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

JUN 23 1986

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP#4F3081 Amitraz in the Meat, Fat, and Meat
Byproducts of Hogs.
Evaluation of the November 25, 1985, Amendment.
(No Accession No.) [RCB# 278]

FROM: Francis D. Griffith, Jr., Chemist
Residue Chemistry Branch
Hazard Evaluation Division (TS-769C)

A handwritten signature in black ink, reading "Francis D. Griffith, Jr.", written over the typed name and title.

TO: Lawrence J. Schnaubelt, Acting PM 12
Insecticide-Rodenticide Branch
Registration Division (TS-767C)

and

Toxicology Branch
Hazard Evaluation Division (TS-769C)

THRU: Charles L. Trichilo, Chief
Residue Chemistry Branch
Hazard Evaluation Division (TS-769C)

A handwritten signature in black ink, reading "Charles L. Trichilo", written over the typed name and title.

Nor-Am Chemical Company has submitted this amendment consisting of a cover letter and supplementary Section D (a revised protocol for a hog skin processing study with supporting letters from agricultural experts for establishing a pre-slaughter interval [PSI]). The amendment has been submitted in response to several deficiencies outlined in our reviews of amitraz (trade named BAAM®) in meat, fat, and meat by-products of hogs by E.T. Haeberer on July 11, 1984, and F.D. Griffith, Jr., on September 6 and December 19, 1985. The deficiencies are listed below in the order they appeared in the December 19, 1985, Residue Chemistry Branch (RCB) review followed by the petitioner's responses, then RCB comments and conclusions.

Deficiency 1

RCB reiterates its conclusions 1, 2, 3, and 5 of its September 6, 1985, amendment review. They are repeated below as follows:

1. The petitioner should provide additional details of the hog skin study as follows:
 - a. name of the breed of hogs to determine if an economically important breed was used;
 - b. description of the test facilities, including animal care and feeding;
 - c. name and location of the processing plant.
- 2a. The petitioner should demonstrate the basic hydrolysis step in the method used to determine amitraz residues in animal commodities is adequate to recover the possible conjugates of metabolites in animal tissues.
- 2b. Additional extensive recovery data are needed for amitraz, per se, and its formamide and methylmethanimidamide metabolites in/on hog skin, fat, meat, kidney, and liver at or near the limit of detection (L.D.) and proposed tolerances. The petitioner should show the quantitative conversion of amitraz and its metabolites to 2,4-dimethylaniline so RCB may ascertain the total amitraz residues in tissues.
- 2c. The petitioner should determine the limit of detection for the formamide and methylmethanimidamide metabolites.
3. As was noted in the Registration Standard and in previous reviews of amendments to this petition RCB has been unable to locate any storage stability data for amitraz and its metabolites in/on animal tissues. The petitioner should use spiked or weathered residue samples stored at subfreezing temperatures for intervals associated with the treated hog skin samples used to determine the magnitude of the residue. The storage procedure used in this amendment could be validated by preparing samples of hog fat or hog skin spiked with the parent compound and preparing separate samples for each metabolite at several ppm's; i.e., two or three x L.D. and at the proposed tolerances. These samples should be stored under the same conditions as the "field" samples, then periodically remove sample aliquots for analysis.
- 5a. In any future revision of Section F, RCB suggests the petitioner change the phrasing to bring it more in line with the Codex amitraz tolerance expression. Suggested phrasing could be "combined residues of amitraz [N'-(2,4-dimethylphenyl)-N-

methanimidamide) and its metabolites N-(2,4-dimethylphenyl)-N-methyl formamide and N-(2,4-dimethylphenyl)-N-methylmethanimidamide (both calculated as the parent) totaling X part per million."

- 5b. Assuming our method and storage stability questions are resolved without any increase in total amitraz residues, RCB tentatively agrees the proposed amitraz tolerances in hog meat at 0.05 ppm and in hog fat at 0.1 ppm are adequate.
- 5c. In a revised Section F the petitioner needs to propose a separate hog liver and kidney amitraz tolerance. RCB tentatively agrees a 0.2 ppm is adequate.
- 5d. RCB defers judgment on any amitraz in hog meat byproducts proposed tolerance until we have reviewed the amitraz results in cooked hog skin.
- 5e. If the results of the cooked hog skin study show higher amitraz residues than in raw hog skin, a food additive petition and a food additive amitraz tolerance proposal should be presented.
- 5f. RCB reiterates its concerns expressed in conclusion 4b of our July 11, 1984, review.

Assuming the above tolerances are established on hog commodities, they will need to be reevaluated at a later date if future proposals are considered for the possible use of amitraz on potential hog feed items.

Petitioner's Response

The petitioner did not respond to these deficiencies in this submission.

RCB Comments and Conclusions

These conclusions remain unresolved and thus outstanding. RCB recognizes it is not necessary to answer them completely at this time for the review of this protocol and letters. However, they are reiterated to remind the petitioner that when we review residue data submitted from the protocol any deficiency not adequately resolved could adversely affect our recommendations.

Deficiency 2

RCB requests the petitioner identify the amitraz metabolites on which data will be reported. We also suggest these be the same metabolites identified in the Codex tolerance expression.

Deficiency 4

The petitioner needs to show no amitraz is in the test animals' feed and water.

Deficiency 10

Any deviations to the standard commercial hog skin processing to crackling and puff snack food should be described and documented.

Deficiency 11

RCB requests that some recovery data for amitraz and its metabolites using the most appropriate PAM-I procedure(s) be presented.

Petitioner's Response

The petitioner did not respond to these deficiencies in this submission.

RCB Comments and Conclusions

These conclusions continue unresolved and thus remain outstanding. Again, these deficiencies are reiterated to remind the petitioner that any deficiency not adequately resolved when we review residue data generated by running the protocol could adversely impact our recommendations.

Deficiency 3

The petitioner should provide the starting weight and the slaughter weight of the hogs.

Petitioner's Response

In the revised protocol the petitioner proposes to use 28 hogs of a commercial breed selected to bring slaughter weight to 220 to 240 lb.

RCB Comments and Conclusions

For purposes of this protocol, the deficiency is thus tentatively resolved.

Deficiency 5

RCB suggests that some of the hogs to be treated (for example, one per PSI) in the protocol be dosed at an exaggerated level with amitraz. This information could be useful in addressing problems relating to the Delaney Clause. We suggest retaining the 30-day PSI in the study and also suggest animals be included at a seven day PSI.

Petitioner's Response

In the revised protocol the petitioner proposes to treat twelve hogs twice at seven day intervals at the rate of two fluid oz Taktic® EC in three gallons of water (1X rate) and twelve hogs twice at seven day intervals at the rate of six fluid oz Taktic® EC in three gallons of water (3X rate). Four hogs would be kept as control animals. Three animals from each treated group and one control animal would be slaughtered at one, 14, 21, and 30 days after the last treatment. There is no mention of the RCB suggested seven day PSI.

RCB Comments and Conclusions

The requested exaggerated rate residue data are to be provided, as are data for the 30-day PSI.

Letters from various authorities on good agricultural practices for hog ectoparasite control are submitted. These letters suggest PSI's for this type of control ranging from ten to 30 days. Consequently, the petitioner is not including a seven day PSI in his hog skin protocol. The petitioner wants a PSI longer than one to three days.

RCB has recently reviewed its policy regarding practical PSI's (see e.g., Schatzow letter of February 11, 1986, to Dr. M.J. Sloan). The letter points out that we generally accept PSI's of one to three days but do consider each use on a case-by-case basis. Based on this, we suggest that the petitioner include a PSI of three days in his hog protocol. This would give PSI's of one, three, 14, 21, and 30 days. This would provide us with a full complement of residue data to review and upon which to base our decision on an appropriate tolerance level, whether we decide on a one to three day PSI or opt for the petitioner's requested longer interval.

With two treatment rates and PSI's from one day to 30 days the question arises which raw hog skins should be processed into puffed rinds. RCB suggests the petitioner process the hog skins bearing the highest residues.

Based on 1) residue data showing whether residues are concentrated in puffed rinds, 2) the residue level on hog skin at the PSI we determine to be practical and 3) on the

method sensitivity levels for amitraz and its metabolites on hog skin (data we have requested above) RCB will determine whether or not a food additive tolerance is needed on the puffed rinds and, if so, at what level.

Deficiency 6

To accurately determine the proper PSI the petitioner needs to obtain "outside" documentation of good agricultural practices in hog production for ectoparasite control using Taktic[®] EC.

Petitioner's Response

The petitioner has presented photocopies of eight letters from officials knowledgeable in hog production. States represented by these letters are Missouri, Indiana, North Carolina, South Carolina, Minnesota, Oklahoma, Iowa, and Nebraska.

RCB Comments and Conclusions

The petitioner has obtained information on good agricultural practices for ectoparasite control in hogs from major hog-producing States (see USDA Agricultural Statistics, 1982). Officials in all of these States felt a longer preslaughter interval was appropriate with three States suggesting a 30-day PSI, four State officials suggesting 14-day PSI, and one State suggesting a ten to 14-day PSI. We will defer judgment on any PSI until we review the residue data generated by the proposed protocol. As indicated above, the Agency generally accepts only one to three day PSI's but does consider each use on a case-by-case basis.

Deficiency 7

Amitraz and its metabolites residue data should be presented on separate back and belly skin samples from the same hog.

Deficiency 8

RCB suggests the petitioner consider wrapping the high lipid hog skin samples in de-oiled aluminum foil before sealing them in plastic bags.

Petitioner's Response

The petitioner did not respond, per se, to these deficiencies as far as we can tell in this submission.

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RCB Comments and Conclusions

We reiterate that when we review amitraz residue data submitted from running this protocol we should see amitraz and its metabolites residue data on separate back and belly skin samples from the same hogs. We also recognize there is no formal requirement to wrap high lipid hog skin samples in de-oiled aluminum foil. This reviewer's experiences with high lipid samples stored in "plastic" is that there is an increased likelihood of interfering unidentified analytical responses (UAR's) appearing on most chromatograms. RCB will then ask to see all supporting chromatographic data.

The petitioner is reminded that if these deficiencies are not adequately resolved when we review the residue data this could adversely affect our recommendation. The original deficiencies remain unresolved and are thus outstanding.

Deficiency 9

All unused hog skin samples should be retained.

Petitioner's Response

In the revised protocol the petitioner proposes to retain under frozen conditions at least 500 grams of unprocessed hog skin.

RCB Comments and Conclusions

RCB feels 500 grams of sample is a sufficient quantity sample to be retained. If necessary, several additional aliquots of sample can be analyzed. The petitioner is sufficiently aware of our concerns over possible repeat analyses if questions arise. Deficiency 9 is thus resolved.

RCB Recommendation

If the petitioner concurs with all RCB conclusions above and can supply the requested information, then RCB recommends the petitioner proceed with the amitraz on hog skin study.

We particularly want to emphasize the importance of including hog skin residue data reflecting short PSI's (one to three days) as we suggested above.

TS-769C:RCB:Reviewer(FDG):CM#2:Rm708:557-0486:KENCO:JOB:87950:
6/17/86:eg:vo:edited:fdg:6/23/86
cc:R.F.,Circu.,TOX,EAB,EEB,FDA,Reviewer,PP#4F3081,ISS/ISB/PMSD
RDI:Section Head:R.S.Quick:6/6/86:R.D.Schmitt:6/6/86