

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY



WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

April 22, 2004

MEMORANDUM

SUBJECT: Waiver Justification of Inhalation Rat Developmental Neurotoxicity Study With Sulfuryl Fluoride

FROM: Vicki L. Dellarco, Ph.D., Senior Science Advisor
Karl Baetcke, Ph.D., Senior Scientist
Health Effects Division
Office of Pesticide Programs

THRU: Margaret Stasikowski, Director
Health Effects Division
Office of Pesticide Programs

TO: Lois Rossi, Director
Registration Division
Office of Pesticide Programs

We have conducted a review of the waiver justification submitted by Dow AgroSciences for the sulfuryl fluoride inhalation rat developmental neurotoxicity study (DNT). DOW requested this waiver on the basis of:

- Essentially no chronic dietary exposure
- Minimal potential inhalation exposures or short duration (1-2 days)
- Animal welfare concerns (1500 to 4000 animals)
- Potentially confounded scientific and technical aspects of conducting an inhalation DNT

Also, Dow indicated in their waiver justification that they recently conducted a rat metabolism study that showed sulfuryl fluoride is rapidly release to fluoride. Thus, given the known toxicology of fluoride coupled with the minimal inhalation exposure to humans, neurotoxicity to the adult or developmental neurotoxicity would be highly unlikely.

It is important to evaluate the merit of this rat DNT study from a risk perspective that considers realistic circumstances of human exposure. Therefore, we are in

agreement with Dow's scientific arguments concerning the minimal potential for human exposure and the unlikelihood that neurotoxicity or developmental neurotoxicity would occur due to dietary exposure or inhalation exposure to sulfuryl fluoride. Furthermore, a composite uncertainty factor (UF) of 1000 (rather than the standard 100X) is applied and will be retained to account for uncertainties inherent in the extrapolation from laboratory animal data to humans (10X), variations in sensitivity among members of the human population (10X), and for the lack of a DNT (10X) in the sulfuryl fluoride risk assessment. Thus, there is an ample level of protection built into the risk assessment.

cc: Michael Doherty
Dennis McNeilly
Jess Rowland
Karen Whitby