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
B. Fisher
R. Gardner
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J. Doherty

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