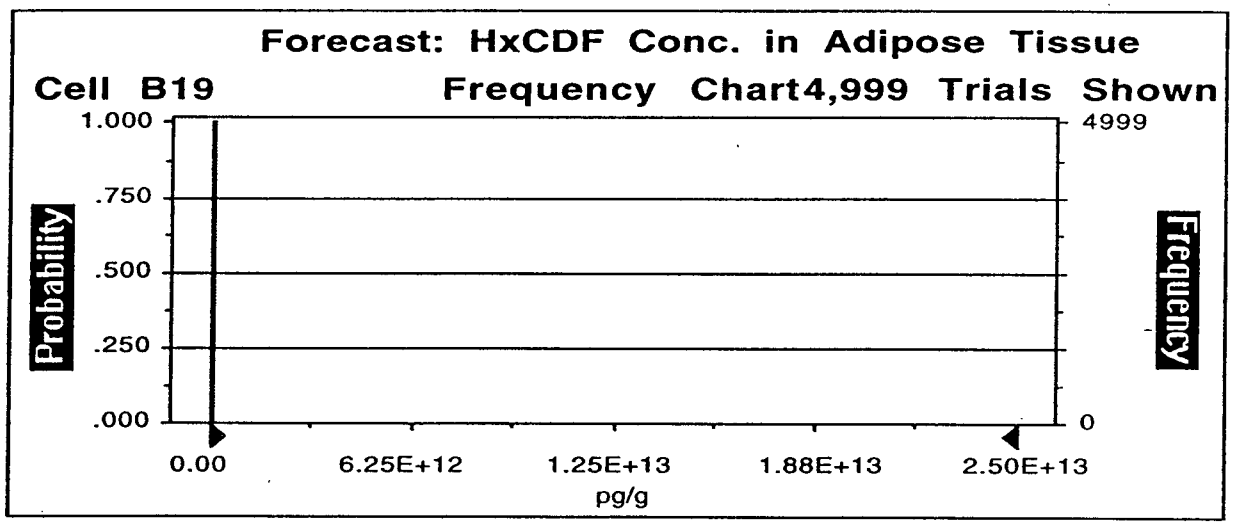
End of Forecast

Forecast: HxCDF Conc. in Adipose Tissue **Cell: B19**

Summary:

Display Range is from 0.00 to 25,000,000,000,000.00 pg/g
Entire Range is from 0.00 to 606,318,618,095,517.00 pg/g
After 5,000 Trials, the Std. Error of the Mean is 121,263,723,570.08

Statistics for Display Range:	Value
Trials	4999
Mean	245,959.47
Median	112.61
Mode	---
Standard Deviation	14,317,994.00
Variance	2.05E+14
Skewness	65.57
Kurtosis	4,446.97
Coeff. of Variability	58.21
Range Minimum	0.00
Range Maximum	2.50E+13
Range Width	2.50E+13
Mean Std. Error	202,507.26



Forecast: HxCDF Conc. in Adipose Tissue (cont'd) **Cell: B19**

Percentiles for Display Range:

Percentile	pg/g
0%	0.00
10%	12.42
20%	29.14
30%	49.74
40%	77.83
50%	112.61
60%	160.79
70%	243.07
80%	406.41
90%	802.11
100%	982,459,442.39

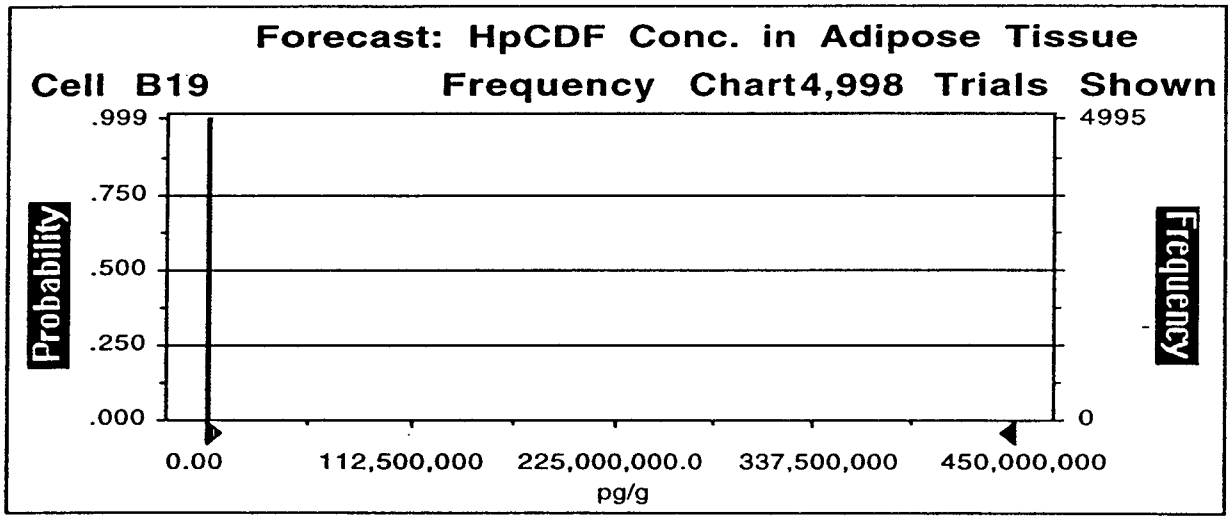
End of Forecast

Forecast: HpCDF Conc. in Adipose Tissue **Cell: B19**

Summary:

Display Range is from 0.00 to 450,000,000.00 pg/g
Entire Range is from 0.00 to 11,216,190,735.72 pg/g
After 5,000 Trials, the Std. Error of the Mean is 2,298,856.50

Statistics for Display Range:	Value
Trials	4998
Mean	9,474.81
Median	90.62
Mode	---
Standard Deviation	346,795.64
Variance	1.20E+11
Skewness	45.29
Kurtosis	2,204.66
Coeff. of Variability	36.60
Range Minimum	0.00
Range Maximum	450,000,000.00
Range Width	450,000,000.00
Mean Std. Error	4,905.41



Forecast: HpCDF Conc. in Adipose Tissue (cont'd) **Cell: B19**

Percentiles for Display Range:

Percentile	pg/g
0%	0.00
10%	6.09
20%	18.89
30%	36.23
40%	57.86
50%	90.62
60%	134.14
70%	211.22
80%	349.58
90%	681.42
100%	18,900,367.63

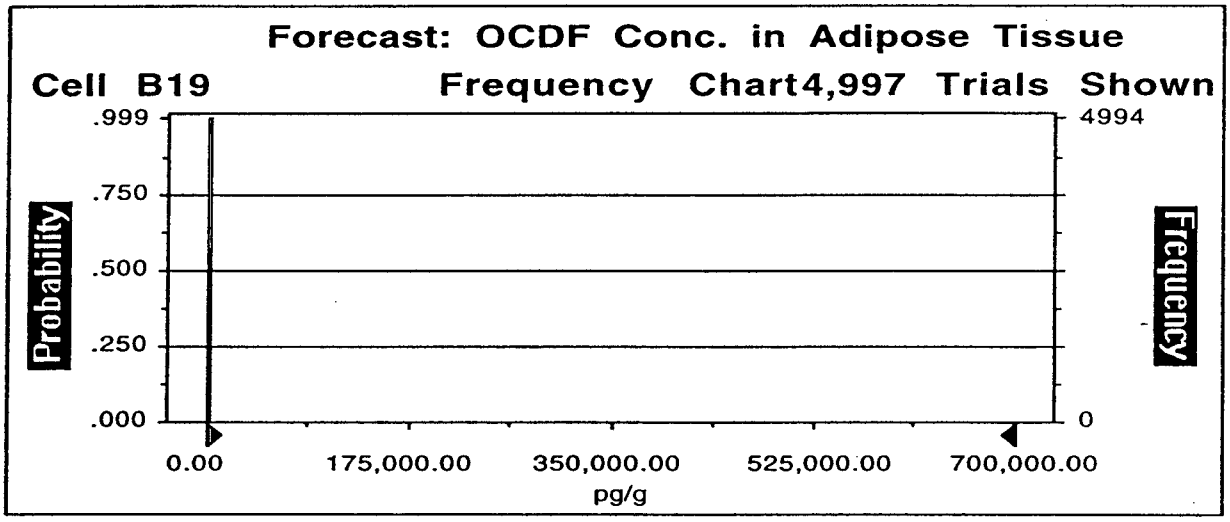
End of Forecast

Forecast: OCDF Conc. in Adipose Tissue **Cell: B19**

Summary:

Display Range is from 0.00 to 700,000.00 pg/g
Entire Range is from 0.00 to 16,661,831.96 pg/g
After 5,000 Trials, the Std. Error of the Mean is 3,534.84

Statistics for Display Range:	Value
Trials	4997
Mean	66.66
Median	8.47
Mode	---
Standard Deviation	756.05
Variance	571,617.00
Skewness	45.52
Kurtosis	2,469.11
Coeff. of Variability	11.34
Range Minimum	0.00
Range Maximum	700,000.00
Range Width	700,000.00
Mean Std. Error	10.70



Forecast: OCDF Conc. in Adipose Tissue (cont'd) **Cell: B19**

Percentiles for Display Range:

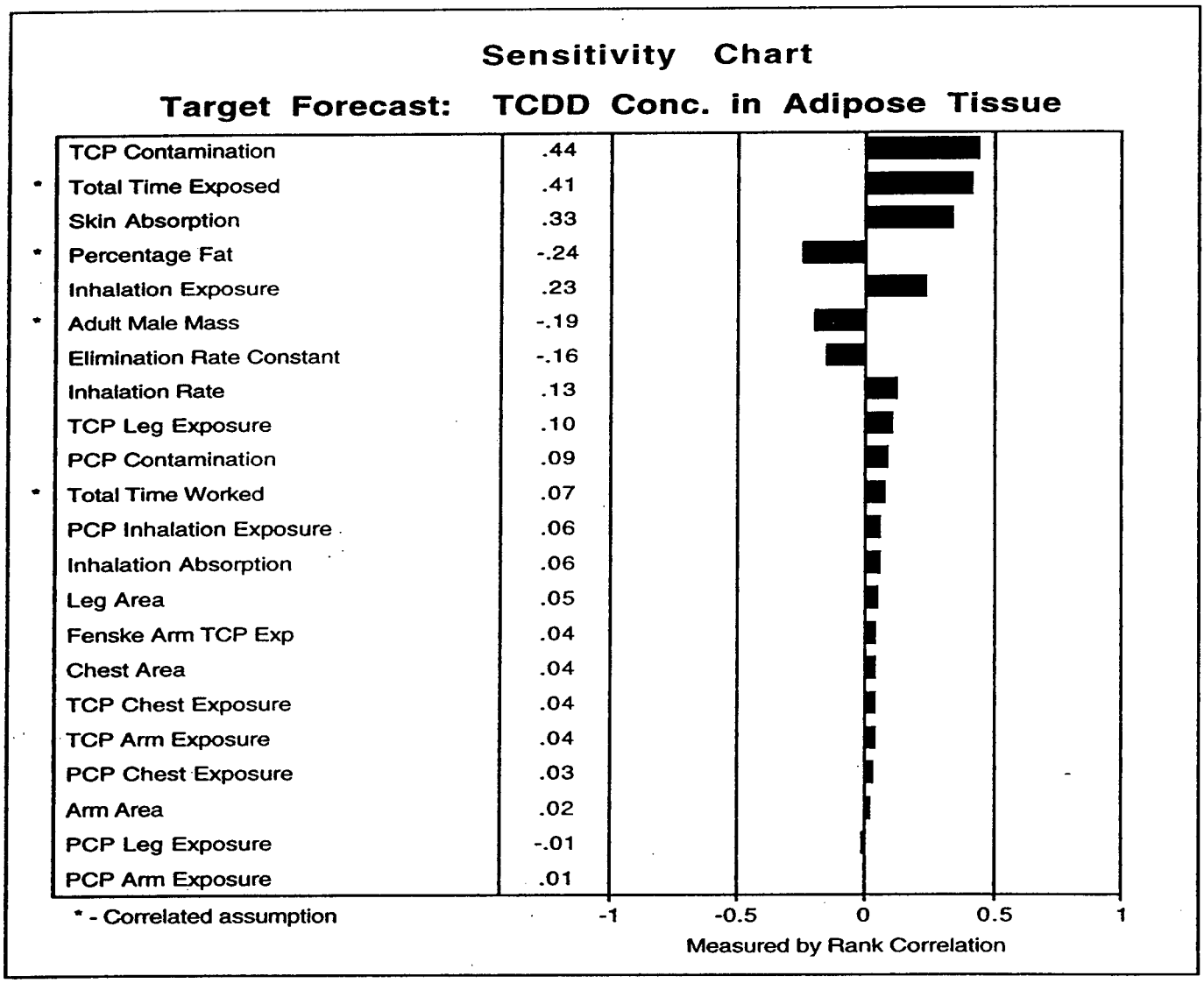
Percentile	pg/g
0%	0.00
10%	0.24
20%	1.09
30%	2.56
40%	5.09
50%	8.47
60%	13.88
70%	22.83
80%	41.75
90%	89.08
100%	44,354.95

End of Forecast

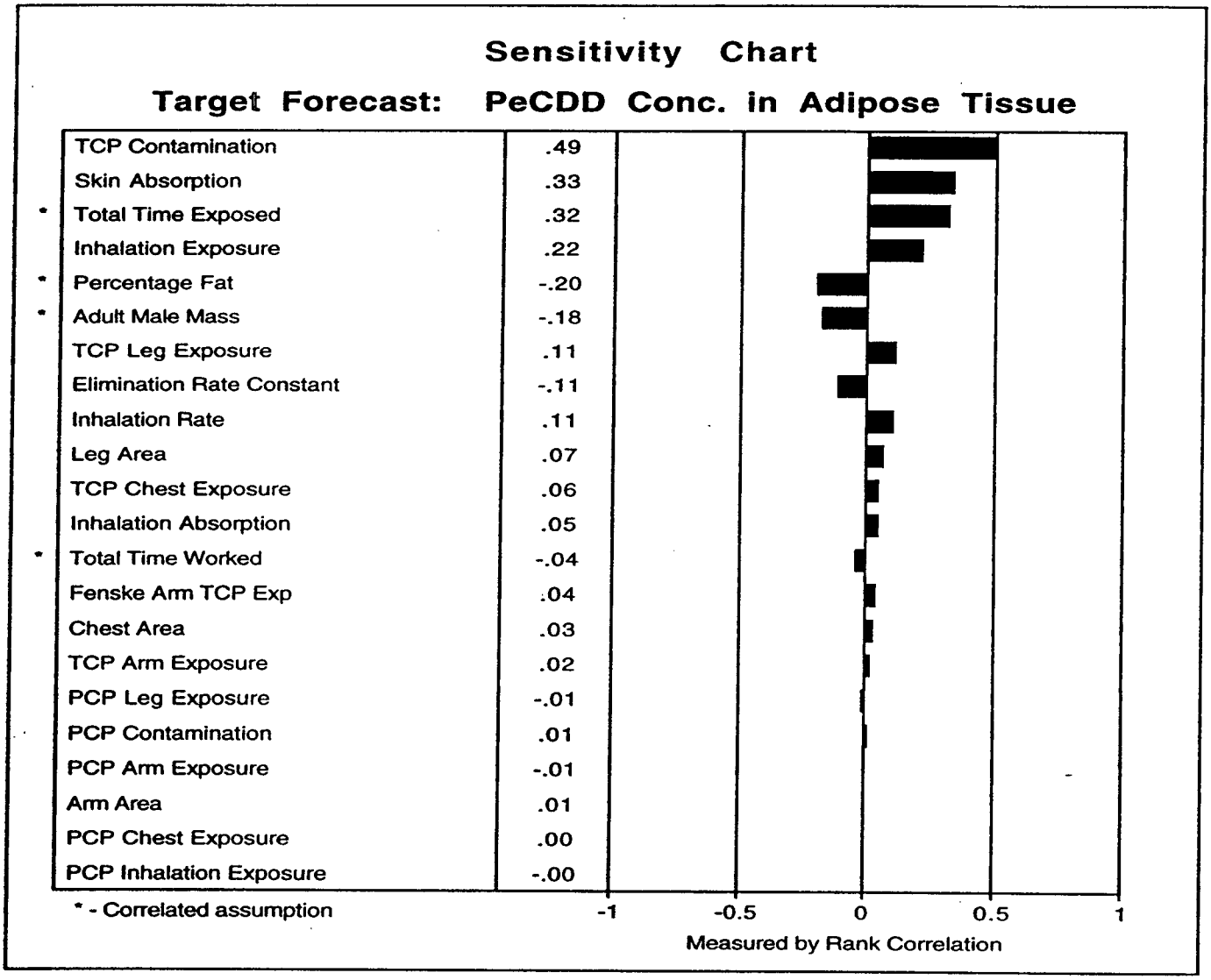
APPENDIX IV

SENSITIVITY ANALYSES: AEROSOL ASSUMPTION

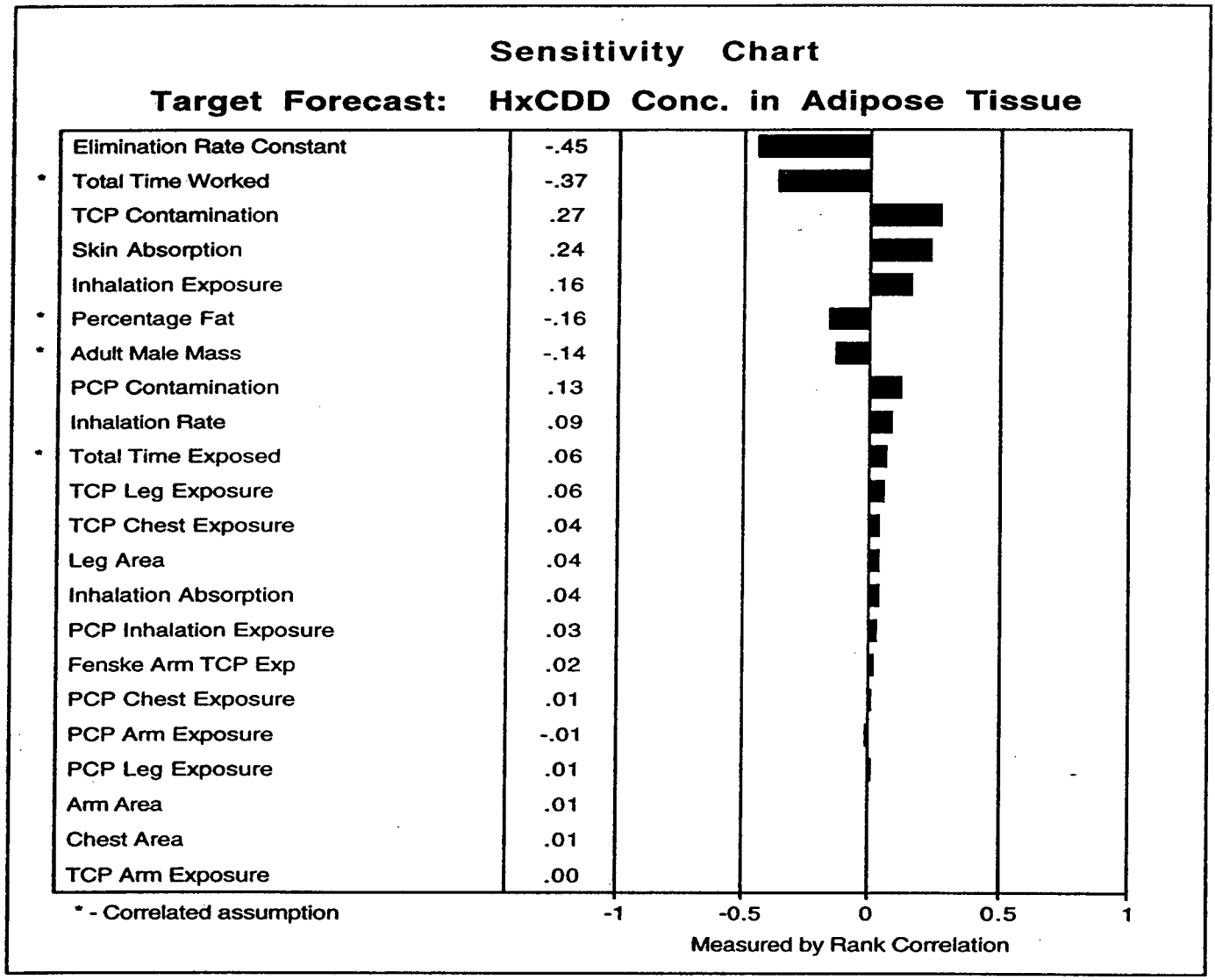
Crystal Ball Report
Simulation started on 9/18/95 at 5:56:02
Simulation stopped on 9/18/95 at 6:48:10



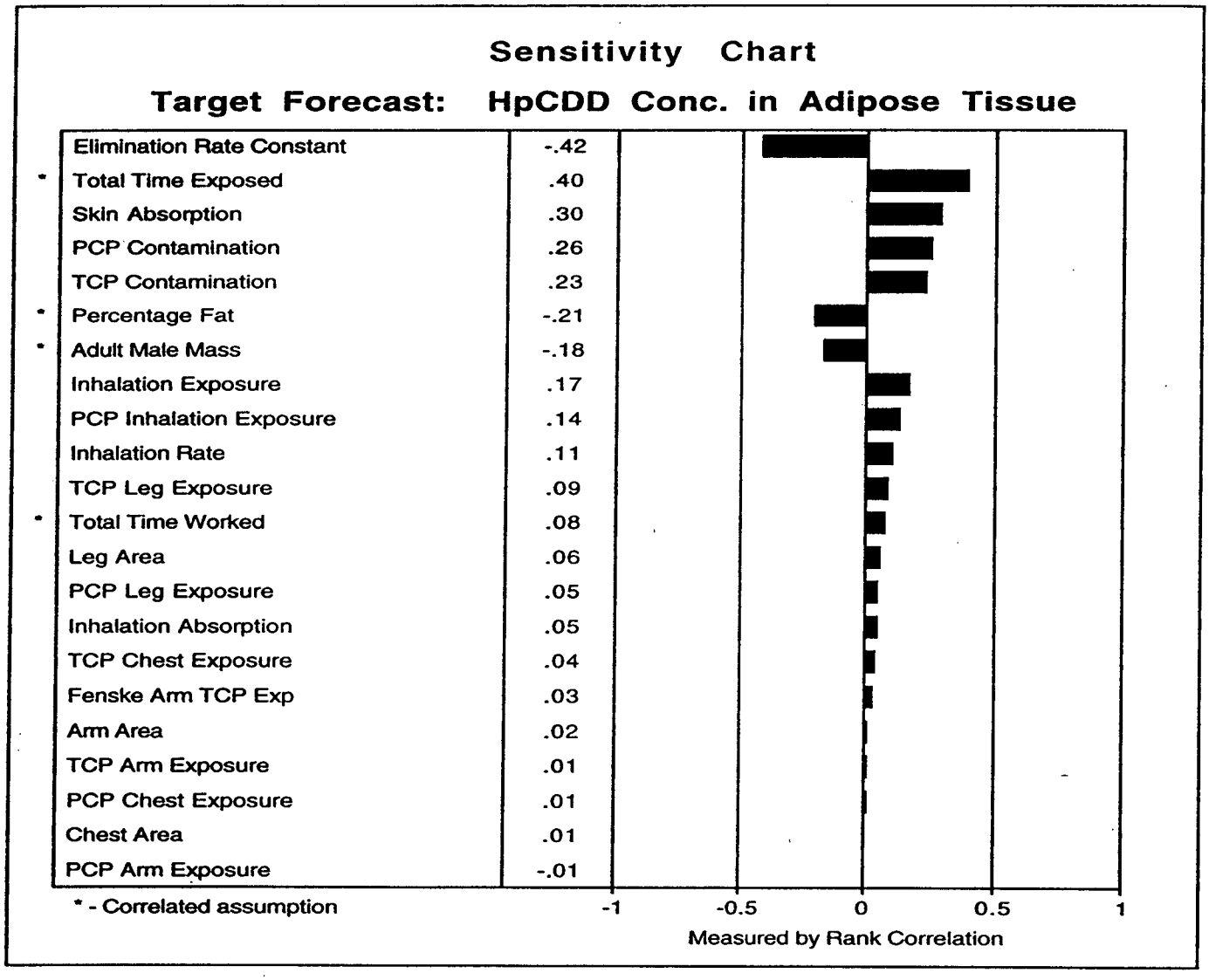
Crystal Ball Report
Simulation started on 9/18/95 at 16:11:11
Simulation stopped on 9/18/95 at 17:03:31



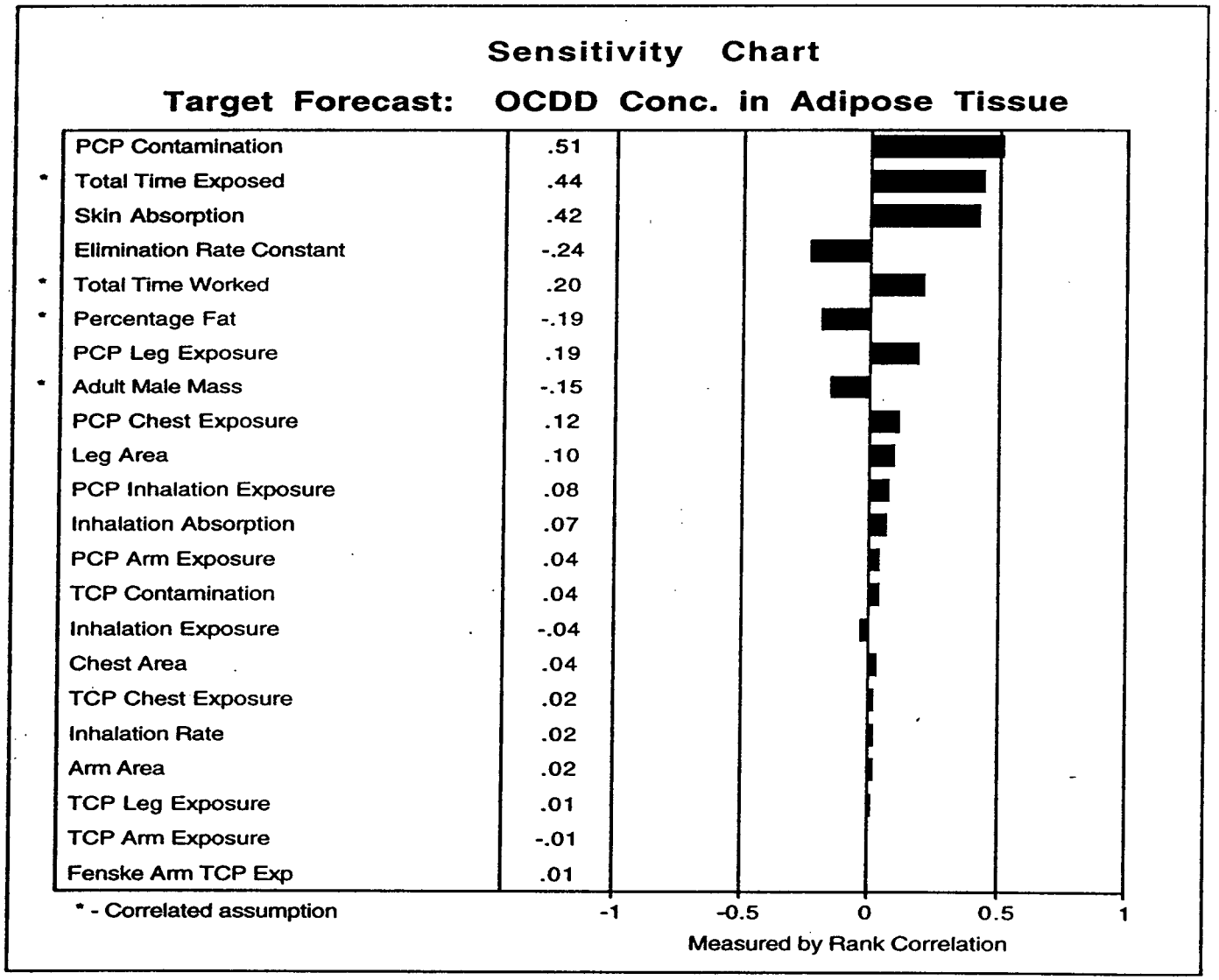
Crystal Ball Report
Simulation started on 9/18/95 at 17:18:06
Simulation stopped on 9/18/95 at 18:11:21



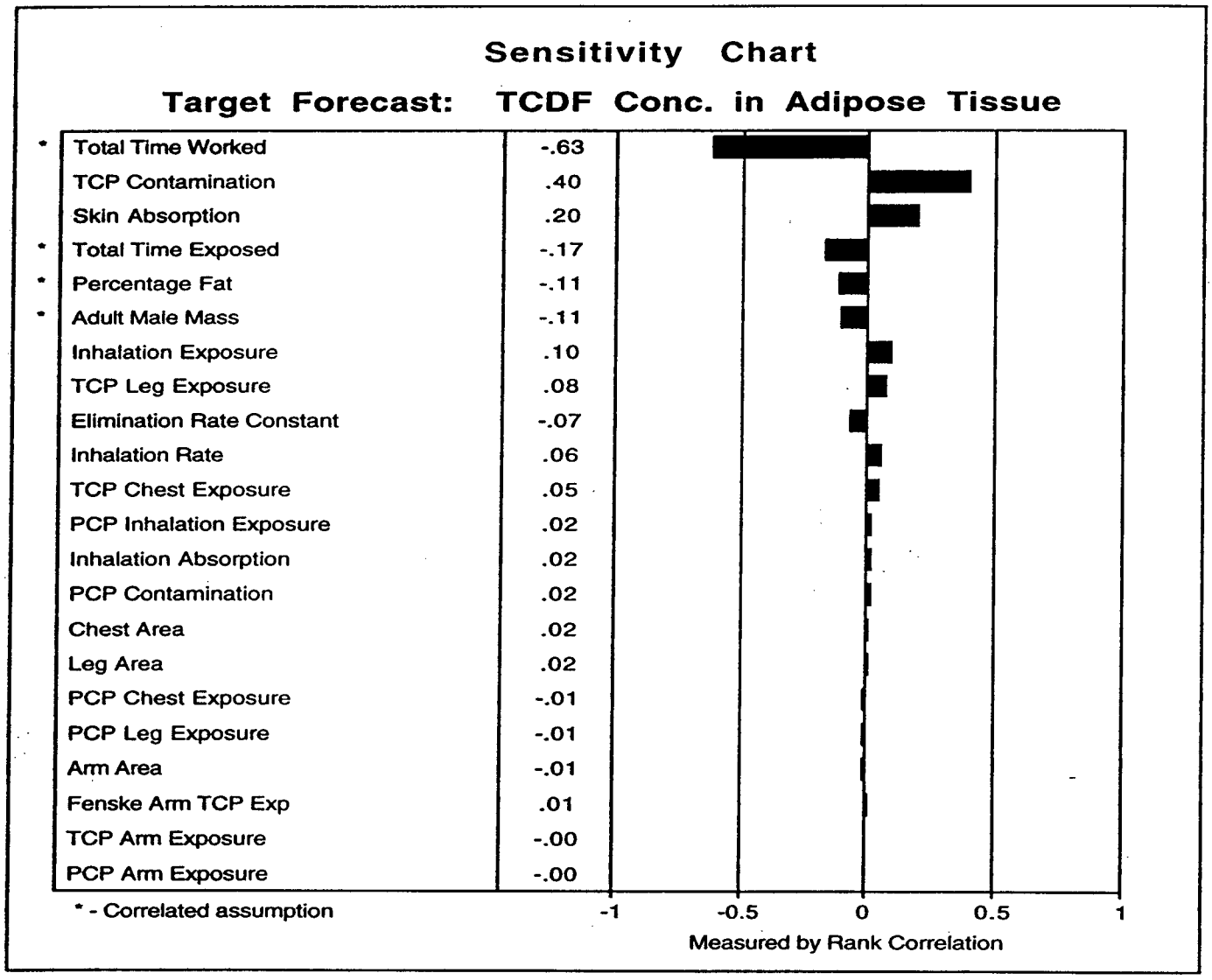
Crystal Ball Report
Simulation started on 9/18/95 at 18:21:19
Simulation stopped on 9/18/95 at 19:14:25



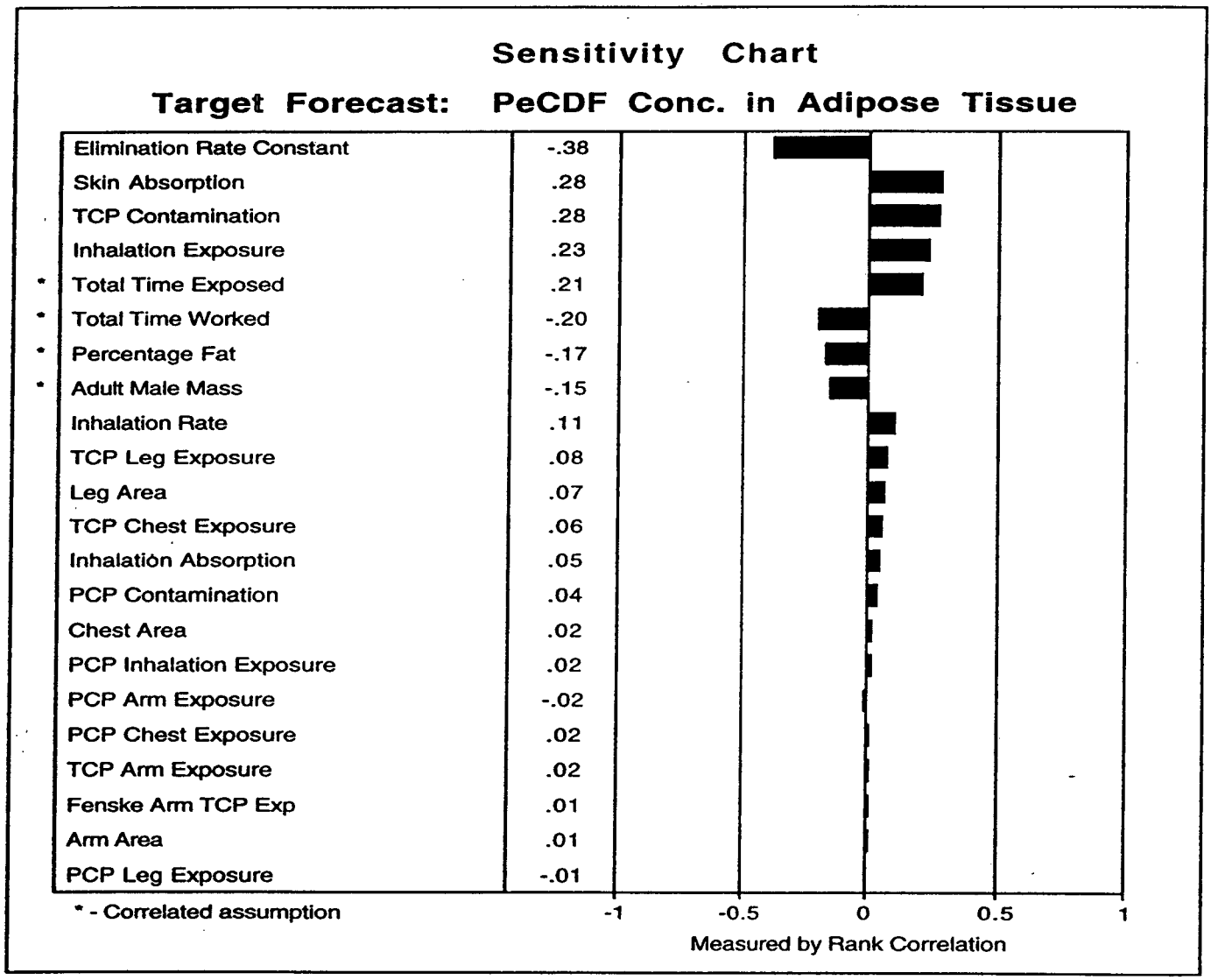
Crystal Ball Report
Simulation started on 9/18/95 at 19:23:46
Simulation stopped on 9/18/95 at 20:16:19



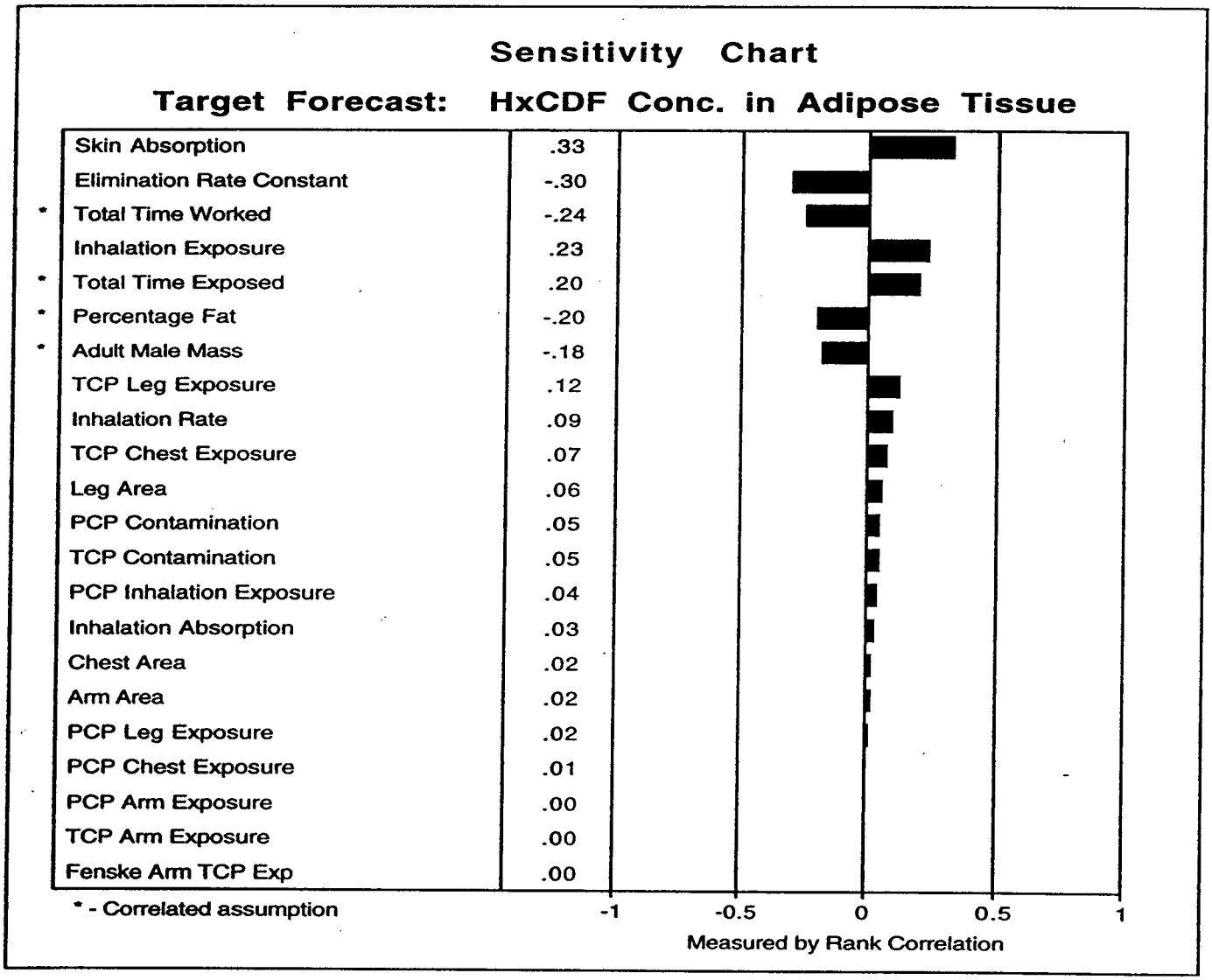
Crystal Ball Report
Simulation started on 9/19/95 at 17:08:47
Simulation stopped on 9/19/95 at 18:03:40



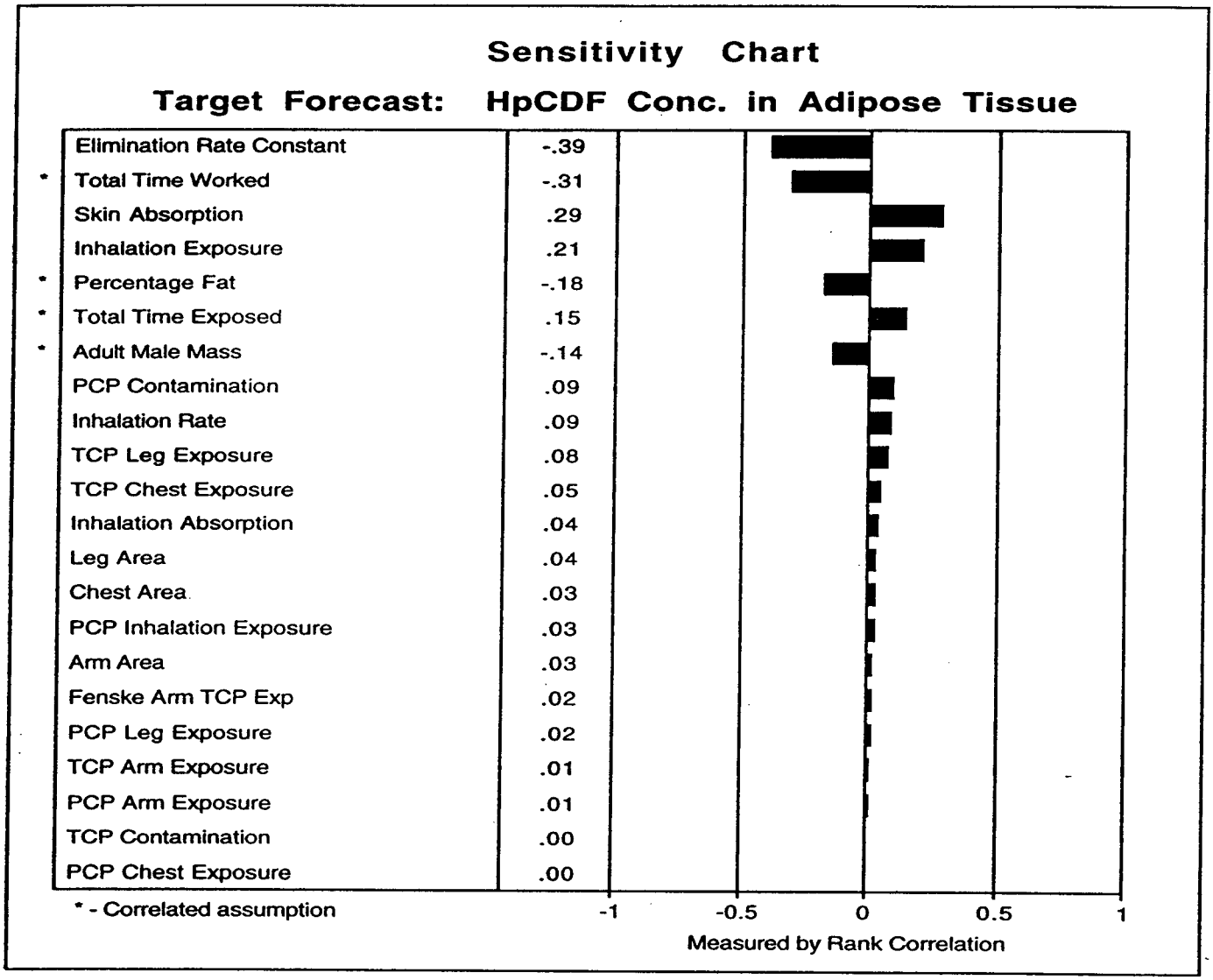
Crystal Ball Report
Simulation started on 9/19/95 at 18:11:51
Simulation stopped on 9/19/95 at 19:06:46



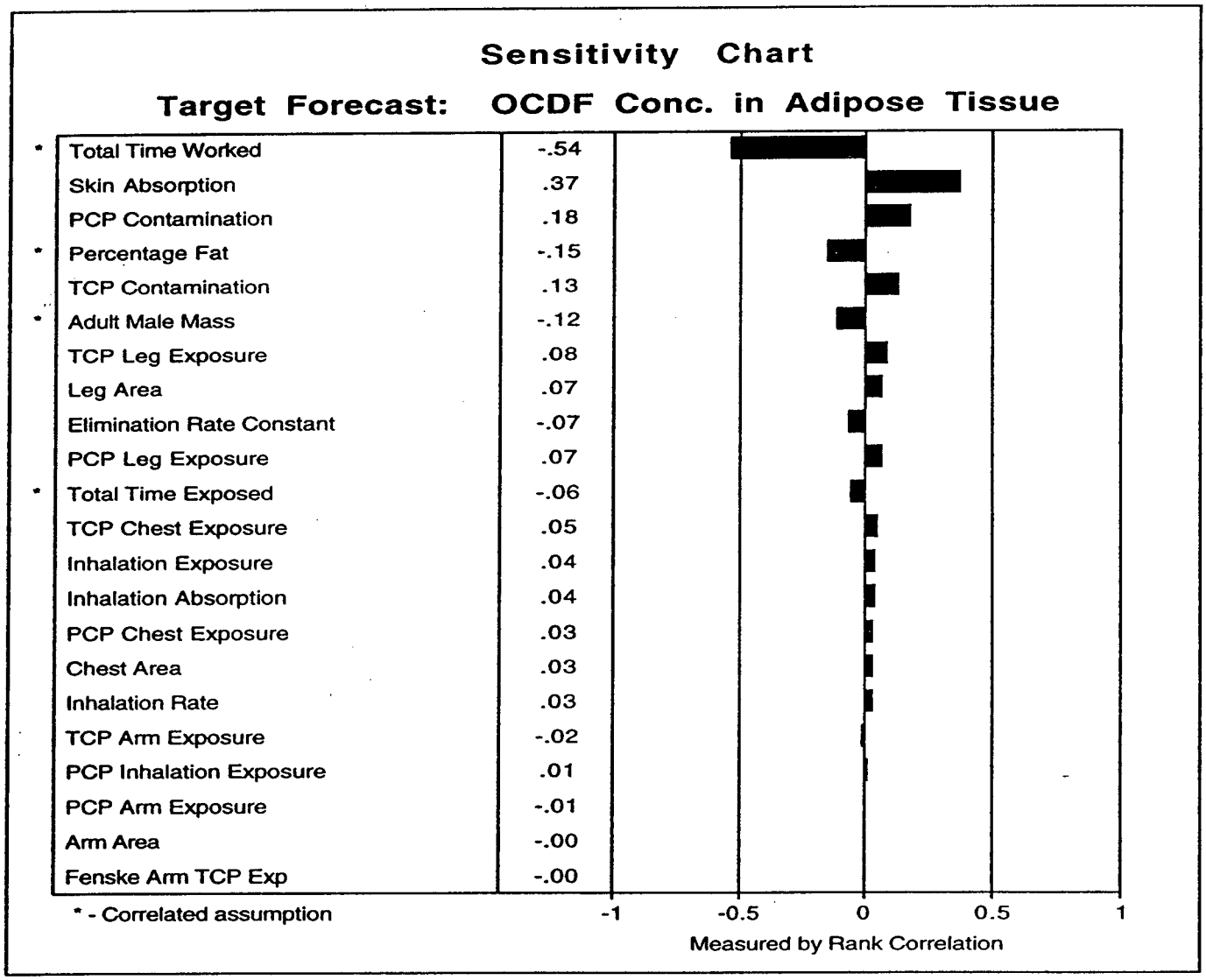
Crystal Ball Report
Simulation started on 9/19/95 at 19:23:50
Simulation stopped on 9/19/95 at 20:18:44



Crystal Ball Report
Simulation started on 9/19/95 at 20:26:13
Simulation stopped on 9/19/95 at 21:20:30



Crystal Ball Report
Simulation started on 9/19/95 at 21:27:55
Simulation stopped on 9/19/95 at 22:22:59



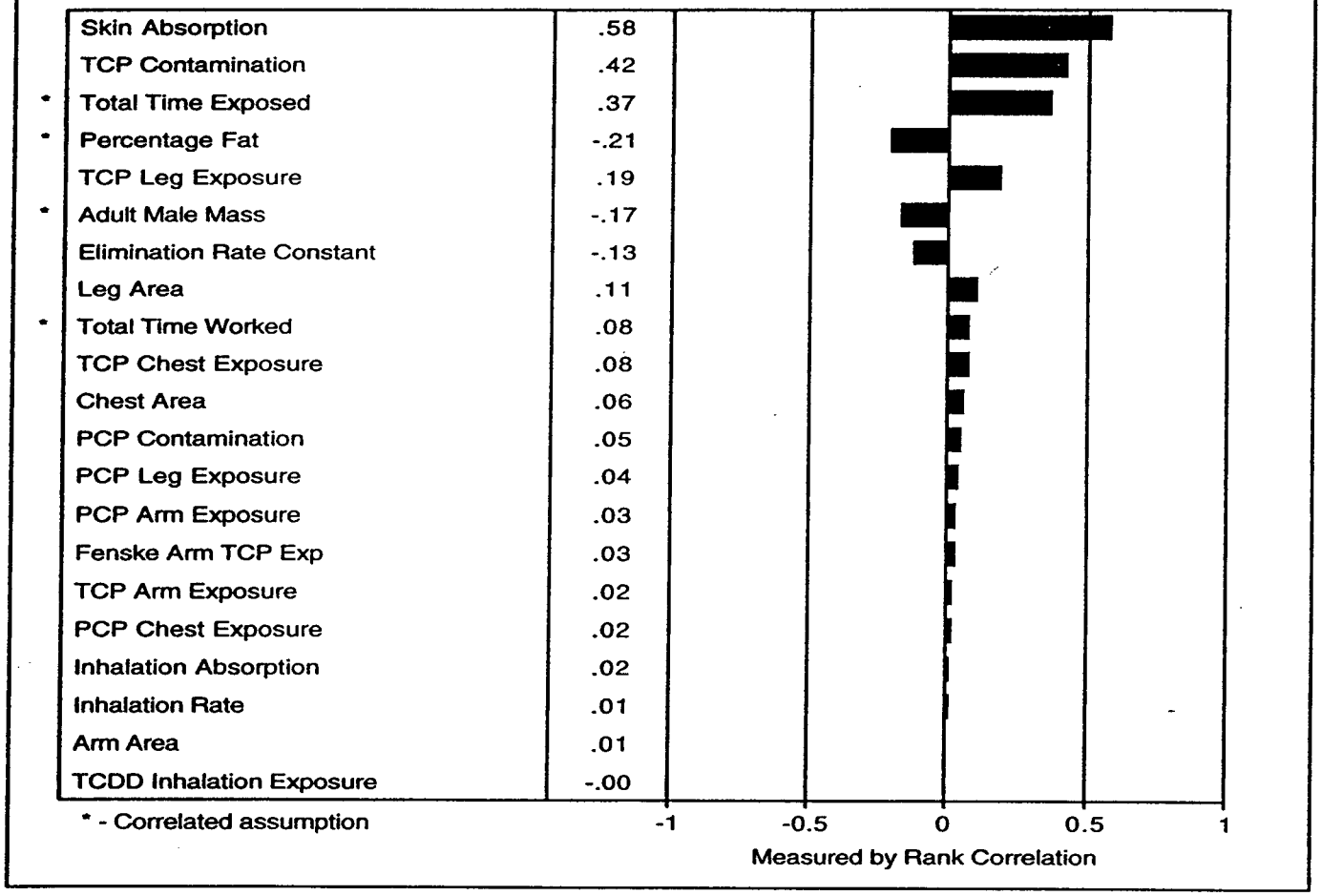
APPENDIX V

SENSITIVITY ANALYSIS: VAPOUR ASSUMPTION

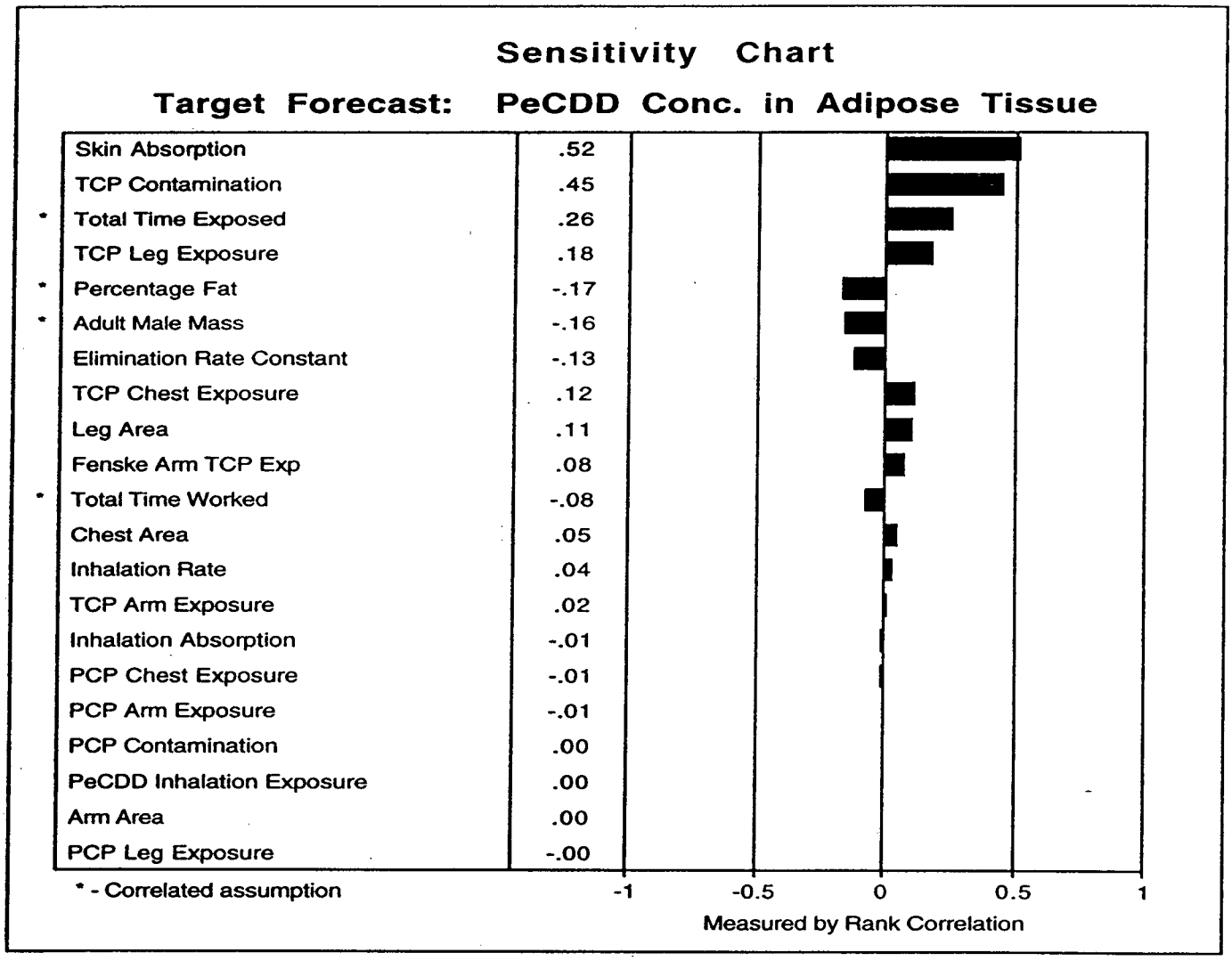
Crystal Ball Report
Simulation started on 9/17/95 at 16:07:14
Simulation stopped on 9/17/95 at 16:57:50

Sensitivity Chart

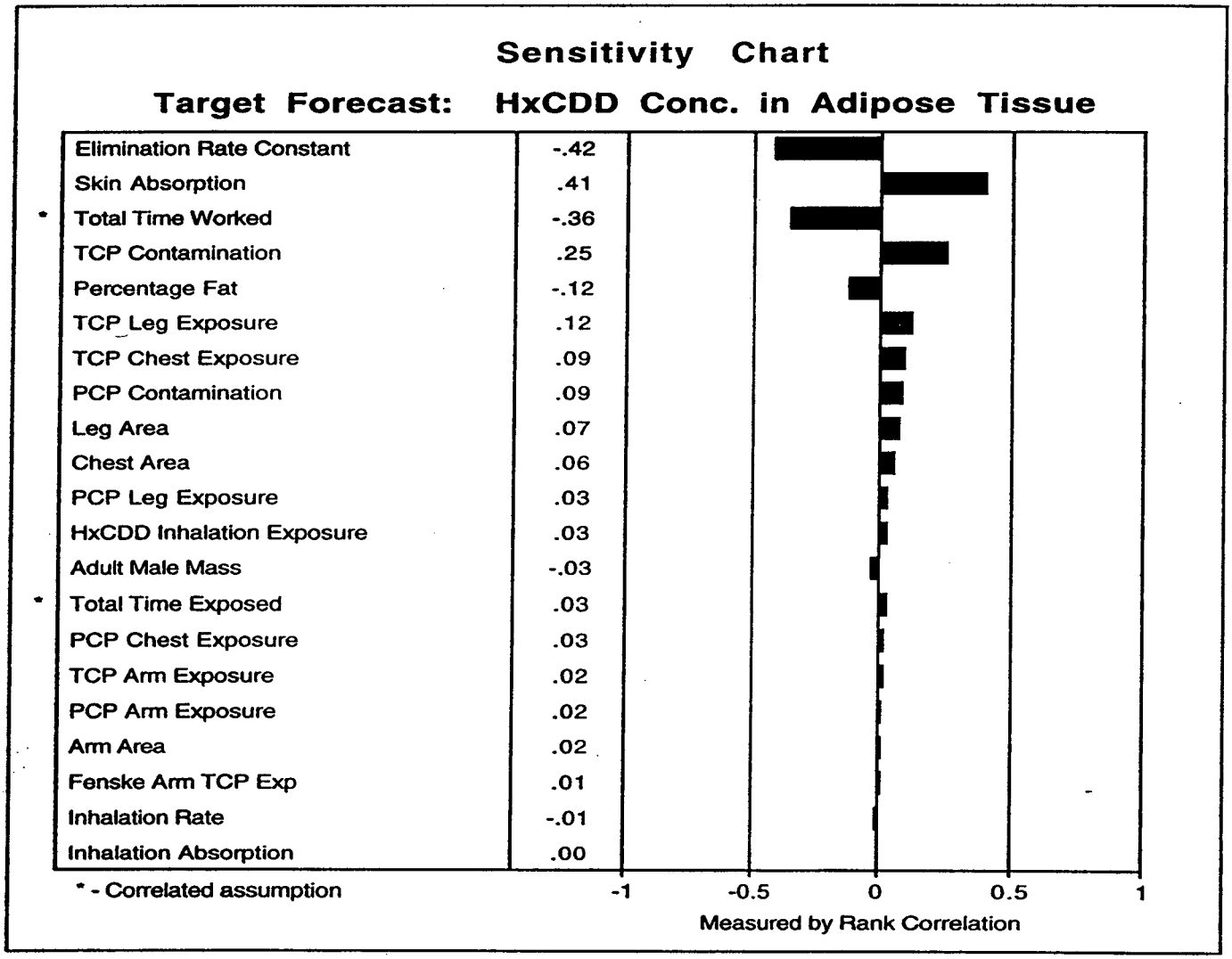
Target Forecast: TCDD Conc. in Adipose Tissue



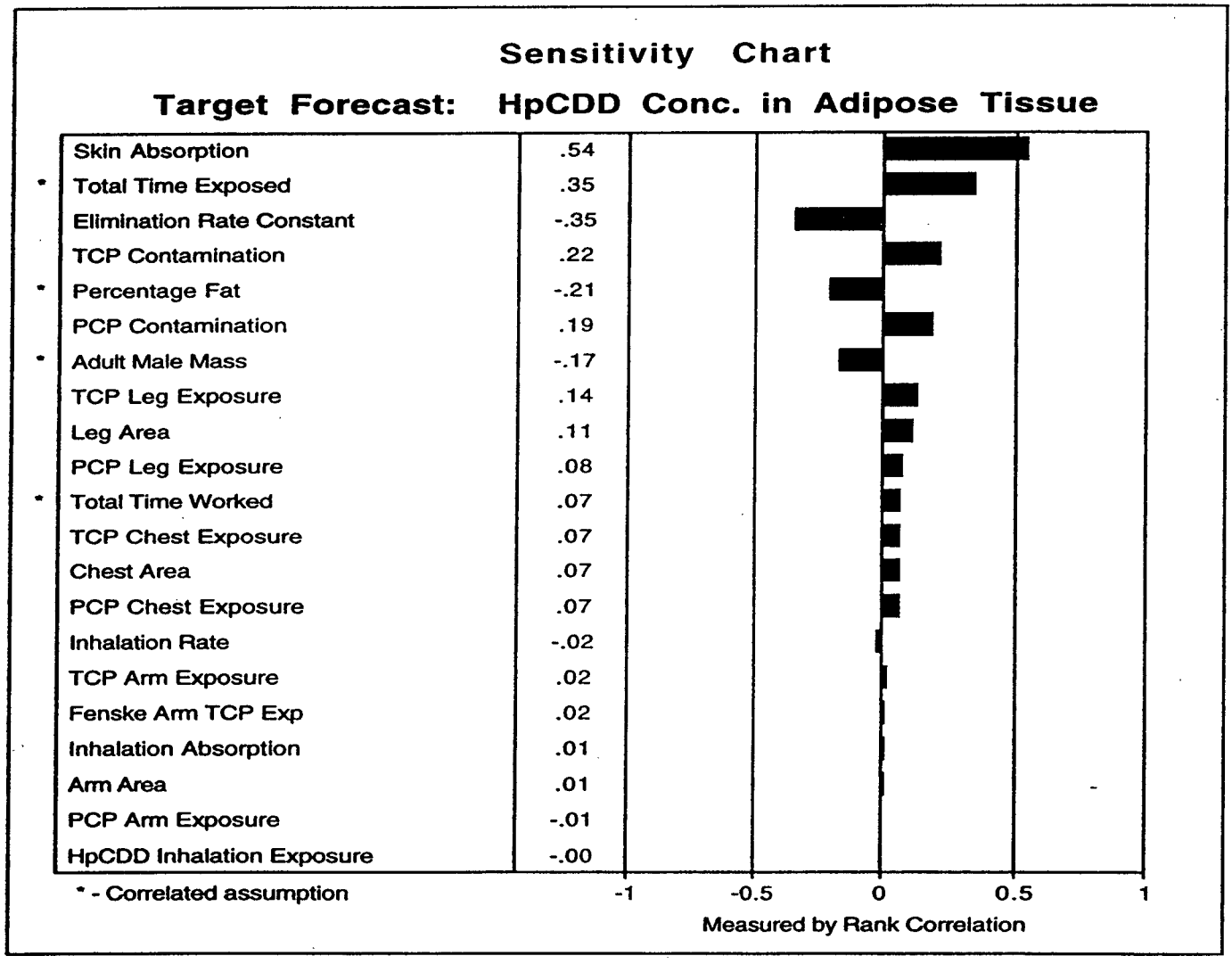
Crystal Ball Report
Simulation started on 9/17/95 at 17:10:55
Simulation stopped on 9/17/95 at 17:54:26



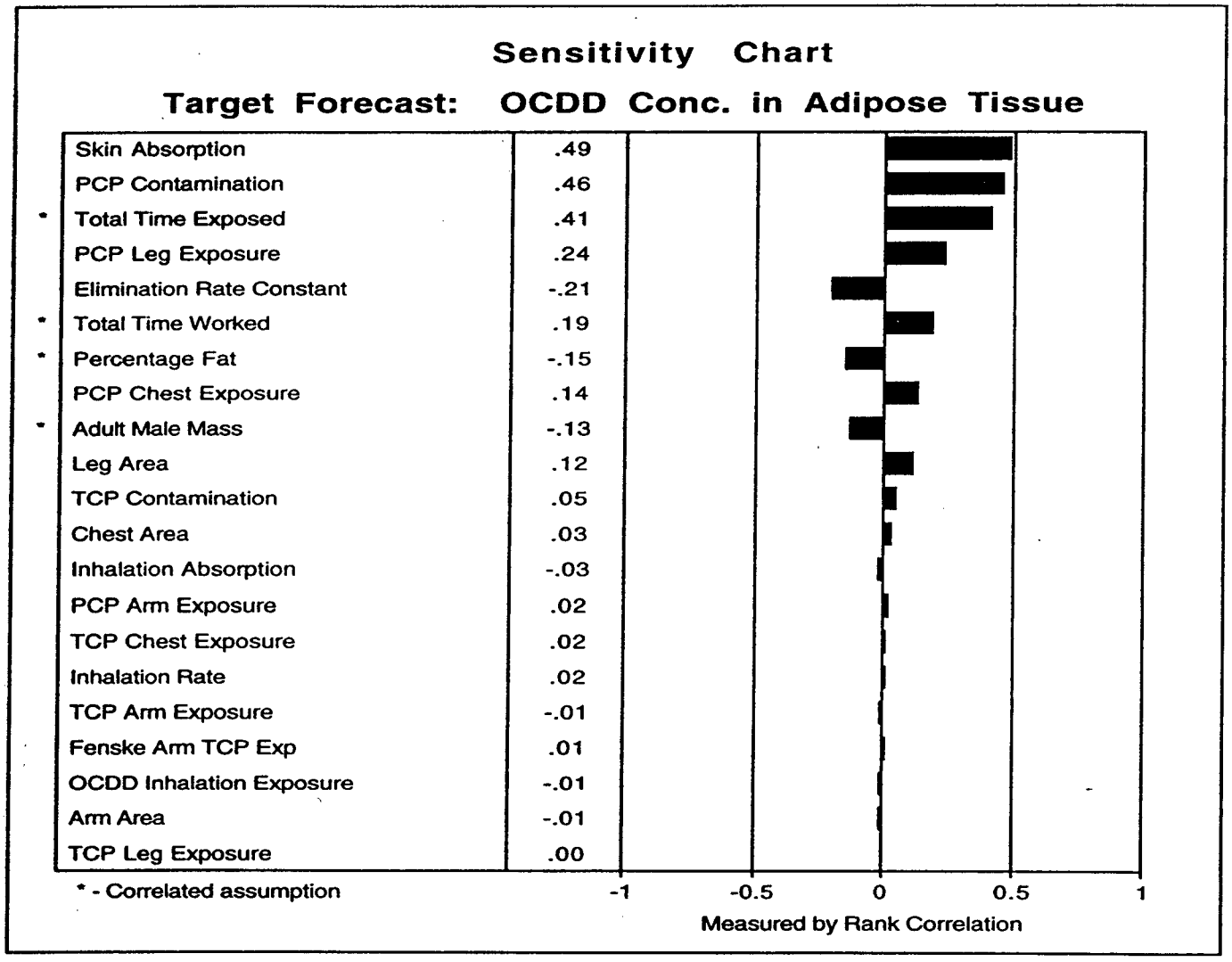
Crystal Ball Report
Simulation started on 9/17/95 at 18:04:60
Simulation stopped on 9/17/95 at 18:54:19



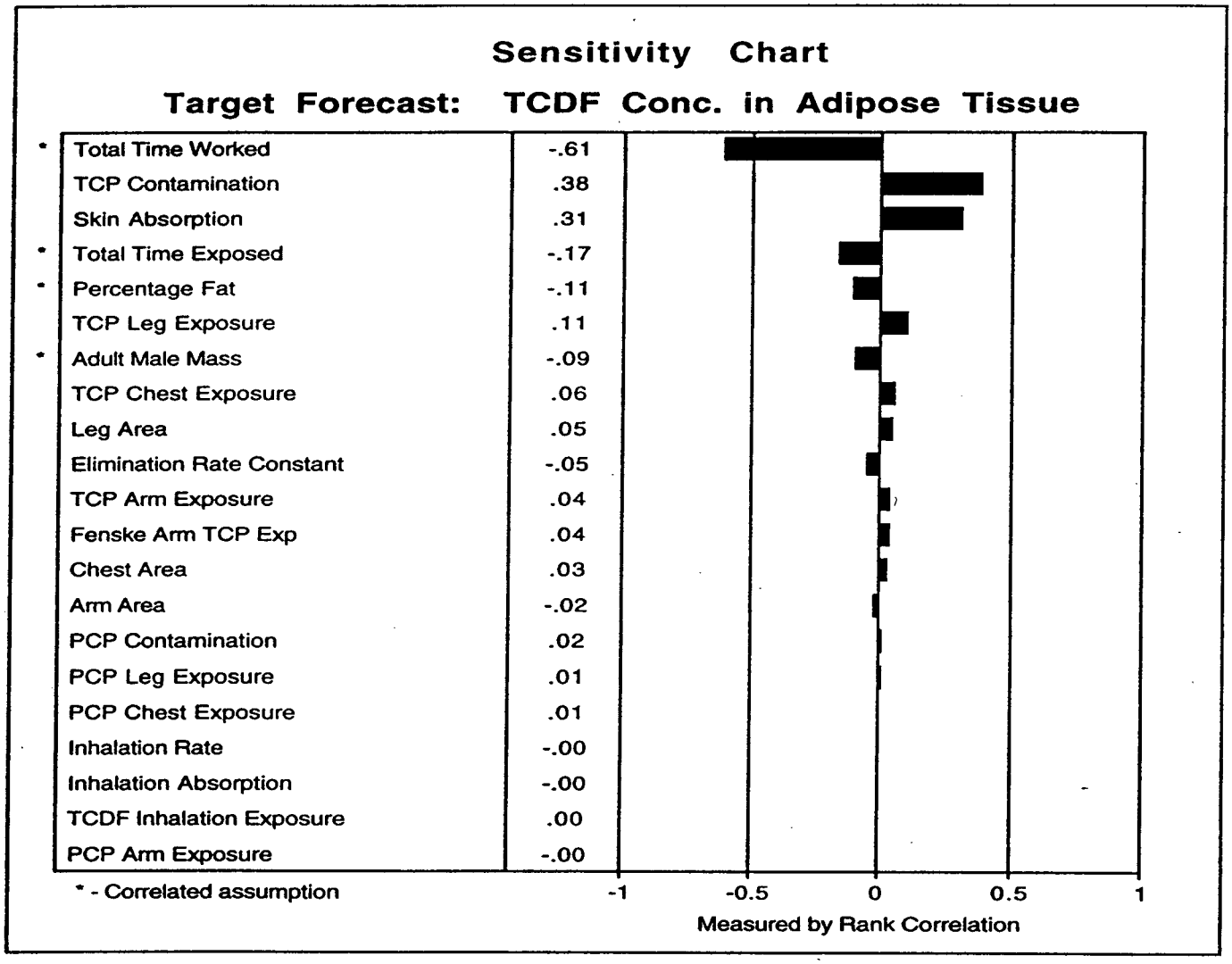
Crystal Ball Report
Simulation started on 9/17/95 at 19:05:20
Simulation stopped on 9/17/95 at 19:55:18



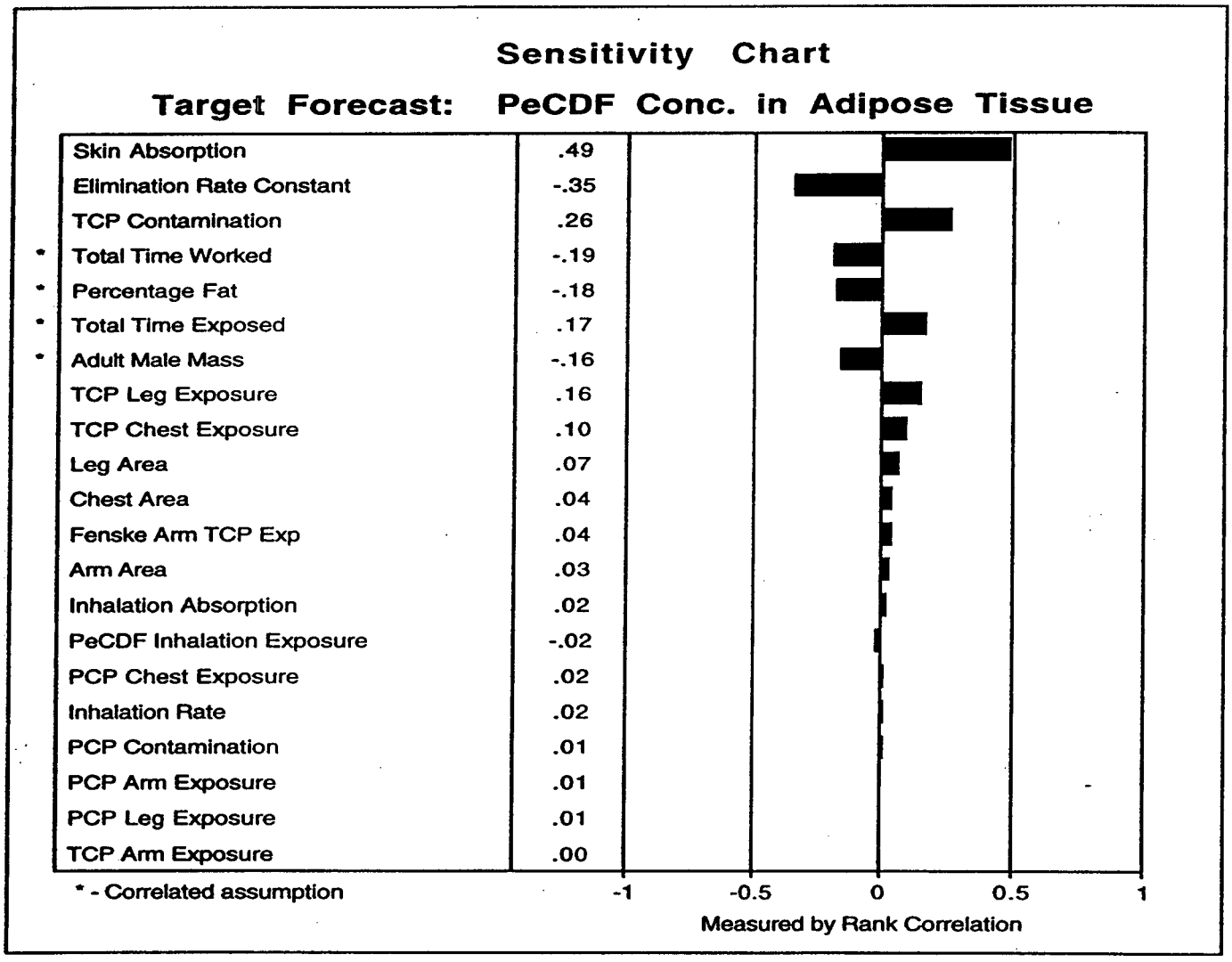
Crystal Ball Report
Simulation started on 9/17/95 at 20:05:16
Simulation stopped on 9/17/95 at 20:56:00



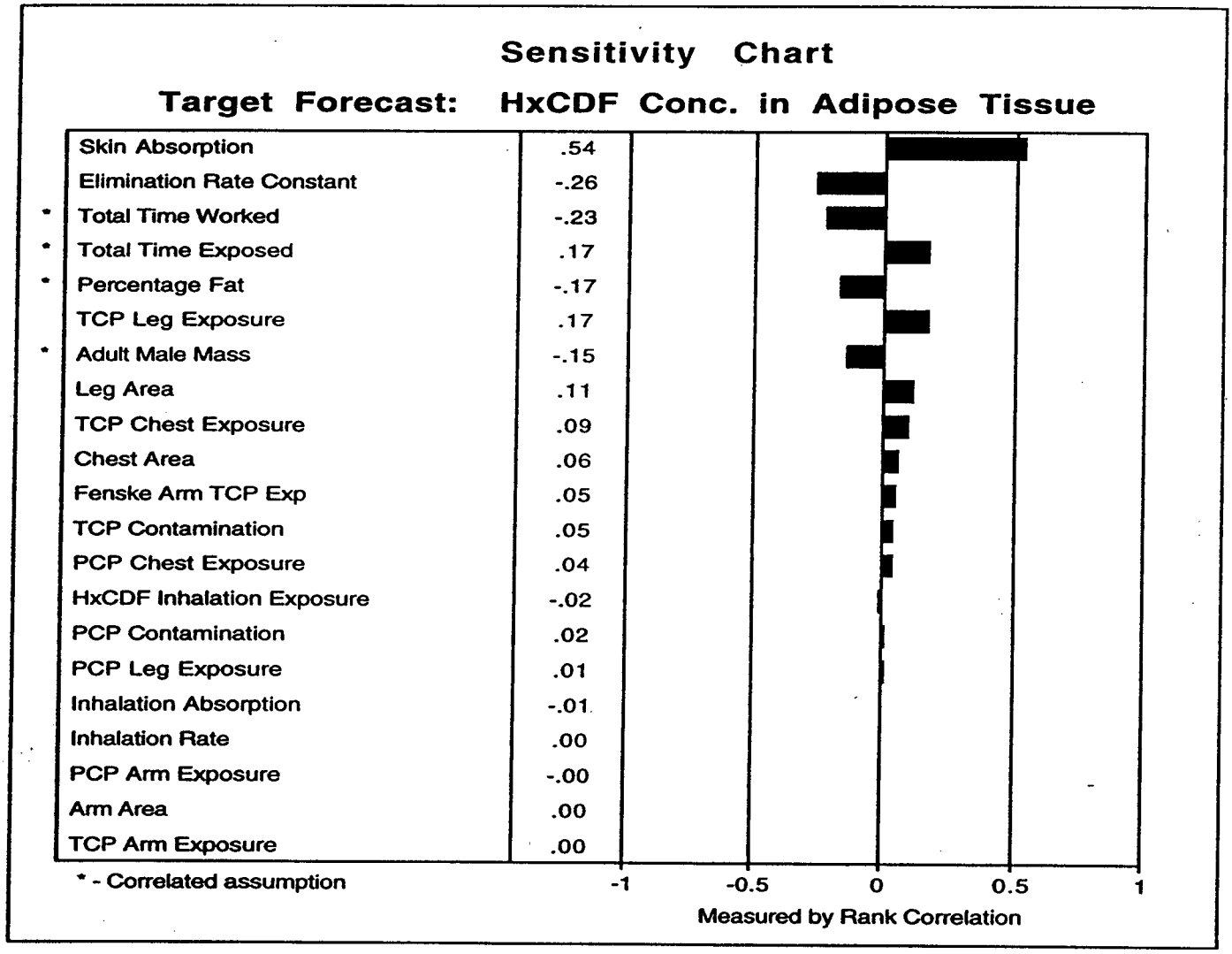
Crystal Ball Report
Simulation started on 9/18/95 at 20:24:41
Simulation stopped on 9/18/95 at 21:13:59



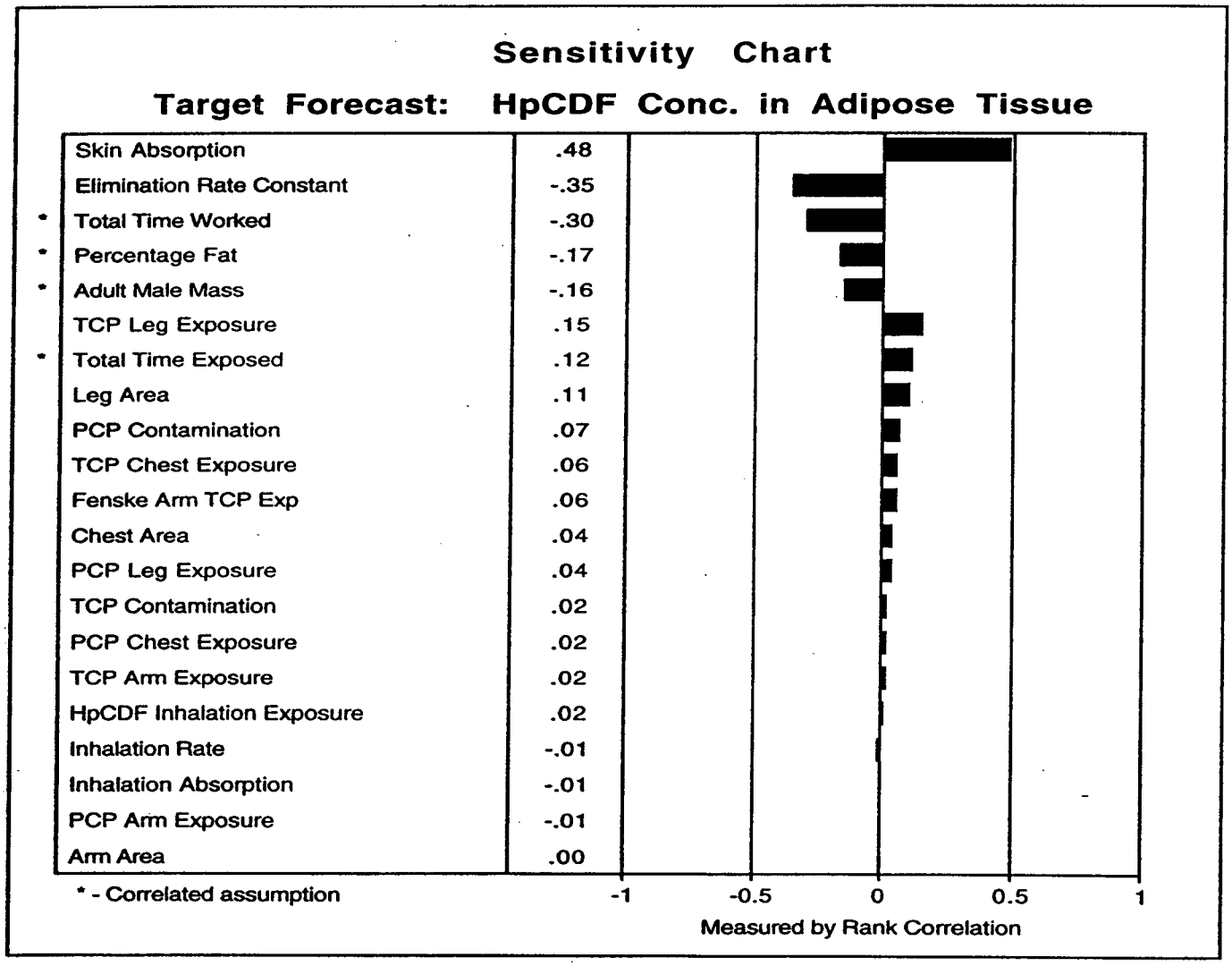
Crystal Ball Report
Simulation started on 9/18/95 at 21:22:42
Simulation stopped on 9/18/95 at 22:11:50



Crystal Ball Report
Simulation started on 9/19/95 at 0:48:38
Simulation stopped on 9/19/95 at 1:37:13



Crystal Ball Report
Simulation started on 9/19/95 at 5:48:41
Simulation stopped on 9/19/95 at 6:37:01



Crystal Ball Report
Simulation started on 9/19/95 at 16:09:24
Simulation stopped on 9/19/95 at 17:00:52

Sensitivity Chart

Target Forecast: OCDF Conc. in Adipose Tissue