Cum. Risk

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August 9, 2002

Honorable Christine Todd Whitman
Administrator
US Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington, DC 20406

Dear Administrator Whitman:

We commend the EPA for its development of scientific methods to evaluate the cumulative risks from multiple pathways of exposure. We share the Agency's goal of making regulatory decisions that are protective of human health, particularly for infants and children.

We met on June 12-13, 2002 to consider how the Agency is applying these new scientific methods in the ***Application of the 10X Safety Factor in Cumulative Risk Assessment***, and the ***Cumulative Risk Assessment for Organophosphate (OP) Pesticides***. We discussed several important issues and would like to share some concerns for the Agency as it moves forward. We intend our comments to address EPA's cumulative risk assessment methods using the OP Cumulative Risk Assessment as an example, where appropriate. We look forward to seeing these concepts reflected in the revised ***Cumulative Risk Assessment for Triazine Pesticides.***

Cumulative Risk Assessment

An important issue is selection of the common mechanism of action that serves as the basis of the cumulative risk assessment. Once EPA has chosen a common mechanism of action it risks missing other common mechanisms of action that may result in more sensitive endpoints. When evidence of more sensitive endpoints is present, the EPA should explore the possibility that other common mechanisms exist.

For example, the December 2001 draft of the OP Cumulative Risk Assessment uses brain cholinesterase inhibition as the common mechanisms of action. Some of the OP pesticides have been shown to cause developmental neurotoxicity that may or may not result from brain cholinesterase inhibition. Choosing brain cholinesterase inhibition as the common mechanism of action may overlook developmental neurotoxicity potential. EPA should aggressively seek information on additional mechanisms important to developmental neurotoxicity to determine if there are additional common mechanisms of action causing this endpoint.

When there is a more sensitive endpoint for which the mechanism of action is unclear, the EPA should consider this when applying the FQPA safety factor.

Application of FQPA

The February 28, 2002 draft document, *Consideration of the FQPA Safety Factor and Other Uncertainty Factors in Cumulative Risk Assessment of Chemicals Sharing a Common Mechanism of Toxicity,* provides general guidance regarding application of the FQPA factor. The guidance document outlines three possible methods to apply an FQPA factor:

- Applying the factor during development of the Relative Potency Factors for each member of the Cumulative Assessment Group (CAG) where data are unavailable for the chosen toxicological endpoint;
- Applying the factor where there are deficiencies in the database that apply to the entire CAG; and
- Applying the factor as a combination of the above two.

In cumulative risk assessment, when children's health is at issue, the agency should use the method for applying the FQPA safety factor that is most protective of infants and children.

Transparency

Since application of the FQPA safety factor affects the final risk assessment, a transparent process is essential. The cumulative risk assessment should document data gaps at each decision point that may affect the choice of the FQPA safety factor. This information should include gaps in the toxicological database, gaps in the exposure assessment, and decisions to include or exclude available data. For example, use of the USDA Food Consumption Survey data alone to estimate food intake results in data gaps particularly for infants and adolescents. As another example, the decision to exclude data on agricultural drift or pesticide misapplication may underestimate risks to children, as would the absence of data about home, school, and day care exposure. We urge the EPA to clearly convey the process and data used to identify and characterize the risk to susceptible sub-populations of children, such as farm worker children, children living near farms, children living on subsistence diets and urban and ethnic populations.

Impact of Cumulative Risk Assessment on Registration Review

If a cumulative risk assessment results in an unacceptably high-risk assessment, this will presumably necessitate a new process to determine impact on individual pesticide registration. We urge the EPA to make this an open public decision making process and to make decisions that are most protective of infants and children. Risks to infants and children should specifically be considered in individual pesticide re-registration as well as the registration review process for a Cumulative Assessment Group.

Thank you and we look forward to your response on the issues raised above regarding cumulative risk assessment, application of the FQPA safety factor, transparency, and the pesticide re-registration review processes.

Sincerely,

J. Routt Reigart, MD
Chair, Children's Health Protection
Advisory Committee

JRR/pc

Copy to: Joanne Rodman, OCHP