3-9-87

CASWELL FILE

007679

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

MAR 9 1987

MEMORANDUM:

SUBJECT: Propanil; Twenty-four Month Dietary Oncogenicity Study in Mice; Special Review Criteria (40 CFR 154.7)
OFFICE OF PESTICIDES AND TOXIC SUBSTANCES

Caswell No. 325

TO: Robert Taylor
Product Manager (25)
Registration Division (TS-767)
and
Jan Auerbach, Chief
Special Review Branch
Registration Division (TS-767)

THRU: Edwin Budd, Section Head
Review Section II
Toxicology Branch
Hazard Evaluation Division (TS-769)
and
Theodore M. Farber, Chief
Toxicology Branch
Hazard Evaluation Division (TS-769)

FROM: William Dykstra
Toxicology Branch
Hazard Evaluation Division (TS-769)

During review of the chronic mouse feeding study (MRID 155215, Hazelton No. 417-400; December 21, 1983) with propanil, as part of the Propanil Registration Standard, it was observed that STAM, technical (85.4% purity) produced increased incidences of moderate and moderately severe bilateral retinal degeneration in both male and female mice at 180 ppm, the only dose tested (with 85.4% a.i.).

The seriousness of this lesion was discussed with the Toxicology Branch pathologist, Dr. Kasza.

The incidences and grades of this lesion are presented below:

Retinal Degeneration, Bilateral

	Males						Females					
Group	1	2	3	4	5	6	1	2	3	4	5	6
Number Exmained	25	26	2	4	35	38	31	30	1	3	39	35
Not Affected	24	24	2	4	32	31	31	29	1	3	39	31
Slight	0	1	0	0	1	0	0	0	0	0	0	0
Moderate	1	1	0	0	2	2	0	1	0	0	0	3
Moderately Severe	0	0	0	0	0	5	0	0	0	0	0	1
Total Affected	1	2	0	0	3	7	0	1	0	0	0	4

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Unilateral retinal degeneration was not increased by treatment in this study. Additionally, an increased incidence of thyroiditis in female mice was observed at 180 ppm (85.4% purity). The significance of this lesion was not considered as serious as the eye effects by Dr. Kasza.

The dosages for the mouse study are as follows:

Group 1	:	Control	
Group 2	:	Control	
Group 3	:	5.0 ppm a.i.,	98.0% purity technical
Group 4	:	30 ppm a.i.,	98.0% purity technical
Group 5	:	180 ppm a.i.,	98.0% purity technical
Group 6	:	180 ppm a.i.,	85.4% purity technical

A NOEL for both bilateral retinal degeneration and thyroiditis were not established for the 85.4% technical. Therefore, the chronic feeding mouse study may need to be repeated at lower dosages with STAM technical, 85.4% purity, to establish a NOEL.

Toxicology Branch does not understand the purposes for which 98.0% a.i. and 85.4% a.i. were both tested in this study. Attached are copies of earlier memos (Hammernik, 10/22/86 and Dykstra, 11/5/86) relating to these issues. Toxicology Branch again requests that the information requested in the 11/5/86 memo be submitted. Additionally, historical control data for these lesions are required.

The STAM technical that is believed being marketed is of approximately 85.4% purity. It is expected that a final review of the entire study will be completed within two months.

On the basis of this information, Toxicology Branch believes that propanil may have exceeded special review criteria.

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

NOV 5 1986

MEMORANDUM:

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: Information Regarding Stam Technical (Propanil); Possible 6(a) 2 data

Caswell No. 325

TO: Robert Taylor
Product Manager (25)
Registration Division (TS-767)

THRU: Edwin Budd, Section Head
Review Section II
Toxicology Branch
Hazard Evaluation Division (TS-769)

FROM: William Dykstra
Toxicology Branch
Hazard Evaluation Division (TS-769)

Based on a recent audit of a 24-month dietary oncogenicity study in mice with Stam technical (report date 3/10/82, Hazelton Project No. 417-400), an association could not be excluded between the administration of 85.4% Stam technical and thyroiditis and retinal degeneration. The lesions associated with the 85.4% technical, according to a recent memo from K.L. Hamernik to W. Dykstra, "do not appear to have been reported to the EPA in an expedient manner in accordance with Section 6(a)2 of FIFRA." The memo from K. Hamernik is attached. Toxicology Branch has no review in its files on the 24-month mouse oncogenicity study. Toxicology Branch requests that hard copy of the study in question be obtained for review or that accession numbers be provided.

Toxicology Branch also requests a complete audit report by members of the audit team regarding all aspects of the audit.

Finally, Toxicology Branch requests that the registrant, Rohm and Haas Co., provide confidential statements of composition on the technical grade and Batch No. of the test materials used in the Stam 2-year dog study, 2-year rat study, 3-generation rat reproduction study and rat and rabbit teratology studies, as well as the 2-year mouse oncogenicity study.

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from Hamernik
on 10/22/86

MEMORANDUM

SUBJECT: Information Regarding STAM Technical (Propanil) 007679

TO: William Dykstra, Ph.D., Toxicologist
Toxicology Branch
Hazard Evaluation Division (TS-769)

FROM: Karen L. Hamernik, Ph.D., Toxicologist
Toxicology Branch
Hazard Evaluation Division (TS-769)

10/22/86

As a result of a recent EPA audit of Hazleton Laboratories, Vienna, VA, in which I participated, several pieces of information came to light with regard to STAM technical, a product of Rohm and Haas Co., Spring House, PA. I spoke with you previously about this subject (since I was informed that you were the primary reviewer for STAM) and I am now providing you with more formal notification by way of this memo. The items I wish to inform you of are presented below:

1. Dr. W. T. Lynch, Research Section Manager, Toxicology Dept., Rohm and Haas, informed me via personal communication that the purity of the technical material that is currently being marketed is of approximately 85.4% purity. However, it emerged from the audit, that tests conducted with the technical material in support of regulatory requirements under FIFRA may have been performed with a technical of substantially different purity than 85.4%.

2. According to the results of one of the studies audited, a 24-Month Dietary Oncogenicity Study in Mice with STAM Technical, Rohm and Haas Report No. 82rc-68, report date 3/10/82, Hazleton Project No. 417-400, an association could not be excluded between the administration of the 85.4% purity technical and the finding of at least two lesions (i.e. thyroiditis and retinal degeneration). Apparently, these lesions were not associated with a technical material of 98% purity also tested in this study.

3. The lesions associated with the 85.4% purity technical do not appear to have been reported to the EPA in an expedient manner in accordance with Section 6(a)2 of FIFRA.

Further evaluation of these matters would seem to be in order. I also call to your attention, that M. Adrian Gross, also an audit team member, has discussed some of these issues in his audit report. You might wish to get a copy of the final audit report for this study, since other members of the audit team may have provided, therein, information useful to you in your evaluation of STAM. In addition, I enclose some correspondence and data ("Stam (R): A 3-month dietary study in mice", Rohm and Haas Report No. 82R-065), which came to me by way of the audit.

cc E. Budd
T. Farber
A. Kocialski
R. Taylor

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