10/3/1988

Reviewed by: John Doherty
Section I, Tox. Br., Insecticide, Rodenticide Support (TS-769C)
Secondary reviewer: Edwin Budd 10/3/88
Section I, Tox. Br., Insecticide, Rodenticide Support (TS-769C)

DATA EVALUATION REPORT

STUDY TYPE: Special Study: Shimkin Mouse Lung Bioassay.

ACC.No.: 407668-17 TOX. CHEM. NO.: 652BB

TEST MATERIAL: Technical permethrin (92.5% pure, 40/60 cis/trans ratio, Lot #8599-RA, Penick Corp.)

SYNONYMS:

STUDY NUMBER(S): DAAD05-84-C-0234

SPONSOR: U.S. Army

TESTING FACILITY: BIOCON, Inc. 649 Lofstrand Ln. Rockville, Md.

TITLE OF REPORT: Shimkin Mouse Lung Bioassay.

AUTHOR(S): Lawrence E. Cunnick

REPORT ISSUED: September 13, 1985

CONCLUSIONS:

No evidence that permethrin treated mice (285 mg/kg/treatment, highest level of assessment) developed significant differences in adenoma formation relative to the control groups. The positive control (urethane) produced the expected positive result. Levels tested: 285, 475, 713.5 and 1425 mg/kg/treatment, death rate at 475 mg/kg and above precluded assessment.

Classification: SUPPLEMENTARY

Special Review Criteria (40 CFR 154.7): N/A

Quality Assurance Statement:

A Quality Assurance Statement signed by Judith T. Snow indicated that inspections were made on five occasions.

Table 7. Permethrin, Mouse Study - Male Liver Tumor Rates and Peto Prevalence Test Results

Tumor	Dose (ppm) 0	20	500	2000
Adenoma	6/66	17/63	15/63	17/57
(%)	(9)	(27)	(24)	(30)[a]
p =	0.0034**	0.0058**	0.0150*	0.0003**
Carcinoma	16/68	12/64	19/64	8/60
(%)	(24)	(19)	(30)[b]	(13)
p =	0.1797	0.3481	0.1381	0.1819
Both	22/68	29/64	36/64	25/60
(%)	(32)	(45)	(56)	(42)
p =	0.0973	0.0618	0.0083**	0.0215*

[†]Number of tumor-bearing animals/Number of animals at risk, excluding those that died before observation of the first tumor.
[a]First adenoma at week 56.
[b]First carcinoma at week 47.

Note: Significance of trend denoted at control.
Significance of pairwise comparison with control denoted at dose level.
*p < .05.
**p < .01.

Table 6. Permethrin, Mouse Study - Male Lung Tumor Rates[†] and Peto Prevalence Test Results

Tumor	Dose (ppm) 0	20	1500	5000
Adenoma	16/73	15/71	15/68	17/69
(%)	(22)	(21)	(22)[a]	(25)
p =	0.1175	0.4651	0.4823	0.1707
Carcinoma	7/49	5/52	13/54	4/30
(%)	(14)	(10)[b]	(24)	(13)
p =	0.3989	0.2217	0.1276	0.1722
Both	23/73	20/71	28/68	21/69
(%)	(32)	(28)	(41)	(30)
p =	0.1329	0.3585	0.1535	0.1722

[†]Number of tumor-bearing animals that died/Number of animals at risk, excluding those that died before observation of the first tumor.
[a]First adenoma at week 25.
[b]First carcinoma at week 81.

Note: Significance of trend denoted at control.
Significance of pairwise comparison with control denoted at dose level.
*p < .05.
**p < .01.

Table 5. Permethrin, Mouse Study - Female Liver Tumor Rates[†] and Cochran-Armitage Trend Test and Fisher Exact Test Results

Tumor	Dose (ppm) 0	20	2500	5000
Adenoma	2/66	4/62	22/63	28/65
(%)	(3)	(6)	(35)[a]	(43)
p =	0.0000**	0.2994	0.0000**	0.0000**
Carcinoma	4/49	3/55	3/49	2/51
(%)	(8)	(5)	(6)	(4)
p =	0.2534	0.4312	0.4938	0.3082
Both	6/66	7/62	25/63	30/65
(%)	(9)	(11)	(40)	(46)
p =	0.0000**	0.4519	0.0000**	0.0000**

[†]Number of tumor-bearing animals that died/Number of animals at risk, excluding those that died before observation of the first tumor.
[a]First adenoma at week 54.
[b]First carcinoma at week 81.

Note: Significance of trend denoted at control.
Significance of pairwise comparison with control denoted at dose level.
*p < .05.
**p < .01.

Table 4. Permethrin - Mouse Study, Female Lung Tumor Rates[†] and Cochran-Armitage Trend Test and Fisher Exact Test Results

Tumor	Dose (ppm) 0	20	2500	5000
Adenoma	9/71	17/68	24/68	29/69
(%)	(13)	(25)	(35)[a]	(42)
p =	0.0002**	0.0495*	0.0015**	0.0001**
Carcinoma	6/66	7/62	11/59	15/62
(%)	(9)	(11)[b]	(19)	(24)
p =	0.0047**	0.4519	0.0977	0.0187*
Both	15/71	24/68	35/68	44/69
(%)	(21)	(35)	(52)	(64)
p =	0.0000**	0.0473*	0.0002**	0.0000**

[†]Number of tumor-bearing animals/Number of animals at risk, excluding those that died before observation of the first tumor.
[a]First adenoma at week 39.
[b]First carcinoma at week 62.

Note: Significance of trend denoted at control.
Significance of pairwise comparison with control denoted at dose level.
*p < .05.
**p < .01.

Table 3. Permethrin, Mouse Study - Female Mortality Rates[†] and Cox or Generalized K/W Test Results

Dose (ppm)	Weeks 0-26	27-52	53-78	79-104	105[a]	Total
0	3/75	3/72	13/69	34/56	22/22	53/75 (71)
20	1/75	7/74	10/67	23/57	34/34	41/75 (55)
2500	4/75	7/71	13/64	27/51	24/24	51/75 (68)
5000	4/75	5/71	14/66	30/52	22/22	53/75 (71)

[†]Number of animals that died/Number of animals alive at the beginning of the interval.
()Percent.
[a]Final sacrifice.
Note: The above time intervals are for display purposes only.
Significance of trend denoted at control.
Significance of pairwise comparison with control denoted at dose level.
*$p < .05$.
**$p < .01$.

Table 2. Permethrin, Mouse Study - Male Mortality Rates[†] and Cox or Generalized K/W Test Results

Dose (ppm)	Weeks 0-26	27-52	53-78	79-104	105[a]	Total
0	1/75	6/74	17/68	31/51	20/20	55/75 (73)**
20	4/75	6/71	10/65	28/55	27/27	48/75 (64)
500	6/75	4/69	9/65	30/56	26/26	49/75 (65)
2000	5/75	9/70	27/61	22/34	12/12	63/75 (84)**

[†]Number of animals that died/Number of animals alive at the beginning of the interval.
()Percent.
[a]Final sacrifice.
Note: The above time intervals are for display purposes only.
Significance of trend denoted at control.
Significance of pairwise comparison with control denoted at dose level.
*$p < .05$.
**$p < .01$.

References

Armitage, P. (1955) Tests for Linear Trends in Proportions, Biometrics 11, 375-386.

Cochran, W.G. (1954) Some Methods for Strengthening the Common X^2 Test, Biometrics 10, 417-451.

Cox, D.R. (1972) Regression Models and Life Tables (with discussion) J. Royal Stat. Soc. Ser. B. 34, 187-220.

Peto, R., Pike, M., Day, P., Gray, P., Parish, S., Peto, J., Richard, S., and Wahrendorf, J. (1980) Guidelines for Simple, Sensitive, Significant Tests for Carcinogenic Effects in Long-term Animal Experiments. - Monograph on the Long-term and Short-term Screening Assays for Carcinogens: A Critical Appraisal. International Agency on Research on Cancer Monograph - Supplement 2., 311-426. Lyons, France.

Thomas, D.G. Breslow, N., and Gart, J.J. (1977) Trend and Homogenity Analysis of Proportions and Life Table Data, Computers and Biomedical Research 10, 373-381.

Reviewer's Peer Review Package for 2nd Meeting

5/24/89

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, DC 20460

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MAY 24 1989

MEMORANDUM

OFFICE OF
PESTICIDES AND
TOXIC SUBSTANCES

SUBJECT: Reevaluation of Permethrin and Express Following SAP Review

FROM: Esther Rinde, Ph.D. E.R.
Manager, ONCO Peer Review
Health Effects Division (TS-769c)

TO: Addressees

On May 9, 1989, the SAP reviewed these two chemicals which were previously evaluated by the Peer Review Committee. A meeting to discuss the issues on Permethrin and Express is scheduled for Thursday, June 1, 1989, from 9:00 to 10:00 in Room 821.

Permethrin will be discussed from 9:00 to 9:30

Express will be discussed from 9:30 to 10:00

Copies of the Peer Reviews and SAP reports are attached.

Addressees

P. Fenner-Crisp
W. Burnam
R. Engler
R. Hill
K. Baetcke
E. Budd
M. Van Gemert
M. Copley
J. Quest
L. Slaughter
K. Dearfield
R. Levy
W. Sette
G. Ghali
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R. Gardner
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J. Doherty

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