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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, DC 20460

CASWELL FILE

FEB 14 1990

OFFICE OF
PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Iprodione- Response to the TB review of 1-year feeding study in dogs

TO: Susan Lewis/Jim Stone PM 21
Registration Division (H7505C)

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Registrant: Rhone-Poulenc

Action requested

Address registrant's arguments.

Background

The current submission represents another response to the TB evaluation of a 1-year feeding study in dogs with Iprodione (Memorandum, van Gemert, TB, to Forrest, RD, May 18, 1987). In a study in which dogs were administered 100, 600 or 3600 ppm of Iprodic technical for 1 year, TB concluded that the LEL was 600 ppm (4.2 mg/kg/day) based on decreased prostate weights and the presence of erythrocytes with Heinz bodies in males. The registrant responded to the TB review by expressing the opinion that these changes were not toxicological effects. The TB reviewer asked the registrant to submit historical control data from the test laboratory in the same strain of dog for these parameters to support their argument. However, during a meeting between TB and Rhone-Poulenc on October 12, 1987, the registrant indicated that they were not able to present the requested historical control data. Instead they reiterated arguments that TB had previously considered.

The registrant is concerned about the review of this study because it was used to establish the RfD (0.04 mg/kg/day), so obviously they would prefer a NOEL higher than 100 ppm. TB has suggested that the registrant repeat the study because a higher NOEL could probably be established. The registrant has objected to this approach, instead, they have proposed to perform a 90-day feeding study to provide bridging data. TB is concerned that a 90-day study may not be of adequate duration to detect the noted effect on prostate.

Registrant's current response

The registrant reiterated previous arguments that they do not consider the following changes observed at 600 ppm to be toxicological effects:

a/ Increased number of erythrocytes with Heinz bodies, especially in males
b/ Decreased prostate weights
c/ Renal proximal tubule lipofuscinosis in females
d/ Retinal hyperreflection

TB response

The May 18, 1987 review (cited above) of this study did not conclude that the changes noted above for kidneys and eyes were toxicological effects. It remains TB's opinion that the observed increases in Heinz bodies and decreases in prostate weights are toxicological effects from the ingestion of Iprodione.