US EPA ARCHIVE DOCUMENT

17 / OPPTS

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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

APR 30 1998

NOTE

SUBJECT: Upgrading of Acute Oral Study for the Cry9C Protein

TO: Michael Mendelsohn
Regulatory Action Leader
Biopesticides & Pollution Prevention Division (7511W)

FROM: John L. Kough, Ph.D., Biologist
Microbial & Plant-Pesticide Branch
Biopesticides & Pollution Prevention Division (7511W)

ACTION REQUESTED
To confirm the acceptability of the acute oral toxicity study submitted by Plant Genetic Sciences (PGS now part of AgrEvo) to support the registration of the Cry9C protein.

BACKGROUND
PGS submitted an acute oral study utilizing a purified preparation of the Cry9C protein along with other information to support a safety assessment of that protein as expressed in corn. The company analyzed the test substance for the presence of the Cry9C protein to determine the concentration of the protein in the dose administered. Several methods were utilized to determine protein concentration: Bradford analysis, OD_{280}, ELISA and insect bioassay. The initial review indicated a discrepancy between the Cry9C concentrations by the different methods (memorandum from J. Kough to M. Mendelsohn, 6 January 1998). While discrepancies between the different methods is to be expected, the most reasonable method to give an accurate Cry9C concentration in a protein matrix background, the ELISA, gave a lower reading but was not selected to calculate the dose administered. The company chose the OD_{280} method corrected by an SDS-PAGE, the least specific method for Cry9C, to calculate the values of the dose administered. Since this method choice was not adequately rationalized or supported with data, the administered dose was recalculated by the Agency and lowered from 5,525mg/kg to 3,760mg/kg bodyweight.

192

RECOMMENDATION

With the company's acceptance of the Cry9C recalculation, the acute oral toxicity study (MRID 442581-07) can be upgraded from SUPPLEMENTAL to ACCEPTABLE. It is not clear at the present time what an appropriate limit dose should be in toxicity testing for proteins through the oral route of exposure. There is no indication that there is a significant hazard of oral toxicity that would be not detected by testing the protein substance at 3,760mg/kg rather the 5,525mg/kg bodyweight.