PC 125501

R.F.

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

MAR 23 1995

MEMORANDUM

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

Subject: **PP# 6F3392/FAP# 6H5500 - CLOFENTEZINE (APOLLO®) ON APPLES.** Evaluation of the Tolerance Method Validation Reports. (No MRID #)[CBTS #s 15269 and 15270]{DP Barcode D213231 and D213237}

From: Francis D. Griffith, Jr., Chemist
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Health Effects Division (7509C)

To: Dennis H. Edwards, Jr., PM-19
Insecticide - Rodenticide Branch
Registration Division (7505C)

and

Donald A. Marlow, Chief
Analytical Chemistry Branch
Biological and Economic Analysis Division (7503W)

Thru: E. Zager, Acting Chief
Chemistry Branch I - Tolerance Support
Health Effects Division (7509C)

CONCLUSIONS

1. There has **not** been a successful Tolerance Method Validation (TMV) for the Nor-Am method RAM J/02/92 as written using either cleanup column to determine clofentezine residues in apples at 0.01 ppm. However, for the purposes of a time limited tolerance, we would not object to limited distribution of the method to enforcement authorities provided the Analytical Chemistry Branch (ACB) reports accompany the method to describe needed changes in the clean-up and determinative steps.

2. The method using either the florisil or silica gel cleanup column is suitable to gather data on the magnitude of the clofentezine residues on apples at 0.01 ppm submitted in the petition.

3. The petitioner needs to extensively revise the method to incorporate the various ACB suggestions and to have the method meet all Agency Guidelines for an enforcement procedure. The clean-up and determinative steps will need the most revisions. CBTS reminds the

petitioner we do not consider it reasonable to have limit of detection (LD) tolerance enforcement methods.

4. The extensively revised clofentezine on apples at 0.01 ppm method will need a new Independent Laboratory Validation (ILV) prior to a repeat Agency TMV.

RECOMMENDATION

CBTS recommends that the Nor-Am method RAM J/02/92 **NOT** be forwarded to FDA for publication as a generally acceptable residue analytical enforcement method for clofentezine on apples at 0.01 ppm.

However, CBTS can support a 1 year time limited tolerance of 0.01 ppm clofentezine on apples to allow the petitioner time to correct all method deficiencies. If IRB/RD agree with this proposal, then CBTS can forward this method to FOD for limited distribution with the following disclaimer: "This method is for use only by experienced chemists who have demonstrated **knowledge** of the principles of trace organic analysis; and have proven **skills and abilities** to run a complex residue analytical method obtaining accurate results at the part per billion level." In addition, a copy of both ACB reports must accompany each method distributed.

CBTS suggests that the petitioner quickly take steps to correct the many method deficiencies and develop a plan to keep the Agency informed of the progress made in correcting the deficiencies.

DETAILED CONSIDERATIONS

CBTS has been informed by the Analytical Chemistry Laboratory of ACB of the completion of the requested clofentezine TMVs for method RAM J/02/92. The results of the TMVs were reported by Paul Golden in his February 21 and March 14, 1995, memoranda. The TMVs were requested for clofentezine, trade named Apollo®, on raw apples at 0.01 ppm using the petitioner's method titled "Analytical Method for Residues of Clofentezine in Fruit and Vegetables" dated July 7, 1992, and coded RAM No. J/02/92 (see memorandum by M. Bradley dated Sept. 16, 1994 to ACB).

The TMV was run initially using the petitioner's method as written and used to generate his crop field trial residue data; ie use of the florisil SPE cleanup. When it became apparent that the results would not be acceptable the petitioner provided the lab with additional information and requested RD have the lab rerun the TMV using the silica gel SPE.

In the ACB screen several points were noted that would require clarification. These points along with the additional comments noted in both reports are included herein by reference. The petitioner needs to include them in any method revision as additional instructions. We place particular emphasis on identification of the SPE

cartridges and how they are to be prepared for use. We suggest the petitioner consider an alternate determinative step(s) as one way to overcome the significant positive interferences. The revised method needs to have more detailed, better written with easy to follow instructions. Details included in the petitioner's memo to the Chief of ACB are also to be included in the revised method.

CBTS requested validation of the method in duplicate at 0.01 on raw apples only. Using the florisil SPE cleanup recoveries ranged from 65 to 85%. When the TMV was repeated using the silica SPE clofentezine recoveries were 80 and 82% from the 0.01 fortification. CBTS points out that the chromatographic profiles in the spiked samples around the elution of clofentezine are different than that displayed in the blank/control samples. CBTS concurs with the laboratory conclusion that the method does not meet Agency guidelines for an enforcement residue analytical method. We do not agree with the petitioner that the silica SPE cartridge is better than the florisil SPE cartridge cleanup. If anything the cleanups presented the same chromatographic profile. Agency recovery data indicate a crop co-extractive interference is present on the chromatograms regardless of the cleanup that could easily be calculated at 33 to 50+% of the proposed tolerance. That is not method specificity.

In summary, the petitioner has presented a residue analytical method that in the hands of a knowledgeable chemist possessing well above average skills and abilities can determine clofentezine at 0.01 ppm. Our TMV confirms that the magnitude of the residue data presented are acceptable; however, the method is **NOT** suitable to enforce the proposed 0.01 ppm tolerance. We do not feel it is reasonable to accept a method at the LD where extensive skill is required for each sample to **manually** determine the appropriate clofentezine elution time and what is clofentezine in the presence of closely eluting crop co-extractives or unidentified analytical responses. The petitioner needs to determine what is the method LD and LOQ with supporting method validation data at the LOQ.

CBTS concludes that the method in its present form is not suitable as a method ready for publication in FDA's PAM Vol II. We recommend limited distribution of the method with the laboratory reports attached if RD establishes a time limited tolerance.

cc:R.F.,Circu.,Reviewer(FDG),PP#6F3392.
7509C:CBTS:Reviewer(FDG):CM#2:Rm804Q:305-5826:FDG:3/21/95:edit:fdg:3/23/95.
RDI:SecHd:RSQuick:3/21/95:BrSrSci:RALoranger:3/21/95:ActBrCh:EZager:3/23/95.