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WASHINGTON, D.C. 20460

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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: HED Metabolism Committee Meeting of 6/20/96.
New Chemical - **Chlorfenapyr** (i.e. Alert/Pirate®).
PP#5F04456. Insecticide/Miticide on Cotton/Oranges/Lemons and
Tomatoes/Lettuce/Cabbage/Potatoes. Barcode D227383. CBTS#
17304.

FROM: Gary F. Otakie, P.E., Chemist
Tolerance Petition Section III
Chemistry Branch I, Tolerance Support
Health Effects Division (7509C)

Gary F. Otakie
6/27/96

THRU: Edward Zager, Acting Branch Chief
Chemistry Branch I, Tolerance Support
Health Effects Division (7509C)

Edward Zager

TO: HED Metabolism Committee Members¹

QUESTIONS DISCUSSED

Plants

1. Is a permanent tolerance expression for plants containing only the parent acceptable (are there any other residues of toxicological concern)? Is use of only parent residues acceptable for dietary risk assessments for a crop such as tomatoes where the parent is 38-50% TRR?

Animals

Ruminant Commodities Excluding Meat ByProducts

2. Is a permanent tolerance expression for ruminant commodities (i.e. milk/milkfat, fat and meat; excluding meat byproducts) containing only the parent acceptable (are there any other residues of toxicological concern)? Is use of only parent residues acceptable for dietary risk assessments for ruminant commodities?

¹Richard Loranger, Michael Metzger, Alberto Protzel, Karl Baetcke, William Burnam, Mike Ioannou, Byong-Han Chin, Randy Perfetti

Ruminant Meat Byproducts

3. Is a permanent tolerance expression containing only the parent serving as a marker compound for metabolite residues acceptable for ruminant meat byproducts (are there any other residues of toxicological concern)? Since metabolites can account for 13-39X the parent residues in ruminant byproducts should they be included in the dietary risk assessment (i.e. a factor could be used for the risk assessment based on the ratio of the sum of all the metabolite mixtures, conjugates and metabolites of toxicological concern to the parent marker; see Attachment 7; 13X for liver and 39X for kidney includes all metabolites and mixtures)?

Poultry

4. Although tolerances on poultry commodities are not yet required based on the current proposed uses they may be required for additional new uses for this new chemical. Are the metabolism decisions for ruminant commodities applicable to poultry? If not proceed to 5. and 6.

Poultry Commodities Excluding Meat ByProducts

5. Is a permanent tolerance expression for poultry commodities (i.e. meat, fat and eggs; excluding meat byproducts) containing only the parent acceptable (are there any other residues of toxicological concern)? Is use of only parent residues acceptable for dietary risk assessments for poultry commodities?

Poultry Meat Byproducts

6. Is a permanent tolerance expression containing only the parent, serving as a marker compound for metabolite residues, acceptable for poultry meat by-products (are there any other residues of toxicological concern)? Since metabolites can account for 11-16X the parent residues in poultry meat byproducts should they be included in the dietary risk assessment (i.e. a factor could be used for the risk assessment based on the ratio of the sum of all the metabolites, to the parent marker; see Attachment 5; 13X for liver and 16X for kidney includes all metabolites and mixtures)?

INDIVIDUALS IN ATTENDANCE

METABOLISM COMMITTEE: (Signatures indicate concurrence unless otherwise stated)

Randy Perfetti

R. Perfetti

Richard Loranger

Richard Loranger

Michael Metzger

Michael Metzger

Alberto Protzel

Alberto Protzel

Mike Ioannou

Mike Ioannou

Byong-Han Chin

Byong Han Chin

William Burnam

William Burnam

SCIENTISTS: Non-Committee members responsible for the data presentation (signatures indicate technical accuracy of the report)

G. Otakie

G. Otakie

G. Reddy

G. Reddy

METABOLISM COMMITTEE MEMBERS IN ABSENTIA: (Signatures indicate concurrence with the overall conclusions of the Committee.)

Karl Baetcke

Karl Baetcke

MATERIAL REVIEWED

The Committee reviewed the CBTS briefing paper, which included chlorfenapyr plant and animal metabolism data and metabolic pathways. The Committee also reviewed tox data on the metabolism of chlorfenapyr in rats.

CONCLUSIONS REACHED

The conclusions reached follow the numbering of the questions iterated above.

1. For plant commodities there is no scientific objection to establishing the chlorfenapyr permanent tolerance expression in terms of parent only. Use of only parent residues is acceptable for chlorfenapyr dietary risk assessments on plant commodities based on the parent comprising such a high percentage of the residue.

2. For ruminant commodities (excluding meat byproducts) there is no scientific objection to establishing the chlorfenapyr permanent tolerance expression in terms of parent only. Use of only parent residues is acceptable for chlorfenapyr dietary risk assessments on ruminant commodities (excluding meat byproducts).
 3. For ruminant meat byproducts there is no scientific objection to establishing the chlorfenapyr permanent tolerance expression in terms of parent only. However, chlorfenapyr dietary risk assessments on ruminant meat byproducts should include the two metabolites CL 303,268 and 325,195 as well as the parent (303,630). Although the metabolites have different acute toxicities and CL 303,268 has a lower LD₅₀ than the parent, the metabolites were detected in the rat metabolism study and are therefore included in the toxicology endpoints. For risk assessment, the three moieties are assumed to have comparable toxicity taking into account their relative residue levels. The ruminant meat byproduct risk assessment will use a factor (i.e. ratio parent plus metabolites/parent) multiplied by the parent based tolerance determined from the residue levels of the three moieties in the ruminant metabolism studies.
 4. The metabolism decisions for ruminant commodities are not fully applicable to poultry commodities. It was noted that based on the **current** proposed uses tolerances on poultry commodities are not required. However, poultry was addressed in the event that future proposed uses for this new chemical require tolerances on poultry commodities.
 5. For poultry commodities (excluding meat byproducts) there is no scientific objection to establishing the chlorfenapyr permanent tolerance expression in terms of parent only. Use of only parent residues is acceptable for chlorfenapyr dietary risk assessments on poultry commodities (excluding meat byproducts).
 6. For poultry meat byproducts there is no scientific objection to establishing the chlorfenapyr permanent tolerance expression in terms of parent only. However, chlorfenapyr dietary risk assessments on poultry meat byproducts should include the four metabolites CL 303,268, 325,195, 152,835 and 325,157 as well as the parent (303,630). Although the metabolites have different acute toxicities and CL 303,268 has a lower LD₅₀ than the parent the metabolites were detected in the rat metabolism study and are therefore included in the toxicology endpoints. For risk assessment the five moieties are assumed to have comparable toxicity taking into account their relative residue levels. The poultry meat byproduct risk assessment will use a factor (i.e. ratio parent plus metabolites/parent) multiplied by the parent based tolerance determined from the residue levels of the five moieties in the poultry metabolism studies.
- 4

cc: G. Otakie, R.F., S.F., circ, PP#5F04456, PM 19 (D. Edwards), D
McCall (RCAB), R. Griffin (RCAB), Met. Comm. File (R. Loranger).
RDI: EHaeberer 6/25/96; RLoranger 6/25/96

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