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May 21, 1998

**MEMORANDUM**

OFFICE OF PUBLIC INQUIRY

OFFICE OF PESTICIDES AND TOXIC SUBSTANCES

**Subject:** Parathion (057501). The outcome of the HED Metabolism Assessment Review Committee Meeting Held on March 11, 1998. DP Barcode: D245193

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And

Richard Loranger, Chair  
Metabolism Assessment Review Committee  
Health Effects Division [7509C] *R. Loranger*

**To:** George Kramer, Executive Secretary  
Metabolism Assessment Review Committee  
Health Effects Division [7509C]

**Background**

Parathion was previously discussed by the HED Metabolism Committee on 1/30/95. Available animal metabolism data were presented and discussed. Livestock feeding studies were not available. [Note: The Committee did not discuss parathion residues of concern in plant commodities.] The Committee concluded the following (memo by S. Hummel dated 2/10/95):

- It was postulated that deethylation of the phosphorodithioate or phosphorothioate would lower the toxicological activity. The electron donating properties of NH<sub>2</sub> substitution in

the para position on the phenyl ring produce a metabolite less toxic than parathion. Some evidence suggests that 4-acetamidoparaoxon may be less toxic than parathion, but in the absence of toxicology on that compound, it will be assumed to be as toxic as parent.

- The parathion residue to be regulated will include parathion, paraoxon, and 4-acetamidoparaoxon. *p*-Nitrophenol is not a residue of concern. If the registrant can demonstrate that 4-acetamidoparaoxon is much less toxic than parathion, feeding study data may not be needed for 4-acetamidoparaoxon. 4-Acetamidoparaoxon will not be considered a residue of concern if the acute oral LD<sub>50</sub> is more than 200 mg/kg. If the acute oral LD<sub>50</sub> is less than 200 mg/kg, additional toxicological testing may be required.

### Current Considerations

In light of FQPA requirements to perform cumulative risk assessments and the associated issue of addressing common metabolites, previous conclusions reached by the HED Metabolism Committee on 1/30/95 concerning *p*-nitrophenol needed to be reconsidered since *p*-nitrophenol is also a metabolite of methyl parathion. Moreover, to insure consistency between methyl parathion and parathion, the HED Metabolism Assessment Review Committee met on 3/11/98 to discuss both chemicals and determine what residues of parathion need to be regulated/included in the risk assessment from plant and animal commodities.

Available plant and animal metabolism data were presented and discussed. [NOTE: No new animal metabolism or animal magnitude of the residue data had been submitted since the previous meeting of the HED Metabolism Committee on 1/30/95.] The HED Chapter of the Paranitrophenol Reregistration Eligibility Decision (RED) document was briefly discussed. The Committee concluded the following:

- Based on available plant metabolism data, parathion residues of concern in/on plant commodities are parathion, paraoxon, and *p*-nitrophenol. Parathion residues of concern to be included in the risk assessment for plant commodities based on cholinesterase inhibition will include parathion and paraoxon. The tolerance expression may be based on parathion only since detectable levels of paraoxon have not been found in/on commodities tested by FDA monitoring. Residues of *p*-nitrophenol resulting from the use of parathion do not have to be included in the tolerance expression or considered in the aggregate risk assessment for parathion with respect to cholinesterase inhibition, but should be considered in conjunction with the cumulative risk assessment for *p*-nitrophenol. The risk assessment for *p*-nitrophenol will be based on its own toxicological endpoints (rather than cholinesterase inhibition) and should include exposure to *p*-nitrophenol from its use as a fungicide on leather. Residues of parathion, paraoxon, and *p*-nitrophenol should be determined in/on plant samples collected from future plant magnitude of the residue studies.

- Based on available animal metabolism data, parathion residues of concern in animal commodities are parathion, paraoxon, *p*-nitrophenol, and 4-acetamidoparaoxon. [Note: Livestock feeding studies remain outstanding.] Parathion residues of concern to be included in the risk assessment for animal commodities based on cholinesterase inhibition will include parathion, paraoxon, and 4-acetamidoparaoxon. As with plants, the tolerance expression may be based on parathion only. Residues of *p*-nitrophenol do not have to be included in the tolerance expression or considered in the aggregate risk assessment for parathion but should be considered in conjunction with the cumulative risk assessment for *p*-nitrophenol. The risk assessment for *p*-nitrophenol will be based on its own toxicological endpoints (rather than cholinesterase inhibition) and should include exposure to *p*-nitrophenol from its use as a fungicide on leather. Residues of parathion, paraoxon, *p*-nitrophenol, and 4-acetamidoparaoxon should be determined in meat, milk, poultry, and egg tissue samples from the required livestock feeding studies.

NOTE: Toxicology deems 4-acetamidoparaoxon of concern due to potential cholinesterase inhibition. However, if the registrant can demonstrate that 4-acetamidoparaoxon is much less toxic than parathion, feeding study data will not be needed for 4-acetamidoparaoxon and 4-acetamidoparaoxon residues in animal commodities will not need to be included in the risk assessment for parathion. 4-Acetamidoparaoxon will not be considered a residue of concern if the acute oral LD<sub>50</sub> is more than 200 mg/kg. If the acute oral LD<sub>50</sub> is less than 200 mg/kg, additional toxicological testing may be required.

- For the aggregate risk assessment for parathion with respect to cholinesterase inhibition, the residues of concern in drinking water are parathion and paraoxon. Residues of *p*-nitrophenol in drinking water should be included in the cumulative risk assessment for *p*-nitrophenol.

• Committee Members in Attendance:

R. Loranger  
C. Olinger  
G. Kramer  
A. Protzel  
L. Cheng  
K. Farwell  
J. Peggins

cc: HED Metabolism Assessment Review Committee file (G. Kramer), BLCKohlligian, Parathion Reg. Std. File, Parathion SF, RF.

7509C:RRB2:BLCKohlligian:CM#2:Rm 804E:703-305-7462:4/10/98.