UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Submission of the Toxicology Branch Chapter of the Registration Standard for Lindane

Tox Chem No. 527

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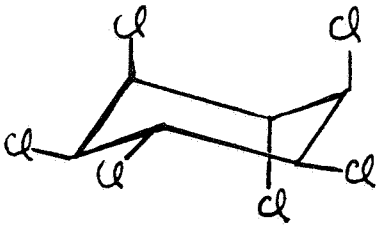
Enclosed is the Toxicology Branch (TB) chapter for the Registration Standard for lindane including the following three parts.

I. Lindane Policy Discussion(s)
II. Table A. Generic Data Requirements for Lindane
III. Summary of Evaluated Data -"one-liners" and review of selected studies. Additional "one-liners" and study reviews will be submitted at a later date.

I. Lindane Policy Discussions

A. Introduction

Lindane is the common name for preparations of the gamma isomer of 1,2,3,4,5,6- hexachlorocyclohexane (see structure below). Technical preparations of lindane must contain 99.5% or more of the gamma isomer. Other names used for the chemical lindane are gamma BHC and gamma HCH (BHC = benzene hexachloride, HCH = hexachlorocyclohexane). It should be noted that use of the term BHC in describing lindane is misleading because lindane does not contain an unsaturated benzene ring. Lindane must be distinguished from hexachlorobenzene a fungicide, which has separate pesticidal uses and its own toxicity data base. HCH exists in several isomeric forms because of the spatial orientation of the chlorine atoms on the cyclohexane ring. Thus preparations of technical HCH contain mixtures of chiefly alpha, beta, gamma, delta, epsilon and minor quantities of other isomers (up to eight). Technical HCH was once used as an insecticide and earlier toxicity data was generated using the mixture of the isomers. Later studies have indicated that the different isomers have different toxicity profiles Because of lindane's close relationship to the benzene derivative and because there are several isomers of hexachlorocyclohexane any discussion of the toxicity of lindane must carefully assess the exact composition of the test material used in the study. The chemical structure of lindane is as follows:



Other commercial names for lindane include: Exagama, Forlin, Gallogama, Gamaphex, Gammex, Inexit, Isotox, Lindafor, Lindagam, Lindagrain, Lindagranox, Lindalo, Lindamul, Lindpoudre, Lindaterra, Novigam, Silvanol.

Lindane has been used as an insecticide since the 1940's. There are currently numerous tolerances for residues of lindane in/on various agricultural commodities (see Tolerance Reasssessment). The following table outlines the distribution of the usage of lindane in 1978 (this information was obtained from "Preliminary Benefit Analysis of Lindane" prepared by the U.S. EPA and USDA in June 1978):

Estimated Pounds of Gamma Isomer Used by Site

	lbs ai (gamma)	% of total[a/]
hardwood logs, lumber	200,000	23.0
seed treatment	426,000	48.0
forestry	4,000	0.5
livestock	140,000	16.0
pineapples	19,000	2.0
ornamentals	17,000	2.0
Christmas trees	unknown	
pecans	27,000	3.0
pets	30,000	3.0
structures	1,000	0.1
household	12,000	1.0
cucurbits	11,000	1.0
Total	887,000	100.0

[a/] May not add to 100% due to rounding error.

According to Mark I. Dow, Ph.D., BUD/EPA, the net poundage and use distribution for the use of lindane probably has not changed significantly from the 1978 estimates.

As indicated in the above table there are a large variety of usages as well as exposure conditions for lindane. In addition to the uses indicated in the table, lindane is also used on humans to control lice and scabies. The use of lindane directly on humans is regulated by the Food and Drug Administration and will not be further evaluated in this Registration Standard.

The regulatory history of lindane at EPA includes a full Rebuttable Presumption Against Registrataion (RPAR) review. Position Documents were published in 1977 (PD1), in 1980 (PD2/3) and in 1983 (PD4). PD4 addressed several toxicity issues of immediate concern, but did not provide a comprehensive evaluation of the full toxicity data base supporting the registration of lindane. Although there have been numerous publications in the scientific literature, there has been only a limited amount of new data submitted to the Agency since completion of the PD4. This Registration Standard reassesses the toxicity data base for lindane and specifies additional studies which are required to support the registration(s) of lindane. The discussions presented in PD4 for the most part will not be reiterated in this Registration Standard.

B. Data Summary

1. Table A - Generic Data Requirements for Lindane - See Part II.

2. Summary of Evaluated Data ("one liners" and review of selected studies)- See Part III.

3. Data Gaps and Special Toxicity Problems

a. Data Gaps

The following toxicity studies are data gaps which should be filled to support the continued registration of various uses of lindane.

i. acute inhalation LC_{50} - rats
ii. dermal sensitization
iii. 21-day dermal-rabbits
iv. 90-day inhalation
v. chronic feeding/oncogenicity-rats
vi. general metabolism (including pharmacokinetics)
vii. special testing - aplastic anemia
viii. mouse oncogenicity-this requirement is being reevaluated (see part c ii below)

b. Explanation for Data Gaps.

i. Acute inhalation LC_{50}-rats. There is no available study which adequately determines the LC_{50} of technical lindane.

ii. Dermal sensitization. A dermal sensitization study is required because lindane products are likely to result in repeated human skin contact under conditions of use.

iii. 21-day dermal-rabbits. Registered uses of lindane include livestock and pet treatment products. These and certain other products may require frequent handling by the user/applicator. Thus, a 21-day dermal toxicity study with rabbits is required to support these uses.

iv. 90-day inhalation. Registered uses of lindane include products intended for repeated indoor uses in the form of aerosols, sprays, etc. A 90 day inhalation study is required to support these and certain other uses such as soil treatments and subterranian termite control (refer to the Data-Call-In notice dated Feb. 23, 1984).

v. Chronic Feeding/Oncogenicity-Rats. A chronic feeding/oncogenicity study in rats is required to support uses on agricultural commodities and certain other uses involving repeated long-term exposure to lindane. The chronic feeding aspects of this study must include an emphasis on kidney and liver function and pathology. Pathology of the testes should be included. Critical assessments of all blood elements and the spleen and bone marrow should also

be included in addition to the usual parameters of a chronic feeding study. Extra slides of the kidney, testes, liver, spleen, and bone marrow should be prepared and examined. The oncogenicity aspects of this study should particularly include critical assessment of the liver and the hematopoietic system.

vi. General metabolism. A general metabolism study is required to support uses on agricultural commodities and certain other uses involving repeated long-term exposure to lindane (e.g. soil treatment and subterranian termite control (refer to the Data-Call-In notice dated Feb. 23, 1984).

vii. Special testing-aplastic anemia.

Lindane has been associated with possible induction of aplastic anemia (a more specific term for blood dyscrasias) in humans. The PD4 concluded that there were insufficient data to establish a cause-effect relationship between lindane and blood dyscrasias. The possibility that lindane may induce aplastic anemia in certain susceptible humans still remains. For this reason a special study is requested to assess whether lindane can induce or increase the frequency of anemia in test animals. A suggested protocol for this study is briefly outlined below.

It is suggested that the test animals (preferably rats or mice) first be exposed to known inducers of aplastic anemia such as radiation or certain chemicals. A standard curve for induction of anemia by the agent(s) should be constructed. Then additional animals should be dosed with both lindane and the inducing agent. An enhancement of aplastic anemia by lindane would be the criterion for a positive result. This experiment was suggested by Dr. Louis Kasza, Pathologist, Toxicology Branch.

The registrant is strongly encouraged to discuss this study in advance with the Agency and then design the study and submit the protocol to the Agency for review. Discussions on chemical and radiation induced aplastic anemia can be found in the following references (the registrant is welcome to use other appropriate references):

(a) Hematology, 3rd Edition, (1983), W.J. Williams, E. Beutler, A.J. Erslev, and M.A. Lichtman, McGraw-Hill Book Company, pages 151-170.

(b) Veterinary Pathology, 5th Edition, (1983), T.C. Jones and R.D. Hunt, Lea-Febiger, pages 886-894.

(c) Pathology of Laboratory Animals, Volume I, (1978), K. Benirschke, F.M. Garner and T.C. Jones (editors), Springer-Verlag, pages 890-1050.

c. Special Toxicity Problems

i. Teratology and reproduction studies

[The following statements were provided by William L. Burnam, Deputy Branch Chief, Toxicology Branch.]

The potential of lindane to induce teratogenic and fetotoxic effects has been adequately characterized by studies in the rat, rabbit and mouse in which the routes of administration were by gavage and subcutaneous injection. In these studies which were reviewed previously by the Agency and referenced in Lindane Position Document 4, no teratogenic effects were noted and adverse fetal effects were seen only at doses which also caused maternal toxicity.

Oral (gavage) intubation in rats indicated a NOEL of 5 mg/kg/day for maternal effects and a NOEL of 10 mg/kg/day for fetal effects. Similar NOELs were noted in a gavage study in rabbits. In a gavage study in mice, both the maternal and fetal NOEL was 30 mg/kg/day. No further teratogenicity testing is required with lindane.

Doses up to 100 ppm produced no adverse reproductive effects in rats fed lindane for three generations. No further reproduction testing is required with lindane.

ii. Oncogenicity in mice

The Carcinogenesis Assessment Group (CAG) of the Office of Research and Development (ORD) of EPA has reviewed the issue of lindane oncogenicity in mice and has determined that lindane has been demonstrated to be associated with increased incidences of liver tumors in at least two studies. These studies are the NCI study (1977) and the Thorpe and Walker (1973) study conducted at the Shell Research Laboratories in England. For a more detailed discussion of this determination, see PD4. The conclusion that lindane causes increased liver tumors in mice was also made by the International Agency for Research on Cancer (IARC, 1979). Other studies have indicated that the alpha isomer of hexachlorocyclohexane consistently increases liver tumors in both rats and mice and a metabolite of lindane in humans (2,4,6-trichlorophenol) is associated with leukemia in rats and with liver tumors in mice.

For the preparation of this Registration Standard, Toxicology Branch has taken into consideration seven studies designed by the investigators to assess the oncogenic potential of lindane in mice. For various reasons none of these studies could be classified as CORE MINIMUM or better in terms of current review criteria. The principal reasons that these studies could not be

classified as CORE MINIMUM is that only summary tables were presented and an independent analysis of the data by Toxicology Branch could not be made. Other reasons include that some of the studies were of too short a duration of dosing and still others used too few mice at initiation of the studies and the studies were run concurrently with other test materials.

On June 28, 1985, Hazard Evaluation Division (HED) staff met with the CAG to discuss the issue of lindane oncogenicity in mice. As a result of this meeting it was agreed that CAG would reconsider the issue of lindane oncogenicity in mice and on July 3, 1985, HED forwarded a request to CAG to provide specific responses to the following items (refer to Anne Barton memo to Dr. Elizabeth Anderson dated July 3, 1985):

"1. A rat chronic feeding/oncogenicity study with lindane has been identified as a data gap for this insecticide. Are additional mouse studies with lindane necessary to assess for oncogenic effects in this species.

2. Do the available oncogenicity studies provide a satisfactory assessment for other organs/tissues being possible target organs/tissues for an oncogenic effect of lindaner in mice.

3. If the available data are appropriate, classify lindane per proposed Agency Guidelines according to the weight of available evidence. The attached summary of mutagenicity experiments with lindane prepared by Dr. I. Mauer should be incorporated into the classification.

4. Confirm that the appropriate Q_1^* for the risk assessments for lindane is 1.33 $(mg/kg/day)^{-1}$."

An additional oncogenicity study with mice may or may not be a requirement (data gag) for lindane pending receipt of responses to be provided by CAG.

iii. Mutagenicity

[The following summary was provided by Dr. I. Mauer, Geneticist, Toxicology Branch.]

As summarized in Appendix IV of PD4, lindane has demonstrated little if any mutagenic or genotoxic activity. Except for two Salmonella studies by Rohrborn (1975, 1976), lindane has been reported to be negative for gene mutation in bacterial Ames assays (Shirasu et al., 1976; Lawler et al., 1975; Purchase et al., 1978;

van Dick and van der Voorde, 1976), in a Drosophila sex-linked recessive lethal assay (Benes and Sram, 1969), in yeast cells (Schuber, 1969; Shahin, 1977) as well as in host-mediated assays (Buselmaier et al., 1972). Although a few in vitro studies with human lymphocytes (Zimonjic et al., 1981; Tzoneva-Maneva et al., 1971) or Chinese hamster lung cells (Ishidate and Odashima, 1977) have suggested lindane may induce chromosome breakage at toxic concentrations, in vivo cytogenetic studies were negative (Rohrborn, 1976, 1977; Dikshith et al., Reno, 1976; Gencik, 1977; Buselmaier et al., 1972; Epstein et al., 1972; Jenssen and Ramel, 1980), or equivocal (Nigam et al., 1981; Shtannov et al., 1980, Cerey et al., 1975). The beta-isomer of HCH has been reported to cause chromosome breakage in rat bone marrow cells (Shimazu et al., 1976). Except for one "weakly" positive in vitro study for unscheduled DNA synthesis in rat thymocytes and human lymphocytes by Rocchi et al., (1980), lindane has been reported as negative in other in vitro assays for DNA damage/repair in bacteria (Lawler et al., 1979; Shirasu et al., 1972, van Dijck et al., 1976), in transformed human (VA-4) cells (Ahmed et al., 1977), as well as in rat and mouse hepatocytes (Probst et al., 1981). Finally, mammalian cell transformation assays were negative employing human WI-38, Chang liver and hamster BHK21 cells (Purchase et al., 1978).

Some studies have reported spindle inhibition with lindane, but these have not been validated by EPA. That lindane may act as a spindle inhibitor is suggested by cytological activity in plant cells, in which it produces c-mitosis and polyploidy (Jeanne, 1979; Das and Singh, 1978; Kar and Singh, 1979; Nyborn, 1947; Anderegg et al., 1977; Baqar et al., 1971) and in rat liver cells, where it increaes mitotic indices and tetraploidy (Hitachi et al., 1975). However, other studies reported negative results (e.g., deBrabander, 1976).

In response to the Special Data Call-In Notice (February 23, 1984), more recent mutagenicity testing submitted by registrants through the Centre International d'Etudes du Lindane (CIEL) have confirmed that lindane has little or no genetic activity, even when employing more sensitive tests for detecting DNA events. For example, negative results were reported in bacterial Ames testing in the presence of a microsomal metabolic activation system (S-9) from the tumor-susceptible mouse strain, CF-1. Negative results were also obtained in the presence of inactivators of potential nucleophilic reacting products, such as the epoxide hydrase inhibitor and glutathione depletor, 1,1,1-trichloropropene (TCPO), as well as following preincubation with nor-harman, a DNA intercalator and co-carcinogen, which is a known inhibitor of DNA synthesis and repair. Negative results have also have reported in adequate mammalian assays for gene mutation at the HGPRT locus of Chinese hamster lung (V79) cells, and for sister chromatid exchanges in CF-1 mice administered lindane by both the oral and parenteral (ip) routes.

Hence, the weight-of-evidence based on conventional genotoxicity testing indicates that lindane does not interact directly with DNA or interfere with genetic mechanisms. Moreover, further standard mutagenicity assays are unlikely to alter this assessment.

No further mutagenicity studies are required at this time.

[Note: Refer to PD4 for the list of references.]

C. Risk Assessment/Tolerance Reassessment

1. Risk Assessment

HED has requested the CAG to reevaluate the oncogenicity of lindane in mice and to confirm the appropriate Q_1^* for use in risk assessments (see section c ii-Oncogenicity in mice - above). Until the Q_1^* value is confirmed by the CAG, oncogenic risk assessments for lindane cannot be provided.

2. Tolerance Reassessment

Tolerances ranging from 0.01 ppm to 7.00 ppm for residues of lindane in/on various agricultural commodities have been established (40 CFR 180.133).

The best available study for determining the ADI for lindane is the recently submitted subchronic feeding study in rats (1983) which has a NOEL of 4 ppm. Based on dietary analysis, food intake and body weight data from this particular study, the NOEL of 4 ppm is equivalent to 0.3 mg/kg/day. Using this latter value and a safety factor of 2000, the provisional Acceptable Daily Intake (ADI) is 0.00015 mg/kg/day and the Maximum Permissible Intake (MPI) for a 60 kg person is 0.0090 mg/day. The Theoretical Maximum Residue Contribution (TMRC) for lindane based on established tolerances is 1.4189 mg/day/1.5 kg of diet. The percent of the MPI used up is thus 15765.64%. See the attached computer printout.

It should be recognized that even if the safety factor was 100 the percent MPI used up would be 788.28%.

Thus, the sum of the TMRCs from existing tolerances greatly exceed the MPI.

Note: Although the TMRC from existing tolerances greatly exceeds the MPI, the actual residues of lindane in foodstuffs may be lower. Information on the actual residue levels of lindane has been sought (refer to the Residue Chemistry Branch Chapter for the lindane registration standard).

CFR 180.1 Linuron 7/11/89

Unverified Printout

TOLERABLE DAILY INTAKE DATA

NOEL Change not recorded

NAME, CLOVER ROOT	SPECIES	NOEL	PI
mg/kg	[redacted]	mg/kg/day	mg/day/60kg
0.300		0.0002 (0.00015)	0.0090

Published Tolerances

CROP	Tolerance	Food Factor	mg/day/1.5kg
Cattle(26)	7.000	7.18	0.75437
Goats(82)	7.000	0.03	0.00315
Sheep(145)	7.000	0.19	0.02039
Hogs(69)	4.000	3.43	0.20063
Cucumbers, inc pickl(46)	3.000	0. 3	0. 3265
Lettuce(74)	3.000	1.31	0.05617
Melons(92)	3.000	2.00	0.08014
Mushrooms(97)	3.000	0.03	0.00135
Pumpkin, inc squash(131)	3.00	0.11	0.00506
Summer squash(133)	3.000	0.03	0.00135
Tomatoes(163)	3.000	2. 7	0.12537
Apples(4)	1.000	2.33	0. 3795
Apricots(5)	1.000	0. 1	0.00405
Asparagus(5)	1.000	0.14	0. 0215
Avocados(6)	1.000	0. 3	0. 0345
Broccoli(19)	1.000	0.10	0.00135
Brussel sprouts(20)	1.000	0.03	0.00045
Cabbage, sauerkraut(44)	1.000	0.74	0.01104
Cauliflower(47)	1.000	0.07	0.00107
Celery(2)	1.000	0. 9	0. 0429
Cherries(30)	1. 00	0.1	0.00153
Collards(37)	1. 00	0.08	0.00123
Eggplant(53)	1.000	0.03	0.00045
Grapes, inc raisins(60)	1.000	0.49	0.00736
Guava(164)	1.000	0.03	0.00045
Kale(75)	1.000	0.03	0.00045
Kohlrabi(76)	1.000	0.03	0.00045
Mangoes(85)	1.000	0.03	0.00045
Mustard Greens(95)	1.000	0.06	0.00092
Nectarines(100)	1.000	0. 3	0.00045
Okra(103)	1. 00	0.07	0.00107
Onion(dry bulb)(106)	1.000	0.72	0.01073
Peaches(114)	1. 00	0. 9	0. 1349
Pears(110)	1.000	0.26	0.00383
Peppers(120)	1.000	0.12	0. 0164
Pineapple(123)	1.000	0.30	0.00445
Plums, inc prunes(125)	1.000	0.13	0. 0195
Quinces(132)	1.000	0.03	0.00045
Spinach(150)	1.000	0.05	0.00077
Strawberries(152)	1.000	0.18	0. 0270
Swiss Chard(156)	1.000	0. 3	0.00045
Pecans(116)	0. 1	0. 3	0. 0000

TDI	TMRC	% ADI
0.0090 mg/day/60kg	1.4169 mg/day/1.5kg	15760.94

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Commodity	Parts per million
Tomatoes	10

(Sec. 408(d)(2), 68 Stat. 514 (21 U.S.C. 346(d)(2))

[46 FR 27938, May 22, 1981, as amended at 48 FR 32015, July 13, 1983]

§ 180.130 Hydrogen cyanide; tolerances for residues.

Tolerances for residues of the insecticide hydrogen cyanide from postharvest fumigation are established as follows:

250 parts per million in or on the following spices: Allspice, anise, basil, bay, black pepper, caraway, cassia, celery seed, chili, cinnamon, cloves, coriander, cumin, dill, ginger, mace, marjoram, nutmeg, oregano, paprika, poppy, red pepper, rosemary, sage, savory, thyme, tumeric, white pepper.

75 parts per million in or on barley, buckwheat, corn (including popcorn), milo (grain sorghum), oats, rice, rye, wheat.

50 parts per million in or on citrus fruits.

25 parts per million in or on almonds, beans (dried), cashews, cocoa beans, peanuts, peas (dried), pecans, sesame, walnuts.

§ 180.131 Endrin; tolerances for residues.

Tolerances are established for residues of the insecticide endrin (hexachloroepoxyoctahydro-endo, endo-dimethanonaphthalene) in or on the following raw agricultural commodities:

Commodity	Parts per million
Beets, sugar	0
Beets, sugar, tops	0
Broccoli	0
Brussels sprouts	0
Cabbage	0
Cauliflower	0
Cottonseed	0
Cucumbers	0
Eggplant	0
Peppers	0
Potatoes	0
Squash, summer	0
Tomatoes	0

[42 FR 9178, Feb. 15, 1977]

§ 180.132 Thiram; tolerances for residues.

Tolerances for residues of the fungicide thiram (tetramethyl thiuram disulfide) in or on raw agricultural commodities are established as follows:

7 parts per million in or on apples, celery, peaches, strawberries, tomatoes.

7 parts per million in or on bananas, (from preharvest and postharvest application) of which not more than 1 part per million shall be in the pulp after peel is removed and discarded.

0.5 part per million in or on onions (dry bulb).

[36 FR 22540, Nov. 25, 1971, as amended at 37 FR 3182, Feb. 12, 1972]

§ 180.133 Lindane; tolerances for residues.

Tolerances are established for residues of the insecticide lindane (gamma isomer of benzene hexachloride) in or on raw agricultural commodities as follows:

7 parts per million in or on the fat of meat from cattle, goats, horses, and sheep.

4 parts per million in or on the fat of meat from hogs.

3 parts per million in or on cucumbers, lettuce, melons, mushrooms, pumpkins, squash, summer squash, and tomatoes.

1 part per million in or on apples, apricots, asparagus, avocados, broccoli, brussels sprouts, cabbage, cauliflower, celery, cherries, collards, eggplants, grapes, guavas, kale, kohlrabi, mangoes, mustard greens, nectarines, okra, onions (dry bulb only), peaches, pears, peppers, pineapples, plums (fresh prunes), quinces, spinach, strawberries, and Swiss chard.

0.01 part per million (negligible residue) in or on pecans.

[36 FR 22540, Nov. 25, 1971, as amended at 39 FR 13776, Apr. [illegible], 1974]

§ 180.134 Ovex; tolerances for residues.

Tolerances for residues of the insecticide ovex (*p*-chlorophenyl-*p*-chlorobenzenesulfonate) are established as follows:

5 parts per million in or on grapefruit, lemons, oranges, tangerines.

3 parts per million in or on apples, peaches, pears, plums (fresh prunes).

§ 180.135 Aldrin; toler

Tolerances for tol
insecticide aldrin a
product dieldrin, res
cation of aldrin, in
tural commodities a
follows:

0.1 part per millio
gus, broccoli, brus
bage, cantaloups, c
cherries, cranberries
plant, grapes, lettuc
melons, nectarines,
pimentos, pineapp
prunes), potatoes, p
ries, summer squash
tomatoes, watermel

Zero in or on alf
cots, beans, black-e
clover, collards, c
grain, cowpeas, co
(escarole), garden b
tops, garlic, grain so
ghum forage, horse
rabi, leeks, lespede
onions, parsnips, p
pears, peas, pea hay,
radishes, rutabagas,
fy roots, shallots,
hay, spinach, sug
tops, Swiss chard, t

Additional toleran
dues of aldrin are
interim basis pendi
all tolerances for th
new toxicity and re
available on or befo
0.1 part per millio
barley, oats, rice, r
0.05 part per millio
fruit, lemons, lim
grain, and tangerine
million in or on th
oats, rye, and wheat.

**§ 180.136 Basic copp
ance for residues.**

The tolerance for
fungicide basic copp
on pears from post-
chemical is 3 parts p
bined copper.

§ 180.137 Dieldrin; tol

Tolerances for resi
ticide dieldrin in or
al commodities are
lows:

TABLE A
GENERIC DATA REQUIREMENTS FOR LINDANE

Data Requirement		Composition	Use Patterns	Does EPA Have Data To Satisfy This Requirement? (Yes, No or Partially)	MRID NO.	Must Additional Data Be Submitted Under FIFRA Section 3(c)(2)(B)7
§158.135 Toxicology						
ACUTE TESTING:						
81-1	Oral LD_{50}-Rat	TGAI	All	Partial	00049330 and 00109141	No
81-2	Dermal LD_{50}	TGAI	All	Partial	00049330 and 00109141	No
81-3	Inhalation LC_{50}-Rat	TGAI	All	Partial	---	Yes
81-6	Dermal Sensitization	TGAI	All	No	---	Yes
81-7	Acute Delayed Neurotoxicity-Hen	N/A				
SUBCHRONIC TESTING:						
82-1	90-Day Feeding-rodent - rat	TGAI	All	Yes	00128356	No
	nonrodent-dog	TGAI	All	No	---	No (see chronic toxicity-dog)
82-2	21-Day Dermal	TGAI	All	No	---	Yes (depending on use)
82-3	90-Day Dermal	TGAI	---	No	---	No
82-4	90-Day Inhalation	TGAI	E,F,I	No	---	Yes
82-5	90-Day Neurotoxicity -hen	N/A				

TABLE A
GENERIC DATA REQUIREMENTS FOR LINDANE

Data Requirement	Composition	Use Patterns	Does EPA Have Data To Satisfy This Requirement? (Yes, No or Partially)	MRID NO.	Must Additional Data Be Submitted Under FIFRA Section 3(c)(2)(B)7
§158.135 Toxicology (continued)					
CHRONIC TESTING:					
83-1 Chronic Toxicity-					
rat	TGAI	A,E	No	---	Yes
dog	TGAI	A,E	Yes	---	No
83-2 Oncogenicity -					
rat	TGAI	A,E	No	---	Yes
mouse	TGAI	A,E	Partial	---	Pending[1]
83-3 Teratology -					
1st species (rat)	TGAI	All	Yes	---	No
2nd species (hamster)	TGAI	All	Yes	---	No
83-4 Reproduction - 2 generations	TGAI	A,E	Yes	---	No
MUTAGENICITY TESTING					
84-2 Gene Mutation	TGAI	All	Yes	---	No
84-3 Chromosomal Aberration	TGAI	All	Yes	---	No
84-2 Other Mechanisms of Mutagenesis	TGAI	All	Yes	---	No

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TABLE A
GENERIC DATA REQUIREMENTS FOR LINDANE

Data Requirement	Composition	Use Patterns	Does EPA Have Data To Satisfy This Requirement? (Yes, No or Partially)	MRID NO.	Must Additional Data Be Submitted Under FIFRA Section 3(c)(2)(B)7
§158.135 Toxicology (continued)					
SPECIAL TESTING:					
85-1 General Metabolism -	PAI or PAIRA	A,E	Partial	---	Yes[2]
Aplastic Anemia -	TGAI	All	No	---	Yes[3]
Dermal Absorption	PAIRA or PAI	All	Yes	---	No

Composition: TGAI = technical grade of the active ingredient. PAI=pure active ingredient. PAIRA=pure active ingredient, radiolabelled. The use patterns are coded as follows: A = terrestrial, food crop, B = Terrestrial, nonfood, C = Aquatic, food crop, D = Aquatic, nonfood, E = Greenhouse, food crop, F = Greenhouse, nonfood, H = domestic, outdoor, I = indoor. Data must be submitted no later than _____.

1. The need for an additional oncogenicity study in mice has not yet been determined. See discussion of this issue in the Policy Discussion section.

2. Recently acquired data are currently in review. Additional metabolism data may not be required pending review of these submissions.

3. See discussion of this requirement in the Policy Discussion section.