(Document has been retyped 9/10/96MPC. Handwritten notes in italics)

(Fenvalerate - MRID No. 00071949)

[***TXR # 0052457***]
(From: pp# 71-2013, 7/21/78; R. Engler)

Review

1. 18-Month chronic toxicity study of S5602 in mice. Sumitomo AT-70-0176, Dec. 29, 1977 (tab 125, 127 and 128)

Pydrin was administered in the diet to ddy mice for 18 months. The dose levels and number of animals assigned were as follows:

Dose (PPM)	Males	Females
0	29	35
100	37	25
300	30	30
1,000	30	30
3,000	29	31

Mice were observed daily, after 78 weeks they were sacrificed (3000 PPM males and sacrificed after 72 weeks). Hematology, Blood Chemistry, gross pathology (including organ weights and ratio), and histopathology was performed. All animals were examined histologically, the number of apparently autolyzed animals is small.

Results:

Clinical signs of hypersensitivity were seen at 1000 and 3000 PPM, these subsided gradually. Mortality was increased for both sexes at 3000 PPM and the males only at 1000 PPM; increase in early deaths occurred at about 40 weeks of the study. The body weights (and gains) were affected at 3000 PPM and for males at 1000 PPM. Females at 100, 300, and 1000 PPM had somewhat lower body weights than controls but the effect was not significant. Hematology and blood chemistry were affected at 1000 and mostly 3000 PPM in such parameters as decreased Hbg and RBC, increased leukocytes and monocytes, increased GPT, GOT, LAP and LDH. Organ weights and ratios were also affected at 1000 and more so at 3000 PPM. Histopathologically granulomatous changes were observed in liver and lymph nodes. The incidence and severity were dose related. The histopathological findings were reviewed by a second pathologist (Dr. Ito) who also reported giant cell infiltration of the spleen. 100 PPM was a NEL for these changes, or very conservatively the lowest effect level. The incidence of parasites (nematodes) was determined by Ito as well but no correlation was found between parasitic nematodes and granulomata and it was thus concluded that the effect was compound related. The effect is further discussed by Okuno and Myamoto. Their conclusion corroborate the LEL of 100 PPM and they also suggest that the granulomatas are a reversible organ reaction. This conclusion is also corroborated by Dr. Long, EPA pathologist. Increases in tumor frequency was not observed in this study.

Conclusion:

The mouse study (ddy strain), shows a NEL of about 100 PPM or possibly less for granulomatous changes in liver and spleen, but no oncogenic potential. Granulomatas are usually the result of microbial infection or irritation by metals. The outcome of the second mouse study initiated by Shell and a demonstration that the effect seen in ddy mice is in fact reversible should clarify the situation.

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