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DATA EVALUATION RECORD

TRICHLORFON

Carcinogenicity: Oral feeding in rats

CITATION: Grundmann E, Hobik HP. 1966. Bay 15922: Two year feeding experiment on rats: Histology. (Unpublished study prepared by Farbenfabriken Bayer, AG. Submitted by Chemagro Corp., Kansas City, MO. CDL 097552-AO).

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ACCESSION NUMBER: Not available.

MRID NUMBER: 00080596.

LABORATORY: Farbenfabriken Bayer A.G., West Germany.

TEST MATERIAL: Bay 15922 [trichlorfon]; purity not stated.

PROTOCOL:

1. This study presents only histologic findings for selected organs of animals in a two-year study. Full details of the experimental procedures, clinical and pathologic findings are not presented in the report.

2. The test animals were as follows:
   Species/Strain -- Rats (strain not specified)
   No. of animals -- 600. (300 males and 300 females)

3. Concentration (size of group): control (100/sex); 50 ppm, 250 ppm, 500 ppm, and 1,000 ppm (50 animials of each sex/group)

4. The experimental parameters investigated were as follows:

   o Tissues were examined histologically.

   For 5 male and 5 female rats receiving 1,000 ppm BAY 15922 over two years and for 3 male and 3 female controls, the following tissues were examined: liver, kidneys, adrenals, heart, lung, testes/ovaries and uterus, spleen, thyroid, stomach, small intestine, bladder, cerebrum, brain stem, cerebellum, and medulla oblongata.

   The ovaries of an additional 30 controls and 15 females at 1,000 ppm were examined.

Random samples of pituitaries were examined for 10 control animals and 4 animals at 1,000 ppm and 3 animals in the 500 ppm group with macroscopically enlarged glands.

A total of 104 tissues from all experimental groups of animals that died during the study or were sacrificed at 24 months with suspect tumors were examined histologically.

RESULTS:

Histologic observations for the animals examined are summarized in Table 1.

The histologic findings in the liver, kidneys, spleen, and lungs were the result of chronic infections that occurred in both control and dosed animals. The enlargement of the pituitaries was common in aging rats. There was no difference in findings between high dose and control animals. Incidence of lesions in the ovaries were also characteristic of aging rats and was not compound related.

Incidence of malignant tumors examined histologically is summarized in Table 2. The number of tumors in animals surviving 2 years was not presented separately, nor was the number of animals dying with tumors and their age at death presented.

CONCLUSIONS:

Trichlorfon was fed to rats for two years at levels of 0, 50, 250, 500, and 1,000 ppm. Histopathologic examinations were performed on 5 males and 5 females at the 1,000 ppm dose and 3 males and 3 females in the control group. Ovaries of 30 control and 15 rats at 1,000 ppm were examined and suspected tumors (104) were examined histologically. Selected pituitaries (17 of 73 observed to be enlarged at necropsy) were also examined histologically. There were no increases in histologic lesions in liver, kidney, spleen, adrenal, lungs, testes, or ovaries of rats at 1,000 ppm trichlorfon compared to controls. There was no increase incidence of malignant tumors compared to controls in any test group at doses from 50 to 1,000 ppm.

This study does not adequately assess carcinogenicity because of limited histopathology, lack of mortality data, and lack of data on the age of animals that died with tumors before the end of the study. Only 6 of 200 controls and 10 of 100 high dose animals had extensive histologic examination. Suspect tumors were examined in other animals in the study. A total of 73 animals had grossly enlarged pituitaries but only 17 of those were subjected to microscopic examination. The histologic findings in both control and test animals were attributed to chronic infections; however, there were no clinical observations to assess the general health or debility of the animals.

TABLE 1. Histologic Findings in Rats Fed Trichlorfon for Two Years[a]

	Controls	1,000 ppm
Liver		
Vacuolar swelling of cytoplasm	3/6	4/10
Diffuse fatty degeneration	0/6	2/10
Necrosis of individual cells	1/6	0/10
Kidneys		
Swelling of the basal membranes of the glomerules due to pyelitis	6/6	8/10
Swelling of tubular cells	4/6	3/10
Fatty degeneration of tubular cells	2/6	0/10
Spleen		
Hyperplasia of the reticular cells	4/6	8/10
Adrenal glands		
Cortical adenomas	1/6	1/10
Lipoid degeneration of the cortex	0/6	2/10
Lungs		
Pulmonary hemorrhage and edema	3/4	3/10
Testes		
Reduction of spermatogenesis	3/3	3/5
Ovaries		
Follicular cysts	14/33	8/20
Interstitial fibrosis	5/33	2/20
Tubular hyperplasia of the interstitial tissue	4/33	2/20

[a] These were indicated as the most important findings, not the complete findings.

TABLE 2. Incidence of Malignant Tumors in Rats Fed Trichlorfon

Dietary Level (ppm)	No. Animals	Malignant Tumors	Malignant Mammary Tumors (females)
0	200	15	8
50	100	4	4
250	100	3	5
500	100	6	6
1,000	100	7	8

CORE CLASSIFICATION: This study is classified as Core Invalid since the histopathology was limited. The following deficiencies in the study were noted by this reviewer:

- Only 5 animals of each sex at the 1,000 ppm dose and 3 of each sex in controls were examined histologically after 730 days.
- The number of animals surviving 2 years was not stated.
- Mortality data were not presented.
- The ages of animals that died with tumors were not presented.
- Tumor incidence at 2 years could not be determined.
- It was not clear if animals whose ovaries were examined (33 controls and 20 at 1,000 ppm) survived to final sacrifice.
- It is not clear if Table 1 (histologic findings) presents nontumorigenic data or if none of the 6 controls and 10 test animals at 730 days had tumors.
- Although 73 animals had macroscopically enlarged pituitaries only random samples (10 controls, 4 at 1,000 ppm, and 3 at 500 ppm) were subjected to microscopic examination.