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

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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MAY 30 1986

MEMORANDUM

CASWELL 435

SUBJECT: EPTC - Acute Toxicity Studies Submitted under Accession No. 261729 - EPA Registration No. 748-223

FROM: Irving Mauer, Ph.D.
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TO: Robert Taylor/J. Miller, PM 25
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THRU: Jane E. Harris, Ph.D. 5/27/86
Head Section VI
Toxicology Branch
Hazard Evaluation Division (TS-769C) 5/30/86

Registrant: PPG Industries
Pittsburgh, PA

Action Requested (655):

Review and evaluate six acute studies on EPTC technical, submitted by the registrant February 25, 1986.

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TB Conclusions: (TB Data Reviews, attached):

Study	Reported Results	TB Eval/Core
Acute oral LD_{50} - rat (WIL - 13035, 06/03/85)	LD_{50} (males) = 1465 (1290-1663) mg/kg LD_{50} (females) = 1712 (1324-2214) mg/kg LD_{50} (combined) = 1599 (1294-1976) mg/kg	Guidelines Tox Cat. III
Acute dermal LD_{50} - rabbit (WIL - 13036, 12/18/84)	LD_{50} > 2000 mg/kg	Guidelines Tox. Cat. III
Acute inhalation - rat (Toxigenics 420-1853, 04/10/85)	LC_{50} (combined) = 1.39 (0.97-2.00) mg/L (analytical)	Guidelines Tox. Cat. II
Primary eye irritation - rabbit (Toxigenics 410-0910, 04/12/82)	PIS (24-hr) = 2.2 Reversed within 3 days	Minimum Tox. Cat III (males)
Primary dermal irritation - rabbit (WIL - 13037, 12/12/84)	PII = 1.4	Guidelines Tox. Cat. IV
Skin sensitization - guinea pig (WIL - 13038, 03/28/85)	Very slight sensitizer	Guidelines

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TOXICOLOGY BRANCH: DATA REVIEW

Chemical: EPTC

Caswell: 435
EPA Chem. 04101

Study Type: Acute oral LD_{50} - rat

Citation: Acute Oral Toxicity (LD_{50}) Study in Albino Rats with EPTC Technical

Accession No./MRID No.: 261729

Sponsor/Testing Lab: PPG/WIL Research Labs

Study No./Date: WIL-13035/June 3, 1985

Test Material: EPTC technical, lot #518-996, a light-yellow liquid (% ai not stated).

Procedures:

Groups of fasted young adults Sprague-Dawley rats (5/sex/group) were intubated with undiluted test material at levels of 991, 1427, 2055, 2959, and 5000 mg/kg, observed three times on the day of dosing and once daily thereafter for 14 days. Body weights were recorded 1 day before dosing, just prior to dosing, and on study Days 7 and 14; animals that died were weighed as soon as found. Gross necropsies were performed on all animals.

Results:

Dose-related lethargy, salivation, decreased limb tone, and ataxia were noted in test animals, persisting to death (within 2 to 4 days) at the higher dosages. Recovery in survivors was also directly related to dose. Based on mortality in the five treated groups, the acute LD_{50} and 95 percent confidence limits were calculated (Litchfield and Wilcoxon) as: Males = 1465 (1290-1663) mg/kg
Females = 1712 (1324-2214) mg/kg
Combined = 1599 (1294-1976) mg/kg

Except for weight loss in one animal each in the two lower dose groups, no other ponderal changes were noted during the study period. No significant gross alterations in major thoracic or visceral organs were found in animals surviving to Day 14. In contrast, almost all rats that died during the study period displayed brain hemorrhages and/or congestion, as well as hemorrhages and/or erosion of the GI tract. In addition, hyperemia and/or congestion of lungs and liver were found in a lesser number of dead animals. Hemorrhagic thymus glands were recorded in all four rats that died following

administration of 1427 mg/kg (in addition, two had blood in the urinary bladder), but these findings were not observed in any other group.

TB Evaluation: Core-Guidelines Data.

Toxicity Category: III.

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TOXICOLOGY BRANCH: DATA REVIEW

Chemical: EPTC

Caswell: 435
EPA Chem.#: 041401

Study Type: Acute dermal LD_{50} - rabbit

Citation: Acute Dermal Toxicity (LD_{50}) Study in Albino Rabbits with EPTC Technical

Accession No./MRID No.: 261729

Sponsor/Testing Lab.: PPG/WIL Research Labs

Study No./Date: WIL-13036/December 18, 1984

Test Material: EPTC technical, lot #518-996, a yellowish liquid (% ai not stated)

Procedures:

The backs of young adult New Zealand White rabbits (5/sex/group) were shaved, and 2000 mg/kg undiluted test material applied to cover approximately 25 percent of intact body surface. Test sites were bandaged and taped for 24 hours, following which bandages were removed and sites wiped with wet paper towelling. Animals were observed for treatment-related effects three times shortly after dosing, and daily thereafter for 14 days. Signs of dermal irritation were recorded 30 minutes after bandage removal, and daily thereafter. Body weights were recorded on the day of dosing, and on study Days 7 and 14. Gross necropsy examinations were performed on all animals at termination.

Results:

No animals died and no significant body weight changes or clinical effects were noted during the study period. Very slight to slight (Grade 1 to 2) erythema and/or edema were recorded on the first day of dermal observation, persisting in a few animals to day 14. Desquamation and fissuring were recorded in all animals on Days 5 through 11, and persisted in three after Day 11.

Except for abcessed lungs and "a gray and soft spleen" in one female (considered by the authors as unrelated to treatment), no gross postmortem pathological changes were recorded in major thoracic or visceral organs.

Conclusions: The acute dermal LD_{50} was greater than 2000 mg/kg.

TB Evaluation: Core-Guideline Data.

Toxicity Category: III.

TOXICOLOGY BRANCH: DATA REVIEW 005170

Chemical: EPTC

Caswell: 435
EPA Chem.#: 041401

Study Type: Acute inhalation LC_{50} - rat

Citation: Four-hour Acute Aerosol Inhalation Toxicity Study in Rats of EPTC

Accession No./MRID No.: 261729

Sponsor/Testing Lab: PPG/Toxigenics (American Biogenics Corporation)

Study No./Date: ABC-420-1853/April 10, 1985

Test Material: EPTC technical, lot #518-996 (% ai not stated)

Procedure:

Groups of young adult albino Sprague-Dawley rats (5/sex/group) were exposed for 4 hours to whole-body aerosol atmospheres (MMAD = 2.2 um) of test material at gravimetric concentrations of 0.85, 1.84, 2.31 and 5.62 mg/L (analytically determined for the three lower levels as 0.73, 1.58 and 2.34 mg/L). Animals were observed hourly during the exposure period, and daily thereafter for 14 days. Body weights were recorded immediately before exposure and on study Days 7 and 14 (or at death). All animals were necropsied, and the FIFRA Guidelines roster of organs and tissues examined.

Results:

No animals survived the highest concentration of test article, all but one dying 1 day after exposure (one female died shortly after removal from the chambers). Mortality at the three next lower concentrations were 8/10, 5/10 and 2/10.

Increased severity and incidence of dose-related irregular breathing, crusty eyes, nose and muzzle, lethargy, damp fur, exophthalmos, lacrimation, prostration, and poor coat quality were common observations during and shortly after exposure, for some effects persisting in survivors to termination. Postmortem changes in animals that died on test included abnormalities in nasal passages, liver, caecum, ears, small intestine, eyes, tail, kidney, stomach and lungs; with the exception of pulmonary inflammation in one low-dose male, no gross lesions were noted in survivors to Day 14.

Conclusions:

The combined acute inhalation LC_{50} was calculated to be 1.39 (0.97-2.00) mg/L, measured analytically (not including

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the highest gravimetric level of 5.62 mg/L, since no analysis was performed).

TB Evaluation: Core-Guideline Data.

Toxicity Category: II.

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TOXICOLOGY BRANCH: DATA REVIEW

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Chemical: EPTC

Caswell: 435
EPA Chem.#: 041401

Study Type: Primary eye irritation - rabbit

Citation: Primary Eye Irritation Study in Rabbits of 237-2651

Accession No./MRID No.: 261729

Sponsor/Testing Lab.: PPG/Toxigenics

Study No./Date: TX-410-0910/April 12, 1982

Test Material: "237-2651, a yellow liquid (supplied by the sponsor" (no other information provided in the report, but presumably, the TGAI).

Procedure:

[Procedures as described in 43 FR 37336, Part 163.81-4 of the 1978 FIFRA Guidelines were stated to have been followed.]

0.1 Milliliter of test article ("neat" as received, i.e., not diluted) was instilled into the right eye of 9 young adult New Zealand White rabbits; 3 of these treated eyes were washed with warm tap water 30 seconds later. The left eyes served as untreated control. Eyes were examined 24, 48 and 72 hours posttreatment, and again on Days 4 and 7 (termination); ocular reactions were scored according to Draize (1979).

Results:

The unwashed eyes in 2 of the 6 treated animals exhibited Grades 1 or 2 conjunctivitis at 24 hours, persisting in one animal as Grade 1 to 48 hours); Grade 1 chemosis and corneal opacity was also observed in the second affected animal. Eye irritations were reversed in the unwashed eyes by day 3, and no irritation was recorded in the group of 3 rabbits whose eyes were washed.

No deaths occurred, and no abnormal clinical signs were observed.

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Conclusions:

Mean primary eye irritation scores (PIS) were reported as follows:

Group (No.)	24 HR	48 HR	72 HR	4 DA	7 DA
UNWASHED (6)	2.2	0.3	0.0	0.0	0.0
WASHED (3)	0.0	0.0	0.0	0.0	0.0

TB Evaluation: Core-Minimum Data (Females were not tested).

Toxicity Category: (Males) III.

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TOXICOLOGY BRANCH: DATA REVIEW

Chemical: EPTC

Caswell: 435
EPA Chem.#: 041401

Study Type: Primary dermal irritation - rabbit

Citation: Primary Dermal Irritation Study in Albino Rabbits with EPTC Technical

Accession No./MRID No.: 261729

Sponsor/Testing Lab.: PPG/WIL Research Labs.

Study No./Date: WIL-13037/December 12, 1984.

Test Material: EPTC technical, lot #518-996, a light yellow liquid (% ai not stated)

Procedures:

0.5 mL of test material (as received) was applied to the shaved, intact dorsum (test site, approximately 1 inch square) of 3 male and 3 female young adult New Zealand White rabbits. Test sites were bandaged and taped for 4 hours, then coverings removed and sites washed with wet paper towels. Dermal examinations (scored according to Draize) were made 30 minutes after bandage removal, and again at 24, 48 and 72 hours postdosing. Animals free of irritation at 72 hours were sacrificed; those with any degree of irritation were maintained and observed daily until irritation disappeared.

Results:

No animals died during the test and no changes in body weights recorded.

Slight degrees (Grades 1 or 2) of erythema and/or edema were recorded in all animals within 24 hours, persisting (as Grade 1) for 7 days in two females and 11 days in one male.

Conclusions:

The primary irritation index (PII) was calculated as 1.4.

TB Evaluation: Core-Guideline Data.

Toxicity Category: IV.

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TOXICOLOGY BRANCH: DATA REVIEW 005170

Caswell: 435
EPA Chem.#: 041401

Chemical: EPTC

Study Type: Skin sensitization - guinea pig

Citation: Skin Sensitization Study in Albino Guinea Pigs with EPTC Technical.

Accession No./MRID No.: 261729

Sponsor/Testing Lab.: PPG/WIL Research Labs

Study No./Date: WIL-13038/March 28, 1985

Test Material: EPTC technical, lot #518-996, a yellowish liquid (% ai not stated)

Procedures:

[The study was stated to have been carried out according to FIFRA Guidelines, Section 81-6, November 1982]. Briefly, after selection of an irritating concentration (15% w/v), the backs of young adult Hartley guinea pigs were depilated (with NEET), and 0.4 mL of this test material applied to the shaved intact skin of the left shoulders of 10 males and 10 females three times, one week apart (Induction Phase). A Naive Control Group of 5 males and 5 females remained untreated during this induction phase. Two weeks later, 0.4 mL of a 3 percent w/v mixture (previously determined to be nonirritating) was applied to the right flank/hip areas of all animals, test and control (Challenge Phase). During all dosing phases, test material remained in contact under an occlusive dressing for 6 hours, following which dressings were removed and test sites washed with wet paper towels.

Skin reactions were graded 24 and 48 hours after removal of bandages and test material for each phase, according to the following system:

0 = No reaction
+ = Slight patchy erythema
1 = Slight confluent or moderate patchy erythema
2 = Moderate erythema
3 = Severe erythema (with or without edema)

Results:

No animals died, and no adverse clinical effects were noted. No significant changes in body weight were recorded.

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The 15 percent concentration employed for dose determination produced slight to moderate skin reactions (Grades 1 or 2) which included eschar, necrosis, fissuring and edema. During application of the 15 percent mixture for induction, generally slight to moderate skin reactions were again noted, including fissuring and desquamation for the majority of sites. Except for Grade 1 irritation in one test male and one test female in response to the 3 percent challenge dose, all other animals in both test and Naive Control groups showed slight to no reaction at 24 or 48 hours.

Conclusions:

On the basis of this test, EPTC was defined as a "very slight sensitizing agent." The Irritation Incidence Index was calculated as 0.1 for the Test Group and 0 for the Naive Control Group. Severity Indices for each group at 24 hours and 48 hours were as follows:

	24 Hours	48 Hours
Test Group	6.5/20 = 0.325	2.5/20 = 0.125
Naive Control Group	2/10 = 0.2	1/10 = 0.10

TB Evaluation: Core-Guideline Data.

Toxicity Category: Very slight sensitizer.