12/26/82

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

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MEMORANDUM

OFFICE OF PESTICIDES AND TOXIC SUBSTANCES

TO: Robert Taylor, Product Manager #25
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Hazard Evaluation Division (TS-769)

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SUBJECT: Evaluation of a Draft Report Entitled "Paraquat: Combined Toxicity and Carcinogenicity Study in Rats". Life Science Research, Stock, Essex, England. Study No. 82/ILY 217/328 (no date). Submitted by Chevron Chemical Company, Richmond, California.
EPA Accession No. 248201-248208
EPA Record No. 77324 TOX Chem. No. 634

Because this submission is only an unsigned draft copy and not a final authoritative report, only a cursory review has been performed by Toxicology Branch/HED. The most important points are listed below.

1. Treatment of Animals:

Rats of the Fischer 344 strain, 70/level/sex, were fed a powdered diet containing 0, 25, 75 or 150 ppm of paraquat ion. The source of the ion was "Paraquat Concentrate" (technical grade paraquat [redacted] containing 32.69% w/w of paraquat ion. The animals were sacrificed after 113 weeks (males) and after 122 weeks (females). The study was extended before the originally planned duration of 104 weeks because of a low incidence of mortality on the completion of that period. The animals were housed in groups of five/cage.

2. Parameters Evaluated:

Daily observations for toxic reactions
Mortality
Food and water intake
Body weight changes
Efficiency of food utilization
Ophthalmoscopy
Hematology, blood chemistry and urinalysis
Organ weights
Levels of paraquat in urine and tissues
Macroscopic and microscopic pathology

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INFORMATION WHICH MAY REVEAL AN INERT INGREDIENT IS NOT INCLUDED

Data were evaluated statistically using several procedures.

3. Results:

a. This treatment had no effect on hematology, blood chemistry, urinalysis and the incidence of mortality.

b. There was a dose-related increase in the progression and severity of lenticular cataracts. The highest incidence occurred after the test week 102 (or late in the lifespan of the animals) and especially in the 75 and 150 ppm groups. Irrespective of the time of occurrence, the incidence was always higher in the females. This is illustrated in the attached graphs, prepared by the reviewer, and based on data from Tables 2, 3 and 4 (pages 36, 37 and 38, respectively) of Vol. I (accession No. 248201) of the submitted documents.

c. There were pulmonary changes in male and female rats. In the males, the changes observed were predominantly proliferative changes of the alveolar epithelium. In the females, pulmonary adenomas were generally observed. However, the four pathologists who examined lung tissue could not agree on the classification of the pulmonary lesions.

d. Non-neoplastic changes (excluding eyes and lungs) that were considered to be associated with paraquat treatment comprised hydrocephalus, degeneration of the nerve fibers of the sciatic nerve and an increase in the number of cysts or cystic spaces in the spinal cord. Hydrocephalus occurred in the females and the other changes in the males.

e. With regard to the neoplastic findings during the second year of study, there was a low incidence of squamous cell carcinoma in the nasal cavity of the paraquat-treated rats. This tumor was present only in three males and one female from the 150 ppm group and in two females from the 75 ppm group.

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Other neoplasms present were similar in type and incidence to those considered usual in the Fischer 344 rats. These included mammary gland benign fibroepithelial tumors, pituitary adenomas and carcinomas, benign thyroid parafollicular cell adenomas and carcinomas, adrenal pheochromocytomas, skin and subcutis fibromas and lipomas, monocytic leukemia, pancreatic islet cell adenomas and testicular interstitial cell tumors. There were no differences in the distribution of benign and malignant neoplasms or in the number of different neoplasms per animal. Very few neoplasms were present during the first 52 test weeks and none was attributed to paraquat.

f. The following findings were reported for the 150 ppm level: 1) slight to moderate decrease in the food intake, body weight and food utilization efficiency in the males during the first 52 test weeks; 2) slight depression in the body weight gain of the females during the test weeks 53-122; and 3) decrease in the absolute liver weight (males and females) and the testicular weight.

g. No-Observable-Effect-Level (NOEL) was not really determined in this study because an increase in the incidence of lenticular lesions was also observed at the 25 ppm level (lowest tested), at the termination of the study. However, because of the appearance of these lesions at the end of the lifespan of the animals, the 25 ppm level was considered ".....to lie close to the no-effect level for lenticular change".

h. Classification of these data: Supplementary.

Krystyna K. Locke 11/9/83

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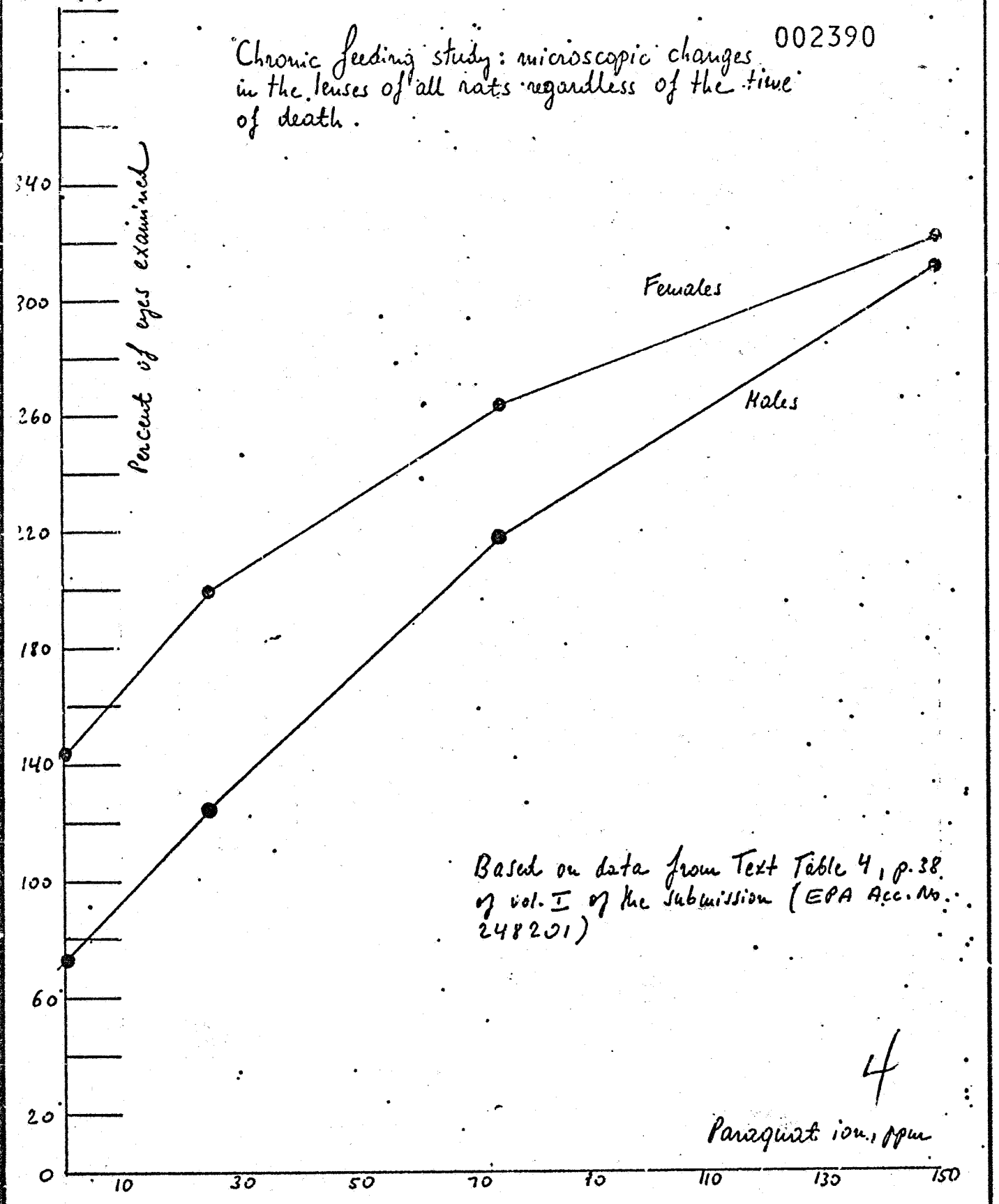
Chronic feeding study: microscopic changes in the lenses of all rats regardless of the time of death.



Based on data from Text Table 4, p. 38 of vol. I of the submission (EPA Acc. No. 248201)

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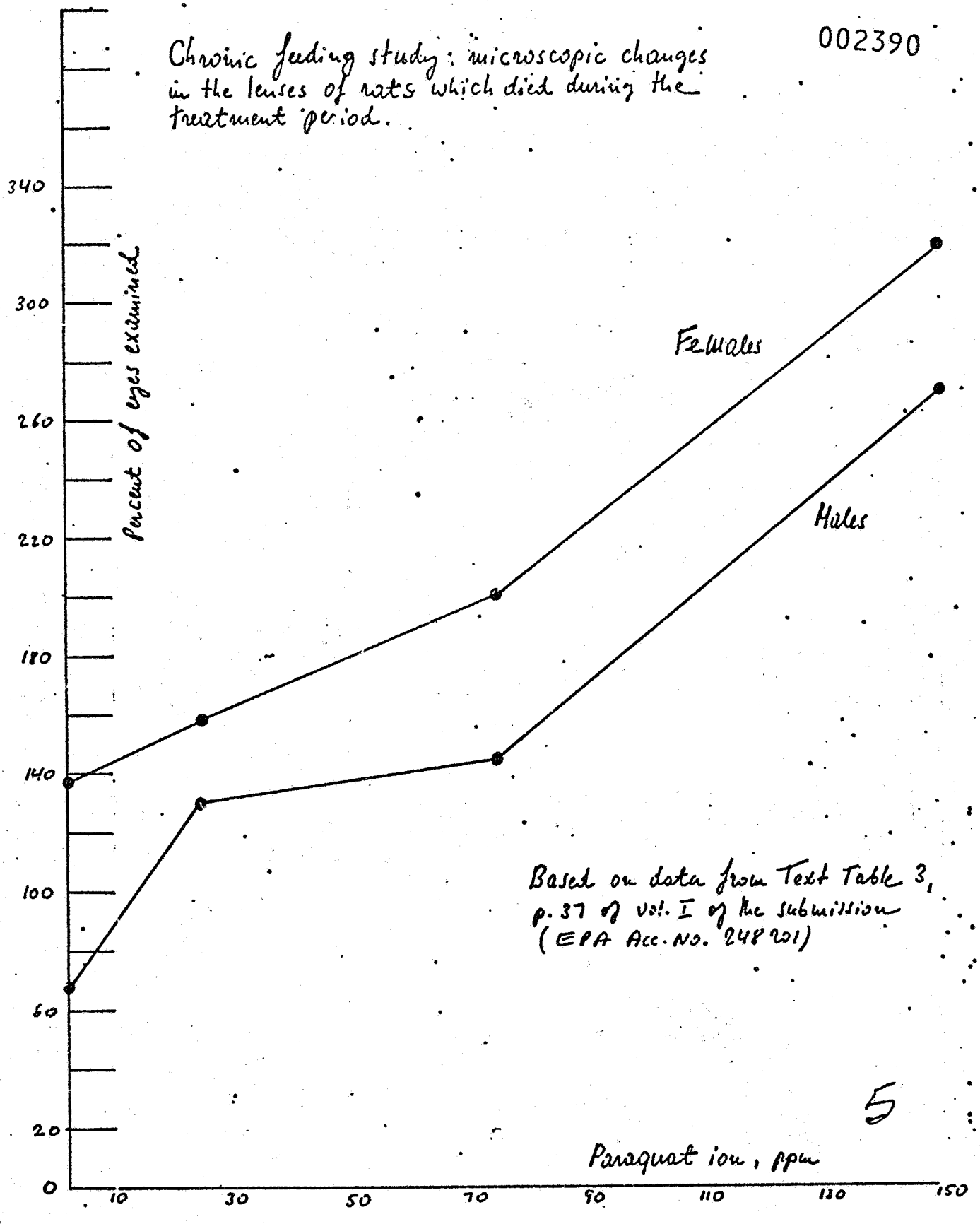
Chronic feeding study: microscopic changes in the lenses of rats which died during the treatment period.



Based on data from Text Table 3, p. 37 of Vol. I of the submission (EPA Acc. No. 248201)

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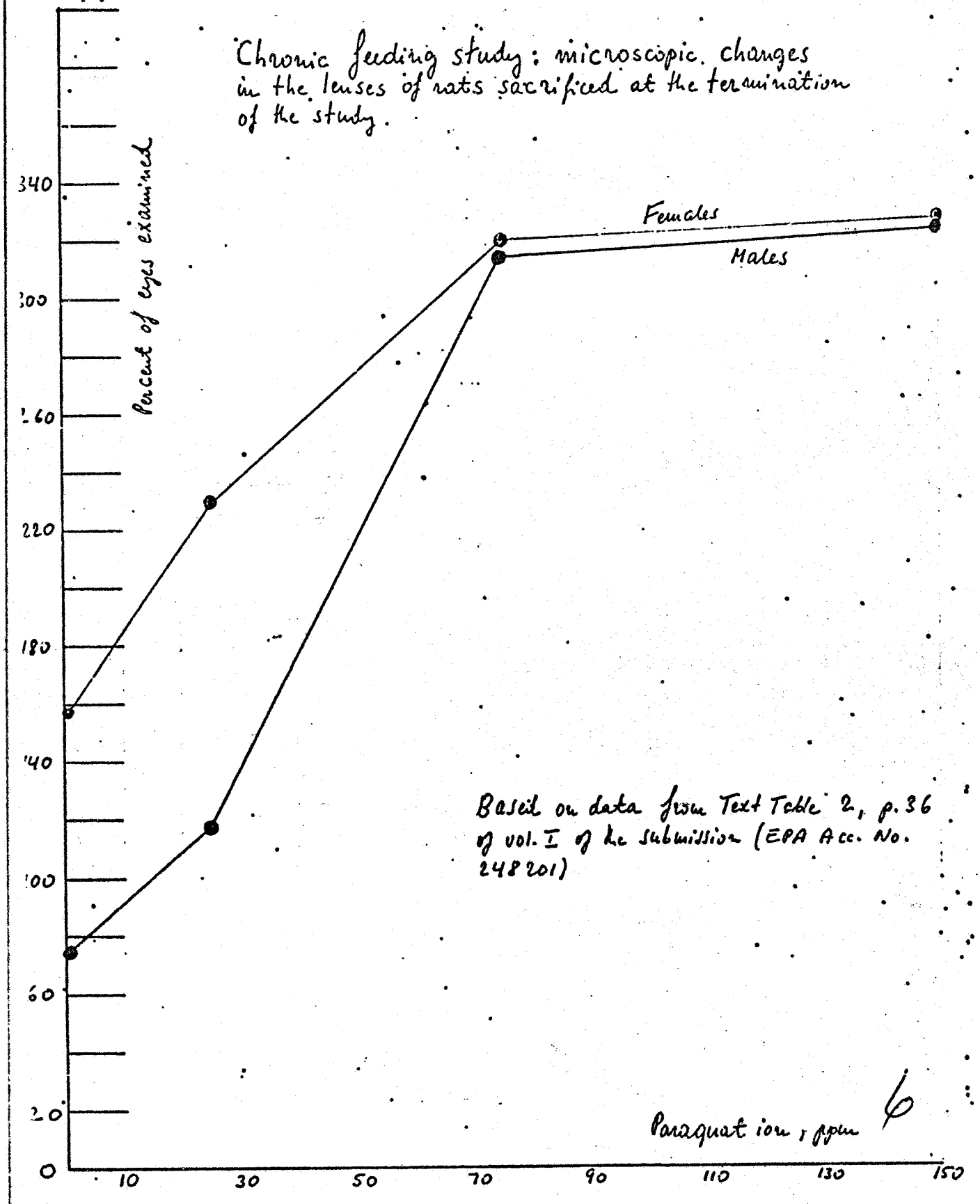
Chronic feeding study: microscopic changes in the lenses of rats sacrificed at the termination of the study.



Based on data from Text Table 2, p. 36 of vol. I of the submission (EPA Acc. No. 248201)

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