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

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MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

Subject: SELECT 2 EC Herbicide
Tox Chem No. 721F

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Review of the Registrant's Response to the Previous Toxicology Branch II Comments Concerning the Large Droplet Size Reported in the SELECT (clethodim) Acute Inhalation Studies, MRID Nos. 40974512 and 40974513

1. Acute Inhalation Toxicity of RE-45601 Technical (SX-1688) in Rats
Study No. S-2783

Registrant's Response: "RE-45601 (SELECT) technical is a viscous liquid with a vapor pressure less than 10-7 mm Hg which cannot be aerosolized with typical equipment at ambient temperature." "In spite of its physical nature, every effort was made to obtain useful information relative to this material's inhalation toxicity." "In order to generate an aerosol from the technical material, it was diluted slightly with acetone to reduce its viscosity." "Two large nebulizers were used to generate the test aerosol in order to obtain a total concentration near the limit test concentration of 5 g/m^3. These nebulizers were usually operated by aspirating the liquid from the test material

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reservoir but pumps were used in this study in order to obtain the desired aerosol concentration. The initial droplet size from typical compressed air nebulizers is greater than 5 um. These droplets then shrink to smaller sizes depending on the vapor pressure, solute concentration, etc., of the liquid being aerosolized. Given the physical nature of SELECT Technical and the concentration being generated, and MMAD much smaller than the one tested was not possible. Approximately 30 percent of the aerosol had an aerodynamic diameter smaller than 2 um and this particle size is definitely respirable for the rat."

Reviewer's Comments: The submitted report amendment providing necessary explanations for the difficulty to produce the desired aerodynamic diameters (i.e., 1 um or less) in this study, is considered reasonable. Since the relationships of particle size and deposition in laboratory rodents have not been adequately characterized, the reported results in terms of the particle sizes(i.e., 30% of the aerosol had an aerodynamic diameter smaller than 2 um) appear to be justified for this study (References: SEP/Inhalation Toxicity Testing EPA-540/09-88-101; Comments on SEP/Inhalation Toxicity Testing from Stanley Gross, Ph.D., dated April 18, 1989).

Recommendation: The study is upgraded to Core Minimum LC_{50} > 3.9 mg/L (both sexes); Toxicity Category III

2. Acute Inhalation Toxicity of Select 2.0 EC (CC-14900;SX-1721) in Rats. Study No. S-2856

Registrant's Response: "The aerosol generated in this study appeared to deviate somewhat from lognormality. Although the caluculated MMADs were 2.7 and 4.2 um, an examination of the cascade impactor data (Tables 2 and 3 in the final report) indicates that 23 to 27 percent of the aerosol had an aerodynamic diameter smaller than 1.1 um which is the cutoff diameter of the second to the last stage before the final filter. This indicates that a substantial portion of the tested aerosol was respirable."

Reviewer's Comments: Toxicology Branch II agrees with the Registrant's explanations that the reported results in terms of particle sizes (i.e., 23-27% of the aerosol had an aerodynamic diameter smaller than 1.1 um) appear to be justified in this study. However, the Registrant submitted no response to the deficiency concerning the LC_{50} value reported in this study. Since the median lethal concentration (LC_{50}) obtained from this study is very low (i.e., 0.033 mg/L lower than 0.2 mg/L classified as Toxicity Category I), the Registrant must provide detailed explanations why higher concentration was not achievable in this study. In view of the severe ocular irritation (Toxicity Category I) demonstrated in the primary eye irritation study with Select 2EC (Study No. S-2854), this product may be potentially poisonous if inhaled.

Recommendation: Until the reporting deficiency concerning the LC_{50} value in this study is clarified and resolved, this study remains to be rated supplementary.

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