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Summary of a Meeting Report on February 4, 1983.

A meeting was convened with members from the Environmental Protection Agency in Washington, DC. A list of the attendees is attached. At this meeting possible modes of exposure for people in contaminated environments were discussed. Specifically, what is the dose received by people living in areas where soil is contaminated at measurable levels with 2,3,7,8 tetrachlorodibenzodioxin?

It was agreed that a number of assumptions could be made in place of concrete data. For instance, it can be assumed that people living in such areas may work in their garden or yard 150 days a year. They probably receive an amount of contamination from soil on their skin of about 100 mg daily. This would result in a yearly contamination of 15 g, and it might be assumed that the lifetime exposure would be to 600 g of soil. Dermal absorption from this chemical lies somewhere within a range of 1 to 10%. The 10% figure may actually be high and further information on that should be obtained from Dr. Reggiani. In areas with heavy vegetation dust levels are probably negligible. They will be of concern in riding arenas and in areas where there are dirt roads on which cars travel. In such situations, dust levels are probably in the nuisance range as defined by NIOSH. It can also be assumed that 70-90% of the dust which is inhaled will stay in the body and since there is no data at this point it will be assumed that 100% of the amount of chemical on the inhaled dust would be absorbed. An additional source of contamination might be ingestion of soil. This is primarily a problem in children particularly in toddlers. There was much debate of how much dirt children might eat. A number of assumptions were made ranging from 100 mg to 10 grams. It was decided to make an additional effort to determine whether any concrete information is available on this question. It was decided that most likely 40% of the ingested chemical absorbed on soil would be absorbed into the body. It can be assumed that the time period for ingestion of soil in children would be primarily from ages 2 to 5. In other words, the extent of the exposure by this route would be 3 years.

Renate Kimbrough, MD

CDC

12/2/82
DRAFT

Risk assessment* of TCDD (2378 tetrachlorodibenzo-p-dioxin) in soil.

Introduction.

In the past a number of groups have made attempts to develop or to determine what an acceptable risk for the exposure to TCDD would be. As more information on the toxicity of this chemical has become available, these levels have generally been reduced. To develop an acceptable risk level for exposure to TCDD is particularly difficult because TCDD has such unique properties. It is one of the most toxic man-made organic chemicals known. In addition to being extremely toxic when it is given as a single dose, it is persistent in the environment and in living organisms. TCDD has a very pronounced cumulative toxicity. In animals TCDD has been shown to affect reproduction, to cause suppression of the immune response and to be carcinogenic in rodents. In rats, a daily dietary dose of 0.001 ug/kg body weight is a "quasi no effect level." Lifetime studies have not been conducted in species other than rodents. Subhuman primates and guinea pigs are extremely sensitive to the toxic effects of TCDD. The oral LD_{50} for female guinea pigs, for example, is 0.7 ug/kg b.w. while it is 44 ug/kg b.w. in rats. The ratio between the rat oral LD_{50} dose and the no-effect level of 0.001 ug/kg is 44,000. If this ratio was the same for all species, then in the guinea pig the no-effect level for lifetime exposure would be 0.7 ug/kg divided by 44,000 or the same as 0.016 ng/kg b.w./day. Unfortunately, no long-term studies on any species that are extremely sensitive to the toxic

*This risk assessment does not apply to soil and ranges and other areas where cattle, for instance, is grazing.

effects of TCDD are available. It is therefore not known whether such ratios exist in reality.

In general, animals studies show that there is great variability in response to TCDD among species. It is not clear where on this response scale humans fit. It is assumed they would be more sensitive than the rats, but less sensitive than the guinea pig, that is, any amount of TCDD detected with presently available analytical methods would still present some although poorly defined risk if absorbed by humans.

Within the last few years TCDD has been identified in our environment in several areas in the United States and other parts of the world. Fish in Lake Ontario have TCDD levels from undetected levels to 162 ng/kg; and in Lake Huron levels they range from undetected to 29 ng/kg. TCDD levels in fish near chemical companies in the Arkansas River and in the Titthawassee River and Signaw have ranged from 50 to 480 ppt (ng/kg). TCDD has also been found in beef fat and in fly ash from incinerators. Furthermore, the mean yearly exposure to TCDD from cigarette smoking has been calculated to be 2 ng per smoker (NRCC 1981). All of these findings suggest that a general background contamination of the environment with TCDD exists at extremely low concentrations.

TCDD is highly hydrophobic, degrades rapidly on exposure to ultraviolet light if hydrogen donors are available, is persistent in soil with a half life of anywhere from 1 to 10 years, does not readily migrate through soil, and is only slightly taken up by root plants. A few strains of soil bacteria are able to degrade it at a very slow rate.

Exposure.

In order to determine whether a specific concentration of TCDD in soil presents a risk to humans, it is first necessary to examine how humans might absorb TCDD from such soil. Unfortunately, it is not well-known how much of any chemical that is present in soil, may be absorbed by humans that come in contact with such soil. Most risk assessments that have been made in the past have been made for such media as food, where it is assumed that a certain amount of food with a certain concentration of the chemical in it, is consumed; for air, where it simply needs to be calculated how much air is inhaled, or for chemicals in water, where again the only number needed is the amount of water consumed. Unfortunately, this is more complicated for soil. No good data exists delineating with any degree of certainty what this type of exposure might consist of. There are basically three types of exposure routes that must be considered. One is dermal absorption through direct contact with the soil, another would be ingestion of soil, and the third would be inhalation of dust to which TCDD is attached. Another issue which does not directly enter in this risk assessment is the fact that any TCDD in the environment will eventually end up in the food chain and in that regard presents a risk to a larger undefined population. There is some evidence that at least part of the TCDD binds relatively tightly to the soil and would not be as easily available for absorption. However, information on this aspect is very limited at present and it is also not known whether this is true for all types of soil. According to the literature (Poiger and Schlatter, 1980) anywhere from 1 to 10 percent of the TCDD which is in the soil may be absorbed through the skin. This may to some extent depend on the amount present in the soil and may be greater at higher concentrations. Feeding studies in animal

suggests that 10-30% TCDD adsorbed on soil will be absorbed in the gastrointestinal tract. Furthermore, TCDD may be inhaled through dust from contaminated areas. There is also very little information available on the amount of the dust that may be present in the air in such situations. When this was measured in Seveso, it was found that the amount of dust in air was 0.14 mg/m^3 air (Di Domenico et al., 1980). It would be possible that in some situations such as riding arenas or in rather dry areas the amount of dust would be higher. On the other hand, immediately after a rainfall, there would probably be less dust. Another unknown is the amount of material that could be carried into the house from the outside. In order to err on the conservative side, it was assumed that the exposure in side a house would be similar to what would occur if people spent their entire time in very close contact with the contaminated soil. Thus, the following assumptions for exposure were made:

ingestion: 10 to 30% is absorbed from soil

dermal: 10% is absorbed from soil

inhalation: dust would be present in air in a concentration of 0.14 milligrams per cubic meter.

In the studies conducted in Seveso (Di Domenico, 1980), depending on the type of samplers used, the amount of TCDD per gram of dust ranged from 0.06 to 2.1 ng/gr TCDD per gram of dust.

Another unknown in these studies, as well as the dioxin determinations in Missouri, is the fact that it is really not known what the recovery is when the soil is extracted by various solvents. No recovery data for instance was given in the Di Domenico paper. According to experience in the New York State Health Department (Patrick O'Keefe, personal communication) recovery of these

types of compounds from soot may be very poor with a recovery of anywhere from 18 to 50%. If the data given in the Di Domenico paper is reviewed, it is clear that the concentrations of TCDD in dust from different areas is similar to what was measured in the soil so it can therefore be assumed that the concentration of TCDD in dust from a soil area with 1 part per billion TCDD would roughly also be 1 part per billion or slightly less and at 100 parts per billion you would assume that the dust concentration would be in the same order of magnitude. Thus, it can be assumed that in an area where the soil contained 1 part per billion TCDD, the amount of TCDD in 140 ug of dust would be 0.14 pg. The total amount of air inhaled for a 24-hour period by an adult if this person was resting would be 10 m^3. These 10 m^3 of air would contain 1.4 mg of dust and the 1.4 mg of dust would contain 1.4 pg of TCDD. If the soil contained 100 times as much TCDD, then, of course, the concentration in the dust would most likely be 100 times as high.

The amount of TCDD that could be received from ingesting soil, and this would be particularly true for children, but it is conceivable that adults working in the yard would also get soil contamination of their hands from which they could inadvertently ingest some soil, would again depend on the amount of TCDD that was in the soil. If it was assumed, for instance, that 1 gram of soil is ingested per day which contains 100 ppb of TCDD, and if it is further assumed that 10 to 30% of the TCDD in the soil was actually absorbed from it, then the dose that a person would receive would be 10 to 30 pg/person. If 10 grams of soil were ingested, that contained 100 ppb of TCDD, then the dose, of course, would 100 to 300 pg/person. The other exposure that could occur would be through dermal absorption of TCDD from soil that had inadvertently contaminated the skin and in this case if for instance, 10 grams

of dirt were present on the skin and if it is assumed that 10% of the TCDD present in that dirt were absorbed, the dose at 100 ppb would be 100 ng/person. If the skin was only contaminated with 1 gram of soil, then, of course, the amount absorbed through the skin could be as much as 10 ng/person. Thus, at a concentration of 100 ppb of TCDD in soil, if 10 grams of soil contaminated the skin daily, and 10 grams were ingested, the conceivably total dose per person from these two sources would be 200 to 400 ng and the contribution from air would be ~~114~~ 14 pg so the air contribution would actually not add very much to the contribution from dermal absorption and ingestion. It would probably be more reasonable to assume that the daily contamination of the skin and the possible daily ingestion would be closer to 1 gram in each instance which would reduce the contribution of dermal and oral absorption from 200-400 ng to 20-40 ng per person. It is also not clear whether such exposures would occur daily.

If only 1 ppb of TCDD was present in soil, then the amount that would be absorbed through ingestion and dermal contamination of 1 gram of soil per day, would have to be divided by 100 and would be reduced to 0.2 to 0.4 ng/person to which a 1.4 picogram dose in air would have to be added. It can be assumed that actual exposure of TCDD from soil on the skin as well as from ingestion is probably lower than the assumed daily exposure dose to soil of 1 or 10 grams by both routes. The reason for this is that most people are probably not exposed daily and that most of the soil which they come in contact with will be washed off. An exception are small children who habitually eat some soil while playing outside.

Safe levels for dioxin.

The National Research Council of Canada (NRCC) has recently published a report reviewing available toxicity data for TCDD and related compounds and also various procedures that can be used to calculate from such animal data a virtually safe dose for TCDD. A Table out of this document is appended (Table 1) giving the various models, the virtually safe dose, the approximate 95% confidence levels and references to the different models which were used. Basically only one chronic study in rats is available which gives several dosage levels and a no-effect level. The lower confidence limits with these different models if that data is used are of the same order of magnitude of about 30 ng/kg b.w. of TCDD per day for lifetime exposure. Using another model, the Crump one hit model, EPA in 1981 calculated the risk of oncogenicity for TCDD of one additional cancer in a million (10^{-6}) to be about 170 fg/kg of b.w. per day. There is no scientific method for choosing which of the models gives the most reasonable assessment of the virtually safe dose at various assumed risk levels especially since the mechanism whereby TCDD elicits its carcinogenic response is not known. However, if it is assumed that the virtually safe dose of TCDD would lie somewhere between 30 and 90 fg/kg of b.w. per day or between 2.1 and 6.3 pg per day per person, this would be less than the amount of TCDD conceivably absorbed by a person from soil containing 1 ppb of TCDD. According to the calculations made above a person could from such soil absorb somewhere in the neighborhood of 400 pg/person per day if 1 gram of soil was ingested and 1 gram of soil got on the skin. The amount contributed through dust by inhalation does not appreciably alter these levels. This dose would be 100 times higher than what the NRCC had calculated as a virtually safe dose. This would change the acceptable

risk level from one case of cancer in a million to one case of cancer per 10,000 individuals.

If instead of using cancer as the endpoint, reproduction is used as the endpoint, then, again, information is only available in rats. The no-effect dose for reproductive effects in rats is 0.001 ug TCDD per kg of body weight per day, or 1 ng/kg. Subhuman primates which are much more susceptible to the effects of TCDD, if fed for 6 months at a daily dose of 1.8 ng/kg b.w. per day, still show an effect on reproduction. Thus, if for the reproductive studies in rats a safety factor of 100 is chosen, then a virtually safe dose would be a daily dose of 0.7 ng per person per day. On the other hand, if the toxicology data from subhuman primates is used, the lowest dose of 1.8 ng/kg b.w was not a no-effect level and was also not obtained from a chronic study. Therefore, a 1000-fold safety factor would have to be used at a minimum. Thus, a daily dose of 0.0018 ng/kg or for a 70 kg person a daily dose of 0.126 ng/person or 126 pg/person would be acceptable.

As these calculations show, even 1 ppb TCDD in soil may not represent an acceptable risk if the estimates for exposure are accepted. However, for practical purposes the reliability of the chemical methods for soil is not as good in the ppt range and as we measure more environmental samples, it is possible that TCDD will be present in ppt concentrations in soil in many areas. Furthermore, it is impractical to move large quantities of dirt from 1 site to another (landfill) since degradation by bacteria will probably be more effective if the material is spread out. The amount of TCDD in the soil would be gradually decreasing and would not be replenished minimizing the possibility of lifetime exposure. The acceptable dosage levels of TCDD, on the other hand, were calculated for lifetime exposures. If excavation took

place to a concentration of 1 ppb, uncontaminated soil would have to be put into its place and topsoil could also be added to areas where no excavation is necessary diluting the available TCDD to ppt levels and further reducing the risk..

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Table 1 Estimates and approximate 95% lower confidence limits (LCL) for "virtually safe dose" (VSD) of 2,3,7,8-T_4CDD at three risk levels, using various extrapolation procedures[α] (NRCC 1980).

	Estimate (LCL) (fg.kg-bw^{-1}.d^{-1})		
Risk Level	10^{-4}	10^{-6}	10^{-8}
Procedure			
Multistage model[β]	8.2×10^3 (6.5×10^3)	87(65)	87(0.65)
Multistage model[β] omitting top dose group	176×10^3 (2.16×10^3)	17.6×10^3(21.6)	1.76×10^3 (0.216)
Weibull model[γ]	107(0.524)	0.118(3.96×10^{-5})	1.31×10^{-4} (2.98×10^{-9})[ζ]
Linear extrapolation[δ] from .01 μg.kg^{-1}	3.91×10^3 (2.64×10^3)	39.1 (26.4)	.391 (.264)
Linear extrapolation[γ,δ] from .001 μg.kg^{-1}	ε (3.07×10^3)	ε (30.7)	ε (.307)

[α] Data from Kociba et al. (1978) are as follows: number with tumour/number examined (dose in μg.kg-bw^{-1}.d^{-1}) 9/86(0); 3/50(.001); 18/50(.01); 34/48(.1).

[β] (Crump, Guess and Deal (1977) fitting polynomial of maximum estimable degree. Confidence limit based on model with positive estimate for highest degree term.

[γ] Kovar and Krewski (1981) calculating confidence limit after log transformation.

[δ] Gaylor and Shapiro (1979) using normal approximation for confidence interval.

[ε] No point estimate given because of inversion in observed dose response.

[ζ] 1 molecule 2,3,7,8-T_4CDD weighs 3.21×10^{-6} fg.

[12]

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Special Studies Br
12/5/82 CDC

Habitability of TCDD Contaminated Areas

Questions as to the habitability of any area contaminated with 2,3,7,8-TCDD are necessarily linked to considerations of excess risks of developing specific adverse health effects as a result of the total cumulative dose which an individual receives. In turn, this cumulative dose is a function of several factors:

1) concentrations of environmental contaminations
2) location of and access to contaminated areas
3) type of activities in contaminated areas
4) duration of exposure.

In addition, questions of continued habitability must also include considerations of the potential for limiting or eliminating ongoing exposures.

As a first approach, a series of risk assessment estimates based on several of these factors has been utilized in the past by a number of groups which have made attempts to determine what an "acceptable" risk for exposure to TCDD would be. As more information on the toxicity of this chemical has become available, these levels have generally been reduced.

The development of an acceptable risk level for exposure to TCDD is particularly difficult because TCDD has such unique properties:

1) it is one of the most toxic man-made organic chemicals known when given as a single dose at extremely low levels;
2) it is persistent in the environment (with a half-life of 1 to 10

[13]

3) TCDD has a very pronounced cumulative toxicity;

4) in animals, TCDD has been shown to affect reproduction, to cause a variety of systemic effects including hepatotoxicity, suppression of the immune response, and carcinogenesis;

5) TCDD is highly lipophilic, degrades rapidly on exposure to ultraviolet light if hydrogen donors are available, does not readily migrate through soil, appears to be only slightly taken up by root plants, and only a few strains of soil bacteria are able to degrade it (at a very slow rate).

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In rats, a daily dietary dose of 0.001 ug/kg body weight is a "quasi no-effect level". Lifetime studies have not been conducted in species other than rodents. Subhuman primates and guinea pigs are extremely sensitive to the toxic effects of TCDD. The oral LD_{50} for female guinea pigs, for example, is 0.7 ug/kg while it is 44 ug/kg in rats. The ratio between the rat oral LD_{50} dose and the no-effect level of 0.001 ug/kg is 44,000. If this ratio was the same for all species, then in the guinea pig the no-effect level for lifetime exposure would be 0.7 ug/kg divided by 44,000 or the same as 0.016 ng/kg/day. Unfortunately, no long-term studies on any species that are extremely sensitive to the toxic effects of TCDD are available. It is therefore not known whether such ratios exist in reality.

In general, animal studies show that there is great variability in response to TCDD among species. It is not clear where on this response scale humans fit. It is assumed they would be more sensitive than the rats, but less sensitive than the guinea pig; i.e., any amount of TCDD detected with presently available analytical methods would still present some (although poorly

In order to determine whether a specific concentration of TCDD in soil presents a risk to humans, it is first necessary to examine how humans might absorb TCDD from such soil. Unfortunately, it is not well-known how much of any chemical that is present in soil may be absorbed by humans that come in contact with such soil. Most risk assessments that have been made in the past have been made for such media as food where it is assumed that a certain amount of food with a certain concentration of the chemical in it is consumed, for air where it simply needs to be calculated how much air is inhaled, or for chemicals in water where the only number needed is the amount of water consumed. Unfortunately, the analogous series of estimates is more complicated for soil.

DRAFT

There are basically three exposure routes that must be considered: dermal absorption through direct contact with the soil, ingestion of soil, and the inhalation of dust to which TCDD is attached. Another issue which does not directly enter in the current risk assessment is the fact that TCDD in the environment could eventually end up in the food chain and, in that regard, presents an unknown additional risk to those individuals most highly exposed to contaminated soil as well as a risk to a larger, undefined population.

In regards to the first route, there is some evidence that at least part of the TCDD binds relatively tightly to the soil and would not be as easily available for absorption. However, information on this aspect is currently limited— such as whether this is true for all types of soil. According to the literature (Poiger and Schlatter, 1980) anywhere from 1 to 10 percent of the TCDD which is in the soil may be absorbed through the skin and is likely to be dependent on the amount present in the soil (i.e., it may be greater at

In regards to the portion of total dose due to ingestion of soil particles, feeding studies in animals suggest that 10-30% TCDD adsorbed on soil will be absorbed in the gastrointestinal tract. Therefore, the calculations to follow will also consider these differing gastrointestinal absorption rates.

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In regards to inhaled doses, there is little information available on the amount of dust that may be present in the air in situations of known soil contamination; measurements in Seveso showed that the amount of dust in air was 0.14 mg/m^3 air (DiDomenico et al., 1980). It would be possible that in situations such as riding arenas or in relatively drier areas the amount of dust would be higher. On the other hand, immediately after a rainfall there would probably be less dust. Furthermore, based on the same investigation, it was shown that TCDD levels in dust were comparable to those found in soil. Another unknown is the amount of material that could be carried into the house from the outside. In order to err on the conservative side, it is assumed that the exposure inside a house is similar to that which would occur if people spent their entire time in close contact with the contaminated soil outside. It is further assumed that an average adult at rest exchanges approximately 10 m^3 of air per 24-hour period. Finally, it is assumed that all of TCDD adsorbed on inhaled dust particles are absorbed either through deposition in the respiratory tract or ingested after being brought up by the ciliary action of the respiratory tract epithelial cells.

For the sake of comparison, all of the above-discussed assumptions (and variations thereof) were applied in a series of total dose calculations where it was further assumed that individuals at risk are exposed to the maximum soil concentrations (e.g., 1 PPB and 100 PPB levels were used) at all times

The estimates of contribution to total daily dose from percutaneous absorption given varying levels of TCDD concentrations in soil, quantities of soil on exposed skin surfaces and absorption rates are presented in Table 1. Table 2 contains the estimates of the daily dose derived from ingestion of varying amounts of soil contaminated at different levels with variable rates of gastrointestinal absorption. Finally, Table 3 represents the estimates of the contribution to total daily dose from inhalation of contaminated dust particles given the above assumptions.

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A large number of estimated total daily doses can be derived from the many combinations of the exposure route-specific doses (given different sets of assumptions as to absorption rates, soil contamination, etc.). For the sake of brevity, the two most extreme total daily dose estimates were compiled and are as follows:

Lowest Daily Dose 111.4 picograms/day

Assumptions: 1 PPB in soil; 1 gram of soil ingested (10% absorbed); 1 gram soil on skin (1% absorbed)

Highest Daily Dose 400.14 nanograms/day

Assumptions: 100 PPB in soil; 10 grams of soil ingested (30% absorbed); 10 grams soil on skin (10% absorbed).

Of course, any other combinations of these varying factors can be used to derive intermediate or farther outlying daily dose estimates.

The final step in assessing individual risks at these estimated dose levels must incorporate a comparison to known (or estimated) "safe" levels of

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TABLE 1
Percutaneously Absorbed Dose

Amount of Soil on Skin	TCDD-Concentration in Dirt	Amount Absorbed Through Skin	Daily Dose (in ng)
1 gram	1 PPB	1%	0.01
		10%	0.10
	100 PPB	1%	1.00
		10%	10.0
10 grams	1 PPB	1%	0.10
		10%	1.00
	100 PPB	1%	10.0
		10%	100.0

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TABLE 2
Ingested Dose

Amount Soil Eaten	Absorption Rate	Concentration in Dirt	Daily Dose (in ng)
1 gram	10%	1 PPB	0.10
		100 PPB	10.0
	30%	1 PPB	0.30
		100 PPB	30.0
10 grams	10%	1 PPB	1.00
		100 PPB	100.0
	30%	1 PPB	3.00
		100 PPB	300.0

TABLE 3
Inhaled Dose

Concentration in Dirt and Dust	Daily Dose (in pg)	(in ng)
1 PPB	1.40	0.0014
100 PPB	140.0	0.14

The National Research Council of Canada (NRCC) has recently published a reviewing available toxicity data for TCDD and related compounds as well various procedures to calculate a "virtually safe dose" (VSD) for TCDD f such data. Table 4 is taken from this document and lists the various mod estimated VSDs, approximate 95% confidence levels and references to the different models which were used.

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Basically only one chronic feeding study in rats is available which gives several dosage levels and a no-effect level. Using these data, the lower confidence limits for a virtually safe dose from these different models ca estimated and are all of a similar order of magnitude. There is no scienti method for choosing which of the models gives the most reasonable assessmen of the VSD at various assumed risk levels especially since the mechanism whereby TCDD elicits its carcinogenic response is not known. However, if it is assumed that the VSD of TCDD would lie somewhere between 30 and 90 fg/kg per day (or between 2.4 and 7.2 pg/day for an average 80 kg person) this is less than the amount of TCDD conceivably absorbed from soil containing 1 PPB of TCDD. According to the calculations made above, a person could take up as much as 400 pg of TCDD per day if only 1 gram of soil was ingested and 1 gram of soil got on the skin (the amount contributed through dust inhalation does not appreciably alter these total dose levels). This dose would be 100 times higher than what the NRCC had calculated as a VSD. Alternatively stated, this would mean an elevation in risk level from one case of cancer in a million to one case per 10,000 individuals, assuming extrapolation from a linear model.

(8)

Table 4 Estimates and approximate 95% lower confidence limits (LCL) for "virtually safe dose" (VSD) of 2,3,7,8-T_4CDD at three risk levels, using various extrapolation procedures[α] (NRCC 1980).

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	Estimate (LCL) ($fg.kg\text{-}bw^{-1}.d^{-1}$)		
Risk Level	10^{-4}	10^{-6}	10^{-8}
Procedure			
Multistage model[β]	8.2×10^3 (6.5×10^3)	87(65)	87(0.65)
Multistage model[β] omitting top dose group	176×10^3 (2.16×10^3)	17.6×10^3(21.6)	1.76×10^3 (0.216)
Weibull model[γ]	107(0.524)	0.118(3.96×10^{-5})	1.31×10^{-4} (2.98×10^{-9})[ζ]
Linear extrapolation[δ] from .01 $\mu g.kg^{-1}$	3.91×10^3 (2.64×10^3)	39.1 (26.4)	.391 (.264)
Linear extrapolation[γ,δ] from .001 $\mu g.kg^{-1}$	ε (3.07×10^3)	ε (30.7)	ε (.307)

[α] Data from Kociba et al. (1978) are as follows: number with tumour/number examined (dose in $\mu g.kg\text{-}bw^{-1}.d^{-1}$) 9/86(0); 3/50(.001); 18/50(.01); 34/48(.1).

[β] (Crump, Guess and Deal (1977) fitting polynomial of maximum estimable degree. Confidence limit based on model with positive estimate for highest degree term.

[γ] Kovar and Krewski (1981) calculating confidence limit after log transformation.

[δ] Gaylor and Shapiro (1979) using normal approximation for confidence interval.

[ε] No point estimate given because of inversion in observed dose response.

[ζ] 1 molecule 2,3,7,8-T_4CDD weighs 3.21×10^{-6} fg.

Applying the Crump "one-hit" model (for which it is estimated that a daily dose of about 170 fg/kg will increase the risk of carcinogenicity by 10^{-6}) from the perspective of an affected individual with an assumed lifetime of 70 years, an estimate of the total dose required to induce an excess risk in this context would come out to be approximately 0.35 micrograms of TCDD. At the lowest daily dose levels estimated above (i.e., 111.4 pg/day) it would take just over 6 1/2 years to accumulate a total dose sufficient to increase an individual's risk of developing cancer by one in a million. However, the highest daily dose estimated above given the most extreme set of assumptions (i.e., 400.14 ng/day) would induce a 10^{-6} incremental risk <u>each day</u> of continued exposure. Of course, these interpretations carry the implicit assumption (for which no corroborating data exist) that dose rate does not affect the process by which cancerous effects are manifested.

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Using reproductive effects as the end-point (where information is available only in rats) the no-effect dose is 1 ng/kg TCDD per day. Subhuman primates (which are much more susceptible to the effects of TCDD) show an effect on reproduction if fed for six months at a daily dose of 1.8 ng/kg. Thus, based on the reproductive studies in rats and choosing a safety factor of 100, a VSD in humans would be a total daily dose of 0.8 ng per day; on the other hand, if the toxicology data from subhuman primates is used, the lowest dose of 1.8 ng/kg per day (which was a no-effect level and was not obtained from a chronic feeding study), a 1000-fold safety factor would have to be used. Thus a daily dose rate of 0.0018 ng/kg-- corresponding to a total daily dose of 144 pg-- would be acceptable for an average 80 kg person. Thus at the lowest daily dose likely to obtain as estimated above, both of these extrapolations from reproductive studies in animals appear to suggest a situation of no

excess risk in humans. However, at virtually all other estimated levels of daily dose (i.e., under more severe sets of assumptions) one might expect the induction of adverse reproductive health effects.

It should be stressed that both considerations of carcinogenicity and reproductive health effects contain critical assumptions which may not obtain in reality. Most prominent of these are the assumptions of uniform levels of contamination throughout the living space and constant, total access to these areas. In fact, the situation is likely to be such that areas with elevated TCDD levels which, of themselves, can be expected to decrease in time, are found in specific, well-defined locations which have concomitant unique use and access characteristics. Therefore, in such a situation where access is less than total and constant, the actual daily dose will be lower than calculated above. Similarly, different usage patterns of affected areas (e.g., sports activities, gardening, horseback riding) or an individual's characteristics (e.g., pica in children) will have differing effects on the determination of total cumulative dose.

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Therefore, final decisions on habitability may range from recommendations to avoid identified "hot spots" or limit specific activities in these areas (if possible) or temporary relocation while clean-up and/or onsite stabilization of the contaminations are performed to permanent relocation and access restriction for a given site. In addition, such recommendations will have to be prepared in terms of situations which range from the need for near-term action to those of a less emergent nature. In all of these scenarios, however, these decisions must be made on a site-specific basis as indicated by

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