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

Analytical Chemistry Section
Building 306, BARC-East
Beltsville, Maryland 20705

September 17, 1996

OFFICE OF PREVENTION, PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Pre- Review of Request for Petition Method Validation of Isoxaflutole in/on Field Corn and Animal RACs (PP# 6F04664).

FROM: Dallas Wright, Jr., Chemist DDW
Analytical Chemistry Section

THRU: Harvey Huntley, Head
Analytical Chemistry Section

THRU: Donald Marlow, Chief
Analytical Chemistry Branch

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

ACL has reviewed the analytical method and ILV report for the chemical isoxaflutole in the request from the Health Effects Division dated June 14, 1996. Because of the following problems, we have determined that the method is generally not suitable as a regulatory method as written.

COMMENTS ON MILK METHOD

1) Control samples for the parent compound contained interferences as high as 11 ppb while the request calls for analyzing samples at 10 ppb.

2) Recoveries for the metabolite RPA 203328 were lower than permitted in the Residue Chemistry Guidelines.

COMMENTS ON EGG METHOD

1) The method was developed to analyze only the metabolite RPA 202248 and not the parent compound. ACL was asked to validate the method on both the parent and the RPA 202248 metabolite.

COMMENTS ON CATTLE LIVER METHOD

1) There is no data from the registrant or the ILV for recoveries of the parent compound on beef liver.

2) The control samples for metabolite RPA 202248 showed significant interferences.

3) Recovery data for metabolite RPA 202248 were higher than permitted in the Guidelines.

4) ACL was asked to run recoveries at one half of the method LOQ. The registrant reported data at this level, but the recoveries were unacceptable, over 300% in one case, indicating that there was significant interference. Validation data below the LOQ would not be meaningful.

COMMENTS ON CHICKEN MUSCLE METHOD

1) There was no data either from the registrant or the ILV for recovery of the parent compound.

2) The recoveries for the metabolite RPA 202248 were higher than permitted in the Guidelines.

3) ACL was asked to run recoveries at one half the method LOQ. The registrant submitted data for that level, but the recoveries were unacceptably high. Validation data below the LOQ would not be meaningful.

COMMENTS ON ILV DATA

1) The ILV was run on milk and beef kidney. While ACL was not requested to run the validation on beef kidney, this data was reviewed since the method is the same as that for beef liver, which ACL was asked to validate.

2) The results of the ILV were similar to those of the registrant. Significant interferences were reported for both matrices. Since the recoveries were reported corrected for control values, it is not possible to tell if they would be acceptable otherwise.

3) The experimental design of the ILV trials does not meet the requirements of PR 88-5. The ILV lab ran recoveries at the LOQ, at ten time the LOQ, and reagent blanks.

4) The ILV lab reported that it took 29 hours or 5 calendar days, not including chromatography time to run a set of milk samples. Since the milk method requires injecting the samples using three different mobile phases, this would make the method substantially longer. They also reported that it took 21 hours, not including chromatography time, to analyze a set of beef kidney samples. This lengthy analysis time does not meet the Guidelines requirement of 24 hours to complete a set of samples.

CONCLUSION

ACL has reviewed the method for Isoxaflutole in animal products and found serious problems which have caused it to fail our pre-review. While the method as a whole does not appear to be suitable for regulatory use, ACL could attempt to validate a smaller subset of commodities and fortification levels listed in the table below.

Commodity	Chemical Added	PPM Added
Milk	Isoxaflutole	0 0.02
	RPA 202248	0 0.01 0.02
Eggs	RPA 202248	0 0.01 0.025 0.05
Cattle Liver	RPA 202248	0 0.10 0.20

These combinations of commodities and spiking levels have acceptable supporting data either from the registrant or the ILV.

ACL will put this validation in abeyance until we receive additional specific guidance from HED.