

ssr/TOX:10/22/85

Toxicology Branch/HED Form for Updating ADI's

004839

Tox. Chem. No./Name: 174-Chlordane (177, 22)

Acceptable Daily Intake -
EPA/OPP/HED/TOX:

Material: Technical

Doc No. for Updated ADI:

ADI / PADI / PLD: 0.00002
~~0.00005~~ mg/kg/day

004839

Safety Factor: 3000

OK'd 12/13/85

Dated: ~~12/9/85~~

*S. Swanda
D. Bowen
H. Spencer*

Updated: 12/9/85

*C. Frick
R. Frick*

Study: 30 month Rat Feeding / Onco-genic

NOEL: < 0.05 mg/kg

Lab.: Research Institute for Animal Science in Biochemistry
and Toxicology

Study No.:

Section Head

Study Date: 12/1/83

*Allen Kowalski
Henry Spencer*

Doc. No.: 004635

Comments: Q*

A review of the Tox. Branch files indicates that the 30-month rat feeding study yielded the most sensitive value for determining an ADI for Chlordane. Since the systemic NOEL is less than 0.05 mg/kg or not determined, an additional safety factor of 10 was given to the 30-month rat feeding study.

Q*: This agent is a positive carcinogen; it produces hepatocellular adenomas and hepatic hemangiomas.

1711

174-Chlordane

004839

Data Considered for Establishing an ADI, a PADI or PLD

1. 30-month Feeding/Oncogenic - rat (Dys. NOEL < 1 ppm or 0.05 mg/kg; minimum)
2. 2-Year Feeding ~~toxicity~~ - ~~rat~~ (NOEL = 3 ppm or 0.375 mg/kg; no core grade)
3. 2-year Feeding - rat (NOEL (?) = 25 ppm [detailed data needed to confirm microscopically changes in liver and kidney]; no core grade)
4. 3-Generation Reproduction - rat (NOEL = 30 ppm; no core grade)
5. Reproduction - rat (NOEL = 5 ppm or 0.25 mg/kg; no core grade)
6. Teratology - rabbit (maternal NOEL = 5 mg/kg; Pilot Study)

Data Gap(s)

1. Teratology - rat
2. Teratology - rabbit
3. 2-Year Feeding - rat

Other Data Considered

1. 2-Year Feeding/Oncogenic - mice (Oncogenic LEL = 12.5 ppm; increased formation of hepatocellular adenomas and hepatic hemangiomas; Dys. NOEL = 1 ppm; minimum)



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

004839

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Verification of New ADI
TO: Section Heads/Reviewers
FROM: William Burnam, Deputy Chief
Toxicology Branch

The ADI for the attached pesticide has been discussed by the Branch ADI Committee. According to our records, an ADI or PADI does not exist for this pesticide due to, for example, its oncogenic effects, the erosion of the data base, etc. The Committee has attempted to follow the new Branch SOP "Establishing an ADI for Pesticide Chemicals" #1002 in determining a new ADI for the pesticide.

Within the week, review the attached information, discuss it with your reviewers and sign the cover sheet if you agree with the conclusions of the group. If you and the reviewer disagree, write a cover sheet, return it to me and we will discuss it at our next Committee meeting.

2,4,5-T
Chlordane
Pesticide

Albin X
Section Head

W. Spencer
Reviewer

Note: Return cover sheet and/or comments to Charles Frick

Study/Lab/Study #/Date	Material	EPA Accession No.	Results:	TOX Category	CORE Grade/Doc. No.
2-Year oncogenic - mice; Research Institute for Animal Biochemistry	unknown purity	248331	LD50, LC50, PIS, NOEL, LEL		Invalid 002217
30 Month feeding/onco-rat interim report.	Technical Lot # B-9129 A	352267	Data are summary information and inadequate for review. Fischer 344 rats were reported by authors to have liver necrosis at 25 ppm (HDT), and adenomas greater than controls. Increased mammary tumors were reported at 1 ppm in females.		Supplementary 003659
Mutagenic - ames; Chemicals Inspection & Testing Institute; 6/1/80	Tech (100%)	243704	Significant increase in the number of revertant colonies per plate for <u>Salmonella typhimurium TA-100</u> but not to <u>TA-98</u> .		Acceptable 000935
Mutagenic - Ames; Chemicals Inspection & Testing Institute of Japan; 8/1/80	Technical chlordane		Significant increase in number of revertant colonies in histidine deficient strain of <u>Salmonella typhimurium TA 100</u> but not <u>TA 98</u>		Acceptable 000935
Mutagenic - ames; Chemicals Inspection & Testing Institute; Japan; 8/1/80	Gamma-chlordane (99.2%)	243704	Negative on histidine deficient strains of <u>Salmonella typhimurium TA-98</u> and <u>TA-100</u> .		Acceptable 000935
Mutagenic - ames; Chemicals Inspection & Testing Institute; Japan; 8/1/80	Gamma-chlordane (99.5%)	243704	Negative on histidine deficient strains of <u>Salmonella typhimurium TA-98</u> and <u>TA-100</u> .		Acceptable 000935
Mutagenic - ames; Chemicals Inspection & Testing Institute; Japan; 8/1/80	Alpha-chlordane (100%)	243704	Negative on histidine deficient strains of <u>Salmonella typhimurium TA-98</u> and <u>TA-100</u> .		Acceptable 000935

004839

Tox Chem No. 174 Chlordane EPA File Last Updated _____ Current Date _____
 Study/Lab/Study #/Date Material Accession No. Results: TOX Category CORE Grade/Doc. No.

Study/Lab/Study #/Date	Material	Accession No.	Results:	TOX Category	CORE Grade/Doc. No.
2-Year-feeding/oncogenic-mice; Research Institute for Animal Science in Biochemistry and Toxicology, Japan; 12/1/83	Technical Lot#B-9129A 100%	254665 251815	LD50, LC50, FIS, NOEL, LEL Levels tested in ICR strain-0, 1, 5 and 12.5 ppm Oncogenic NOEL = 5 ppm Oncogenic LEL = 12.5 ppm (hepatocellular adenomas and hepatic hemangiomas) Systemic NOEL = 1 ppm Systemic LEL = 5 ppm (hepatocellular swelling and necrosis in males; hepatocyte swelling in males; increased liver weight in male and female).		Minimum 004635
30-Month-feeding/oncogenic - rat; Research Institute for Animal Science in Biochemistry and Toxicology, Japan; 12/1/83	Technical 100%	252267	Levels tested in Fischer 344 Strain-0, 1, 5 and 25 ppm Oncogenic NOEL = 5 ppm, Oncogenic LEL = 25 ppm (increased incidence of benign hepatocellular) Systemic NOEL < 1 ppm (increased incidence of hepatocellular swelling and hepatocellular necrosis in males.)		Minimum 004635

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Tox Chem No. 174 - Chlordane

File Last Updated _____

Current Date 12/7/85

Study/Lab/Study #/Date	Material	EPA Accession No.	LD50, LC50, FIS, NOEL, LEL	Results:	TOX Category	CORE Grade/Doc. No.
2-Year feeding - rat; Lehman (1952)	Chlordane		Level tested: 0, 2.5, 5, 10, 25, 50, 75, 150, and 300 ppm NOEL (?) = 25 ppm Detailed data needed to confirm microscopically changes in liver and kidney			004829
3-Generation Reproduction - rat;	Technical		Levels tested: 0, 0.3, 15, 30, and 60 ppm NOEL = 30 ppm LEL = 60 ppm (increased mortality of pups, decreased litter size, and slight liver hypertrophy in pups)			004830
2-Year feeding - dog; IRDC; 10/65	Technical		Levels tested: 0, 0.3, 3, 15, and 30 ppm NOEL = 3 ppm LEL = 15 ppm (lesions in liver and liver hypertrophy)			004830
Reproduction - rat; Instk (1952); Group Med. 6, 357, 1952.	Technical		Levels tested: 0, 5, 10, 30, and 150, and 300 ppm Reproduction NOEL = 5 ppm (6D)			004831

Tox Chem No. 174 - Chloroform

File Last Updated _____

Current Date 12/7/85

EPA

Accession

No.

Results:

LD50, LC50, FIS, NOEL, LEL

TOX

Category

CORE Grade/

Doc. No.

Study/Lab/Study #/Date

Material

Toxicology - irritability;
IRDC; 12/71

Technical

Pilot Study

Levels tested: 1, 5, 10, 25,
50, 50 mg/kg

Maternal NOEL = 5 mg/kg
Maternal LCL = 10 mg/kg
(decrease in body weight)

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004839

Tox Chem No. 174 - Chlordane

File Last Updated

Current Date

EPA

Accession No.

TOX Category

CORE Grade/Doc. No.

Study/Lab/Study #/Date

LD50, LC50, PIS, NOEL, LEL

Results:

Acceptable Daily Intake-
EPA/ OPP/ HED TOX.

PADI= 0.00002 mg/kg/day
Safety Factor = 3000

TECH

Dated:

Updated: 12/9/85

Study: 30 Month Rat Feeding/Onco-
genic

NOEL: < 0.05 mg/kg

Lab.: Rés.Inst.for An.Sci.in Bio. and Tox.

Study No.:

Study Date: 12/1/83

Doc.No.: 004635

Comments: Q*

A review of the Tox. Branch files indicates that the 30-month rat feeding study yielded the most sensitive value for determining an ADI for Chlordane. Since the Systemic NOEL is less than 0.05 mg/kg or not determined, an additional safety factor of 10 was given to the 30 month rat feeding study.

Q* This agent is a positive oncogen; it produces hepatocellular adenomas and hepatic hemangiomas.

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Tox Chem No. 174 - Chlordane

EPA

File Last Updated

Current Date

Accession No.

Results: LD50, LC50, FIS, NOEL, LEL

TOX Category CORE Grade/Doc. No.

Study/Lab/Study #/Date

Material

Data considered for establishing an ADI, a PADI or PLD

- 1. 30-Month Feeding/Oncogenic-rat (Sys.NOEL < 1ppm or 0.05 mg/kg; minimum)
- 2. 2-Year Feeding-dog (NOEL=3 ppm or 0.075 mg/kg; no Core grade)
- 3. 2-Year Feeding-rat (NOEL (?)=25 ppm [detailed data needed to confirm microscopically changes in liver and kidney]; no core grade)
- 4. 3-Generation Reproduction-rat (NOEL=30 ppm; no Core grade)
- 5. Reproduction-rat (NOEL=5 ppm or 0.25 mg/kg; no Core grade)
- 6. Teratology-rabbit (Maternal NOEL= 5 mg/kg; Pilot Study)

Data Gaps

- 1. Teratology - rat
- 2. Teratology - rabbit
- 3. 2-Year Feeding - rat

Other data considered

- 1. 2-Year Feeding/Oncogenic-mice (Oncogenic LEL=12.5 ppm; increased formation of hepatocellular adenomas and hepatic hemangiomas; Sys. NOEL=1 ppm; minimum)

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File last updated 1/14/66

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ACCEPTABLE DAILY INTAKE DATA

RAI, Older CHILD	S.F.	P 101	P 101
mg/kg	ppm	mg/kg/day	mg/day/60kg
0.050	1.0	0.0000	0.0010

Published tolerances

CROP	Tolerance	Food Factor	mg/day/1.5kg
Apples(2)	0.300	2.53	0.01139
Apricots(3)	0.300	0.11	0.00051
Beans(5)	0.300	2.04	0.00918
Beets(14)	0.300	0.77	0.00078
Beet greens(15)	0.300	0.03	0.00014
Blackberries(15)	0.300	0.03	0.00014
Blueberries(16)	0.300	0.03	0.00014
Buckberries(74)	0.300	0.03	0.00014
Boysenberries(17)	0.300	0.03	0.00014
Broccoli(19)	0.300	0.10	0.00046
Brussel Sprouts(20)	0.300	0.03	0.00014
Cabbage, sauerkraut(22)	0.300	0.74	0.00331
Carrots(24)	0.300	0.48	0.00216
Cauliflower(27)	0.300	0.07	0.00032
Celery(28)	0.300	0.03	0.00129
Cherries(30)	0.300	0.10	0.00046
Citrus fruits(33)	0.300	3.01	0.011715
Collards(37)	0.300	0.03	0.00037
Corn, all types(38)	0.300	2.51	0.01130
Cucumbers, inc pickl(46)	0.300	0.73	0.00327
Lewberries(52)	0.300	0.03	0.00014
Eggplant(53)	0.300	0.03	0.00014
Grapes, inc raisins(60)	0.300	0.49	0.00221
Kale(75)	0.300	0.03	0.00014
Kohlrabi(76)	0.300	0.03	0.00014
Lettuce(84)	0.300	1.31	0.00589
Loganberries(86)	0.300	0.03	0.00014
Melons(92)	0.300	2.00	0.00901
Nectarines(100)	0.300	0.03	0.00014
Okra(103)	0.300	0.07	0.00032
Onions(105)	0.300	0.03	0.00373
Papayas(109)	0.300	0.03	0.00014
Peaches(114)	0.300	0.90	0.00405
Peanuts(115)	0.300	0.36	0.00161
Pears(116)	0.300	0.26	0.00115
Peas(117)	0.300	0.09	0.00313
Peppers(120)	0.300	0.72	0.00055
Pineapple(123)	0.300	0.30	0.00133
Plums, inc prunes(125)	0.300	0.13	0.00060
Potatoes(127)	0.300	5.43	0.02442
Quinces(132)	0.300	0.03	0.00014
Radishes(133)	0.300	0.03	0.00014
Raspberries(135)	0.300	0.03	0.00014
Rutabagas(139)	0.300	0.03	0.00014
Pumpkin, inc squash(131)	0.300	0.11	0.00051
Strawberries(152)	0.300	0.18	0.00083

