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WASHINGTON, D.C. 20460

05/01/98  
     
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May 21, 1998

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MEMORANDUM

OFFICE OF  
PESTICIDES AND TOXIC  
SUBSTANCES

Subject: **Methyl Parathion (053501)**. The Outcome of the HED Metabolism Assessment Review Committee Meeting Held on March 11, 1998. DP Barcode: D245127

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Through: Alan P. Nielsen, Branch Senior Scientist *Al Nielsen*  
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And

Alberto Protzel, Branch Senior Scientist *Alberto Protzel*  
Toxicology Branch I  
Health Effects Division [7509C]

And

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

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

Background

Methyl parathion was previously discussed by the HED Metabolism Committee on 3/11/92. Available plant metabolism, animal metabolism, and plant magnitude of the residue data were presented and discussed. Livestock feeding studies were not available. The Committee concluded the following (memo by R. Perfetti dated 3/16/92):

- The terminal residue of concern in the extractable portion of the TRR in the methyl parathion plant metabolism studies was tentatively determined to be parent and paraoxon, pending submission of additional information required in the update. The Committee

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decided that *p*-nitrophenol need not be regulated because it is not a cholinesterase inhibitor as is methyl parathion. Also, the no observable effect level for cholinesterase inhibition for methyl parathion is low so that protection for any possible systemic effects arising from exposure to *p*-nitrophenol would be provided (Note: This does not mean that toxicity data for *p*-nitrophenol may not be required in the future.).

- In the case of milk, eggs, and animal tissues, if it is determined that tolerances are needed for these commodities, then the parent and paraoxon are to be regulated. Therefore, feeding studies for ruminants and poultry are needed. These experiments should reflect feeding of parathion *per se* at 1, 3, and 10X the maximum expected dietary burden for the subject species. However, in addition to analysis for parent and paraoxon, the following compounds should also be determined in milk, egg, and tissue samples; *p*-nitrophenol, *p*-aminophenol, and conjugates of these compounds.

### 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 3/11/92 concerning *p*-nitrophenol and *p*-aminophenol needed to be reconsidered since they are also metabolites of parathion. Moreover, to insure consistency between methyl parathion and parathion, the HED Metabolism Assessment Review Committee met on 3/11/98 to consider both chemicals and reconsider the question of what residues of methyl parathion need to be regulated/included in the risk assessment from plant and animal commodities.

Available plant metabolism, animal metabolism, and plant magnitude of the residue data were presented and discussed. [Note: No new plant metabolism, animal metabolism, or animal magnitude of the residue data had been submitted since the previous meeting of the HED Metabolism Committee on 3/11/92.] The HED Chapter of the Paranitrophenol Reregistration Eligibility Decision (RED) document was briefly discussed. The Committee tentatively concluded the following:

- Based on available plant metabolism and magnitude of the residue data, methyl parathion residues of concern in/on plant commodities are methyl parathion, methyl paraoxon, and *p*-nitrophenol. [Note: A new lettuce metabolism study remains outstanding.] Methyl parathion residues of concern to be included in the risk assessment for plant commodities based on cholinesterase inhibition will include methyl parathion and methyl paraoxon. The tolerance expression may be based on methyl parathion only since detectable levels of methyl paraoxon have not been found in/on commodities tested by FDA monitoring. Residues of *p*-nitrophenol do not have to be included in the tolerance expression or considered in the aggregate risk assessment for methyl 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

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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 methyl parathion, methyl paraoxon, and *p*-nitrophenol should be determined in/on plant samples collected in future plant magnitude of the residue studies.

- Based on available animal metabolism data, methyl parathion residues of concern in animal commodities are methyl parathion, methyl paraoxon, *p*-nitrophenol, and amino-paraoxon-methyl. [Note: Livestock feeding studies remain outstanding.] As with plants, methyl parathion residues of concern to be included in the risk assessment for animal commodities based on cholinesterase inhibition will include methyl parathion and methyl paraoxon. The tolerance expression may be based on methyl parathion only. Residues of

*p*-nitrophenol do not have to be included in the tolerance expression or considered in the aggregate risk assessment for methyl 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. Toxicology deems amino-paraoxon-methyl of concern due to neuropathy of unknown origin and not due to cholinesterase inhibition. Once outstanding livestock feeding studies have been submitted, the Agency will determine how to include amino-paraoxon-methyl in the risk assessment. Residues of methyl parathion, methyl paraoxon, *p*-nitrophenol, and amino-paraoxon-methyl should be determined in meat, milk, poultry, and egg tissue samples from the required livestock feeding studies.

- For the aggregate risk assessment for methyl parathion with respect to cholinesterase inhibition, the residues of concern in drinking water are methyl parathion and methyl 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, Methyl Parathion Reg. Std. File, Methyl Parathion SF, RF.

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

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