Item ID Number 05530 ☐ **Not Scanned**

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Report/Article Title Comments to the EPA Draft Document "Estimating Exposures to 2,3,7,8-TCDD" (June 1987)

Journal/Book Title

Year 1987

Month/Day

Color ☐

Number of Images 0

Description Notes Also included is a cover letter from Dennis Paustenbach to Alvin L. Young.

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September 1, 1987

Dr. Alvin Young
Executive Office of The President
Office of Science & Technology Policy
726 Jackson Place, N.W.
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Dear Al:

Enclosed please find Syntex's comments on the EPA draft (June 1, 1987) document entitled "Estimating Exposures to 2,3,7,8-TCDD" by the Exposure Assessment Group. We hope you will have the opportunity to bring these comments to the attention of appropriate individuals at EPA.

The draft, in general, does a credible job of reviewing the literature. However, we take serious issue with some of the exposure scenarios which the EAG constructs to assess human exposure. Using some of their assumptions and exposure scenarios, TCDD in soil would need to be restricted to the 1 ppt level. Equally serious is the EAG's omission of exposure scenarios which reflect the levels of TCDD to which some persons might be exposed; specifically, those having to do with typical residential and occupational settings.

We appreciate your providing us with the draft document and with the opportunity to comment on it. It is our hope that the final version will present a more balanced view of human exposure to TCDD contamination.

Sincerely yours,

Dennis Paustenbach/DZ

Dennis Paustenbach, Ph.D.
Manager, Environmental and Occupational Toxicology

wp/0237e-7

Enclosures

Comments to the EPA Draft Document
"Estimating Exposures to 2,3,7,8-TCDD" (June, 1987)

Table of Contents

Executive Summary. 1

Introduction 7

General Comments 7

  Exposure Scenarios 7

  Risk Criteria for Small Populations. 11

  Virtually Safe Dose for TCDD 14

Line-by-Line Comments. 21

Fruit and Vegetable Ingestion. 84

Incinerator Exposure Parameters. 84

Alternate Scenario/Alternate Approach. 85

References 88

Comments to the EPA Draft Document
"Estimating Exposures to 2,3,7,8-TCDD"
(Draft of June, 1987)

Executive Summary

The draft document entitled "Estimating Exposure to 2,3,7,8-TCDD" written by EPA's Exposure Assessment Group (EAG) represents a conscientious effort to explore an important aspect of risk assessment. It appears to be a thoroughly researched document which addresses the question of how to estimate exposure to an environmental contaminant. However, the document contains a number of commissions and omissions which detract from its capacity to address accurately the problem of environmental contamination by TCDD. These include:

- Uneven organization - The information needed to reconstruct exposure is presented in various places in the draft document; better organization would make the document more readable.

- Inappropriate exposure scenarios - The proposed exposure scenarios are extreme and do not represent many people who may be exposed to TCDD.

- Excessive reliance on mathematical modelling - Mathematical models are only as good as the data inputted and the available data are often incomplete or unsubstantiated; thus, the final output is suspect.

- Inappropriate selection of exposure parameters - Although most relevant data were reviewed, the EAG did not adopt some of the reported values; the EAG did not adequately explain why they were not used nor why the selected values were selected. Of particular concern is the use of two incompatible assumptions: a high level of exposure from the inhalation of TCDD vapors due to rapid volatilization and a long environmental half-life of TCDD.

- Inadequate documentation of the number of people exposed for each proposed scenario - The EAG defined in quantitative terms the "reasonable worst case" scenario and should also define the "typical" scenario. In addition, the number of people exposed for each scenario should be presented to justify that these scenarios actually comply with EAG's definitions.

- Adoption of linearized, multistage model for deriving the cancer potency value and upper bound incremental risk - The conservatism of this model should be explained if it is used.

A major error of commission which needs rectifying involves the inconsistencies between exposure parameters the authors discuss in the text and those the authors use to estimate human exposure in their sample calculations. For example, scientific papers dealing with environmental half-life were reviewed early in the document, but, in many of the scenarios evaluated, no environmental degradation was assumed to occur. Also, the draft

document reviewed data estimating dermal contamination by soil, but used an arbitrary value rather than the literature values in its calculations. Such inconsistencies may arise from multiple authors writing this draft document without the benefit of a final blending process (where the writers reconcile inconsistencies to devolve a coherent document). Furthermore, perhaps due to multiple authorship, similar information is presented in various sections of the draft document. The information required for estimating exposure is found in various sections but never in one section which makes reconstructing how the EAG developed their exposure values more time-consuming than it should be.

Most importantly, the document often addresses settings which are not applicable to those situations which exist, or are likely to exist, and these settings are therefore not of primary concern to risk managers. Many of the exposure scenarios constructed for approximating human exposure to TCDD appear to be extreme situations which probably do not exist or, if they might exist, are likely to involve few people. For example, all of the scenarios assume ingestion of varying quantities of fish, beef and diary products produced on small farms having TCDD contamination. Since the majority of populations potentially affected by TCDD contamination are urban or suburban and do not ingest TCDD contaminated food, these scenarios would not apply to that majority. It is suggested that the document develop scenarios which address urban or suburban dwellers who do not consume food items produced on contaminated sites.

The authors also need to distinguish explicitly between those scenarios where the TCDD contamination occurred as a one time event and those in which the possibility exists for recurring contamination. For example, situations like Times Beach or Seveso would be one time events, while TCDD emissions from incinerators could well be on-going. Clearly, potential exposures would differ under these two classes of scenarios, with the possibility of recurring contamination likely to pose a higher level of concern.

The authors rely heavily on mathematical modelling to derive many exposure parameters. These mathematically-derived exposure parameters are only as reliable, and often much less reliable, as the inputted data. This is because errors within each input value is compounded when several input values are needed to calculate the exposure parameters. Often, a great deal of uncertainty surrounds each inputted value. Thus, it is advisable that all measurable parameters (e.g., TCDD concentration in fish, beef, milk) be substituted for mathematically-derived parameters. The approach presented in the draft document gives too much credibility to these mathematically-derived parameters.

Another serious shortcoming of the EAG draft document is that it assumes simultaneously that environmental TCDD volatilizes at a rate sufficient to pose a significant exposure via inhalation, and yet that TCDD does not degrade in many of the scenarios evaluated. These two assumptions are incompatible. If TCDD were as volatile as described, the half-life would be weeks, not years. In all likelihood, the volatile component of TCDD is negligible and not worthy of concern.

The risk criteria under which regulatory agencies take action rest mainly on the size of the exposed population. Agencies with remarkable consistency have evolved the position that for small populations, individual risks below 10^{-4} are generally considered de minimus, i.e., one which is below a level of concern. The EAG document would benefit from some estimate of the numbers of people to which the various exposure scenarios describe. More importantly, does EAG know how many people potentially exposed to TCDD contaminated sites who are not described by the proposed exposure scenarios?

The EAG document makes a number of assumptions concerning quantitative risk assessment issues which should be acknowledged. The document has adopted the application of the linearized multistage low dose extrapolation model for deriving the cancer potency value and the upper-bound incremental risk. Although due to policy constraints the document has chosen to use this modelling approach, this does not represent the only scientifically valid approach to assessing TCDD's carcinogenic risk at low doses. In fact, in light of TCDD's lack of genotoxicity, it represents an untenable scientific position. The EAG document need not make this assumption on TCDD's quantitative risk, since it is a document intended to estimate exposure and uptake. This policy issue could be avoided entirely by expressing the exposure estimates in terms of dose rather than in terms of risk, as is done in Table VI-5.

Due to TCDD's lack of genotoxic activity, the scientific evidence convincingly argues for alternative ways to assess TCDD's activity at low doses. Many non-U.S. regulatory agencies have adopted Virtually Safe Doses (VSDs) which are 600-1500 times higher than the VSD implied by the EAG draft document.

In short, the EAG presents a useful review of the pertinent literature. However, we take exception with the application of some of this information. We recommend the EAG give serious consideration to the following recommendations and incorporate them in the revised document.

A. Introduction

EPA's Exposure Assessment Group (EAG) has circulated a document entitled "Estimating Exposure to 2,3,7,8-TCDD" dated June 1, 1987 in draft form for review. According to the forward, the purpose of the document is "to provide the most recent exposure and risk estimation methodology for application to 2,3,7,8-TCDD contaminated sites. This methodology will help us set priorities and make decisions required to address this important problem."

The following comments pertain primarily to the sections in the EAG document entitled: IV. Exposure; VI. Use of Methodologies to Estimate Exposure to 2,3,7,8-TCDD; and VII. Uncertainty Evaluation.

B. General Comments

Exposure Scenarios

We assume that the Exposure Assessment Group (EAG) prepared this document, "Estimating Exposure to 2,3,7,8-TCDD," for use by risk managers in making regulatory decisions concerning TCDD contaminated sites. The document categorizes TCDD sites into "contaminated soil scenarios" and "dump/landfill

scenarios." We do not believe this way of categorizing sites optimizes the usefulness of the information to the risk manager or accurately characterizes the nature of current exposure to TCDD.

One distinguishing feature among contaminated sites which greatly influences any exposure assessments is whether the contamination represents a one-time event (episodic site) or a recurring event (recurring site). The TCDD can only decrease with time at episodic sites, while at sites next to dumps, landfills or incinerators, the contamination may recur because of the nearby presence of the source. More importantly, for recurring sites, the risk manager needs to make policy decisions regarding the location and operation of future dumps/landfills/incinerators and the potential for increasing numbers of people to be exposed. Unlike the recurring sites, the episodic sites are fewer in number and the potential numbers of people exposed are smaller. Consequently, managing the risks at recurring sites must occupy higher priority than those at episodic sites because of the ongoing nature of TCDD exposure.

The issue of the potential numbers of people affected at each type of site will influence any risk management decisions. Travis et al. (1987) conducted a retrospective examination of the level of risk which triggered regulatory action in 132 cases. They considered three variables: (1) Individual risk (an upper-limit estimate of the probability that the most highly exposed individual in a population will develop cancer as a result of a lifetime

exposure), (2) population risk (an upper-limit estimate of the number of additional incidences of cancer in the exposed population), and (3) population size. The findings of Travis et al. (1987) can be summarized as follows:

1. Every situation presenting with an individual lifetime risk above 4×10^{-3} received regulatory action. Those with values below 1×10^{-6} remained unregulated.

2. For small populations, regulatory action never resulted for individual risks below 1×10^{-4}.

3. For effects resulting from exposures to the entire U.S. population, a risk level below 1×10^{-6} never triggered action; a risk level above 3×10^{-4} always did.

Consequently, regulatory agencies have taken different action, depending on the magnitude of the risk and the size of the population. Travis et al. (1987) summarized their conclusion as follows:

> "Perhaps the most surprising aspect of our study is the consistency found among federal agencies' methods in the use of cancer risk estimates for regulatory decisions. With the possible exception of FDA decisions concerning de minimus risks,the history of federal decision making indicates that all agencies are fairly consistent in their implicit definitions of de manifests and de minimus levels of risk. If the above three guidelines were adopted explicitly, consistency with past decisions would be maintained and the process of regulatory decision making would be simplified considerably."

While the exposure scenarios formulated in the EAG draft document may be of theoretical interest, they appear not likely to be of direct use for risk management in many situations. Further, for the example scenarios to be useful, the EAG should estimate the numbers of people who reside at sites described by the exposure scenarios. For example, the majority of TCDD sites in Missouri, which resulted from the spraying of TCDD-contaminated oil in the

early 1970's, are in urban or suburban areas. Consequently, human exposures in these areas are more likely to resemble those for residential and industrial areas as described by Paustenbach et al. (1986) than those described in this EAG document. The number of people in Missouri who may be exposed under scenario 1-4 (a small farm with a pond where the residents consume fish and cattle raised on the farm for 70 years) or under scenario 5-7 (a small farm with a stream where the residents consume fish and cattle raised on the farm for 40 years) undoubtedly is less than 20, if that many. We know of no regulatory actions which address such a limited population. In contrast, the number of people described by residential and occupational exposure to low levels of TCDD are likely to be in the thousands.

The EAG characterization of the above exposure scenarios as "reasonable worst case" (for scenario 1-4) and "typical" (for scenario 5-7) appear to be quite misleading. These scenarios are not applicable to the majority of the potentially exposed U.S. population, and are neither reasonable worst case nor typical.

The EAG document (P. VI-4) states:

> "Describing a "reasonable worst case" involves specifying situations where there is a reasonable probability (e.g., 1% to 10%) of individual events occurring, rather than looking at a situation which would maximize all exposure pathway risks simultaneously. While risks for all scenarios and pathways considered in this chapter are summarized later in a single table [VI-5], it is very unlikely that people would experience the highest risk for all exposure pathways simultaneously. It would be reasonable to assume than an individual could experience the calculated risk of one to several of the pathways simultaneously."

The label "reasonable worst case" should only be applied to situations that have a reasonable chance of occurring. If a scenario has, for example, 20 events, as is the case for a typical scenario described in Table VI-4, and each has a 10% probability, then that scenario has a probability of 1×10^{-20}, a very low probability. Although each individual event has 10% probability, which the EAG characterizes as reasonable, 20 events at 10% individual probability result in an unreasonable scenario.

The judgment by the EAG that it is highly unlikely that people would experience the highest risk for all exposure pathways simultaneously (p. VI-4) should be highlighted and presented as a caveat to those who use Table VI-5. The temptation is too great for the hasty reader to add up the risks across the rows and misapply the information.

Risk Criteria for Small Populations

The EPA has historically regarded one in one million as a de minimus risk, one defined by regulators as not meriting concern. The choice of the de minimus risk needs to be put into perspective. For example, how does this degree of risk compare with the background value for cancer in the U.S., the risk of everyday activities, or with levels which have traditionally triggered action by various U.S. regulatory agencies?

As we discussed earlier, Travis et al. (1987) reviewed past regulatory decisions by the EPA, FDA, and OSHA and noted a remarkable consistency in the degree of risk and the population size which trigger regulatory action. In particular, for small populations, risks below 1×10^{-4} never triggered regulatory action.

Not only have regulatory agencies taken exception to the unilateral application of one in one million risk, but also many common human activities entail risks greatly in excess of one in one million. Wrenn (1986) has discussed these:

> "Examination of the risks of common human activities demonstrates . . . a lifetime risk of 1 in 100,000 or more is within the realm of, or orders of magnitude below, everyday risks that generally do not cause undue concern. These are risks that people, while they are aware of them and may have some concern of fear over them, do not in general alter their behavior to avoid. As Table 1 illustrated, the risks from many activities greatly exceed the level of 1 in 100,000. In comparison to these background risks of "everyday activities," a lifetime risk of 1 in 100,000 is relatively small. Accordingly, regulatory action will not generally be justifiable unless risks are substantially higher than this 1 in 100,000 "benchmark".

Table 1: Lifetime Risk of Death Per 100,000 Persons from Selected Common Human Activities (Wrenn, 1986)

Activity	Lifetime Death Rate per 100,000
Motor-vehicle accidents	1,372
Home accidents	770
Fall	343
Drowning	168
Poisoning (accidental)	161
Fires, burns	140
Suffocation	91
Firearms (accidents)	56
Electrocution	37
Air travel (radiation from one transcontinental trip/year)	14
Tornado	

Finally, the incidence of cancer for the American population and for people in highly industrialized countries is about 1 in 4. Smoking and lifestyle factors such as diet are believed to account for the bulk of this background rate. If regulatory action were taken to limit further risk to one in one million, this would be equivalent to lowering the cancer incidence in a million people from 250,001 to 250,000.

Given the above examples, the unqualified use of the one in one million risk criteria in managing TCDD risk lacks a strong rationale, and these points should be raised with risk managers who must make such decisions. The inclusion of risks greatly below one in one million in Table VI-5 of the EAG's draft document misleads the reader as to the health significance of these risks.

The Virtually Safe Dose for TCDD

The current U.S. regulatory position on TCDD is articulated in two publications, one by EPA (1985) and the other by the Centers for Disease Control (CDC) (Kimbrough *et al.*, 1984). Both agencies treated the TCDD mutagenesis, carcinogenesis, and tumor promotion data similarly in their estimates of the potential human cancer risk posed by exposure to TCDD at low doses. Both agencies assume that TCDD is a mutagen, that the supposed DNA damage it inflicts may progress to tumor formation, and that any exposure contributes to a lifetime cancer risk. The tumor promotion data on TCDD are not considered in these risk estimations despite the overwhelming evidence that TCDD has no mutagenic activity (see Shu *et al.*, 1987 for a review).

Upon the assumption that TCDD possesses mutagenic activity, the EPA has estimated a virtually safe dose (VSD) for TCDD at one in one million risk of approximately 0.64×10^{-14} g/kg/day (EPA, 1985) (= 6.4 fg/kg/day) and the CDC of 28 to 1428×10^{-15} g/kg/day (= 28 to 1428 fg/kg/day) (Kimbrough et al., 1984). These estimates are derived from a low-dose linear extrapolation of the tumor data obtained in animal tests, the traditional approach used for tumor initiators. The cancer potency value of 0.156 $(ng/kg/day)^{-1}$ adopted in the draft document (p. VI-2) implies that EAG has adopted the EPA approach.

In the American Industrial Health Council (AIHC) comments to EPA on risk assessment guidelines (AIHC, 1985), it stated:

> It is also important that the assumptions and constraints included in the models be explicitly noted and evaluated. The Proposed Guidelines make the linearized multistage model the model of choice. Dr. Roy Albert (then Chairman of the Cancer Assessment Group) described Agency use of that model and the way data are treated in applying the model (Albert 1982):
>
> - non-threshold: "if a carcinogenic response occurs at the dose levels used in the study, then responses will also occur at lower doses with incidence determined by the . . . [linearized multistage model]."
>
> - "Whenever the multistage model does not fit the data sufficiently well, the data at the highest dose is deleted and the model refitted to the rest of the data. This is continued until an acceptable fit to the data is obtained."
>
> The mathematics in the model have been disclosed, but the characteristics and assumptions of the model have not been fully explained. AIHC believes that these assumptions and characteristics must be taken into account so that the values generated by the programs can be fully and fairly evaluated in the multidisciplinary step of risk characterization.

Three characteristics of the computer programs of the multistage model used by the Agency (Global 79 or Global 82) are particularly worth noting:

(i) the program has a procedure for calculating a linearized 95% upper confidence limit on added risk, */ but does not apply that procedure to calculate the 95% lower limit on added risk.

(ii) the model does not calculate confidence limits in a statistical fashion, independent of the linearized constraint.

(iii) the calculation of the most likely value is constrained by rejection of negative parameter values, so that all points on the projected dose response curve are forced to be positive and the response is forced to increase with dose despite data to the contrary.

Generation of an unconstrained most probable estimate of added risk, as well as unconstrained values for upper and lower bounds, would provide data that assist in judging the biological relevance of the model and the values it generates. This additional information would assist in the exercise of scientific judgment in interpreting the results as part of the risk characterizing process.

In contrast to the EPA approach, non-U.S.regulatory agencies have applied safety factors to the results of the 2-year chronic bioassay (Kociba et al., 1978) of 0.001 μg/kg to derive allowable exposure estimates. These limits are significantly above those of the EPA and the CDC. For a comparison of allowable TCDD levels estimated by various regulatory agencies, see Table 2.

*/ The linearized multistage model does not incorporate background tumor rates in the calculation. The term "added risk" or "extra risk" represents calculation of the amount of "risk" at particular dose levels over the background rate. Both upper and lower bound limits, therefore, converge on zero.

The Ontario Ministry of the Environment (OME), the State Institute of National Health (SINH) in The Netherlands, and the Federal Environmental Agency (FEA) of the Federal Republic of Germany have estimated TCDD risk to humans that is significantly lower than EPA. The OME risk assessment uses a no-observable effect level (NOEL) of 0.001 μg/kg/day and a safety factor of 100 to obtain a maximum allowable daily intake of 1×10^{-11} g/kg/day (= 10 pg/kg/day) for humans (Ontario Ministry of the Environment, 1985). EPA's value of 1×10^{-14} g/kg/day is approximately 1000 times lower than the OME value.

Table 2

Comparison of Allowable TCDD Intake Calculated by Governmental Agencies

Agency	Risk Analysis Approach	Allowable TCDD Intake (fg/kg/day)
EPA[1]	Linearized Multistage	6.4
CDC[2]	Linearized Multistage	28-1428
SINH[3]	Safety Factor (250)	4,000
OME[4]	Safety Factor (100)	10,000
FEA[5]	Safety Factor (100-1000)	1000 - 10,000
FDA[6]	Safety Factor (77)	13,000

1 EPA Health Assessment Document for Polychlorinated Dibenzo-P-Dioxin (1985).

2 Kimbrough et al. (1984).

3 Vander Heijden et al. (1982), State Institute of National Health, The Netherlands.

4 Ontario Ministry of the Environment (1985).

5 Federal Environmental Agency, The Federal Republic of Germany (1984).

6 Cordle, F. (1981)

(Shu et al., 1987)

The fundamental difference in the analyses by the EPA, OME, SINH and FEA is how each treats the data on TCDD's likely mechanism of action. Scientists from OME, SINH and FEA regard TCDD as a tumor promoter in animals whereas EPA regards TCDD as a tumor initiator.

The following rationale articulated by the OME in its assessment of TCDD risk in carcinogenesis exemplifies the reasoning of these regulatory bodies. In particular, the OME assessment embraces a theoretical threshold, based on TCDD's activity as a promoter in animals, and an observable threshold, based on the NOEL identified in chronic animal studies (Ontario Ministry of the Environment, 1985) the OME report noted that:

- The NOEL (0.001 μg/kg/day) identified in rodent carcinogenicity bioassay studies indicates where the threshold level for tumor production by TCDD exists.
- While TCDD has been rated as the most potent carcinogen in animals using absolute quantities as a criterion, this must be viewed in the context that its carcinogenic properties are expressed at concentrations 2 to 3 orders of magnitude below the LD_{50} range.
- Mutagenicity studies, judged on a battery of short-term tests, indicate that TCDD is not a mutagen in the classical sense. The lack of evidence to suggest that TCDD or its metabolites can directly alter DNA physically or chemically also supports this conclusion.
- From the data in the above section, it can be concluded that PCDDS and PCDDs and PCDFs, especially TCDD, can produce tumors in rodents by an indirect mechanism. A threshold dose exists, as indicated by NOELS from long-term animal studies.

The OME risk assessment rejects the quantitative risk analysis approach which uses mathematical models to extrapolate from animal dose-response data to obtain the VSD (Ontario Ministry of the Environment, 1985). In particular, it notes the following weaknesses in quantitative low dose extrapolation by mathematical models:

- There are many types of mathematical models and they produce very different risk estimates from the same biological data,

- current models assume only direct action by the chemical; current models do not incorporate indirect modes of action (e.g. tumor promoters),

- current models extrapolate probabilities from measurements made in the 10^{-1} to 10^{-2} range down to 10^{-5}, 10^{-6} or 10^{-8}, i.e., well beyond the realm of biological certainty.

The OME rejects the use of the mathematical modeling approach in setting standards (Ontario Ministry of the Environment, 1985) in the following manner:

- Use of these risk-analysis models, in this instance, should therefore be more to indicate the potential range of safe doses rather than to form the basis of a standard.

- The non-linear and sex-specific nature of the rodent bioassay data used and the presence of dose-related primary liver damage at treatment levels causing hepatocellular neoplastic change (Kociba et al., 1978, 1979; NTP, 1980) suggest that these risk estimates for cancer incidence may be confounded by direct tissue damage. Lack of knowledge of the mode of action of 2,3,7,8-TCDD also precludes selection of a specific risk-analysis model.

The use of the 100-fold safety factor for noncarcinogens by regulatory agencies extends over three decades (Lehman and Fitzhugh, 1954). The OME defended its choice of 100 as the safety factor for TCDD (Ontario Ministry of the Environment, 1985) in the following manner:

- This 100-fold safety factor is a practical means to handle the uncertainties in extrapolating from animals to humans. It includes a factor of 10 to extrapolate from animals to humans assuming that animals are less sensitive than humans and another factor of 10 to account for differential sensitivities within the human population.

- This factor incorporates a number of considerations to account for uncertainty in extrapolating from animal data to humans, particularly an allowance in case humans are more sensitive than the animal species tested.

- Since acute toxicity and long-term animal studies are available, and since the short-term mutagenicity studies and the human epidemiology studies are generally negative, a safety factor of 100 is recommended.

- The NOEL of 0.001 μg/kg/day for 2,3,7,8-TCDD, determined in the three-generation reproductive study of Murray et al. (1979) and the two-year oncology study of Kociba et al. (1978) (both using rats), is recommended as a prudent basis for developing a maximum allowable daily intake for human PCDD and PCDF intake.

The FDA, like the OME and SINH, has also estimated TCDD a cancer risk to humans which is significantly lower than that estimated by the EPA (see Table 2). The FDA calculated an allowable TCDD dose level of 13,000 fg/kg/day in its fish advisory (Cordle, 1981). This value is comparable to the estimate calculated by the OME and is approximately 2000-fold higher than EPA's value (Cordle, 1981).

The FDA (Cordle, 1981) assigned the following interpretation to the results of Kociba et al. (1978):

Dose μg/kg/day	Biological Response	FDA Interpretation of Data
0.001	No observable adverse effect	No-observable effect level
0.01	Enzyme induction and liver cell response	Lowest effect level
0.1	Increase in liver carcinoma	Carcinogenic level

The FDA took the 0.001 μg/kg/day dose in Kociba et al. (1978) as a no-observable effect level, applied a safety factor of 77, adjusted for the amount of fish consumed by the 99th percentile of the U.S. population, and concluded that 25 ppt of TCDD in fish was an acceptable level. Specifically, FDA's reasoning was as follows: If fish containing average TCDD residue levels of 25 ppt (determined by sampling fish) were consumed at the level of

the 99th percentile (= 36.8 g/day) by the U.S. population, the total human daily intake of TCDD would be 0.92 ng or 13 pg/kg/day (= 13,000 fg/kg/day) for a 70-kg person (Cordle, 1981).

The FDA reasoned that 13 pg/kg/day was less than 1/70th of the no-observable effect level, was less than 1/700th of the lowest-effect level, and was less than 1/7000th of the carcinogenic level (Cordle, 1981). The FDA further states that for the U.S. population which consumed fish at the 90th percentile, the safety margin would be even greater than for those who consumed at the 99th percentile.

The FDA has recently reaffirmed 25 ppt TCDD in fish as an acceptable level (Anonymous, 1986). However the FDA has also stated that this level corresponds to a risk of 3 in 1 million, derived by the linear extrapolation approach (Anonymous, 1986). The FDA has offered the following reasoning for its conclusions. In order for fisheries not to exceed the acceptable level established at 25 ppt, the average TCDD in fish must be below 25 ppt and, in fact, the average is 8 ppt. Further, since fish consumption is not restricted to fresh water fish, and since not all fresh water fish are contaminated or are bottom feeders such as carp or catfish, the percent of contaminated fish consumed is closer to 10% rather than 100%. Also, fish consumption at the 90th percentile would be used in exposure calculations. If these considerations are taken into account, the daily consumption of TCDD is 13 pg/day (or 0.18 pg/kg/day). This corresponds to a 3 in 1 million risk according to FDA's linear extrapolation approach (Anonymous, 1986).

C. Line-By-Line Comments

The following are comments on specific statements contained in the document:

1. Page I-5. This report states "While reasonable worst case scenarios illustrate that in the absence of any controls on disposal of 2,3,7,8-TCDD-contaminated material at the 1 ppb level may result in risks in the 10^{-4} to 10^{-2} range."

   It is difficult to reconstruct what the risks are from exposure to 2,3,7,8-TCDD in the various scenarios presented. The equation containing the necessary parameters, the rationale for the parameters, and the results are presented in different sections of the document. For example, the parameters for beef ingestion is presented on p. VI-22, the rationale for these parameters are found on p. III-18, IV-30, VI-17, VI-38 and other places in the document, and the equation for calculating risk on p. VI-2.

   The parameters that were used in this draft document often are more conservative than a "reasonable worst case", and we have made comments in the appropriate sections.

2. Page I-5. This report states "Risks calculated for contaminated materials of 1 ppt or below in land-related scenarios were below about 10^{-6} in all cases regardless of controls, except for the reasonable worst case soil contamination scenarios, where the highest pathway was in the range of 10^{-5}."

   Kimbrough et al. (1984) estimated that at the 1 ppb "level of concern", average exposure to TCDD is 634 fg/kg/day with a resultant cancer risk of about 10^{-6}. Paustenbach et al. (1986) has commented extensively on the inappropriateness of Kimbrough's assumptions and Kimbrough has admitted her exposure assumptions were overly conservative. The 10^{-5} risk calculated in this draft document at a

level of soil contamination of 1 ppt is due to unreasonable selection of exposure parameters and unreasonable exposure scenarios. We have commented on their inappropriateness elsewhere.

3. Page I-5. This report states "Recent literature is divided and seemingly contradictory on the issue of whether, and how much, 2,3,7,8-TCDD is taken up into plants from contaminated soil. The authors of this report conclude that there is evidence that 2,3,7,8-TCDD is taken up by plants growing in contaminated soils, but the amount taken up, or subsequent transport within the plant itself (say, to edible portions) is very uncertain."

   More studies have been conducted on plant uptake of TCDD than on most of the other parameters discussed in this document, and the authors chose to use them in various exposure estimates, e.g., environmental half-life, dermal bioavailability, GI bioavailability of beef and fish, fish-to-sediment ratio. Although the data are mildly conflicting, all the data indicate that plant uptake is low. This makes sense in light of TCDD's very low water solubility. As shown at last years International Dioxin meeting in Japan, the amounts present are so low that labs are generally unable to accurately conduct the analyses. Some reasonable value could be assumed for certain vegetables if this route of entry needs to be addressed. In all likelihood, TCDD uptake by humans from vegetables is low compared with potential uptake through meat and milk.

4. Page I-6. This report states "For systems where two distinct liquid phases exist (water and a relatively nonpolar organic solvent), much greater mobility of 2,3,7,8-TCDD is thought possible, with associated threat to ground water."

   There are little field data to verify this statement. It is, of course, true that this may be possible, but the bottom line is that

the oils will migrate and move the TCDD only a short distance vertically, as is seen in Times Beach. It has been suggested that, in fact, the affinity of TCDD for soil is sufficiently great that the presence of organic solvents does not affect its migration (Yanders, personal communication).

5. Page I-6. This report states "The weight of evidence indicates that 2,3,7,8-TCDD is often bioavailable from various materials, although certain materials may bind 2,3,7,8-TCDD very tightly, decreasing the bioavailability by an order of magnitude or more. The data base upon which this conclusion is drawn is very slim."

   The present data base clearly indicates that TCDD bioavailability is media-dependent and less bioavailable from aged soil or fly ash (van den Berg _et al_., 1985; Umbreit _et al_., 1986a). The authors made no effort to factor this into their exposure parameters and this should be reconsidered. It seems inappropriate to suggest that not much is known about TCDD bioavailability on soil. In fact, probably more is known about TCDD on these media than about any other chemical.

6. Page I-6. This report states "Pharmacokinetic considerations, including back-calculating "background" doses in the U.S. population (if any) from body tissue data, would be a very helpful "reality check" for 2,3,7,8-TCDD risk assessments. At present, however, the published data base is small and cannot easily be used to answer the question of whether a "background" level exists in the general population."

There is considerable evidence that a "background" level of TCDD of between 5 and 12 ppt in adipose tissue exists in the general population (Sielken, 1987, Byard, in press). Gehring (1984) and Commoner (cited in this draft document by the authors) have proposed methods for back-calculating exposure levels from body burdens. The exposure levels needed to produce the background level of TCDD in adipose tissue is much higher than the exposure levels estimated for most pathways in this draft document. This would suggest that either the general population is at much greater risks from their exposure to TCDD than the people exposed to TCDD in the scenarios proposed in this draft document or that the exposure parameters/mathemtatical models used in this draft document are inappropriate.

A paper by Leung and Paustenbach (submitted), contains a discussion of how TCDD uptake could influence the eventual body burden. A review paper by Byard (in press) suggests that adipose tissue concentration less than 1000 ppt probably poses no incremental risk to humans.

7. Page I-6. This report calls for "a limited research program addressing the areas where critical information is needed."

A critical area of needed research is dermal bioavailability of TCDD from different types of soil. There are many shortcomings in Poiger and Schlatter (1980). In addition, the amount of soil that is in actual contact with skin and thus available for absorption needs to be addressed. We would refer the authors to the references discussed in Paustenbach (1987).

Another important area of needed research is species differences in the pharmacokinetics of TCDD. More research data supporting the development of a physiologically-based pharmacokinetic model (PB-PK) for TCDD would be extremely helpful. By extrapolating the results of this type of model from experimental animals to man, one will be able to better estimate human risk.

8. Page II-1. The report states "Possible exceptions are the new information on the volatilization potential of 2,3,7,8-TCDD, as predicted by revised information on Henry's Constant and recent work on increased solubility of 2,3,7,8-TCDD when other organic materials are present."

There is no new information on the volatilization potential of TCDD. While the value of Henry's constant may be somewhat higher than thought years ago, owing to lower solubility values, there are no experimental data for the rate of volatilization of TCDD (or TCDD isomers) from either water or soils. The use of Smith's equation by Podoll, Jaber, and Mill is valid only for molecules that partition freely between the liquid and the two-dimensional gas phase. The model is inappropriate when there is interaction of the participating molecule at the liquid interface, and such is invariably the case for TCDD.

Further, if a mass balance were to be conducted using the high rate of volatilization of TCDD proposed by Freeman and Schroy, it would be readily shown that the TCDD at Times Beach and elsewhere would no longer be present. Of course, the rapid loss described in this document is inconsistent with the estimations of a long environmental half-life of TCDD. Volatility of TCDD may depend heavily on the matrix, i.e., the presence of co-contaminants (Spencer and Farmer, 1980); this seems to have been overlooked by Freeman and Schroy. Analogous to the handling of the plant uptake data, the authors should reserve judgment until the data can be reassessed.

Recent work by Dr. Armon Yanders at the University of Missouri has clearly shown that the predictions of Freeman and Schroy are dramatically inconsistent with actual field laboratory studies. Discussions with Freeman and Schroy indicate that they are well aware of the shortcomings of their original model and plan to revise their work soon. In light of the shortcomings of the old Freeman and Schroy model, we would suggest that reference to it be deleted until they can revise the model so as to account for the field experience.

We would suggest that you review Haque's book, Dynamics, Exposure and Hazard Assessment of Toxic Chemicals, pp. 143-161, which we believe would clearly show that the vapor hazard for chemicals like TCDD is virtually nonexistent.

9. Page III-2. The report states "Freeman and Schroy (1985b, 1986) and Tung et al. (1985) simulated the concentration profile of 2,3,7,8-TCDD in soil with initially uniform contamination. As time progressed, the simulated concentration profile tended to be bell-shaped, with a maximum concentration somewhere in the core of the soil column."

   The migration of TCDD is generally dependent on the mode in which TCDD is applied to soil, the presence or absence of co-contaminants, the soil type, and numerous meteorological conditions. Further, field and simulated data do not support the "bell shaped" nature of the distribution of TCDD in soil (Palausky et al., 1986).

10. Page III-1. The report states: "Except in unusual cases involving mobile, organic co-contaminates, large-scale leaching of 2,3,7,8-TCDD to groundwater from soil is thought to be unlikley." (Note, however, that some landfills may have these very conditions.)

    The calculations shown on page II-6 show that the concentration of a co-contaminant, in which TCDD is very soluble, would have to be in the 10% range in order to significantly increase the TCDD solubility. It is misleading for the draft report to refer to 10% solvent loading as having any usefulness in estimating the effect of solvents which might be present in landfills at the ppb or ppm level; fully 3-9 orders lower than the conditions of the test. The statement that landfills may have these very conditions seems highly unlikely.

11. Page III-3. The report states "The authors noted that 'the floods at Times Beach, Missouri, have not redistributed the TCDD over a large area' and concluded that based on a simulation of the measured concentration profile at some time periods, the volatilization process is a major mechanism by which 2,3,7,8-TCDD is depleted from the soil."

The authors also estimated an environmental half-life of TCDD in soil to be much shorter than that estimated by other researchers, and than the environmental half-life used in this draft document. If TCDD is actually depleted by volatilization at the rate estimated by Freeman and Schroy, the sites contaminated at 1 ppb, 1 ppt, and 1 ppq which are assumed in the scenarios used in this draft would be depleted of TCDD very quickly. In Spencer and Farmer (1980), the vaporization rate (flux) of DDT from inert surfaces (soil) was reported as 0.004 $\mu g/cm^2/hr$. Since the vapor pressure of TCDD is similar to that of DDT, the flux of TCDD from soil can be assumed to be the same as that of DDT. If the concentration of TCDD in soil is 1 ppb, and the depth of contamination is 10 cm, then the TCDD is spread over a 50 cm^2 surface [1 ppb = 1 μg TCDD/kg soil = 1 μg TCDD/(50 cm^2 surface x 10 cm depth), assuming a soil density of 2 g/cm^3]. If all of the TCDD is available for vaporization, then all of it would be vaporized within 5 hours, based on the vaporization rate of DDT. It follows then that individuals would not be exposed over their entire life spans. We believe that if EPA conducts a mass balance of the TCDD in the soil versus that predicted to be lost per unit time, it will be clear that inhalation of vapor at six feet above the ground does not pose a hazard.

12. Page III-4. The report states "Although the surface concentration may theoretically appear to be relevant in some cases, the soil surface is not always quiescent, and could be subject to disturbances due to construction activities, erosion, or digging. These activities will expose the subsurface soil and make these soils available for human exposure."

The use of a 10 cm depth of soil uniformly contaminated with TCDD in some scenarios or a 1 cm depth of soil uniformly contaminated in other scenarios does not factor into account the above statement. Soil turnover will accelerate environmental degradation rates (volatilization, photodegradation, etc.), and while this may increase short-term exposure (if possible), it should also decrease the long-term exposure potential.

13. Page III-6. The report states "Czuczwa and Hites (1986) studied lake sediments and concluded that little photolysis occurred during the long-range transport of atmospheric 2,3,7,8-TCDD on particulates. This finding appears to discredit the theory that 2,3,7,8-TCDD rapidly photolyzes on the soil surface under sunlight."

This inference is probably not correct. First, the tenacious binding of TCDD to fly ash which has been discussed by van den Berg et al. (1983, 1985) and Silkworth et al. (1982) suggest that sunlight probably doesn't penetrate the pores of ash. Secondly, one would need to know the initial concentration of the fly ash to know that there has been no degradation. In our opinion, the data collected by Young et al. (1983) at Eglin and the Seveso exposure (di Domenico et al. 1980c) suggest that degradation at the soil surface almost surely occurs, although it may not be as significant as initially believed.

14. Page III-6. The report states "The concentration of 2,3,7,8-TCDD in environmental media may depend on the degradation of related congeners as well as that of 2,3,7,8-TCDD itself, since more highly chlorinated congeners may degrade to 2,3,7,8-TCDD."

There is no evidence that more highly chlorinated PCDDs are degraded to the 2,3,7,8-isomer. In fact, the available data strongly suggest that this is <u>not</u> the case. EPA's Health Assessment Document for Polychlorinated Dibenzo-p-Dioxins (USEPA, 1985), states,

> Although the degree of photolysis may be related to the extent of chlorination, positional isomerization also plays a critical and perhaps dominant part in the photolysis of higher PCDDs. In higher PCDDs, there appears to be preferential loss of chlorine from the 2, 3, 7 and 8 positions (Nestrick et al., 1980; Buser and Rappe, 1978; Choudhry and Hutzinger, 1984). However, Buser (1979) observed the formation of 2,3,7,8-TCDD in trace quantities, and PeCDD form photolysis of 1,2,3,6,7,8-HxCDD and 1,2,3,7,8,9-HxCDD. PCDD compounds with chlorine substitutions in positions 2,3,7 and 8 are likely to photodegrade faster than compounds not having these positional substitutions. According to such a predicted rule, it is not likely that photodegradation of OCDD and other higher PCDDs will yield a high quantity of 2,3,7,8-TCDD as the stable end product.

15. Page III-6. The report states "However, very few studies have been done on the biodegradation of 2,3,7,8-TCDD in soil."

Numerous investigators have looked at the microbial degradation of 2,3,7,8-TCDD. Matsumura and Benezet (1973) evaluated 2,3,7,8-TCDD biodegradation by 100 microbial strains and found only five strains showed some ability to degrade the compound. Camoni <u>et al</u>. (1982) found that the addition of organic compost rich in organic matter and microbial flora had little influence on 2,3,7,8-TCDD degradation. Kearney <u>et al</u>. (1972) studied the persistence of 2,3,7,8-TCDD in soil from two Maryland locations and found an environmental half-life of

about one year. The environmental persistence of 2,3,7,8-TCDD in the Seveso area was estimated to be greater than ten years (di Domenico et al. 1980) and at Eglin Air Force Base in Florida 10 to 12 years (Young, 1983).

It is clear that the type of microbial flora among other factors greatly influences 2,3,7,8-TCDD biodegradation. The rationale for knowing the 2,3,7,8-TCDD biodegradation rate in order to conduct an exposure assessment is not clear. What is needed for exposure assessment is the overall environmental half-life (the sum of degradation by photolysis, volatilization, migration, microbial degradation, etc.). In this regard, we agree that the half-life of TCDD on soil not exposed to sunlight is probably between 10 and 30 years (Young, 1983, di Domenico et al., 1980c).

16. Page III-7. The report states "Although he [Young] stated that the role of volatilization and microbial degradation in removing 2,3,7,8-TCDD from soil is not clear, he estimated the half-life as 10 to 12 years, based on observed changes in soil concentrations."

The environmental persistence of 2,3,7,8-TCDD depends on site-specific conditions, as demonstrated by environmental half-lives ranging from one year to greater than 10 years (Kearney et al., 1972; di Domenico et al., 1980c). When soil from a Missouri horse arena sprayed with 2,3,7,8-TCDD-containing waste oil was removed and used as fill dirt at the Minker and Stout sites in the early 1970's and

was analyzed for 2,3,7,8-TCDD in the early 1980's, it was found that relatively little degradation had occurred. (Final Report of the Missouri Dioxin Task Force, October, 1983). In contrast, di Domenico et al. (1980c) found little TCDD on the soil after only 18 months post-release.

17. Page III-10. The report states "Although the biodegradation rate for 2,3,7,8-TCDD has not been established, it appears that its half-life in soil is in the range of several decades... For a lifetime exposure evaluation, it is appropriate to take into account the gradually decreasing 2,3,7,8-TCDD concentration in soil from which the contaminant is released for human exposure. For a 70-year exposure period, Equation III-3 indicates that a 30-year half-life causes a 50% reduction in exposure relative to an infinite half-life (i.e., no degradation).

    As stated previously, for exposure assessment purposes, only the overall degradation of 2,3,7,8-TCDD in soil is important, not biodegradation. Because the environmental half-life of 2,3,7,8-TCDD has not been established, for illustrative purposes, inclusion of Figure 2 in the exposure assessment of Schaum (1984) in this document would be especially helpful. In addition, a graph of exposure (ng/kg-day) vs. half-life would also be very helpful. A table developed by Paustenbach (1987) also illustrates that the environmental half-life of TCDD and the actual years of exposure to TCDD impact estimated lifetime dose.

18. Page III-15. The report states "Many aquatic organisms, including fish, selectively accumulate polychlorinated dibenzodioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs), which are substituted at the 2, 3, 7, and 8 positions (Rappe et al., 1981; Kuehl et al., 1985, 1986a,b)."

The document goes on to state that this "selective accumulation" may be due to more rapid elimination of other isomers. Kuehl et al. (1986) found that the rate of depuration of PCDD/PCDFs decreased with increasing degree of chlorination. Thus, the draft document should more clearly point out that there is no evidence that aquatic organisms preferentially take up PCDDs substituted at the 2, 3, 7, and 8 positions.

Because bioconcentration of 2,3,7,8-TCDD in fish is difficult to model, an exposure assessment should be based upon the actual measurement of 2,3,7,8-TCDD in fish in a site-specific manner. Only those parameters that cannot be readily measured should be modelled.

Measuring TCDD in fish directly is much more reliable than trying to estimate a value for the distribution factor, which involves too many assumptions. The recent papers by Branson et al. (1985) and Niimi and Oliver (1986) indicate that the BCF in trout is about 10,000 rather than the range of 2,000 to 238,000 suggested by the water solubility equations. In part, the problems with simple approaches to estimating TCDD's BCF is the enormous water solubility data and the inability of the simple formulas to describe behavior at the extremes of lipid and water solubility.

Lastly, the use of an on-site and off-site dilution factor infers that the system is at steady state. If contamination of a site was a one-time or episodic occurrence, then these dilution factors would not be applicable.

19. Page III-18. The report states "The potential for human exposure through consumption of beef and dairy products is greatest where the cattle have contact with the soil; soil ingestion by cattle is the major pathway for the transmission of 2,3,7,8-TCDD residue from soil to these animals. The amount of soil ingested by grazing cattle can vary between 2% and 15% of dry matter intake, depending on whether vegetation is lush or sparse (Healy, 1968)."

Healy's figure represents an extreme which simply is not applicable for the bulk of U.S. cattle. Due to more sophisticated animal management systems in the U.S., the amount of soil ingested by cattle rarely exceeds 2% of dry matter intake (Fries, in press). According to Fries (in press):

> This assessment indicates that there is a high potential for transfer of TCDD from soil to humans through foods of animal origin under some animal management systems. The systems with the most serious potential rarely occur in the U.S. Lactating dairy cows are rarely pastured and some form of supplemental feeding is always employed. Thus, it is unlikely that oil ingestion would ever exceed 1 or 2% of dry matter intake in practical situations. Cattle raised for beef might often be on pastures with no other feed, but it is the general practice to fatten these animals in feed lots before slaughter. This period of time may be as long as 150 days and animals can gain as much as 60 to 70% in body weight. In addition to metabolism, TCDD concentrations would also be reduced by dilution in the expanding body fat pool. Most hogs destined for slaughter are confined and would never be exposed to contaminated soil. Thus, only cull breeding cattle and pigs might be expected to go directly from soil to slaughter.

> The situation may be different in other countries and this evaluation must be adapted to local conditions. Particular care should be exercised in evaluating such factors as the extent pasture is used in the management system and whether animals are fattened on pasture or have a fattening period in feed lots before slaughter. Land unsuitable for livestock production often will not pose a great risk when used for other purposes. Thus, restrictions on animal access to TCDD-contaminated soil may be more practical than rigorous cleanups.

If cattle are placed in feed lots for as long as 150 days before slaughter, much of the ingested 2,3,7,8-TCDD on contaminated soil may have been eliminated depending on the whole body elimination half-life in cattle. Jones and coworkers found that Holstein dairy cattle given 0.05 or 75 ug of TCDD per kg body weight excreted over 50% of the administered dose in the feces, the majority of this being excreted in the first several days post-treatment (presented at the 6th International Symposium on Chlorinated Dioxins and Related Compounds, Fukuoka, Japan, September 16-19, 1986). In short, the approach and assumptions suggested in the document need to be revised.

20. Page III-19. The reports states "Assuming, again, that 2,3,7,8-TCDD behaves in a manner similar to PBB, and that the conditions on the Michigan farms represent the typical situation on U.S. farms, a beef fat/soil bioconcentration ratio of 0.3 to 0.4 and a milk fat/soil bioconcentration ratio of 0.04 are suggested for use in the procedures described for exposure assessment in this document and in Schaum (1984)."

Unless the composition of fat in beef and in milk is substantially different, or the distribution of ingested 2,3,7,8-TCDD is substantially different, on a mass basis, the amount of 2,3,7,8-TCDD

in beef fat and in milk fat should be very similar. Fries (in press) suggested that the ratio of body fat-to-diet and milk fat-to-diet is about 3.5 for 2,3,7,8-TCDD.

In Part Two of the draft exposure assessment, it was assumed for the reasonable worst-case scenarios that individuals in rural farm households consume home-grown beef 44% of the time during their 70 year lifetime. The calculated risks are shown in Table VI-5. One of the considerations in determining what is an acceptable risk is to determine the number of people exposed to a particular scenario. It would be useful for this scenario, and for all the other scenarios, to estimate the number of people who may be exposed in such a fashion. We believe that it is critical for risk managers to know what percentage of the nation is likely to be impacted.

21. Page III-19. The report states "It should be recognized that the significance of soil ingestion as a pathway for animal exposure, and ultimately for human exposure, is greatly reduced under U.S. agricultural conditions (Fries, 1986). Lactating dairy cows are rarely pastured. Beef cattle that may have been on pasture are often fattened for as long as 150 days in feed lots before slaughter, thus giving considerable opportunity for elimination and dilution of tissue residues."

    Since the USEPA is presumably interested in estimating 2,3,7,8-TCDD exposures of individuals in the U.S., there is no need to cite the 2 to 15% range of dry matter intake by New Zealand cattle (Healy, 1968).

22. Page IV-1. The report states "A recent evaluation of the significance of inhaling volatilized 2,3,7,8-TCDD in the vicinity of a contaminated site indicates that this pathway cannot always be treated as negligible."

Although no reference is given for this claim, all the available data indicate that exposure to 2,3,7,8-TCDD by the inhalation route either from particulates or vapor is "negligible" compared to exposure from dermal contact or oral ingestion. A serious problem with the existing air sampling data for TCDD is that when contaminated particles are captured on a filter, the TCDD can be stripped-off due to the superficial face velocity on the filter, and this TCDD is then captured on the back charcoal filter. Its presence on the charcoal, therefore, is not a reflection of TCDD presence in air as a gas.

23. Page IV-3. The report states "Based on the vapor pressure consideration, Paustenbach et al. (1986) discounted the importance of 2,3,7,8-TCDD uptake via vapor inhalation in risk assessment evaluation, and assumed that the human intake via inhalation is related to the intake of airborne, respirable particulates only. On the other hand, Freeman and Schroy (1985a, b, c) considered the vaporization process to be the most important transport process for CDDs present in soils, and compared the results of their modeling with the concentration data obtained at different depths of the soil column and at different times."

If Freeman and Schroy's data are accurate, then hazardous waste sites contaminated to a level of 1 ppb, 1 ppt, 1 ppq would present a very low risk very quickly due to vaporization of TCDD from soil. Also, Freeman and Schroy ignored the fact that the TCDD was in waste oil, which considerably impedes TCDD volatilization.

The phenomenon described by Freeman and Schroy is not inconsistent with Paustenbach et al.'s claim that the vapor hazard is not significant. If only a few nanograms of TCDD are lost per day per cubic foot of soil, this presents considerable loss due to volatility. However, the loss of a few μg over 24 hours, when diluted by the ambient air, represents an insignificant risk to humans via inhalation. Numerous EPA computer models are available which would demonstrate that this is the case. Consequently, Freemen and Schroy's model is in no way inconsistent with the claims by Paustenbach and co-workers.

24. Page IV-3. The report states "Eitzer and Hites (1986), based on a limited experimental study, found that CDD in the ambient air was present primarily in the vapor phase (this study is discussed in more detail below)."

As mentioned previously, most persons believe that the reason why TCDD is not found exclusively in the particles captured in the first half of collection devices is because the TCDD volatilizes off the particles. Consequently, the TCDD found in the foam in Eitzer and Hites (1986) is because of revolatilization, not because TCDD is present in the ambient air. Such phenomenon has been widely recognized for over 10 years in the field of agricultural hygiene. First principles clearly demonstrate that this must be the case.

Almost certainly, these issues plus the break-through phenomenon discussed previously would account for the results.

25. Page IV-3. The report states "For example, Nash and Beall (1980) found ambient air concentrations of 2,3,7,8-TCDD when silvex spiked with 2,3,7,8-TCDD was applied to turf and field sites."

It is unlikely that the authors could have prevented microdroplets or aerosols of silvex (containing 2,3,7,8-TCDD) from entering the air sampling equipment. This could then result in the levels of TCDD detected. In addition, the sampling devices were placed less than two feet above the ground. For a typical 70 kg man who inhales TCDD vapors from a contaminated site, his exposure to the vapors would occur about six feet above the ground. The excess dilution that occurs from two feet above the ground to five feet above the ground certainly reduces exposure considerably. Finally, it is known that the vapor pressure of TCDD is very low. It is probably much lower after it has been in contact with soil for some time (aged). TCDD on aged soil is more difficult to extract off the soil and has been shown to be less toxic than non-aged soil samples containing TCDD.

As mentioned, if TCDD volatilization is significant, this would argue for a much shorter half-life than what has been determined by other investigators and what is being used in this draft document. If TCDD volatilization is significant, there should be very little TCDD remaining at the environmental contamination episodes which have occurred (e.g., Seveso, Missouri, Vietnam).

26. Page IV-9. The report states "In reality, the 2,3,7,8-TCDD concentration at the soil surface will rapidly approach zero, although the 2,3,7,8-TCDD in the bulk soil may have volatilized very little."

As discussed by Paustenbach et al. (1986), this is likely to be the case. Importantly, dermal and inhalation exposure to TCDD for the most part is due to soil at the surface. The concentration of TCDD in upturned soil due to digging, farming, vehicular activity, etc. will also rapidly approach zero. Regrettably, this critical observation was not taken into account in any exposure scenarios modelled in this draft document. In fact, the EAG state several times in the draft document that degradation at the surface is likely to be nonexistent.

27. Page IV-15. The report states "The conditions for photolysis are exposure to sunlight and availability of a hydrogen donor (Crosby and Wong, 1977). Also the presence of a solvent on soil appears to make absorbed compounds more available for photolysis."

It is of interest that under similar experimental conditions, but in the absence of UV radiation, little degradation or loss has been observed. If vaporization were the major process by which TCDD is lost, then the presence or absence of UV radiation would not influence the rate of loss of TCDD from soil.

28. Page IV-15. The report states "They determined the half-lives on leaves as about 1 to 2 hours, and those on soil as longer than 7 hours. All experiments were conducted under natural sunlight without using organic solvents. Accounting for daily and annual fractions of sunlight, Thibodeaux and Lipsky (1985) adjusted the 6-hour half-life derived by Crosby and Wong to obtain an effective photodegradation half-life of 7.2 days."

Virtually all the published data support rapid degradation or loss of TCDD on surfaces. It would be appropriate to try to estimate exposure to TCDD taking this observation into account.

29. Page IV-16. The report states "A preliminary photolysis experiment using 2,3,7,8-TCDD absorbed on fly-ash particulates suspended in recirculating air indicated that the photolysis of 2,3,7,8-TCDD in particulate form underwent virtually no photolytic reactions after 30 hours of illumination (Mill, 1986)."

    The environmental fate and bioavailability of TCDD adsorbed on fly ash are poorly understood. To assume that TCDD on fly ash behaves similarly to TCDD on soil is likely to overestimate markedly exposure to TCDD.

30. Page IV-16. The report states "Eitzer and Hites (1986) reported that 2,3,7,8-TCDD in the atmosphere is all in vapor form. The vapor was captured by adsorption on polyurethane foam. They collected ambient air particulates using a high-volume sampler and 0.1-um pore size filters, and could not detect 2,3,7,8-TCDD in the particulates."

    If this statement were true, then there really is no point modelling an individual's exposure to TCDD adsorbed onto particulates. If fly ash were present, the TCDD on the fly ash would have all vaporized since, according to Mill (1986), no photolysis occurs.

    The most likely explanation is that cited previously. TCDD on particulates is almost certainly revolatilized and subsequently captured on the foam. This is the only reasonable explanation for most of these data.

31. Page IV-17. The report states "In the absence of further experimental data under sunlight conditions, it appears that a reasonable value for 2,3,7,8-TCDD vapor-phase half-life at present is in the range of 2 to 6 hours."

A short half-life supports the observation that concentrations of TCDD at the soil surface rapidly approach zero.

32. Page IV-19. The report states "Hawley (1985) used the results of Lepow et al. (1975) and Roels et al. (1980) in his assessment of risk from exposure to contaminated soil, and used a value of 0.51 mg/cm^2. This value was taken as the soil covering for estimating exposure to children playing outdoors. For adults, Hawley (1985) assumed a value of 3.5 mg/cm^2 from doing yard work. Schaum (1984), after considering Snyder (1975), Lepow et al. (1975) and Roels et al. (1980), assumed a contact range of 0.5 to 1.5 mg/cm^2 and that this range also represents an average for the entire exposed area of the human body for both adults and children."

In Part Two of this draft document, dermal exposure for all scenarios is assumed to be to 1 mg dust/cm^2/day over 1000 cm^2 of surface area exposed, or 1 g dust/day. This appears to be a reasonable value for days when contact to soil/dust occurs. The arbitrary assignment of 80% of days exposed for "reasonable worst case" exposure scenarios and 50% for "typical" exposure scenarios seems unjustified. A better approach would be to base the percentage of days exposed on site-specific climatological conditions. If outdoor soil is covered with snow or if the ground is frozen for six months out of the year, the reasonable worst case exposure scenario should not be 80% of all calendar days but less than 50% of all calendar days. Likewise, the number of exposure days for typical exposure scenarios would be correspondingly fewer. Another climatological consideration would be

the number of rainy days for a particular site. Dermal exposure to soil would be less likely to take place on rainy days. These site-specific climatological data can be obtained readily from local or state agencies.

33. Page IV-20. The report states "A similar issue is the length of time when the soil is in contact with the skin surface. This is an important factor, since it will help determine the amounts absorbed." In Part Two, an absorption fraction of 0.5% was used based on the data of Poiger and Schlatter (1980). There are several shortcomings in using Poiger and Schlatter (1980). First, their data was derived from rats. It has been demonstrated that rats tend to overestimate human dermal exposure by several-fold (Wester and Noonan, 1980). Second, the 2,3,7,8-TCDD was patched onto rat skin for 24 hours. Human exposure to 2,3,7,8-TCDD will rarely be for such a long duration and the contaminated soil will never be patched onto the skin. Using an exposure duration of 24 hours does not appear to be a "reasonable" worst case, but rather an "unreasonable" worst case. A reasonable worst case should be about four hours. Third, the data of Poiger and Schlatter (1980) showed a dose-dependent increase in absorption with 0.07, 2.4, and 3.1% absorption at doses of 346, 4666, and 17333 ppb. If 2,3,7,8-TCDD contamination is at 1 ppb, 1 ppt, or 1 ppq, the data of Poiger and Schlatter (1980) would suggest absorption fractions which would be magnitudes lower than the 0.07%. Fourth, for many solid compounds, there is generally a lag phase

prior to absorption into the bloodstream. This is intuitively obvious since it takes time for a chemical to be desorbed off the soil and then penetrate through the epidermis. When conducting experimental animal studies measuring absorption after 24 or 48 hours of exposure, this lag phase is not apparent. If typical human exposure is for four hours or less, then, perhaps this amount of time is insufficient for 2,3,7,8-TCDD to have desorbed off the soil particle so that no exposure by the dermal route occurs. Due to the lack of data for the dermal absorption of 2,3,7,8-TCDD, perhaps a more fruitful approach would be estimations based on structure-activity relationships and the comparison of physical-chemical properties (e.g., octanol:water coefficient, lipid solubility).

34. Page IV-20. The report states "For older children, he [Hawley] assumed soil contact over both hands, the forearms, and the legs from the knees down (0.16 m^2). For adults, Hawley (1985) assumed contact on both hands and the forearms (0.17 m^2), estimating 3.5 mg/cm^2 of soil on the skin for adults."

The maximum amount of soil per cm^2 available for dermal absorption should not change between children and adults because only the soil directly in contact with the skin is available. For example, if you put ten layers of soil particles onto skin, still only the bottom layer of soil particles will be available for absorption. The maximum amount of soil per cm^2 available for dermal absorption will change for different soil types, however. These types of experiments can easily be conducted and have been done by Duggan and Williams (1977):

> We made an estimate of the amount of dust retained on the pulp of the forefinger and thumb by taking a pinch of dust from a weighted amount, rubbing the finger and thumb together (the surplus falling back into the weighed amount) and re-weighing the dust. The results of a number of tests with several different people were in the range of 2 to 7 mg of dust retained per finger and thumb with a mean of about 4 mg, i.e., about 2 mg per finger or thumb.

If the surface area of the finger or thumb is known, then one can calculate the amount of soil per cm^2 for the "reasonable worst case" scenario.

In Part Two, the amount of surface area used in the exposure assessment is 1000 cm^2. It seems unlikely that all 1000 cm^2 would be contaminated with the same amount of soil playing children get on their hands. It is even less likely that this degree of contamination would occur repeatedly and routinely. Thus, this exposure assessment parameter represents an "unreasonable" worst case.

35. Page IV-23. The report states "Hawley (1985) first considered studies by Bartek et al. (1972) and Feldman and Maibach (1970) on dermal uptake of various compounds in humans when applied as pure compounds or in acetone for 24 hours. On the basis of these studies, he assumed the percutaneous absorption rate to be 11% in 24 hours for adults."

It is not mentioned that the references which Hawley (1985) relied upon, Bartek et al. (1972) and Feldman and Maibach (1975), did not evaluate dermal uptake of 2,3,7,8-TCDD. Moreover, except for caffeine (23.3%), absorption in the first 24 hours ranged from 0.4% of the applied dose to 10.8%. On the basis of these studies, Hawley

(1985) assumed the percutaneous absorption rate to be 11% in 24 hours for adults. As explained in Comment 33, the only data evaluating 2,3,7,8-TCDD dermal bioavailability is from Poiger and Schlatter (1980) and limitations of their study should be stated if their data is to be used. It is not clear to us why Hawley's approach (Hawley, 1985) is explained here but not used later in the exposure assessment section (Part Two). If Hawley's approach is plausible, then it should be used; if it is not plausible, then the reasons that it is not used and the reasons that an alternative approach is used should be stated. The approach suggested by Paustenbach et al. (1986) should also be considered.

36. Page IV-23. The report states "Absorption from soil contact can therefore be estimated as 0.9% for adults and 1.8% for children; or as a range of 0.07% to 3%, as given by Schaum (1984), with no distinction as to age. The duration of contact, both in terms of physical contact and yearly exposure, can be estimated as 12 hours/day for children and 8 hours/day for adults; and this occurs for about 140 days for children and about 45 days for adults."

After summarizing the approach of Schaum (1984) for the duration of contact and the number of days exposed by children and adults, the draft exposure assessment in Part Two uses a different parameter without adequate justification or even explanation. As stated in Comment 32, a reasonable and more justifiable approach to estimating the number of days exposed per year would be to take into account site-specific climatological data.

37. Page IV-29. The report states "The data from the tracer element studies, Binder et al. (1986) and Clausing et al. (1986), provide support for a preliminary estimate of average soil ingestion by children on the order of 100 to 200 mg/day, consistent with the "low" estimate used by Schaum (1984)."

Both the Binder and Clausing studies have been published (Binder et al., 1986, Clausing et al., 1987). These two studies do not support the use of a soil ingestion rate of 1 g/day as a "reasonable worst case" over a 5 year period between ages 2-6 as used in Part Two of the draft document. Further, these studies suggest that a value of 100 mg/day or less for the toddler years is appropriate.

The studies by Binder and Clausing estimated soil ingestion by toddlers, at ages where soil ingestion is greatest. Due to a greater awareness of personal hygiene, it is reasonable to assume adults ingest less soil than toddlers. Kercher and Anspaugh (1984) estimated an adult soil ingestion rate of 10 mg/day; NAS (1980) and USEPA (1984) estimated a rate of 20 mg/day. USEPA (1984) also considered adult soil ingestion to be about one-fifth of the child's rate. Schaum (1984) considered adult soil ingestion to be "negligible." In several risk assessments, the adult rate of soil ingestion was always lower than the child's rate (Kimbrough et al., 1984, Paustenbach et al., 1986, Eschenroeder et al., 1986).

Because adult soil ingestion is not zero and arises out of incidental hand-to-mouth activity, one approach to estimating adult soil ingestion is to base it on the extent to which hands are contaminated, the fraction of the hands that get into an adult's mouth, and the frequency.

38. Page IV-31. The report states "The potential effects of "market dilution" of beef and dairy products on human exposure are discussed briefly in Schaum (1984), at more length by Fries (1986), and at much greater length in U.S. EPA (1985b) for the particular case of cattle production in Missouri."

It is very unlikely that an individual will ingest beef contaminated with 2,3,7,8-TCDD for an entire 70 year lifetime. Environmental contamination occurs episodically and is either remediated or the residents are evacuated. Nowadays, very few people reside at the same location for 70 years.

The 11,000 and 6,400 days of exposure representing a reasonable worst case and a typical case are overly conservative. The value of 44% for the percentage of home-grown beef consumed by rural farm households was obtained in a survey conducted 21 years ago (USDA, 1966). A survey today would certainly show a smaller percentage. In addition, a survey today to determine the number of people who may be exposed for 70 years or even 40 years would probably result in a very small number. The author's own criterion of "reasonable worst case", which involves a probability of 1 to 10%, would most likely not hold.

As for the dilution factors used (Table VI-4), it seems inconsistent that the on-site dilution factor is 1.0 (no degradation or removal) but the off-site dilution factor is greater than zero. Using an on-site dilution factor of 1.0 assumes that the mode of contamination is continuous. It would not hold if the mode of contamination was episodic. Using an off-site dilution factor greater than zero infers that contaminated media leaves the contaminated site (on-site). If that is the case, then, uncontaminated media off-site will also dilute the contaminated media on-site and should be considered.

Finally, as mentioned in the comments herein, the beef fat:soil and dairy fat:soil ratios should be similar. Several investigations have found that 2,3,7,8-TCDD in mother's milk, on a fat basis, is similar to the level found in body fat (Rappe et al., 1984). Under steady state conditions, there is no reason to believe that the 2,3,7,8-TCDD fat level in one region of the body would be different from another region.

39. Page V-1. The report states "Most contaminated soils tested so far (five) show bioavailability of about 25% to 50% that of 2,3,7,8-TCDD in corn oil given by gavage. Three soil samples spiked with 2,3,7,8-TCDD had bioavailabilities in the 40% to 70% range. Based on limited data, 2,3,7,8-TCDD in fly-ash proved roughly 25% as bioavailable as 2,3,7,8-TCDD from solvent extract of the fly-ash."

Several recent studies have addressed the gastrointestinal absorption of TCDD contaminated soil (McConnell et al., 1984; Umbreit et al., 1985; Paustenbach et al., 1986). Paustenbach et al. (1986) reviewed the relevant animal data pertaining to gastrointestinal absorption of TCDD contaminated soil and discussed some of the factors which may have contributed to the range in data reported:

> Poiger and Schlatter (1980) published the first study on this topic. They dosed rats orally with laboratory prepared TCDD contaminated soil and monitored the % of administered dose in the liver. Their data suggest that as the time of contact between the soil and TCDD (known as aging) increased, the oral bioavailability decreased.
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> McConnell et al. (1984) studied Missouri soil contaminated with TCDD. They looked at the liver concentration of TCDD in the guinea pig and rat, and aryl hydrocarbon hydroxylase (AHH) induction in the rat, following soil ingestion. They concluded that TCDD absorption from soil by test animals is highly efficient, but that they had difficulty in arriving at an exact percentage for bioavailability. In the CDC assessment, Kimbrough et al. (1984) used a 30% bioavailability value (1984) and cited McConnell et al. (1984) as the reference. Lucier et al. (1986) republished some of the original data from McConnell et al. (1984) and concluded the oral bioavailability was 50%. However, the data of Lucier et al. (1986), suggested the bioavailability was dose dependent - 24% at 1 μg/kg and 50% at 5 μg/kg TCDD. Lucier et al. (1986) estimated oral bioavailability by comparing the liver TCDD concentration of control rats dosed with TCDD in corn oil with experimental rats dosed with TCDD on Missouri soil.
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> In a recent abstract, Umbreit et al. (1985) reported bioavailability of less than 0.05% for a New Jersey manufacturing site. This work was subsequently published (Umbreit et al., 1986) wherein they reported oral bioavailability of 0.5% for soil at a manufacturing site and 21% for a salvage yard in Newark. In this paper, the authors attributed an oral bioavailability of 85% to the data presented in the paper by McConnell et al. (1984). Umbreit and coworkers did not discuss how they defined or calculated bioavailability for their own data or in their interpretation of the data of McConnell et al. (1984).

Some of the confusion concerning the value for oral bioavailability undoubtedly arises because of the ways investigators have calculated bioavailability. Apparently, some may have used AHH induction as the basis for calculation, while others have used actual liver levels of TCDD. Thus far, none has used a total material balance, including the amount in all tissues and in excreta, as the basis for comparison. Recently, officials of the EPA (Environ. Reporter, 1986) and CDC (Chem. Reg. Reporter, 1986) cited 85% as the bioavailability of dioxin in soil, in spite of the apparent differences between testing methods and methods for defining bioavailability.

Bonaccorsi et al. (1984) have also published a paper on oral bioavailability in the rabbit. They compared liver levels of dioxin 7 days after an oral dose of Seveso soil or a comparable TCDD dose in alcohol. They reported that absorption of soil-bound TCDD from Seveso was 32% that of TCDD in alcohol.

The divergent results on oral bioavailability reported in the literature may occur for several reasons, which will be discussed below. Umbreit and co-workers (1986) and Poiger and Schlatter (1980) have also offered explanations for the discrepancy. The dioxin concentrations in the soil samples for the various laboratories were similar, but other conditions were quite different. For example, the bolus size (the amount of soil administered to the animal) varied markedly among the studies, as did the amount of TCDD taken up in the liver. The data from the three studies suggest that the larger the quantity of soil (i.e., larger dose of dioxin) given to the animal, the larger percentage of uptake by the liver. There are a number of physiological (e.g., residence time and G.I. motility), biochemical (e.g., liver enzyme induction) and physical (e.g., low concentrations bind more tightly to soil, soil type, co-contaminants) reasons why this might be expected. Due to a lack of experimental data, a similar inference cannot be drawn for the rat. The guinea pig data suggest that when the amount of soil ingested is low (on a mg/kg basis) - a condition which more closely resembles that seen in children - the percent GI absorption is lower than the 30% figure used by CDC.

The level of organic matter in soil may also be an important variable. The New Jersey soil used by Umbreit et al. (1986) contained a high organic loading in the form of asphalt-like residues, as well as natural organic content. Interestingly, when this soil was stripped of its organic loading, and the dioxin was reapplied, bioavailability approached 23% (Umbreit et al., 1986), which supports the hypothesis that increasing amounts of organics in the soil may decrease the bioavailability of TCDD.

In summary, 30% bioavailability of TCDD in soil in the G.I. tract appears to be a more reasonable estimate.

Shu et al. (1987b) studied the GI absorption of TCDD in rats fed TCDD contaminated soil. They reported that approximately 43% of the TCDD on Times Beach contaminated soil was absorbed. They also pointed out that the 80% GI absorption value under consideration by EPA (1987) was scientifically groundless:

> The implications to the public health of trace amounts of 2,3,7,8-TCDD in the environment are under evaluation by regulatory agencies in the U.S. and Western Europe. One major consideration in such evaluations is the contribution to human exposure via ingestion of TCDD contaminated soil. An 80% figure is under consideration by some regulators for estimated human exposure. A contractor for one agency has, in fact, used a value of 100% bioavailability for estimating human bioavailability. Several studies have investigated the oral bioavailability of TCDD from contaminated soil in animals. Most have reported estimates of 25-50%, although one has reported <0.5% and 85%, depending on the source of the contaminated soil. This paper reports an oral bioavailability of approximately 43% in the rat dosed with environmentally contaminated soil from Times Beach, Mo. This figure did not change significantly over a 500-fold dose range of 2 to 1450 ng TCDD per kg of body weight for soil contaminated with approximately 2, 30 or 600 ppb of TCDD. This paper also discusses the methodologic shortcomings which underlie the <0.5 and 85% estimate. The relevance of animal oral bioavailability data for the human remains to be evaluated. However, since regulatory agencies use animal data for extrapolating to humans, the 43% figure would be more accurate than the 80% or 100% estimates. Adoption of the 80% estimate would overestimate human exposure from ingestion of TCDD contaminated soil by approximately two-fold.
>
> Various estimates of oral bioavailability of Missouri soil have appeared in the scientific literature. Some of these have derived from original studies, while others have derived from reinterpretation of previously published data. Table II summarizes the origins of these published figures, which range from 25 to 85% for Missouri TCDD-contaminated soil and <0.5 to

21% for New Jersey contaminated soil. These estimates are used by scientists (Kimbrough, et al., 1984; Paustenbach, et al., 1986; Schaum, 1984) and by regulators (Des Rosier, 1986; Houk, 1986; EPA 1987) to calculate exposures of humans to TCDD, and in turn influence regulatory decisions. Because of the considerable social and economic impact of these decisions, the reasons for the discrepancies in the oral bioavailability data for TCDD merit review. The following discussion examines the assumptions underlying the 25, 50, and 85% estimates for Missouri TCDD-contaminated soil, as well as the validity of these assumptions.

The earliest study was conducted in rats and guinea pigs by McConnell, et al. (1984) (Table II). This is the study which Kimbrough, et al. (1984) used to arrive at a figure of 30% for oral bioavailability of TCDD which they used in their evaluation of potential human exposure in residential sites. This study by McConnell, et al. (1984) also provided the raw data for subsequent reinterpretations by Lucier, et al. (1986), who estimated a 25-50% oral bioavailability for TCDD in rats, and by Umbreit, et al. (1986a), who estimated a figure of 85% for oral bioavailability of TCDD in rats based on the guinea pig data of McConnell, et al. (1984) (Table II).

McConnell and coworkers (1984) studied the hepatic uptake of TCDD in the rat and the guinea pig after administration of oral doses of Missouri soil contaminated in-situ with TCDD. The study utilized soil from Times Beach, MO and Minker Stout, MO which was contaminated at 770 and 880 ppb, respectively, with TCDD. The hepatic TCDD concentration in the rat determined on day 6 following dosing was reported only for the highest dose examined (5 μg/kg). Because this dose is significantly lower than the LD50 dose estimated in rats (22 and 45 μg/kg in male and female rats, respectively, Schwetz, et al., 1973), any toxicity in the animals is unlikely to influence the calculation of bioavailability based on liver TCDD levels in these rats. However, this is probably not the case for the guinea pig study, in which liver TCDD, determined 30 days following oral dosing or at time of death, was used to estimate oral bioavailability (Umbreit, et al., 1986, and personal communication). At the lowest dose administered to the guinea pigs (1.1 and 1.3 μg TCDD/kg of Minker Stout and Times Beach soil, respectively), no animals died. At the mid dose (3.3 and 3.8 μg TCDD/kg of Minker Stout and Times Beach soil, respectively), 2/6 and 1/5 animals died, respectively. At the high dose (11.0 and 12.8 μg TCDD/kg of Minker Stout and Times Beach soil, respectively), 6/6 and 5/5 animals died. Because the animals at 30 days following dosing were either dead or were moribund, one would not expect the mid- and high dose data to provide reliable values for estimating bioavailability. For the mid-dose animals

that survived the 30 days, the excretion of TCDD was very likely affected by the toxicity from TCDD. The data for the low dose were not useful for estimating bioavailability since the amount in the amount in the liver fell below the detection limit of 1 ppb. McConnell, et al. (1984), in fact, did not estimate bioavailability in the rat or the guinea pig on the basis of these data.

McConnell, et al. (1984) presented additional evidence that the guinea pig data are unreliable for estimating oral bioavailability. For identically dosed animals, the amount of TCDD found in the guinea pig livers was higher in those that died (before 30 days post dosing) than in those that survived (sacrificed at 30 days). Factors that may be responsible for this effect are (McConnell, et al., 1984): 1) The wasting syndrome, wherein the TCDD initially in the body may mobilize from fat stores and accumulate in the liver. 2) The greater metabolism and excretion of TCDD in the survivors. Consequently, the guinea pig liver levels mainly reflect toxicological aftermaths rather than bioavailability processes which precede the development of toxicity.

McConnell et al. concluded: "Although one has difficulty in arriving at an exact percentage for bioavailability, the absorption of TCDD from soil appears to be highly efficient in the guinea pig and rat models." (McConnell et al., 1984).

Umbreit, et al. (1986a) reported that oral bioavailability of TCDD from contaminated soil obtained from a manufacturing site and metal yard in New Jersey had in the guinea pig was <0.5% and 21.3%, respectively. However, these results were obtained from comparison of hepatic levels of TCDD obtained from positive control animals (TCDD placed on decontaminated soil 1 hr before use) 19 days after dosing and from experimental animals (manufacturing site or metal yard soil contaminated sometime before 1970) 60 days after dosing (Table IV, Umbreit, et al., 1986a; Umbreit, et al., 1986b and personal communication, 1986). These estimates of oral bioavailability are compromised by the fact that hepatic concentrations of TCDD of the positive control and experimental animals were compared at different times. Whether one uses the TCDD half-life in guinea pigs of 30 days (Gasiewicz and Neal, 1979) or 93 days (Olson, 1986), the unexcreted TCDD in the positive control (measured on day 19) would be approximately 3 times higher relative to that in the experimental animals (measured on day 60), based solely on pharmacokinetic considerations. Moreover, by day 19, 7 of the 8 positive control animals had died, a sign of severe toxicity in these animals. Consequently, a bioavailability estimate derived from comparisons of the TCDD levels in these guinea pigs reflects, to a large degree, differences in toxicity and pharmacokinetics rather than bioavailability.

Umbreit, et al. (1986) also recalculated the guinea pig data of McConnell, et al. (1984) and reported an oral bioavailability of approximately 85% for Missouri soil (Table II). Regulators have subsequently focused on the 85% estimate rather than the 30% figure used by Kimbrough, et al. (1984) (Des Rosier, 1986; Houk, 1986; EPA, 1987). For reasons that have already been discussed, the use of the guinea pig data of McConnell, et al. (1984), in which up to 100% of the animals died at the high dose, for calculating oral bioavailability would yield unreliable values. Umbreit also indicated that when he recalculated the data more recently, he obtained a range in bioavailability of approximately 6-60% rather than 85% (Umbreit, personal communication, 1986). According to his calculations, the calculated bioavailability increased 10 fold as administered dose increased 3 fold. This observation constitutes further evidence that the use of liver TCDD levels in these guinea pigs to estimate bioavailability can create artifacts.

On the basis of the estimates obtained from the New Jersey soil studies and their reinterpretation of the guinea pig data of McConnell, et al. (1984), Umbreit, et al. concluded that the oral bioavailability of New Jersey soil is much lower than Missouri soil. For reasons already discussed, estimates of oral bioavailability from the data on the New Jersey soil and from the reinterpretation of the guinea pig data of McConnell, et al., suffer from serious methodological shortcomings.

It should be noted that hepatic levels of TCDD in the rat measured in this study are not directly extrapolatable to levels in humans. Comparisons of hepatic levels of TCDD among different species have indicated that in rats the liver retains TCDD to a greater extent than livers of monkeys (Piper et al., 1973; Allen et al., 1975; Rose et al., 1976; Van Miller et al., 1976). While the liver:fat ratio for TCDD is approximately one or greater than one in the rat, the ratio is substantially less than one in the monkey (Neal, et al. 1982; Byard, 1987). . . Determinations of TCDD levels in human liver and fat indicate the liver:fat ratio more closely resembles that of monkey rather than that of rat (Facchetti et al. 1981; Ryan et al. 1985).

In conclusion, the oral bioavailability of TCDD from Missouri soil contaminated with TCDD in the early to mid 1970's has a mean of 43% in rats. This estimate is higher than the 30% figure used by the CDC (Kimbrough, et al., 1984), but is considerably lower than the 80% and 100% figures which have been suggested by some regulators (Des Rosier, 1985; Houk, 1986; EPA, 1987). Whether the estimated oral bioavailability obtained in rodents is relevant to humans remains to be evaluated. However, if rodent data are used, the 85% estimate was calculated inaccurately and is based on data which are inappropriate for estimating oral bioavailability.

TABLE II. LITERATURE VALUES FOR ORAL BIOAVAILABILITY OF IN-SITU TCDD CONTAMINATED SOILS

Soil Source	Animal	TCDD Dose (ng/kg)	% Bioavailable	Source of Bioavailability Value	Source of Data
Minker Stout, Missouri	Rat	40-5,000	Not estimated	NA	McConnell *et al.* 1984
Minker Stout and Times Beach, Missouri	Guinea Pig	1,100-12,800	Not estimated	NA	McConnell *et al.* 1984
Minker Stout, Missouri	Rat	1,000-5,000	50%	Lucier *et al.* 1986	McConnell *et al.* 1984 and Lucier *et al.* 1986
Manufacturing Site, New Jersey	Guinea Pig	12,000	<0.5%	Umbreit *et al.* 1986	Umbreit *et al.* 1986
Metal Yard, New Jersey	Guinea Pig	320	21.3%	Umbreit *et al.* 1986	Umbreit *et al.* 1986
Minker Stout, Missouri	Rat	1,000-5,000	25-50%	Lucier *et al.*, 1986	McConnell *et al.* 1984
Minker Stout and Times Beach, Missouri	Guinea Pig	1,100-12,800	85%	Umbreit *et al.* 1986	McConnell *et al.* 1984

(Shu *et al.*, 1987b)

40. Page V-6. The report states "Umbreit et al. presented liver concentrations of 2,3,7,8-TCDD after death or sacrifice at 60 days following gavage (see Table V-1). Much lower concentrations of 2,3,7,8-TCDD were found in the livers of animals receiving soil from the manufacturing site compared with those receiving the dose in corn oil."

The healthfulness of the animals needs to be considered when estimating bioavailability by the presence of TCDD in liver. If the health of the animals is seriously compromised, then the ensuing results become difficult to interpret, if not meaningless.

41. Page V-32. The report states "Pharmacokinetic analysis may also allow for predicting the time required for eliminating the body burden after exposure ceases. With sufficient data and proper understanding, these analyses can account for various exposure and physiologic conditions."

Currently, there is considerable effort in trying to estimate "exposure" from measuring an individual's blood or fat levels of 2,3,7,8-TCDD. Biological monitoring can be used to crosscheck an individual's exposure as estimated by the pathway analysis. In order for this to be accomplished effectively, the more data there is of the pharmacokinetics of 2,3,7,8-TCDD in humans, the more reliable it would be to use blood or fat 2,3,7,8-TCDD levels as a surrogate for estimating exposure using the pathway analysis.

Using the approach in Gehring (1984), and adjusting it by using what is known about the disposition of 2,3,7,8-TCDD in humans, one can make a reasonable estimate of what the daily exposure was based on the level of 2,3,7,8-TCDD in fat.

The recent paper by Leung and Paustenbach (submitted) describes how this could be accomplished.

42. Page V-33. This report states "'Commoner Approach': Commoner et al. (1985, 1986) discussed ways to calculate the intake of 2,3,7,8-TCDD per day from human adipose tissue data."

Commoner presented his approach of calculating 2,3,7,8-TCDD intake based on adipose tissue data at two meetings. Thus, his approach has presumably not undergone peer-review. His approach is not available to the reviewers and thus no comments can be made on its validity.

43. The factors used in exposure calculations in the draft document is summarized in Table VI-4, p. VI-22. We would like to comment on each factor used.

SOIL INGESTION

(a) Contact rate - For scenarios 1-4, 8-11, and 15, representative of "reasonable worst case" scenarios, the contact rate is 1 g/day. For scenarios 5-7 and 12-14, representative of "typical" scenarios, the contact rate is 0.2 g/day.

The values above are presumably based on the studies of Binder et al. (1986) and Clausing et al. (1987). These papers have been published since this document was drafted. Binder and colleagues acknowledged in their abstract that they do not consider these estimates "accurate measures of soil ingestion." Furthermore, the preliminary study by Binder et al. (1986) certainly overestimated soil ingestion rates because it did not include a control group. Clausing et al. (1987) used a control group in their study and concluded that a soil ingestion rate in small children was about 55 mg/day.

While the approach taken by Binder et al. and Clausing et al. may lead to more "quantitative" estimates of soil ingestion rates, their preliminary results do not differ from estimates made by numerous other investigators. Duggan and Williams (1977) estimated a soil ingestion rate in children of 50 mg/day. The USEPA Air Quality Criteria for Lead (USEPA, 1984) and Day et al. (1975) estimated a rate of 100 mg/day. Hawley (1985) estimated a rate of 165 mg/day for 2.5 year olds and 24 mg/day for 6 year olds after taking into account their lifestyle patterns. Paustenbach (1987) summarized the literature and selected 100 mg/day as appropriate. Based on existing data, we believe a "reasonable worst case" soil ingestion rate in 2 to 6 year olds should be 165 mg/day and a "typical" soil ingestion rate should be 55 mg/day.

(b) Absorption fraction - The absorption fraction in all scenarios is 0.3.

The available data suggest an oral bioavailability of between 0.2 and 0.4. Recently Shu et al. (submitted) reported a value of 0.43 in rats fed TCDD-contaminated soil from Times Beach, Missouri. Thus, a value of 0.3 used in this draft document is reasonable.

It should be noted that TCDD bioavailability may be dependent upon soil characteristics as well as the mode in which TCDD

contaminates the soil, i.e., co-contaminants, and how long the TCDD has been absorbed to soil prior to human ingestion (aging). (Umbreit et al., 1986a,b). TCDD bioavailability from fly ash may be different from that from soil.

(c) Exposure duration - The exposure duration for "reasonable worst case" scenarios is 1500 days and "typical" scenarios is 910 days based on factors of 0.8 and 0.5 reflecting the fraction of time an individual is likely to spend in the exposure area.

We believe a better approach of estimating the fraction of time an individual spends in the exposure area is to rely upon site-specific meteorological data. The 0.8 and 0.5 values used in this draft document may be representative of geographic locations where the climatological conditions are temperate year round, e.g., Texas, Arizona. However, for locations where the ground may be snow-covered or frozen six months out of the year or rains every other day, then the above factors are clearly overly conservative. For example, in the St. Louis area, Paustenbach et al. (1986) determined that about 50% of the days of the year the ground would be frozen or snow-covered, or receive 0.1 inch of precipitation. These weather conditions would most likely prevent soil ingestion. Applying the factors of 0.8 and 0.5 to the remaining 50% of the days of the year would be a more "reasonable" approach.

(d) Body weight - The average body weight of children 2 to 6 years of age is 17 kg.

It was determined by Diem and Lentner (1973) that the average body weight of boys ages 2 to 6 was 17.8 kg. Thus, the value used in this draft document is reasonable. In terms of using the same body weight for the "reasonable worst case" and "typical" scenarios, for the sake of argument, we wonder why a lesser body weight was not used for the former case. Based on Diem and Lentner (1973), the average body weight in the bottom five percent of boys between ages 2 and 6 is 13.4 kg.

(e) On-site dilution factor - The on-site dilution factor of 1.0 is used for scenarios 1-7.

This is easy to accept since the level of contamination is specified for these scenarios. What is difficult to accept is the unreasonableness of finding a site that is uniformly contaminated with TCDD. Such an occurrence would probably be limited to Seveso-like situations. The uneven distribution of contamination will result in endless possibilities for exposure scenarios. The decision that soil is contaminated down to a level of 10 cm (p. VI-13), although easy to make for modelling purposes, is difficult to envision in actual field situations. This document should discuss in some detail the ramifications of uneven distribution of contamination and the depth of contamination which would be of concern, or, at the very least, to cite specific references where these concerns have been addressed.

(f) Off-site dilution factor - The off-site dilution factor is 0.37 for scenarios 1-4 and 8-11, 0.009 for scenarios 5-7 and 12-14, and 0 for scenarios 15.

The estimation of an off-site dilution factor requires numerous assumptions. These include estimations for: runoff rates, rates for windblown dust, wind direction frequency, location of the site relative to contaminated site, mixing depth of 10 cm of contaminated soil with off-site uncontaminated soil, rainfall, erosivity index, erodibility factor, etc. It is difficult to envision that the derived factors can predict, with any reasonable level of confidence, the level of contamination off-site.

It would be useful to specify in the draft document the range in which the off-site dilution factor could be rather than one particular value. Furthermore, some sort of validation of the above method for any existing site would be very helpful. Finally, it is not apparent whether the on-site level of contamination (e.g., 1 ppb, 1 ppt, 1 ppq) is changing due to either environmental degradation, vaporization or dispersion to surrounding uncontaminated sites, or dilution of the level of contamination from soil dispersion onto the contaminated site from surrounding, uncontaminated sites.

DERMAL EXPOSURE TO SOIL

(g) Contact rate - The dermal contact rate is 1 g/day for all scenarios.

The studies by Lepow et al. (1975), Roels et al. (1980), and Duggan and Williams (1977) all indicated that the amount of soil

deposited on children's hands is approximately 0.5 mg/cm^2. This value should represent a maximum for soil deposition on children as well as on adults. It may be possible to get more dirt per cm^2 than the above value, but it should not result in greater absorption since only the soil particles directly in contact with skin are available for absorption. Studies of this type should be very straightforward to conduct, and the EPA should consider doing these studies using different types of soils.

The draft document uses a dermal surface area for exposure of 1000 cm^2. The 1000 cm^2 value may underestimate the surface area of probable exposure. This area corresponds approximately to the surface area of both hands of an adult. On days when exposure occurs, the surface area of soil contact is most likely not restricted only to the hands. However, as mentioned elsewhere in our comments, it is unlikely that exposure will take place 24 hours per day. Furthermore, the number of days when soil contact does take place is likely to be less than 80% of an individual's lifetime for the "reasonable worst case" and 50% of his lifetime for the "typical case".

(h) Absorption fraction - The dermal absorption fraction is 0.005.

This value was derived from the geometric mean of the three data points presented in Poiger and Schlatter (1980). Poiger and Schlatter (1980) is difficult to interpret for the following reasons. One, their study was conducted in rats. It has been shown that rats tend to overestimate human dermal exposure by several-fold (Wester and Noonan, 1980). Two, TCDD was patched onto rat skin for 24 hours. Patching will enhance absorption, and direct contact with TCDD by humans will rarely be as long as 24 hours. Three, their data indicated a dose-dependent increase in absorption, with 0.07, 2.4, and 3.1% absorbed at doses of 346, 4666, and 17333 ppb, respectively.

If the TCDD contamination on-site is only 1 ppb, 1 ppt, or 1 ppq, by extrapolation of Poiger and Schlatter's data, the absorption fraction would be much lower than the lowest value of 0.07% at a dose of 346 ppb. In fact, the absorption fraction would be several magnitudes lower. And if TCDD contamination off-site is a smaller fraction of what it is on-site (e.g., 0.37, 0.009), then the absorption factor would be even lower. Thus, the basis for an absorption factor of 0.005 is quite weak. A better approach may be to try to estimate the absorption factor by using structure-activity relationships (e.g., octanol: water partition coefficients, lipid solubilities, etc.).

Most dermal absorption kinetics indicate a lag phase of absorption. This is intuitively obvious in that the chemical must first desorb off the soil particle before it can be available to penetrate the epidermis. When experiments are conducted 24 hours after dermal application of the test agent, this lag phase will not be apparent. If human exposure to soil is less than four hours, which is more realistic than using 24 hours, then it is quite likely that little or none of the chemical had time to desorb off the soil particle and consequently, little or no absorption would have occurred.

(i) Exposure duration - For scenarios 1-4, 8-11, and 15, exposure occurs on 20,000 days. For scenarios 5-7 and 12-14, exposure occurs on 7,300 days. This is based upon 80 and 50% of total days in a 70 year lifetime, respectively.

The comments under soil ingestion also apply here. In short, meteorological data should be used to estimate the exposure fraction.

(j) Body weight - The average body weight over a 70-year lifetime is 70 kg for a male.

The average body weight of a female over her 70-year lifetime is less than that of a male. For the purposes of this draft document, the 70 kg value is reasonable.

(k) On-site dilution factor - The on-site dilution factor for all scenarios is 1.0.

Please refer to comments under "Soil Ingestion".

(l) Off-site dilution factor - The off-site dilution factor is 0.37 for scenarios 1-4 and 8-11, 0.009 for scenarios 5-7 and 12-14, and 0 for scenario 15.

Please refer to comments under "Soil Ingestion".

VAPOR INHALATION

(m) Contact rate - The volume of air inhaled per day is 23 m^3. This volume is based upon an average adult who spends 22.4 hours/day engaged in light activity, 1.4 hours/day engaged in moderate activity, and 0.2 hours/day engaged in heavy activity (p. VI-28).

The volume of air inhaled is associated with the size of an individual (e.g., height, weight). Since the 23 m^3/day value is used to estimate air uptake rate by an average adult, it overestimates the air uptake rate of children. If one value is to be used for an individual over his 70 year life span, a more representative air uptake rate, taking into consideration that the individual takes in less air as a child, should be used. Certainly an individual who was exposed for 40 years should have a different inhalation rate from an individual exposed for 70 years (fraction of time as a child would be different).

It is unclear to us why for certain parameters the estimated value for reasonable worst case and typical case is the same. The approach should be consistent in this regard. The values may be subject to discussion once the consistent approach is in place.

(n) Absorption fraction - The absorption fraction of vapors is 0.75.

The authors of this draft document acknowledge that there are no data on the absorption of TCDD vapors by the lungs and that a range between 50 and 100% is reasonable (p. IV-14). Presumably, the 75% value selected represents the average of the range indicated above. Because the vapor concentration of TCDD is extremely low and TCDD has a high affinity for organics, it is likely that the inhaled TCDD vapors are totally absorbed (or at least initially adsorbed onto lung tissue and subsequently absorbed). We would suggest the use of an absorption fraction of 100% rather than 75%. (Using a 75% absorption fraction means 25% is exhaled - that seems very unlikely given the low concentrations of TCDD that we are considering in this draft document).

(o) Exposure duration - The number of days exposed in scenarios 1-4, 8-11, and 15 is 20,000 days and in scenarios 5-7 and 12-14 is 7300 days.

Unlike exposure duration under "Soil Ingestion" or "Dermal Exposure" which are dependent on meteorological conditions, the exposure duration under "Vapor Inhalation" is dependent on the lifestyle of the individuals living in the various scenarios. If the "reasonable worst case" scenario depicts an individual who spends his entire life in a contaminated area, his exposure duration would be 25550 days (70 x 365). Not only is he there every day of his life, but for 24 hours per day as well as dictated by the contact rate of 23 m^3/day. Certainly this would not represent a "reasonable" worst case scenario.

The selection of 80% of a 70 year lifetime as the "reasonable worst case" scenario can also be interpreted that the individual spends 19.2 hours per day every day of his 70 year lifetime in the contaminated area. It would be helpful for the authors to explain the rationale for selecting this 80% as the "reasonable worst case" scenario. Likewise, the basis for the 50% value used to described the "typical" scenario should be defined better. It may be clearer to specify the number of hours per day spent in the contaminated area for the "reasonable worst case" and "typical" case and then to modify the volume of air inhaled for that many hours per day rather than the approach presented.

(p) Body weight - The average body weight over a 70-year lifetime is 70 kg for a male.

Please refer to comments under "Dermal Exposure".

FAT INGESTION

(q) Beef ingestion - The fat ingestion rate from the consumption of beef is 26 g/day in scenarios 1-4, 8-11, and 15 and 14.9 g/day in scenarios 5-7 and 12-14.

In Pennington (1983), the amount of beef ingestion was 66, 89, and 61 g/day for males between the ages of 14-16, 25-30, and 60-65, respectively. Based on a percentage of fat in beef of 22-23%, the fat consumption rate would be in the same range as those used in this draft document. Thus, the values of 26 and 14.9 g/day used in this draft document seem reasonable.

(r) Dairy ingestion - The fat ingestion rate from the consumption of dairy products is 43 g/day in scenarios 1-4, 8-11, and 15 and 18.8 g/day in scenarios 5-7 and 12-14.

In Pennington (1983), the amount of dairy products ingestion was 577, 303, and 232 g/day for males between the ages of 14-16, 25-30, and 60-65, respectively. Based on a percentage of fat in dairy products of 6-7%, the fat consumption rate would be in the same range as those used in this draft document. Thus, the values of 43 and 18.8 g/day used in this draft document appear reasonable. Due to uncertainties in the consumption estimates of both beef and dairy products, it would be more appropriate to round off the values to two significant places rather than three.

(s) Absorption - The absorption fraction of ingested fat in the GI tract is 0.68.

An absorption fraction of 0.68 from the ingestion of beef and dairy products is based on very little information. It is reasonably certain that absorption is media-dependent. There may be data on PBBs that address GI absorption of beef and dairy products in humans that can be applied to TCDD. At this time, 68% seems reasonable.

(t) Beef exposure duration - The beef exposure duration is 11,000 days in scenarios 1-4, 8-11, and 15 and 6,400 days in scenarios 5-7 and 12-14.

Trends on the number of rural households consuming home-grown beef would certainly indicate a marked decline since the USDA-conducted survey of 1966. A graph of percentage home-grown beef consumption versus number of people would indicate whether the 44% value used in this draft document represents a "reasonable" or "unreasonable" worst case scenario. The EPA's definition of a reasonable worst case scenario is "situations where there is a reasonable probability (e.g., 1% to 10%) of individual events occurring." (p. VI-4). The 70-year lifetime exposure used here and elsewhere more closely represents an "absolute" worst case scenario.

(u) Dairy exposure duration - The dairy exposure duration is 10,000 days in scenarios 1-4, 8-11, and 15 and 5,800 days in scenarios 5-7 and 12-14.

The number or rural households consuming dairy products which have not undergone "market dilution" have certainly declined since the USDA conducted survey of 1966. The unreasonableness of using the 40% value would be borne out if a graph of percentage of home produced dairy products versus number of people is plotted. Given how technology has progressed over the last 70 years, it is unreasonable to assume that for future exposure scenarios the value for home-produced dairy products should be 40%, or that the value for home-grown beef should be 44%.

(v) Body weight - The average body weight of a male over a 70-year lifetime is 70 kg.

Please refer to comments under "Dermal Exposure".

(w) On-site dilution factor - The on-site dilution factor is 1.0 for scenarios 1-7.

Please refer to comments under "Soil Ingestion".

(x) Off-site dilution factor - The off-site dilution factor is 0.37 for scenarios 8-11, 0.009 for scenarios 12-14, and 0 for scenario 15.

Please refer to comments under "Soil Ingestion".

(y) Beef fat/soil distribution - The beef fat/soil distribution factor is 0.4 for scenarios 1-4, 8-11, and 15 and 0.3 for scenarios 5-7 and 12-14.

The use of a beef fat:soil distribution of 0.3-0.4 appears to be substantiated by available data.

(z) Dairy fat/soil distribution - The dairy fat/soil distribution factor is 0.04 for all scenarios.

It is unclear to the reviewers whether body fat and milk fat should have different concentrations of TCDD. Preliminary data from Europe has indicated that to the level of TCDD in human milk fat is similar to that in body fat (Rappe et al., 1984).

DUST INHALATION

(aa) Respiration rate - The volume of air inhaled per day is 23 m^3. This volume is based upon an average adult who spends 22.4 hours/day engaged in light activity, 1.4 hours/day engaged in moderate activity, and 0.2 hours/day engaged in heavy activity (p. VI-28).

Please refer to comments under "Vapor Inhalation". In short, the smaller volume of inhaled air of children was not factored into the 23 m^3/day value.

(bb) Absorption fraction - The absorption fraction of TCDD on dust particles is 0.27.

The draft document cites Schaum (1984) as the basis for deriving an absorption fraction of 0.27 but does not explain Schaum's approach. Schaum (1984) based his approach on data from ICRP (1968). In ICRP (1968), it estimated that for not readily soluble particles (e.g., TCDD absorbed onto particles), 25% would be deposited in the lower lungs, 50% in the upper lungs, and 25% exhaled. Of the 25% deposited in the lower lungs, half of that (12.5%) would ultimately be moved up the mucociliary passageway and swallowed. Thus, a total of 62.5% of inhaled particles would end up in the GI tract. Schaum (1984) assumed a range of GI absorption from 20 to 26%, 100% absorption from the lower lungs, and 0% absorption of exhaled particles to derive a range of pulmonary absorption from 25 to 29%. It is important to note that the pulmonary absorption fraction is dependent on the value for GI absorption fraction. The draft document uses a GI absorption fraction of 30%. Using this value, the pulmonary absorption fraction calculates out to be 31% (0.125 x 1.00 + 0.625 x 0.30 + 0.25 x 0.00). If the GI absorption fraction should change, then the pulmonary absorption fraction must also change.

(cc) Exposure duration - The number of days exposed in scenarios 1-4, 8-11, and 15 is 20,000 days and in scenarios 5-7 and 12-14 is 7,300 days.

Please refer to comments under "Vapor Inhalation". In short, it is clearer to think in terms of X hours per day as the "reasonable worst case" scenario and Y hours per day as the "typical" scenario and then to adjust daily breathing volumes to

reflect that number of hours rather than to think in terms of X and Y days exposed and the 24 hour breathing volumes.

(dd) Body weight - The average body weight over a 70-year lifetime is 70 kg for a male.

Please refer to comments under "Dermal Exposure".

FISH INGESTION

(ee) Ingestion - The amount of fish ingested in scenarios 1-4, 8-11, and 15 is 30 g/day and in scenarios 5-7 and 12-14 is 6.5 g/day.

The inclusion of a graph of the amount of fish ingestion versus number of people would be useful to show that the definition of "reasonable worst case" is being complied with in the draft document.

(ff) Absorption - The absorption fraction is 0.68 for fish by the GI tract.

Please refer to comments under "Fat Ingestion".

(gg) Exposure duration - The exposure duration in scenarios 1-4, 8-11, and 15 is 2,600 days and in scenarios 5-7 and 12-14 is 1,500 days.

The use of the 10% value for the amount of contaminated fish consumed is arbitrary. It is unclear to the reviewer why only the number of years is decreased going from a "reasonable worst case" scenario to a "typical" scenario. Both should be decreased.

(hh) Body weight - The average body weight of a male over his 70-year lifetime is 70 kg.

Please refer to comments under "Dermal Exposure".

(ii) On-site dilution factor - The on-site dilution factor in scenarios 1-4 is 1.0 and in scenarios 5-7 is 0.001.

It is difficult to envision that the pond sediment is as polluted as the soil in scenarios 1-4. Please refer to comments under "Soil Ingestion."

(jj) Off-site dilution factor - The off-site dilution factor in scenarios 8-11 is 0.37, in scenarios 12-14 is 0.001, and in scenario 15 is 0.0.

Please refer to comments under "Soil Ingestion".

(kk) Distribution factor - The distribution factor in fish is 5.

The fish sediment distribution ratio available in the literature are for specific fish and/or specific organic content in sediment. Due to the numerous assumptions that need to be made to come up with a distribution ratio of 5, its use may grossly overestimate or underestimate actual exposure and should not be recommended. In actual field conditions, one is unlikely to measure sediment TCDD levels to estimate fish levels; instead one is more likely to measure fish levels directly. Modelling parameters should be filled in with actual values if these values are obtainable.

SURFACE WATER INGESTION

(ll) Ingestion - The average water ingestion rate is 2 L/day.

In Pennington (1983), the amount of water ingested was reported as 548, 512, and 581 l/day for males between the ages of 14-16, 25-30, and 60-65. These values are 3-4 times lower than that used in this draft document. While 2 l/day could represent a "reasonable worst case", 0.5 l/day probably more represents a "typical" case. When a particular value is based on a 70 kg man the use of this parameter overestimates exposure if exposure occurred only when an individual was a child. Because the intent of this draft exposure assessment is to be able to estimate any individual's exposure, it would be extremely useful if values that change with age can be broken down into several age ranges, e.g., ages 0-1, 1-6, 6-13, and 13-70, rather than one value for all ages. If exposure occurred to an individual between the ages of 0-13, then a more representative value for water ingestion, beef ingestion, dairy products ingestion, fish ingestion, body weight, dermal contact rate, body weight, and respiration rate could be used, rather than the value for a 70 kg adult male.

(mm) Absorption - The absorption factor of TCDD in water from the GI tract is 0.5.

There are no data on the absorption fraction of TCDD from water ingestion. It is not readily apparent why the absorption fraction here is lower than that used for fish and beef ingestion.

(nn) Exposure duration - The number of days exposed in scenarios 1-4, 8-11, and 15 is 20,000 days and in scenarios 5-7 and 12-14 is 7,300 days.

It is probably easier to determine the number of hours per day than the number of days per lifetime which an individual spends at a contaminated site. From the number of hours per day, one then assumes that the daily water ingestion rate is reduced proportionately.

(oo) Body weight - The average body weight of a male over his 70-year lifetime is 70 kg.

Please refer to comments under "Dermal Exposure".

One parameter that was not listed under "Surface Water Ingestion" is the TCDD concentration in water. The approach used to estimate this value (p. VI-42) requires too many assumptions to make the outcome credible. The authors of this draft document should consider dropping this discussion in light of TCDD's very low water solubility.

44. Page IV-47. The report states: "At the soil organic carbon-water partition coefficient of 486,000 cm/g organic cargon, and organic carbon content (OC) = 0.0002 for groundwater media, the retardation factor becomes Rd = 973.

The use of the 486,000 cm/g value for Koc does not seem to have experimental backing. No reference to the literature basis is offered. Aquifers that are relatively free of co-contamination should be more like clean silt-loam soils, for which values of 1 x 10^6 have been reported (Marple et al., 1987). Further, it is not clear how the retardation factor was calculated.

45. Page VII-1. The report states "In developing these scenarios, the Exposure Assessment Group tried to construct examples that are relevant to exposure assessment needs faced by the agency. Accordingly, the major focus is on contaminated soil and on landfills containing dioxins and on incinerators emitting dioxins."

It would be useful if the agency provided information on the number of people that may be exposed under each scenario.

46. Page VII-1. The report states "These physical scenarios are intended to represent either reasonable worst-case situations or situations believed to be more typical, i.e., to more closely resemble occurrences that will be encountered in the field."

A definition was given in the draft document of what constitutes a "reasonable worst-case" situation (p. VI-4). A definition should be given of what constitutes a "typical" situation. These can be

supported by indicating the number of people anticipated to be exposed for each situation.

47. Page VII-1. The report states "These scenarios are intended to illustrate a range of circumstances that may be encountered, rather than predict exposures that will occur at specific sites. As such, it is not meaningful to discuss the uncertainty present in the simplified physical scenarios; rather, the test of their construction will be whether they prove useful to the agency as examples of how to evaluate sites in practice."

One of the most difficult questions to be answered regarding a contaminated site is whether the contaminant concentration is uniform throughout the site; generally, it is not. As a result, numerous possibilities for differing extents of exposure exist. This draft document does not address the issue at all.

48. Page VII-2. The report states "Accordingly, variations among behavioral parameters are factored into the exposure scenarios presented."

Many behavioral parameters change with age and with geographic location (meteorological conditions). Except for soil ingestion by children, all exposure parameters have been based on a 70 kg man.

49. Page VII-2. The report states "Determining exposure requires use of measurement data and mathematical models. Uncertainty can be present in measured values that may not be accurate or representative, in mathematical models that do not reflect the processes actually occurring, and in parameters used in models which are also subject to measurement error."

Much of exposure assessment is dependent upon site-specific information. The use of measurement data whenever possible is far more powerful than the use of mathematical models. Thus, wherever possible, the use of mathematical models should be replaced by

measurement data, e.g., TCDD levels in fish, pond sediment, soil on-site, soil off-site.

50. Page VII-4. The report states "The assessment, which is premised upon a thick layer of contaminated soil being present, assumed that no degradation occurred."

The extent of exposure is influenced by the mode that a site is contaminated (being contaminated). If it is a continuous process, then the assumption that no degradation occurs is plausible. If the contamination was a one-time occurrence, then the assumption that no degradation occurs is implausible. How can the authors estimate exposure by inhalation to dusts and vapors and off-site if no degradation occurs?

51. Page VII-5. The report states "In summary it is unlikely that on-site exposure estimates are in error to a large degree, but off-site exposures can be expected to show substantial site specific variation depending on soil concentration."

Certainly when the on-site TCDD concentration is pre-selected and assumed to be uniform, there would be less error in the exposure estimates. In practice, the on-site TCDD concentration is not that well-defined and not uniform.

52. Page VII-8. The report states "The mixing depth was selected as 10 cm, which was judged to be intermediate to what might occur under different agricultural practices. A half-life of approximately 10 years was selected on the basis of experimental data from one study of 2,3,7,8-TCDD in surface soils."

It is not clear why in some scenarios the environmental half-life is 10 years and in others it is infinite (no degradation). This needs further clarification.

53. Page VII-19. The report states "Exposure duration set at 40 or 70 years is considered as a defined part of the exposure scenario, with other durations being easily evaluated if desired."

It is not true that exposures to other durations can be easily evaluated. Many exposure parameters change with age. Except for soil ingestion, no other parameter has been derived for children. If exposure occurred when a child was 0-13 years old, how many exposure parameters presented in the draft document would apply? The effects of environmental half-life for different age groups can be dramatic (Paustenbach, 1987).

54. Page VII-20. The report states "The model is based on theoretical mass-balance calculations, utilizing equations for fundamental physical/chemical transport processes."

The assumption that there is no degradation of TCDD in the environment is implausible when the document is estimating an off-site dilution factor, wind dispersion (and subsequent exposure to dusts by inhalation), vaporization (and subsequent exposure to vapors by inhalation), and other routes of "degradation." There does not appear to be a mass-balance in terms of ultimate exposure to TCDD.

55. Page VII-22: The report states: "Koc has not been measured for 2,3,7,8-TCDD and must itself be calculated using an empirical relationship relating Koc to Kow, the octanol/water partition coefficient."

Koc has been measured for TCDD for two types of clean, uncontaminated soils (Marple et al., 1987), and attempts have been made to measure Koc for several types of contaminated soils (Jackson et al., 1986). While the regression equation of Lyman and Loreti was cited, the equation derived by Karickhoff et al. (Water Research, 13: 241-249, 1979) was not cited, and this equation produces a Koc value much closer to the experimental values for clean soils.

56. Page VII-22. The report states: "Jackson et al. (1985) reported laboratory measurements of the soil/water partition coefficients for 10 soil samples from sites in Missouri and New Jersey . . . The measured partition coefficients (mean of "SWLP-R data) ranged from 4 x 10^4 to 4 x 10^6 with a geometric mean of 5 x 10^5."

The data reported by Jackson suffer from the fact that the results are internally inconsistent. For example, two values of leachate concentration of TCDD exceed the known water solubility. Moreover, concentrations of TCDD in both equilibrated phases (water and soil) were never measured, so that Koc values were determined from both measured and assumed values. Further, micellar solubilization from suspension of co-contaminants was not taken into account and this invariable accounts for much of the spread in Koc values presented. These are just a few of the many faults in this work. In short, in light of these deficiencies, this paper would probably not be publishable using today's standards; at best, it probably presents the range within which the true Koc might reside.

57. Page VII-22. The report states: "In light of the points raised above, the use of the selected value of Kd should be regarded as uncertain to two orders of magnitude."

For clean soils, there is less than one order of magnitude uncertainty in Koc according to values summarized by Marple et al., (1987).

58. Page VII-25. The report states "Since this value is a factor of four below the more reliably established higher dose values, absorption (and thus exposure) may be underestimated by this factor."

There are many problems associated with the use of the data presented in Poiger and Schlatter (1980) and they have been discussed elsewhere.

59. Page VII-26. The report states "Four of the five tested soils are in agreement with an absorption fraction of this magnitude."

It is very unlikely that the GI absorption fraction of ingested fly ash is in the same range as that of ingested soil. In fact, the available data suggest it is much less than soil. This area should receive some attention in order to address properly incinerator exposure scenarios.

60. Page VII-28. The report states "If Hawley's (1985) estimate that an adult ingests an average 0.060 mg/d of soil . . ."

It may only be a typographical error but, due to its importance, it is mentioned here. Hawley (1985) estimated an adult soil ingestion rate of 0.060 g/day rather than 0.060 mg/day.

61. Page VII-30. The report states "A variety of other studies with chlorinated hydrocarbon compounds (reviewed in Fries, 1982), while not allowing comparisons between beef fat and milk concentrations in the same animals, do not suggest that the milk fat distribution ratios should be lower than the beef fat distribution ratios."

There have been preliminary reports that TCDD levels in human milk fat are comparable to TCDD levels in body fat (Rappe et al., 1984). If these reports are substantiated, it would preclude the use of PBB data on which the beef fat:soil and dairy fat:soil distribution factors are currently based.

62. Page VII-35. The report states "Therefore the use of a single fish/sediment distribution ratio, as done in the fish pathway assessment, must be recognized as a broad approximation."

This statement can be used for every mathematically modelled exposure parameter. This is why, if it is possible to obtain measurement data, such data should be substituted for values generated by mathematical models.

63. Page VII-35. The report states "The 6.5 g/d figure is based on data now over a decade old, and fish consumption may have risen somewhat in the intervening period, however this value still appears to be a reasonable typical value."

The percentage of beef and dairy products ingested that are home grown (home produced), on the other hand, was based on a USDA that is over 20 years old. These percentages probably have changed considerably over this period of time. Some have said that the national average may be about 20% of the figures used here.

64. Page VII-45. The report states "Exposure to 2,3,7,8-TCDD through beef ingestion, dairy products ingestion, soil ingestion by children, and soil dermal contact (listed in decreasing order of estimated exposure) were evaluated using similar assumptions as in the land-related scenarios."

A major unresolved issue is whether the bioavailability of TCDD on fly ash is truly much less than the bioavailability of TCDD on soil. As stated previously, all the data suggest that TCDD on fly ash is not very bioavailable.

FRUIT AND VEGETABLE INGESTION

This analysis is not presented in Table VI-4 because the available data are presumably conflicting. These data illustrate the need to interpret existing data in the other sections with caution. Some parameters in the other sections are based on little or no data, but because the data has not been contradicted (or confirmed), they are utilized. The authors of this draft document may have over-extended themselves in this regard.

INCINERATOR EXPOSURE PARAMETERS

The factors used to estimate exposure from TCDD emitted by incinerators is presented in Table VI-7 (p. VI-55). All the parameters except one listed in this table are the same as in Table VI-4 on which we have already commented. The one exception is the distance of the exposed population to the stack. The draft document used a distance of 0.8 km. While it is not

inconceivable to find rural households next to incinerators, it would be hard to believe that the number of people that fit this description is large, especially if this group is assumed to ingest home-grown beef and dairy products and fish from nearby ponds and streams!

ALTERNATE SCENARIO/ALTERNATE APPROACH

(a) One plausible scenario which should be considered is a community which was developed on an abandoned dump site. If TCDD were detected at this site, two different exposure assessments would be necessary. One would be a retrospective exposure assessment which would evaluate residents' past exposure and the other a prospective exposure assessment evaluating potential future exposure.

(b) One major uncertainty would be determining the TCDD concentration throughout the community. Due to non-uniform distribution of contamination, especially considering the soil depth to which residents may be exposed, determination of the representative TCDD within the community may be extremely difficult. Another consideration is the assignment of an environmental half-life for TCDD in soil. According to the draft document, the use of a 10 year half- life, 29 year half-life or infinite half-life (no degradation), impacts exposure by less than a factor of 2 or 3. This is probably not true (see Paustenbach, 1987).

(c) Once the TCDD concentration in soil is specified, an exposure assessment could essentially follow the approach in the draft document. However, the most plausible routes of exposure are expected to be by inhalation, dermal contact, and soil ingestion. No contamination of food sources would be expected for sites similar to the one discussed above.

(d) Exposure assessments should be conducted according to age. For purpose of a draft approach, exposure parameters for several age groups (e.g., 0-1, 1-6, 6-13, 13-70) may be reasonable. Parameters such as body weight, body surface area, inhalation rates, and behavioral patterns of residents for the geographic location (meteorological conditions) in question can be determined.

(e) Dust levels can be obtained from most locations in the U.S. and can be applied on a site-specific basis. Assigning a value for the level of inhalable dust of crustal origin can be estimated and may be more reliable than using wind dispersion models. Inhalation exposure to TCDD vapors can be modeled according to the approach outlined in the draft document. It is anticipated that the inhalation exposure route is de minimus when compared to exposure from dermal contact or soil ingestion.

(f) Dermal contact with TCDD contaminated solid can follow the approach outlined in the draft document. Major uncertainties would be the bioavailability of TCDD from different types of soil. Additional research should be conducted to address the issue of how much soil per cm^2 individuals may be "soiled", and the dermal absorption factor. Only the layer that is directly in contact can be absorbed. It should be determined experimentally using various uncontaminated soil types and human volunteers. An hourly rather than a daily rate of dermal absorption would be useful and should be assessed in experimental animals which best predict human dermal absorption.

(g) Soil ingestion typically occurs from hand-to-mouth behavior, especially in older children and adults. One approach is to estimate the amount of soil on a fraction of one's hands that is ultimately ingested. This approach can be validated for toddlers by the data of Binder et al. (1986) and Clausing et al. (1987). For older children and adults where no data exist, the same approach can be used, and when data become available, also be validated.

(h) The above scenario may represent another "typical" scenario in addition to the ones proposed in the draft document. The above approach of estimating one's exposure should be considered because it attempts to utilize as much as possible site-specific information and age-dependent physiological parameters. This will lead to better estimates of exposure.

ADDITIONAL RECENT PUBLICATIONS ON TCDD AND SELECTED EXPOSURE ASSESSMENT PUBLICATIONS

AIHC (1984). Chemical carcinogens; Review of science and its associated principles.

AIHC (1985). AIHC Submissions to EPA on Risk Assessment Guidelines.

Alzona, J., Cohen, B.L., Rudolph, H., Jow, H.N., and Frohliger, J.O. (1979). Indoor-outdoor relationships for airborne particulate matter of outdoor origin. Atmos. Environ. 13:55-60.

Bartek M.J., La Budde, J.A. (1975). Percutaneous absorption in vivo. In Animal Models in Dermatology, ed. H. Maibach, Churchill Livingstone, New York, pp. 103-120.

Bartek, M.J., La Budde, J.A., Maibach, H.I. (1972). Skin permeability in vivo: Comparison in rat, rabbit, pig and man. J. Dermatol. Invest. 58, 114-124.

Binder, S., Sokal, D., Maughan, D. (1986). Estimating soil ingestion: the use of tracer elements in estimating the amount of soil ingested by young children. Arch. Environ. Hlth. 41(6):341-345.

Bonaccorsi, A., diDomenico, A., Fanelli, R., Merli, F., Motta, R., Vanzati, R., and Zapponi, G.A. (1984). The influence of soil particle adsorption on 2,3,7,8-tetrachlorodibenzo-p-dioxin biological uptake in the rabbit. Arch. Toxicol. Suppl. 7:431-434.

Branson, D.R., Takahashi, I.T., Parker, W.M. and Blau, G.E. (1985). Bioconcentration kinetics of 2,3,7,8-tetrachlorodibenzo-p-dioxin in rainbow trout. Environ. Toxicol. Chem. 4:779-788.

Byard, J.L. (1987). The toxicological significance of TCDD and related compounds in human adipose tissue. Toxicol. Env. Hlth., (in press).

Camoni, I., Di Muccio, A., Pontecorvo, D., Taggi, F., and Vergori, L. (1982). Laboratory investigation for the microbiological degradation of 2,3,7,8-tetrachlorodibenzo-p-dioxin in soil by addition of organic compost. In: Chlorinated dioxins and related compounds. Impact on the Environment. D. Hutzinger, R.W. Frei, E. Merian, and F. Pocchiari, eds., Pergamon Press, New York, pp. 95-103.

Centers for Disease Control (1986). Correlation between human serum and adipose tissue concentrations of 2,3,7,8-tetrachlorodibenzo-p-dioxin.

Clausing, P., Brunekreef, B., Van Wijnen, J.H. (1987). A method for estimating soil ingestion by children. Int. Arch. Occup. Environ. Med., 59:73-83.

Cockerham, L.G. and Young, A.L. (1982). The absence of hepatic cellular anomalies in TCDD-exposed beach mouse-a field study. Environ. Toxicol. Chem. 1:299-308.

Cohen, A.F., and Cohen, B.L. (1980). Protection from being indoors against inhalation of suspended particulate matter of outdoor origin. Atmos. Environ. 14:183-184.

Crosby, D.G., Wong, A.S., Plimmer, J.R., and Woolson, E.A. (1971). Photodecomposition of chlorinated dibenzo-p-dioxins. Science 173:748-749.

Crosby, D.G., Moilanen, K.W., and Wong, A.S. (1973). Environmental generation and degradation of dibenzo dioxins and dibenzofurans. Environ. Health Perspect. 5:259-266.

Crunkilton, R.L., Smith, L.M., Petty, J.D., and Kleopfer, R.D. (1987). Residues of 2,3,7,8-tetrachlorodibenzo-p-dioxin in the Spring River, Missouri. Water, Air, Soil Pollut. 32:219-231.

Crump, K.S. (1987). A critical evaluation of Sielken's dose response assessment for TCDD. Food Chem. Tox. (in press).

Day, J.P., Hart, M., and Robinson, M.S. (1975). Lead in urban street dust. Nature 253:343-345.

di Domenico, A., Silano, V, Viviano, G., and Zapponi, G. (1980a). Accidental release of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) at Seveso, Italy. II. TCDD distribution in the soil surface layer. Ecotoxicol. Environ. Safety 4:298-320.

di Domenico, A., Silano, V, Viviano, G., and Zapponi, G. (1980b). Accidental release of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) at Seveso, Italy. IV. Vertical distribution of TCDD in soil. Ecotoxicol. Environ. Safety 4:327-338.

di Domenico, A., Silano, V, Viviano, G., and Zapponi, G. (1980c). Accidental release of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) at Seveso, Italy. V. Environmental persistence of TCDD in soil. Ecotoxicol. Environ. Safety 4:339-345.

di Domenico, A., Silano, V, Viviano, G., and Zapponi, G. (1980d). Accidental release of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) at Seveso, Italy. VI. TCDD levels in atmospheric particles. Ecotoxicol. Environ. Safety 4:346-356.

di Domenico, A. and Zapponi, G.A. (1986). 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in the environment: Human health risk estimation and its application to the Seveso case as an example. Regulat. Toxicol. Pharmacol. 6:248-260.

Di Toro, D.M., Jeris, J.S., Ciarcia, D. (1985). Diffusion and partitioning of hexachlorobiphenyl in sediments. Environ. Sci. Technol. 19:1169-1176.

Duggan, M.J. and Williams, S. (1977). Lead-in-dust in city streets. Sci. Total. Environ. 7:91-97.

Eduljee, G. (1987). Chemosphere 16.907-20.

Eschenroeder, A., Jaeger, R.J., Ospital, J.J., Doyle, C.P. (1986). Health risk analysis of human exposure to soil amended with sewage sludge contaminated with PCDD's and PCDF's. Vet. Hum. Toxicol. 28(5):435-442.

Final Report of the Missouri Dioxin Task Force, October, 1983.

Fries, G.F. (1987). Assessment of potential residues in foods derived from animals exposed to TCDD contaminated soil. Chemosphere, in press.

Gehring, P.J. (1984). Background exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. In: Public Health Risks of the Dioxins, W.W. Lowrance, ed., William Kaufmann, Los Altos, CA. pp. 151-154.

Graham, M., Hileman, F., Kirk, D., Wendling, J., Wilson, J. (1985). Background human exposure to TCDD. Chemosphere, 14:6/7, 925-928.

Graham, M.A., Hileman, F.D., Orth, R.G., Ryan, J.J., Sebaugh, J.L., Wendling, J.M., Wilson, J.D. (1987). Background concentration of TCDD and related compounds in adipose tissue in the North American population. Arch. Env. Contam. & Tox. (submitted).

Graham, M., Hileman, F.D., Orth, R.G., Wendling, J.M., Wilson, J.D. (1986). Chlorocarbons in adipose tissue from a Missouri population. Chemosphere, 15:9-12, 1595-1600.

Hardell, L., Domellof, L., Nygren, M., Hansson, M., Rappe, C. (1985). Levels of PCDD and PCDF in adipose tissue of patients with soft-tissue sarcoma or malignant lymphoma exposed to phenoxy acids and unexposed controls. American Chemical Soc., pp. 167-168.

Hawley, J.K. (1985). Assessment of health risk from exposure to contaminated soil. Risk Analysis 5(4):289-302.

ICRP, (1968). Report of Committee IV on evaluation of radiation doses to body tissues from internal contamination due to occupational exposure, ICRP Publication 10. Pergamon Press, New York. Wester, R.C. and Noonon, P.K. (1980). Int. J. Pharmacol. 7:99.

Ideo, G., Bellati, G., Bellobuono, et al. (1982). Increased urinary D-glucaric acid excretion by children living in an area polluted with TCDD. Clin. Chem. Acta 120:273-283.

Ideo, G., Bellati, G., Bellobuono, A. and Bissanti, L. (1985). Urinary d-glucaric acid excretion in the Seveso area, polluted by tetrachlorodibenzo-p-dioxin (TCDD): Five years of experience. Environ. Health Perspect. 60:151-157.

Jackson, D.R., Roulier, M.H., Grotta, H.M., Rust, S.W., Warner, J.S., Arthur, M.F., Deroos, F.L. (1985). Leaching potential of TCDD in contaminated soils. EPA/600/9-85/013 Apr.

Jones, D., Safe, S., Morcom E., Coppock, C., and Ivie, W. (1986). Bioavailability of 2,3,7,8-tetrachlorodibenzo-p-dioxin administered to Holstein dairy cows. Presented at 6th International Symposium on Chlorinated Dioxins and Related Compounds. September 16-19, 1986. Fukuoka, Japan.

Jury W., Spencer, W., Farmer, W. (1984). J. Environ Quality 13,580.

Kearney, P.C., Woolson, E.A., and Ellington, Jr., C.P. (1972). Persistence and metabolism of chlorodioxins in soils. Environ. Sci. Technol. 6:1017-1019.

Kercher, J.R. and Anspaugh, L.R. (1984). Analysis of the NAEG model of transuranic radionuclide transport and dose. Lawrence Livermore National Laboratory.

Kimbrough, R., Falk, H., Stehr, P., Fries, G. (1984). Health implications of TCDD contamination of residential soil. J. Toxicol. Env. Health 14:47-93.

Kuehl, D.W., Cook, P.M., and Batterman, A.R. (1986). Uptake and depuration studies of PCDD's and PCDF's in freshwater fish. Chemosphere 15:2023-2026.

LaGoy, P.K. (1987). Estimated soil ingestion rates for use in risk assessment. Risk Analysis (in press).

Lee, L.E., Hobson, L.B. (1985). TCDD in body fat of Vietnam veterans and other men. In Chlorinated Dioxins and Dibenzofurans in the Total Environment II. ed. L. H. Keith, C. Rappe, G. Choudhary. pp. 205-214, Butterworth, Boston.

Leung, H-W, Paustenbach, D.J. A proposed occupational exposure limit for 2,3,7,8-TCDD. J. Amer. Indust. Hygiene Assoc. (submitted).

MacKay, D., Powers, B. (1987). Chemosphere 16, 745-57.

Marple, L, Berridge, B., Throop, L. (1986a). Measurement of the water octanol partition coefficient of TCDD. Environ. Sci. Technol. 20(4):397-399.

Marple, L., Brunck, R., Throop, L. (1986b). Water solubility of 2,3,7,8-tetrachlorodibenzo-p-dioxin. Env. Sci. Technol. 20:180-182.

Marple, L., Brunck, B., Berridge, B., Throop, L. (1987a). Comparison of experimental and calculated physical constants for TCDD. In: Solv. Haz. Waste Prob., Ed. J. Exner, ACS.

Marple, L., Dei Rossi, D., Throop, L. (1987b). Removal of TCDD from wastewater and wellwater by coagulation and flocculation with aluminum salts. In: Solv. Haz. Waste Prob., Ed. J. Exner, ACS.

Miller, M.M., Wasik, S.P., Huang, G-L., Shiu, W-Y., and Mackay, D. (1985). Relationships between octanol-water partition coefficient and aqueous solubility. Environ. Sci. Technol., 19, 522-529.

Mocarelli, P., Marocchi, A., Brambilla, P., Gerthoux, P.M., Young, D.S., Mantel, N. (1986). Clinical laboratory manifestations of exposure to dioxin in children. JAMA, 256:19, 2687-2695.

NAS (1983). Risk assessment in the Federal Government: managing the process, Natl. Acad. Press.

NAS (1980). Lead in the human environment. Washington, D.C., National Academy Press.

Niimi, A.J. and Oliver, B.G. (1986). Biological half-lifes of chlorinated dibenzo-p-dioxins and dibenzofurans in rainbow trout (Salmo gairdneri). Environ. Toxicol. Chem. 5:49-53.

Norris, L.A. (1981). The movement, persistence, and fate of the phenoxy herbicides and TCDD in the forest. Residue Rev. 80:65-135.

Nygren, M., Hansson, M. Rappe, C., Dommellof, L., Hardell, L. (1985). Analysis of PCDD and PCDF in adipose tissue from soft-tissue sarcoma patients and controls. ACS Meeting, pp. 160-163.

Ontario Ministry of the Environment (1985). Scientific criteria document for standard development - PCDD's and PCDF's. OME, 4-84.

Ono, M. Wakimoto, T., Tatsukawa, R. (1986). PCDD and PCDF in human adipose tissues of Japan. Chemosphere 15:1629-1634.

Palausky, J., Harwood, J.J., Clevenger, T.E., Kapila, S., and Yanders, A.F. (1986). Disposition of tetrachlorodibenzo-p-dioxin in soil. In: Chlorinated Dioxins and Dibenzofurans in Perspective, C. Rappe, G. Choudhary, and L.H. Keith, eds., Lewis Publishers, Inc. pp. 211-223.

Patterson, D.G., Jr., Holler, J.S., Smith,. S.J., Liddle, J.A., Sampson, E.J., and Needham L.L. (1986a). Human adipose data for 2,3,7,8-tetrachlorodibenzo-p-dioxin in certain U.S. samples. Chemosphere 15, 2055-2060.

Patterson, D.G., Jr., Hoffman, R.E., Needham, L.L., Roberts, D.W., Bagby, J.R., Pirkle, J.L., Falk, H., Sampson, E.J., and Houk, V.N. (1986b). 2,3,7,8-tetrachlorodibenzo-p-dioxin levels in adipose tissue of exposed and control persons in Missouri. J. Amer. Med. Assoc. 256, 2683-2686.

Paustenbach, D.J., Shu, H.P., Murray, F.J. (1986). A critical examination of assessments of the health risks associated with TCDD in soil.. Reg. Toxicol. Pharmacol., 6, 284-307.

Paustenbach, D.J. (1987). Assessing the potential environment and human health risks of contaminated soil. Comments Toxicol. 1(3-4): 185-200.

Pennington, J.A.T. (1983). Revision of the total diet study. Food list and diets. J. Am. Diet. Assoc. 82:166-173.

Philipp, M., Krasnobajew, V., Zeyer, J., and Hutter, R. (1981). Fate of TCDD in microbial cultures and in soil under laboratory conditions. FEMS Symp. 12:2210-2233.

Pitot Committee Report (1986). Dioxin "update" Committee, convened by EPA, July 1-2., 1986.

Podoll, R.T., Jaber, H.M., Mill, T. (1986). Tetrachlorodibenzodioxin: rates of volatilization and photolysis in the environment. Environ. Sci. Technol., 20, 490-492.

Poiger, H. and Schlatter, C. (1986). Pharmacokinetics of 2,3,7,8-TCDD in man. Chemosphere 15:1489-1494.

Ryan, J.J., Lizotte, R., and Lau, B.P-Y. (1985a). Chlorinated dibenzo-p-dioxins and chlorinated dibenzofurans in Canadian human adipose tissue. Chemosphere 14, 697-706.

Ryan, J.J. (1986). Variation of dioxins and furans in human tissues. Chemosphere 15, p. 1585-1593.

Ryan, J.J. and Schecter, A. (1985). Distribution of dioxins and furans in human autopsy tissues from the general population. Preprint Extended Abstract, presented at the American Chemical Society Meeting, Miami, pp. 158-159.

Ryan, J.J., Schecter, A., Lizotte, R., Sun, W-F., and Miller, L. (1985b). Tissue distribution of dioxins and furans in humans from the general population. Chemosphere 14, 929-932.

Ryan, J.J., Williams, D.T., Lau, B. P-Y., Sakuma, T (1985c). Analysis of human fat tissue for 2,3,7,8-tetrachloro-dibenzo-p-dioxin and chlorinated dibenzofuran residues. In Chlorinated Dioxins and Dibenzofurans in the Total Environment II (L.H. Keith, C. Rappe, and G. Choudhary, Eds.), pp,. 205-214. Butterworth, Boston.

Schaefer, V.J. Mohnen, V.A., and Veirs, V.R. (1972). Air Quality of American Homes. Science 175:173-175.

Schecter, A., Ryan, J.J., Lizotte, R., Sun, W-F., Miller, L., Gitlitz, G., and Bogdasarian, M. (1985). Chlorinated dibenzodioxins and dibenzofurans in human adipose tissue from exposed and control New York State patients. Chemosphere 14, 933-937.

Schaum, J. (1984). Risk analysis of TCDD contaminated soil. EPA.

Shu, H.P., Paustenbach, D.J., Murray, F.J. (1987a). A critical evaluation of the use of mutagenesis, carcinogenesis and tumor promotion data in a cancer risk assessment of TCDD. Reg. Tox. Pharmacol. 7:57-88.

Shu, H., Paustenbach, D., Murray, F.J., Marple, L., Brunck, B., Dei Rossi, D., Teitelbaum, P. (1987b). Bioavailability of Soil-Bound TCDD; Oral Bioavailability in the Rat. Fundam. Appl. Toxicol. (submitted)

Shu, H., Teitelbaum, T., Webb, A.S., Marple, L., Brunck, B. Dei Rossi, D., Murray, F.J., Paustenbach, D. (1987c). Bioavailability of Soil-Bound TCDD: Dermal Bioavailability in the Rat. Fundam. Appl. Toxicol. (submitted)

Sielken, R.L. (1987a). Quantitative cancer risk assessments for TCDD. Food and Chem. Tox., 25(3):257-267.

Sielken, R.L. (1987b). A response to Crump's evaluation of Sielken's dose-response assessment for TCDD. Food Chem. Tox. (in press).

Sielken, R.L. (1987c). Statistical evaluations reflecting the skewness in the distribution of TCDD levels in human adipose tissue. Chemosphere (in press).

Spencer, W.F. and Farmer, W.J. (1980). Assessment of the vapor behavior of toxic organic chemicals. In: Dynamics, Exposure and Hazard Assessment of Toxic Chemicals, R. Hague, (ed.), Ann Arbor Science, pp. 143-161.

Stanley, J.S., Boggess, K.E., Onstot, J., Sack, T.M., Remmers, J.C., Breen, J., Kutz, F.W., Carra, J., Robinson, P., and Mack, G.A. (1986). PCDDs and PCDFs in human adipose tissue from the EPA FY82 NHATS repository. Chemosphere 15, 1605-1612.

Steinberg, K.K., MacNeil, M.L., Karon, J.M., Stehr, P.A., Neese, J.W., Needham, L.L. (1985). Assessment of TCDD exposure using a modified D-glucaric acid assay. J. Toxicol. Env. Health, 16:743-752.

Syntex Agribusiness, Inc. (1987). Comments on EPA document, "Public Comment Draft Feasibility Study" for Times Beach, Missouri.

Travis, C.C., Richter, S.A., Crouch, E.A.C., Wilson, R., and Klema, E.D. (1987). Cancer risk management. Environ. Sci. Technol. 21:415-420.

Umbreit, T.H., Hesse, E.J. and Gallo, M.A. (1986a). Comparative toxicity of TCDD contaminated soil from Times Beach, Missouri, and Newark, New Jersey. Chemosphere 15:2121-2124.

Umbreit, T.H., Hesse, E.J., Gallo, M.A. (1986b). Bioavailability of dioxin in soil from a 2,4,5-T manufacturing site. Science, 232, 497-499.

USEPA (1985a). Superfund health assessment manual.

USEPA (1987). Public comment draft feasibility study, Times Beach site.

van den Berg, M., De Vroom, E., Van Greevenbroek, M., Olie, K., and Hutzinger, O. (1985). Bioavailability of PCDDs and PCDFs adsorbed on fly ash in rat, guinea pig and Syrian golden hamster. Chemosphere 14:865-869.

Wester, R.C., and Noonan, P.K. (1980). Relevance of animal models for percutaneous absorption. Int'l. J. Pharmaceut. 7:99-110.

Wester, R.C. and Maibach, H.I. (1983). Cutaneous pharmacokinetics: 10 steps to percutaneous absorption. Drug Metab. Rev. 14:169-205.

Wester, R.C. and Maibach, H.I. (1975). Percutaneous absorption in the Rhesus monkey compared to man. Toxicol. Appl. Pharmacol. 32:394-398.

Wrenn, G.C. (1986). Testimony of Grover C. Wrenn - asbestos ban and phaseout proposal. EPA.

Young, A.L. (1983). Long term studies on the persistence and movement of TCDD in a national ecosystem. In: Human and Environmental Risks of Chlorinated Dioxins and Related Compounds, R.E. Tucker, A.L. Young, and A.P. Gray (eds.), Plenum Press, New York, pp. 173-190.

Young, A.L. (1984). Determination and measurement of human exposure to the dibenzo-p-dioxins. Bull. Environ. Contam. Toxicol. 33:702-709.

Young, A.L., Cockerham, L.G., Thalken, C.E. (1986). A long-term study of ecosystem contamination with TCDD. 6th Dioxin Symp, Fukuoka, Japan.