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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

Paul Whatling
Jellinek, Schwartz & Connolly, Inc.
1525 Wilson Boulevard, Suite 600
Arlington, VA 22209

Re: Review of 6(a)(2) and Follow-Up Data Submitted for Developmental Neurotoxicity and Acetylcholinesterase Studies in Rats.

Dear Mr. Whatling:

Enclosed is the U.S. Environmental Protection Agency's review of the FIFRA 6(a)(2) data submitted for dose-range finding studies designed for dose selection for definitive developmental neurotoxicity and acetylcholinesterase studies in rats. These range-finding studies were conducted in response to the Agency's September 1999 data-call-in (DCI) for the aforementioned studies. The Agency also reviewed several other documents including letters from Cheminova and literature that addresses issues related to the studies and protocol.

Based on a review of this information, the Agency concludes that these studies and supporting documentation are inconclusive and do not satisfy the DCI. Primarily, the studies did not define a maximum tolerated dose (MTD) for dams nor were the studies designed to yield a clear No-Observed-Adverse-Effect-Level (NOAEL) for cholinesterase inhibition. Though these studies are inconclusive, there is evidence of enhanced sensitivity of pups versus dams based upon serious toxicological effects. In order for the studies to provide the Agency with a definitive analysis of the toxicological effect of malathion on pups, the dose selection for the definitive studies must be designed to 1) secure an MTD, 2) address the question of relative susceptibility, and 3) anticipate the identification of clear NOAELs for cholinesterase inhibition. A more detailed discussion of these findings is outlined in the enclosed review.

MALATHION / SEE 12/14/2000 & 4/19/2001

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If you have any questions concerning this review, please contact me at (703) 308-7038 or Anne Overstreet at (703) 308-8068.

Sincerely,

Carmelita White
Chemical Review Manager
Special Review and Reregistration Division

enclosure

cc: files

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