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

7/11/88

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Lindane: Toxicology Branch response to a letter from the law firm McKenna, Conner and Cuneo regarding the summary of a meeting held on June 9, 1988 in which the potential for lindane to induce kidney lesions and the protocol for a subchronic dermal toxicity study with lindane were discussed.

TOX CHEM. No.: 527

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TO: George LaRocca
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THROUGH: Edwin Budd 7/11/88
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The McKenna, Conner and Cuneo Law Offices on behalf of their client the Centre International d'Etudes du Lindane (CIEL) has submitted a letter (refer to letter from Charles A. O'Connor, III dated June 20, 1988 attached) which summarizes their perspective of a meeting that was held at the Agency facilities on June 9, 1988 to discuss certain toxicity problems related to lindane and the difficulties which the testing laboratory was having in trying to conduct a subchronic dermal toxicity study with rabbits. Toxicology Branch (TB) has already prepared a summary of this meeting (refer to J. Doherty memo dated approximately June 14, 1988).

TB acknowledges receipt of Mr. O'Connor's letter and has the following comments.

Toxicology Branch Comments.

1. Lindane effects in the kidneys of female rats.

Mr. O'Connor states that lindane "did not create kidney effects in the female rat".

TB does not consider this statement to be correct. Although the response to lindane is more pronounced in the male rat, inspection of the data from the subcronic oral study (Research and Consulting Co., Feb. 3, 1983) reveals that the female was also affected by having increased incidences of rats with tubular degeneration as indicated in the Table below (prepared from Dr. K.K. Locke's review dated June 17, 1983).

Group	Incidences of tubular degeneration	
	Females	Males
Control	0	0
0.2 ppm	1	0
0.8 ppm	0	0
4 ppm	0	0
20 ppm	5	5
100 ppm	5	6

15 rats from each dose level were examined.

TB recognizes that the females did not develop increased incidences of lesions "tubular distension", "nephritis, interstitial", "basophilic tubules", "hyaline droplets" or "tubular casts" as were recognized as being of increased incidences in the males in this study. Thus, although the male is considered to be more susceptible to pathological changes in the kidney resulting from lindane exposure, the female rat is also susceptible.

In this regard, all future studies with lindane must give equal care to examining the kidneys of both males and females.

2. Special Review Status.

If the rat subchronic dermal toxicity study scheduled

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to be submitted in July reveals indications of kidney pathology at low doses such that an unacceptable Margin of Safety (MOS) is determined, then a Special Review may be initiated. It is unlikely that a Special Review on lindane will be initiated if the rat dermal subchronic study indicates that an acceptable MOS can be demonstrated. In the latter case, TB expects that the Agency will delay the decision on initiating the Special Review until after the mouse subchronic inhalation study, rabbit subchronic dermal study and the rat chronic feeding/oncogenicity study are submitted and reviewed. If an unacceptable MOS is determined based on any of these three studies, the Special Review may be initiated when such a MOS is demonstrated.

3. Blood samples for determining lindane absorption.

Mr. O'Connor's letter states that "another blood sample will be taken at necropsy, within six hours after feeding". TB is uncertain as to why the sample will be taken relative to the last feeding. It appears that a uniform time interval between the last application of the test material would be a more appropriate time to assess for blood lindane content. Should this statement be reading "after removal of the dosing patch"?

4. Due date for the rabbit subchronic dermal toxicity study.

TB has no objection to extending the due date until December 1989 for submitting the final report of the rabbit subchronic dermal toxicity study.