Image

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

014428

OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

MEMORANDUM

January 4, 2001

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

SUBJECT: Fluazinam Male Rat Thyroid Follicular Cell Peto's Prevalence Analyses Based On Sprague-Dawley Rat Dietary Study

P.C. Code 129098

TO: Edwin Budd, Toxicologist
Registration Action Branch 2
Health Effects Division (7509C)

FROM: Lori L. Brunsman, Statistician
Science Information Management Branch
Health Effects Division (7509C)

Lori L. Brunsman

THROUGH: Jess Rowland, Branch Chief
Science Information Management Branch
Health Effects Division (7509C)

Jess Rowland 1/4/01

On January 3, 2001, the Cancer Assessment Review Committee met to discuss the carcinogenic potential of Fluazinam. During this meeting, the committee requested Peto's prevalence test analyses of the male rat thyroid follicular cell tumors. Though there were no significant survival disparities among the dose groups, the mortality of the controls was 15% higher than that of the male high dose group (Fluazinam Qualitative Risk Assessment Based On Sprague-Dawley Rat and CD-1 Mouse Dietary Studies, L. Brunsman, 12/13/2000). The results of the Peto's prevalence test analyses are presented in this memo.

Background

A combined chronic toxicity and oncogenicity study in Sprague-Dawley rats was conducted by Huntingdon Research Centre, Ltd., Cambridgeshire, England, for Ishihara Sangyo Kaisha, Ltd., Tokyo, Japan, and dated August 25, 1988 (Report No. ISK 8/87263; MRID No. 42248620).

The study design allocated groups of 50 rats per sex to dose levels of 0, 1, 10, 100 or 1000 ppm of Fluazinam for 104 weeks. An additional 10 rats per sex per dose were designated for interim sacrifice at week 52.

Tumor Analyses

Male rats had a significant increasing trend in thyroid gland follicular cell carcinomas at $p < 0.05$. There was a significant difference in the pair-wise comparison of the 1000 ppm dose group with the controls for thyroid gland follicular cell adenomas and/or carcinomas combined at $p < 0.05$.

Table 1. Fluazinam - Sprague-Dawley Rat Study

Male Thyroid Gland Follicular Cell Tumor Rates[+] and Peto's Prevalence Test Results (p values)

	Dose (ppm)				
	0	1	10	100	1000
Adenomas (%)	4/46 (9)	3/33 (9)	5/37 (14)	5[a]/33 (15)	8/41 (20)
p =	0.283	0.144	0.095	0.150	0.079
Carcinomas (%)	0/47 (0)	0/33 (0)	0/37 (0)	1/33 (3)	3[b]/43 (7)
p=	0.038*	-	-	0.079	0.056
Combined (%)	4/47 (9)	3/33 (9)	5/37 (14)	6/33 (18)	11/43 (26)
p =	0.100	0.139	0.093	0.068	0.022*

[+]Number of tumor bearing animals/Number of animals examined, excluding those that died or were sacrificed before observation of the first tumor.

[a]First adenoma observed at week 70, dose 100 ppm.

[b]First carcinoma observed at week 68, dose 1000 ppm.

Note: Interim sacrifice animals are not included in this analysis. There were no thyroid gland follicular cell tumors in any interim sacrifice animals.

Significance of trend denoted at control.

Significance of pair-wise comparison with control denoted at dose level.

If *, then $p < 0.05$. If **, then $p < 0.01$.

References

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

Gart, J.J., D. Krewski, P.N. Lee, R.E. Tarone, and J. Wahrendorf (1986) The Design and Analysis of Long-Term Animal Experiments. In: Statistical Methods in Cancer Research, Volume III. IARC Scientific Publications No. 79. Lyon, France: International Agency for Research on Cancer, p. 18.

Peto, R., M. Pike, N. Day, R. Gray, P. Lee, S. Parish, J. Peto, S. Richard, and J. Wahrendorf (1980) Guidelines for Simple, Sensitive, Significant Tests for Carcinogenic Effects in Long-Term Animal Experiments. In: Monographs on the long-term and short-term screening assays for carcinogens: a critical appraisal. IARC Monographs, Supplement 2. Lyon, France: International Agency for Research on Cancer, pp. 311-426.

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

13544

013128

Chemical:	**Fluazinam**
PC Code:	**129098**
HED File Code	**21200 CARC**
Memo Date:	**01/04/2001**
File ID:	**TX014428**
Accession Number:	**412-02-0006**

HED Records Reference Center
12/04/2001