10-11-95

MEMORANDUM

Subject: **PP# 3F4268 - QUIZALOFOP-P ETHYL ESTER (ASSURE® II) ON LEGUME VEGETABLES (SUCCULENT OR DRIED) AND FOLIAGE OF LEGUME VEGETABLES CROP GROUP, SUGARBEET TOPS, ROOTS, AND MOLASSES, AND COTTONSEED.**
Evaluation of the Analytical Chemistry Laboratory Prereview of the Tolerance Method Validations for Quizalofop-p Ethyl Ester.
(MRID #s 433140-01 and 429275-09))[CBTS # 16260]{PD Barcode D219629}

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and

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Thru: Michael S. Metzger, Chief
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BACKGROUND

CBTS has been informed by the Analytical Chemistry Laboratory (ACL) of the completion of their pre-review of the quizalofop ethyl ester and its acid metabolite method for the requested Tolerance Method Validation (TMV). The results of the pre-review for the method, which was conducted by E. Greer, was reported by H.K. Hundley in his memorandum dated July 21, 1995. Attached to the ACL memorandum were the comments by E. Greer.

One TMV was requested for quizalofop-p ethyl ester, trade named Assure® II, and its acid metabolite quizalofop in cottonseed (see memorandum dated May 26, 1995).

CONCLUSIONS

1. CBTS agrees with all of the data deficiencies that were detected and reported by ACL in their prereview of the method.

2. There has not been a successful method trial for quizalofop-p ethyl ester and its acid metabolite using the revised LAN-1 HPLC-UV method for cottonseed.

2. CBTS concludes the quizalofop-p ethyl ester HPLC-UV method, LAN-1, needs to be revised and revalidated as described in the ACL report.

RECOMMENDATION

CBTS recommends that this review and the attached ACL report be forwarded to the petitioner for revisions to the analytical method, LAN-1. CBTS recommends that the petitioner further revise the LAN-1 HPLC-UV method as soon as possible, generate the additional validation data, and return the revised validated method to the Agency so that a TMV can be reinitiated.

The deficiencies in this method and the lack of a successful TMV will not be a bar to our recommendation for a time limited tolerance/conditional registration if no other significant data gaps exist. However, the lack of a successful TMV report will be a cause of concern when CBTS considers a permanent tolerance.

DETAILED CONSIDERATIONS

In the prereview of the HPLC-UV method, LAN-1, titled "Determination of DPX-79376, DPX-79376 Acid and Conjugates as DPX-709376 Acid in Cottonseed and Fractions Treated with Assure II Herbicide," ACL noted deficiencies in the summary, standard preparations, extraction, cleanup, and determination steps.

SUMMARY

ACL feels that the use of 2 HPLC's is unreasonable, and that 1 HPLC with column switching is more appropriate.

For enforcement labs with limited resources we agree. However, for the larger labs we do not foresee a problem. The petitioner needs to provide for column switching and allow the option to use 2 HPLCs if there are valid reasons for this use. Enforcement laboratories should have the choice of using either determination step.

STANDARD PREPARATION

ACL questions why the acid metabolite must be diluted immediately, yet the petitioner claims it is stable for 6 months at 4°C. Instructions for preparation of the parent quizalofop ethyl ester were not mentioned.

CBTS agrees these apparent contradictions need to be resolved. Instructions for preparation of the parent standard need to be included.

EXTRACTION

ACL inquires how 1 L can be decanted into a 250 ml separatory funnel. The type of equipment used for incubating the sample/enzyme mix is not described, nor is it stated whether the mix is shaken after the addition of the enzymes. Instructions should be included for discarding the hexane layer following partitioning. The final volume of the solution prior to removing an aliquot for cleanup needs to be stated.

CBTS agrees with these comments. The petitioner needs to revise the method to improve the instructions based on ACL's comments.

CLEAN-UP

ACL noted that complete detailed instructions for the HPLC clean-up are lacking.

CBTS agrees with ACL comments and requests the petitioner revise the method accordingly.

DETERMINATION STEP

ACL expresses concern for the variable elution times for the acid metabolite. The supporting chromatographic data suggest there are problems with the method's ruggedness. No recovery data for the parent compound were included. The LOQ (and LD) for the parent were not reported.

CBTS concurs with ACL's comments and feels that this is a critical step. We suggest that the petitioner revise the clean-up step to remove the excess ACN which can cause the shift in retention times and to use peak area as the preferred quantitation technique. The revised method needs to point out potential problems using peak height as a way to quantitate the results. Recovery data for the parent compound should be generated, especially at the LOQ, as noted by ACL, when the method is revised and revalidated. Additional supporting chromatographic data should be submitted.

Nowhere in our request for the TMV did we ask ACL to use radio-isotopes in its validation. The radioisotope validation report was submitted as supporting validation data to show that the method is expected to perform as claimed using cold compounds. The lab is to conduct the TMV using only cold compounds. CBTS will continue to request that petitioners provide us with radio validation data for proposed enforcement methods and will include these data in our TMV package when available.

ACL has concluded a TMV can not be conducted at this time with the number of deficiencies in the LAN-1 HPLC-UV method. There has not been a successful method trial for quizalofop-p ethyl ester and

its acid metabolite using the revised LAN-1 HPLC-UV method for cottonseed. ACL and CBTS conclude the quizalofop-p ethyl ester HPLC-UV method, LAN-1, needs to be revised and revalidated as described in the ACL report.

ATTACHMENT: ACL July 21, 1995, TMV Report, 5 pages.

cc(w/o attachment):R.F.,Circu.,Reviewer(FDG),PP#3F4268,PAM-II File.
7509C:CBTS:Reviewer(FDG):CM#2:Rm804Q:305-5826:FDG:10/3/95:edit:fdg:10/11/95.
RDI:BrSrSci:RALoranger:10/5/95:BrCh:MSMetzger:10/6/95.