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

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MAY 30 1990

MEMORANDUM

SUBJECT: Approximation of acute inhalation toxicity Categories for mice treated by the intratracheal route with Foil OF Insecticide (EPA Reg. No. 55638-RN), Record No. 256,400, MRID No. 413086-03

TO: Mike Mendelsohn/Phil Hutton (PM-17)
Insecticide-Rodenticide Branch
Registration Division (H7505C)

FROM: William S. Woodrow, Ph.D. WSW 5-30-90
Precautionary Review Section
Registration Support Branch
Registration Division

THROUGH: Thomas C. Ellwanger, Ph.D. Thomas C. Ellwanger Jr. 5/30/90
Chief, Precautionary Review Section
Registration Support Branch
Registration Division

Background: Toxicology Branch (Health Effects Division) and the Precautionary Review Section (Registration Division) use a Toxicity Category Criteria table which expresses four inhalation exposure Toxicity Categories qualitatively; in terms of mg toxicant per liter of air.

Inhalation exposure of laboratory animals by the intratracheal route obviously precludes designation of Toxicity Categories for acute inhalation studies based on a qualitative system of mg/L, without special consideration.

The following procedure provides a means for comparing total doses administered to animals by the intratracheal route, with Toxicity Categories expressed as total dose ranges, i.e., amounts of toxicant(s) calculated for theoretical 4 hour exposures.

Part A below presents acute inhalation Toxicity Categories for three intratracheal studies developed using the modified Toxicity Category Criteria Table mentioned earlier. Part B below describes the modified Toxicity Category Criteria Table used to develop Toxicity Categories for the intratracheal studies discussed in Part A above.

A. Task: How to relate mouse intratracheal doses stated as CFU/animal (colony forming units), to Toxicity Categories according to the EPA qualitative scheme (mg/L); for use in determining Product Label Precautionary Statements. The studies of concern were conducted using Foil OF Insecticide (EPA ID No. 55638-RN) which contains Bacillus thuriengensis transconjugant strain EG2424.

a. Total mouse doses in terms of mg/dose. Woodrow obtained the following information by telephone from Bob Sherwood 2-7-90: Three mouse studies (IIT Research Institute)

1) Foil OF Flowable - Male mice: A 0.63 g/10 mL preparation - each animal received 0.05 mL dose; equivalent to 3.15 mg.

2) Foil OF Flowable - female mice: 0.87 g/10 mL diluted 1/40. Each animal received 0.05 mL dose equivalent to 0.109 mg.

3) Foil Technical Powder - male mice: 0.01 g/mL each animal received 0.5 mg/dose.

b. Approximate Toxicity Categories for the three Foil OF Insecticide mouse studies mentioned under a. above; determined using the modified scheme described under Part B below.

1) Foil OF Flowable - male mice. 3.15 mg/mouse. If the LD_{50} were 3.15 mg - the Tox. Category would be Toxicity Category III (according to the scheme); all animals died.

2) Foil OF Flowable - female mice. 0.109 mg/mouse. If the LD_{50} were 0.109 mg - the Tox. Category would be Toxicity Category I (according to the modified scheme); all animals survived.

3) Foil Technical Powder - male mice. 0.5 mg/mouse. If the LD_{50} were 0.5 mg, the Tox. Category would be Toxicity Category II (according to the modified scheme); the animals did survive.

Conclusion regarding assignment of Toxicity Categories for Intratracheal Studies submitted by Ecogen, Inc. to fulfill an acute inhalation study requirement in support of Foil Oil Flowable and Foil Technical Powder (EPA Reg. No. 55638-RN):

A Toxicity Category of II must be designated for Foil Oil Flowable and Foil Technical Powder.

Discussion of conclusion: 3.15 mg dose killed all male mice, 0.109 mg dose did not kill female mice, while a 0.5 mg dose also did not kill male mice. The actual LD_{50} may lie somewhere between 0.109 mg, which did not kill any female mice, and 3.15 mg, which did kill all male mice tested. Until such time as a more definitive study, using male and female mice and multiple dose levels designed to bracket an estimated LD_{50} is conducted, a Toxicity Category of II must be assigned.

B. Modified Scheme suggested for use to convert intratracheal "total doses" to a system allowing designation of Toxicity Categories; using the present EPA Table III -- Toxicity Category Criteria - altered to express total 4 hour exposures.

	Toxicity Category I	Toxicity Category II	Toxicity Category III	Toxicity Category IV
Present EPA Table	up to 0.05 mg/L	>0.05 thru 0.5 mg/mL	>0.5 thru 5.0 mg/L	>5.0 mg/L
Above values*: 4 hr exposure Rats in mg	0.882 mg	>0.882 thru 8.82 mg	>8.82 thru 88.2 mg	>88.2 mg
Mouse 4** hour exposure values in mg	0.293 mg	>0.293 thru 2.93 mg	>2.93 thru 29.3 mg	>29.3 mg

*Rat & mouse breathing rates:
Rat: 85.5 breaths/minute
tidal volume of 0.86 mL/breath
85.5 x 0.86 = 73.53 mL/minute, or 0.0735 liters/rat/minute.
0.0735 L/min. x 240 min. (4 hours) = 17.64 liters of air breathed by 1 rat/4 hour exposure.

Example: Tox. Category I from EPA Table states: 0.05 mg/L. To convert to mg dose/4 hour exposure (rat), 17.64 liters/rat/4 hr exposure x 0.05 mg/L = up to and including 0.882 mg total theoretical dose (/4 hr exposure).

**Convert total mg doses from rats to mice; from values (mg dose/4 hour exposure for rats) -

$$\frac{\text{mg/values, rats}}{3.01} = \text{mg doses for mice for 4-hour exposure;}$$

$$\frac{\text{73.5 mL breathed/rat/minute}}{\text{24.45 mL breathed/mouse/minute}} = 3.01$$

Example: Tox. Category I from modified EPA Table above states: 0.882 mg total theoretical dose/4 hr exposure - for rats:

$$\frac{\text{0.882 mg rats}}{3.01} = \text{0.293 mg dose for 4 hr exposure (for mice).}$$