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DEPARTMENT OF HEALTH SERVICES
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FAX TRANSMITTAL SHEET

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ATTACHMENT IA
PRELIMINARY HEALTH EFFECT LEVEL FOR SOIL ($PHEL_{soil}$)

DDT\DDD\DDE

1.0 SUMMARY. DDT and its metabolites DDE and DDD are carcinogenic in laboratory animals. Malignant and benign liver cell tumors (hepatocellular carcinomas and adenomas) were produced in multiple studies in male and female mice and rats. EPA has given all 3 agents a "B2" classification, that is, they are considered to be probable human carcinogens. Low dose extrapolation of the tumor responses and geometric averaging of the results yielded overall dose-response slope factors of 0.34 kg-day/mg for both DDT and DDE, and 0.24 kg-day/mg for DDD. The maximal exposure level (MEL) for acceptable risk (no more than one excess cancer death per million exposed for a lifetime) calculated with these slope factors is 0.21 ug/day for DDT or DDE and 0.29 ug/day for DDD for a 154 pound adult. The preliminary health effect level (PHEL) for soil calculated with this MEL is 1.7 ppm for DDT or DDE, and 2.4 ppm for DDD. These $PHEL_{soil}$ values represent the concentrations of DDT, DDE, or DDD in soil which would not pose a significant excess risk to an adult exposed by oral ingestion of 0.1 g soil/day and skin contact with 0.45 g soil/day for a 70 year lifetime.

2.0 CHEMISTRY AND USE. DDT consists of two phenyl groups attached to the 1 position of trichloroethane. In the technical grade material, each phenyl group is chlorinated in the para position, although ortho- and meta- isomers may be present in small amounts. DDD and DDE are metabolites of DDT, with dechlorination or dehydrochlorination occurring at the trichloro carbon.

DDT was synthesized in the late 1800s, but its insecticidal properties were not discovered until 1939. An estimated two billion kg of DDT was used between 1940 and 1973, with 80% of that use for agricultural purposes. The remaining 20% was used to kill insects responsible for transmission of disease, such as mosquitos which carry malaria. Agricultural use included registration for use on over 300 commodities, with cotton, peanuts, and soybeans receiving the greatest use in 1972. Due to environmental concerns, the use of DDT in the U.S. was banned in 1972, except for use in public health emergencies. Foreign use continues for agriculture and control of insect-transmitted disease.

The technical grade material is a solid, may exist as a white powder or colorless crystals, and can have a "weak aromatic odor." Solubility in water is 0.0034 mg/L. DDD and DDE are likewise solids, can exist as white powders or crystals, and are odorless. Water solubility is slightly greater than that of DDT, being 0.16 mg/L or 0.12 mg/L for DDD or DDE, respectively. All three compounds are extremely lipid soluble, which accounts for bioaccumulation and environmental persistence (ATSDR, 1987, and USEPA, 1984 and 1988).

3.0 HAZARD IDENTIFICATION

3.1 HUMAN ACUTE TOXICITY. The lethal oral dose of DDT in humans is not well established, but accidental ingestion of doses as great as 285 mg/kg have been survived. In one documented case of fatal poisoning, clinical signs consisted of coughing and vomiting followed by tremors, convulsions, loss of consciousness and death. Clinical signs in human volunteers receiving a single dose of about 22 mg/kg included "...disturbance of equilibrium, dizziness, confusion, tremors, malaise, headache, fatigue, and severe vomiting..." Recovery was nearly complete 24 hours after ingestion. Convulsions have been reported to occur with doses of 16 mg/kg.

The acute toxicity of DDD and DDE is unknown.

3.2 HUMAN CHRONIC TOXICITY. No abnormal changes in blood, cardiovascular, liver, or neurologic function were reported for human volunteers receiving 0.6 mg DDT/kg/day for 12 to 18 months. The effects of DDD or DDE in humans have not been determined.

3.3 HUMAN CARCINOGENICITY. There is no evidence that DDT is carcinogenic in humans exposed occupationally or environmentally in spite of heavy usage for over 30 years with environmental persistence to the present.

3.4 ANIMAL CHRONIC TOXICITY. Due to carcinogenic activity in rodents, systemic effects were not considered in derivation of the Preliminary Health Effect Level for soil ($PHEL_{soil}$).

3.5 ANIMAL CARCINOGENICITY. DDT, DDD, and DDE were carcinogenic in laboratory rats and mice receiving each chemical in the feed for a lifetime (ATSDR, 1987, and USEPA, 1984 and 1988).

3.5.1 DDT. DDT caused malignant and/or benign liver cell tumors (hepatocellular carcinomas and/or adenomas) in female and/or male mice of 3 separate strains, benign liver cell tumors in male and female rats in one study and in female rats of a different strain in a separate study. EPA calculated oral dose-response slope factors (formerly called "cancer potency factors") from the results of these six studies. The slope factors spanned a 13-fold range, from 0.082 to 1.04 kg-day/mg. The geometric mean of all values, 0.34 kg-day/kg, was chosen to represent the overall slope factor for DDT.

3.5.2 DDD. In one mouse study, DDD caused lung tumors in both males and females and liver tumors in males. In a separate mouse study, DDD caused an increase in liver tumors in both sexes, but the difference from control was not significant. Male rats receiving DDD developed thyroid follicular cell tumors, but the

Animal Carcinogenicity: DDD (continued)

results were not statistically conclusive. EPA used the first mouse study to derive an oral slope factor of 0.24 kg-day/mg for DDD.

3.5.3 DDE. DDE caused malignant liver tumors (hepatocellular carcinomas) in both male and female mice, and benign liver tumors (hepatocellular adenomas) in mice of either sex in a separate study. Male and female hamsters receiving DDE developed neoplastic nodules in the liver. EPA derived individual oral slope factors for the results of these 3 studies, and calculated the geometric mean, 0.34 kg-day/mg, for use as the overall slope factor.

In female rats, DDE caused a significant trend for thyroid tumors. This study was not utilized for slope factor derivation.

3.5.4 Comments. DDT, DDD, and DDE collectively caused liver cell tumors in multiple studies in both sexes. EPA has classified all three as "B2" carcinogens, i.e., probable human carcinogens. Note that the slope factor for DDT is identical to that of DDE (0.34 kg-day/mg), and both are close to that of DDD (0.24 kg-day/mg).

4.0 PRELIMINARY HEALTH EFFECT LEVEL (PHEL) DERIVATION.

4.1 MAXIMUM EXPOSURE LEVEL (MEL). The first step involves calculation of the MEL. The MEL is the maximum amount of pesticide that an adult can be exposed to for a lifetime without incurring a "significant" risk of getting cancer. For the purpose of this report, significant risk is defined as risk greater than one cancer case per million humans exposed for their lifetime, i.e., $1x10^{-6}$. Conversely, "acceptable" risk is defined as being no more than one cancer case per million exposed for a lifetime. Note that many regulatory actions currently use one per hundred thousand, i.e., $1x10^{-5}$, as the cutoff point for acceptable/significant risk. Also note that calculated risk is risk in excess of normal "background" risk for the average human population. Lifetime background cancer risk is approximately one in four.

Standard assumptions include an adult body weight of 70 kg (154 pounds) and exposure to pesticides for a 70 year lifetime.

$$MEL = \frac{\text{Acceptable Risk}}{\text{Slope Factor}} \times \text{Body Weight in kg}$$

Maximum Exposure Level (continued)

$$MEL_{DDT/DDE} = \frac{1\times10^{-6}}{0.34\ kg\text{-}day/mg} \times 70\ kg = 2.1\times10^{-4}\ mg/day$$

$$MEL_{DDD} = \frac{1\times10^{-6}}{0.24\ kg\text{-}day/mg} \times 70\ kg = 2.9\times10^{-4}\ mg/day$$

4.2 TOTAL ABSORBED DAILY DOSE (TADD). The amount of pesticide absorbed into the body from soil is calculated next. Two routes of exposure are considered:

1. Ingestion of soil due to hand-to-face activities such as eating, smoking, and finger-nail biting. This is assumed to be 0.1 grams/day for a lifetime (USEPA, 1989); and

2. Skin contact with soil. This is assumed to be 0.45 grams/day for a lifetime (Sedman, 1989).

Alternative scenarios are possible, and USEPA (1989) and Sedman (1989) should be consulted for guidance.

Absorption of DDT/DDD/DDE from ingested soil is assumed to be 100%, in the absence of experimental data. Absorption from soil through the skin (dermal absorption) is assumed to be 5%. Dermal absorption of DDT/DDD/DDE from soil is probably 1% or less, so the use of 5% is sufficiently health protective, in the absence of experimental data.

Let:

ADD_i = Dose which is absorbed following ingestion

= Conc/soil x Soil Ingestion/day x Oral Absorption

= Conc/soil x 0.1 g Soil/day x 1.00

AAD_d = Dose which is absorbed dermally

= Conc/soil x Dermal Contact/day x Dermal Absorption

= Conc/soil x 0.45 g Soil/day x 0.05

$TADD = ADD_i + ADD_d$

Total Absorbed Daily Dose (continued)

$$ADD_i + ADD_d = Conc/soil \times (0.1 + 0.45 \times 0.05)\ g\ soil/day$$

$$= Conc/soil \times 0.1225\ g\ soil/day$$

Since $TADD = ADD_i + ADD_d$

Then: $TADD = Conc/soil \times 0.1225\ g\ soil/day$

$$Conc/soil = \frac{TADD}{0.1225\ g\ soil/day}$$

4.3 PRELIMINARY HEALTH BASED LEVEL$_{soil}$ ($PHEL_{soil}$)

Let TADD = MEL

$$Then: Conc/soil = \frac{MEL}{0.1225\ g\ soil/day}$$

Since MEL is the maximum safe exposure level:

$$PHEL_{soil} = Conc/soil$$

$$Therefore: PHEL_{soil} = \frac{MEL}{0.1225\ g\ soil/day}$$

4.3.1 $PHEL_{soil}$ for DDT or DDE:

MEL (from #4.1 above) = 2.1×10^{-4} mg/day

$$So: PHEL_{soil} = \frac{2.1\times10^{-4}\ mg\ DDT/day}{0.1225\ g\ Soil/day}$$

$$= 16.7\times10^{-4}\ mg\ DDT/g\ Soil$$

$$= 1.7\ ug\ DDT/g\ Soil$$

$$= 1.7\ ppm$$

$PHEL_{soil}$ for DDT and DDE (continued)

The $PHEL_{soil}$ for DDE is identical, because DDE and DDT had identical slope factors.

4.3.2 $PHEL_{soil}$ for DDD:

MEL (from #4.1 above) = 2.9×10^{-4} mg/day

$$\text{So: } PHEL_{soil} = \frac{2.9 \times 10^{-4} \text{ mg DDD/day}}{0.1225 \text{ g Soil/day}}$$

$= 23.6 \times 10^{-4}$ mg DDD/g Soil

= 2.4 ug DDD/g Soil

= 2.4 ppm

5.0 CONCLUSION. The most sensitive endpoint of toxicity for DDT, DDD, and DDE is hepatocellular carcinoma. MELS and PHELS derived from this carcinogenic response are as follows:

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MEL	DDT = 0.21 ug/day	(2.1×10^{-4} mg/day)
	DDE = 0.21 ug/day	(2.1×10^{-4} mg/day)
	DDD = 0.29 ug/day	(2.9×10^{-4} mg/day)
$PHEL_{soil}$	DDT = 1.7 ppm	(1.7 mg DDT/kg soil)
	DDE = 1.7 ppm	(1.7 mg DDE/kg soil)
	DDD = 2.4 ppm	(2.4 mg DDD/kg soil)

Note that these values are for lifetime exposure in a residential setting. USEPA (1989) and Sedman (1989) should be consulted for guidance regarding less than lifetime exposure scenarios, such as occupational, intermittent, or childhood exposures.

In the absence of human effects, in spite of heavy DDT usage, the relevance of these figures to a carcinogenic risk in humans remains unknown.

6.0 REFERENCES

ATSDR (1987). Toxicological Profile for p,p'-DDT, p,p'-DDE, and p,p'-DDD (draft). Prepared by Clement Associates for Agency for Toxic Substances and Disease Registry (ATSDR), U.S. Public Health Service, December, 1988.

Sedman, R. M. (1989). The development of applied action levels for soil contact: a scenario for the exposure of humans to soil in a residential setting. Environmental Health Perspectives, 79:291-313.

USEPA (1984). Health Effects Assessment for DDT. Report No. EPA 540/1-86/026. U.S. Environmental Protection Agency, Washington DC.

USEPA (1989). Risk Assessment Guidance, Volume I, Human Health Evaluation Manual (Part A), Interim Final. Office of Emergency and Remedial Response, U.S. Environmental Protection Agency. Document EPA/540/1-89/002. December, 1989.

USEPA (1990). Integrated Risk Information System (IRIS); Information as of 9/26/90.

ATTACHMENT II

PRELIMINARY HEALTH EFFECT LEVEL FOR ~~SOIL (PHEL soil)~~

ALDRIN

PRELIMINARY

SUBJECT TO REVISION

SUMMARY. Aldrin and its metabolite dieldrin are carcinogenic in laboratory animals. EPA has assigned both aldrin and dieldrin a "B2" carcinogen classification, that is, both are considered to be probable human carcinogens. Low dose extrapolation of the tumor responses in 3 separate studies with aldrin provided a cancer potency factor or 17 mg/kg-day^{-1}. The maximal exposure level (MEL) for acceptable risk (no more than one excess cancer death per million exposed for a lifetime) calculated with this potency factor is 4.1×10^{-6} mg/day, or 4.1 nanograms/day, for a 154 pound adult. The preliminary health effect level (PHEL) for soil calculated with this MEL is 6.8 ppb. This $PHEL_{soil}$ represents the concentration of aldrin in soil which would not pose an excess risk to an adult exposed by oral ingestion and skin contact with 0.6 g of soil/day for a lifetime. Potential exposure via air or water were not included in these calculations.

DRAFT

CHEMISTRY AND USE. Aldrin is an organochlorine insecticide of the cyclodiene type structurally related to chlordane and dieldrin. In fact, dieldrin is the major metabolite of aldrin and probably represents most of the active chemical to which the body is exposed internally.

Aldrin was widely used on corn and citrus, with peak overall usage reaching 19 million pounds in 1966. Based on cancer risk, EPA severely restricted the use of aldrin in 1974, and all foodcrop use was banned in 1985. There is no current manufacture of aldrin in the U.S., and none has been imported since 1985. Current use is restricted solely to termite control by soil injection.

The technical grade material is a tan to dark brown solid "with a mild chemical odor." Solubility in water is 0.027 mg/L (ATSDR, 1987, and USEPA, 1988).

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HUMAN ACUTE TOXICITY. The lethal dose [illegible] not well established, but is known to be as low as 8 mg/kg, the amount ingested by a three year old child which died within 12 hours. This is equivalent to about one-fivehundredth of an ounce in a 30 pound child. In contrast, an adult male survived a suicide attempt with 26 mg/kg.

Clinical signs of acute poisoning are similar to those of other organochlorine pesticides: headache, nausea, vomiting, dizziness, and mild clonic jerking to convulsions.

HUMAN CHRONIC TOXICITY. The signs and symptoms of chronic exposure are similar to those of acute poisoning, and result from a "cumulative intoxication" with regular daily small doses. Electroencephalogram ("brain wave") changes, memory loss, and lack of concentration have also been reported with chronic exposure.

Has not been peer-reviewed

SUBJECT TO REVISION

2. PRELIMINARY HEALTH EFFECT LEVEL$_{soil}$ (PHEL$_{soil}$)

$$PHEL_{soil} = \frac{MEL}{\text{Daily Soil Exposure in g}} \times 1000 \text{ g/kg}$$

$$= \frac{4.1 \times 10^{-6} \text{ mg/day}}{0.6 \text{ g soil/day}} \times 1000 \text{ g/kg}$$

$$= 6.8 \times 10^{-3} \text{ mg/kg soil}$$

$$= 6.8 \text{ ppb}$$

CONCLUSION. The most sensitive endpoint of toxicity for aldrin is hepatocellular cancer. MELS and PHELS derived from this carcinogenic response are as follows:

$$MEL = 4.1 \times 10^{-6} \text{ mg/day}$$
$$PHEL_{soil} = 6.8 \text{ ppb}$$

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The PHEL$_{soil}$ represents the maximum concentration of aldrin in soil which is not likely to pose a significant cancer risk (i.e., greater than 1×10^{-6}) to individuals exposed to aldrin by skin contact and ingestion of soil containing aldrin at the PHEL$_{soil}$.

REFERENCES

ATSDR (1987). Toxicological Profile for Aldrin/Dieldrin (draft). Prepared by Dynamac Corporation for Agency for Toxic Substances and Disease Registry (ATSDR), U.S. Public Health Service, November, 1987.

DHS (1987). The Development of Applied Action Levels for Soil Contact: A Scenario for the Exposure of Humans to Soil in a Residential Setting. Final Draft, December 15, 1987. Toxic Substances Control Division, California Department of Health Services, Sacramento CA.

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Sedman, R. M. (1989). The development of applied action levels for soil contact: a scenario for the exposure of humans to soil in a residential setting. Environmental Health Perspectives, 79:291-313.

USEPA (1980). Ambient Water Quality Criteria for Aldrin/Dieldrin. Report No. EPA 440/5-80-019. Office of Water Regulations and Standards, U.S. Environmental Protection Agency, Washington DC.

USEPA (1988). Integrated Risk Information System (IRIS), 8/22/88 Revision.