



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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

February 16, 2010

Dear Registrant:

The Office of Pesticide Programs (OPP) is actively working on a reevaluation of the human health effects of the synthetic pyrethroids and naturally-occurring pyrethrins under the OPP registration review program, as required under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) [<http://www.epa.gov/oppsrrd1/reevaluation/pyrethroids-pyrethrins.html>]. In addition, OPP has a number of pending requests through the Pesticide Registration Improvement Renewal Act (PRIA) for registration of new pyrethroids and new uses of existing pyrethroids.

In September 2009, Richard Keigwin, Director of the Pesticide Re-evaluation Division, sent a letter to registrants who had not fulfilled the requirement for a Developmental Neurotoxicity Study (DNT) stating that as an "alternative to the generation and submission of a new DNT study, you may instead choose to cite to the six previously submitted DNT studies for pyrethroid pesticides." The September 2009 letter went on to say "EPA has come to the conclusion that the DNT is not a particularly sensitive study for comparing the sensitivity of young and adult animals to pyrethroids" and that "it may be necessary to focus additional experimentation on pyrethroid-specific effects related to the mode of action and pharmacokinetic characteristics of pyrethroids."

The Agency's analysis of the available DNT studies and the scientific literature on comparative sensitivity to pyrethroids is contained in the issue paper entitled: "*Pyrethroids: Evaluation of Data from DNTs & Consideration of Comparative Sensitivity.*" The issue paper describes key scientific evidence, which suggests a concern for age-dependant sensitivity to the young not detected in DNT studies. The Agency believes that pharmacokinetic (PK) factors, particularly the maturation of metabolic processes, are a key component in this potential sensitivity. This paper can be found at <http://www.epa.gov/oppsrrd1/reevaluation/pyrethroids-pyrethrins.html> and provides the scientific support for the information contained in the September 2009 letter. The uncertainties described in this paper will be taken into account in the Agency's regulatory assessments under FIFRA and the Federal Food, Drug, and Cosmetic Act (FFDCA) for this class of pesticides.

This letter is to inform you that the Agency will hold a one-day meeting of the FIFRA Scientific Advisory Panel (SAP) in July 2010 to discuss experimental studies designed to evaluate potential for comparative sensitivity between juvenile and adult rats exposed to synthetic pyrethroids and naturally-occurring pyrethrins. Specifically, the Agency is soliciting proposals for study designs/protocols to evaluate potential differential

sensitivity between juvenile and adult rats. Such proposals submitted to the Agency up to April 16, 2010 will be reviewed by the Agency and provided to the SAP for comment. Like other meetings of the SAP, the July 2010 meeting will be an open, public meeting where the public, including those who submit proposals, will have opportunity to make oral and/or written comments to the Panel. In order to make best use of available experimental techniques appropriate for the toxicological properties of pyrethroids, the Agency will consider protocols which include data from *in vivo*, *in vitro*, and/or *in silico* studies (or combinations thereof).

If you have questions about submitting proposals, please contact Cathryn O'Connell ([oconnell.cathryn@epa.gov](mailto:connell.cathryn@epa.gov); 703-308-0136).

Sincerely,

A handwritten signature in cursive script that reads "Tina E. Levine".

Tina E. Levine, Ph.D.
Director, Health Effects Division
Office of Pesticide Programs