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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

**MEMORANDUM**

Subject: PP#2G04099. Temporary Tolerance Petition and Experimental Use Permit for Use of Fluazinam on Peanuts; 050534-EUP-E. Submission Dated 1/23/95 in Response to the Memo of G.J. Herndon Dated 6/19/92.
MRID#s: 429749-01, 435210-01 thru -03, -11, -13 thru -20 (14 vols.).
DP Barcodes#: D212612, D216941, D217467.
CBTS#: 15184, 15823, 15888.

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In their **original** submission (see memo of G.J. Herndon dated 6/19/92), ISK Biotech Corporation requested the establishment of a temporary tolerance for the residues of the fungicide fluazinam (3-chloro-N-[3-chloro-2,6-dinitro-4-(trifluoromethyl)phenyl]-5-(trifluoromethyl)-2-pyridinamine) in or on peanut nutmeats at 0.01 ppm.

Associated with that temporary tolerance petition ISK Biotech requested an experimental use permit for use of fluazinam on peanuts in 1992 and 1993. Fluazinam was to be applied to peanut plots in 7 states using 4000 pounds of active ingredient over 2000 acres.

(1)

In the current submission (received 1/23/95), ISK Biosciences Corp. has requested the establishment of a temporary tolerance for the residues of the fungicide fluazinam (3-chloro-N-[3-chloro-2,6-dinitro-4-(trifluoromethyl)phenyl]-5-(trifluoromethyl)-2-pyridinamine) in or on **peanut nutmeats at 0.02 ppm**. Associated with the temporary tolerance petition is an EUP for use of fluazinam on 1000 acres in Alabama, Florida, Georgia, North Carolina, Oklahoma, Texas, and Virginia in 1995 and 1996 (2000 total acres for two years), requiring a total of 3120 lbs.ai..

CBTS defers the review of product chemistry for end-use products to the Registration Division.

**Conclusions**

1. **The conclusions drawn in this memo are based on the tolerance expression including only the parent compound, fluazinam, in the regulation of any plant and animal commodity. If the HED Metabolism Committee concludes that the tolerance should include additional and/or different metabolites, additional data will need to be generated for the other sections of this memo.**

2. Data in this petition were generated by the following laboratories:

Ricerca Inc., Painesville, OH
Hazleton Wisconsin, Inc., Madison, WI
Xeno Biotic Laboratories, Plainsboro, NJ

3. For a future, permanent tolerance request, additional product chemistry data will be needed to fulfill 61-1, 61-2, 62-2, 62-3, and 63-17 as detailed in our 6/19/92 memo.

4. Changes are underway to eliminate peanut hulls as a livestock feed item in Table II and allow the grazing/feeding of peanut hay to be restricted (see Conclusion 9a). Therefore, the proposed label, which includes a restriction against grazing/feeding peanut hay, is appropriate.

5a. For the purposes of this EUP and temporary tolerance request, the submitted peanut metabolism study is acceptable. The tolerance expression will include the parent compound, fluazinam, only. For a future, permanent tolerance request, the additional data/information listed in Conclusion 5b. should be provided. For a permanent tolerance request, any conclusions drawn by CBTS are subject to review by the HED Metabolism Committee.

5b. For a Section 3 registration/permanent tolerance request, the registrant will need to provide a complete residue profile outlining and tabulating (% and ppm) the identified, unidentified extractable, and unextractable radioactivity, as well as a proposed degradation scheme outlining the speculated steps from parent compound to natural incorporation. The final peanut metabolism

report should be sent in to the Agency as soon as it is ready, for the reasons outlined in Conclusion 12c.

6a. The nature of the residue in ruminants is adequately elucidated. For the purposes of this EUP/temporary tolerance request, the tolerance expression will include the parent compound, fluazinam, only. Pending review by the HED Metabolism Committee, other metabolites may need to be included in the tolerance expression for a future, permanent tolerance request.

6b. For a future Section 3 registration, the registrant will need to submit a poultry metabolism study.

7a. For the purposes of this EUP/temporary tolerance request, the proposed method is adequate. An independent laboratory validation (ILV) has been submitted. The independent lab believes the method can be improved in the Florisil cleanup step. The registrant may wish to make any modifications/improvements to the method prior to the Beltsville lab validation.

7b. The petitioner is reminded that, for a permanent tolerance on a food use chemical, data on whether the FDA/USDA multi-residue methodology will detect and identify fluazinam are required (see 40 CFR 158.240).

7c. The petitioner should submit the ordering code for the fluazinam standard that has been sent to the EPA Repository.

8. The data shown in Table 13 are adequate to show that fluazinam (parent compound only) is stable in the frozen peanut nutmeat matrix for periods up to 6⅛ months. For the purposes of this EUP request, the submitted storage stability data are adequate. Also, if the additional field trial samples requested (see Conclusion 9b) are held more than 190 days between harvest and analysis, additional storage stability data covering this longer interval will be needed.

9a. Based on recent data the Agency has received, peanut hulls are no longer routinely fed to livestock and, based on current practices, a restiction against feeding peanut hay is practical. These changes will be incorporated into an updated Table II (to be released shortly). Therefore, the current Section F that proposes a temporary tolerance for peanut nutmeats at 0.020 ppm (no temporary tolerances are proposed for either peanut hulls or peanut hay) and Section B which includes a restriction against grazing/feeding peanut hay are appropriate.

9b. Based on the 6/2/94 Field Trial Document, a total of 12 field trial sites (9 if no residues are detected) are required for the registration of a new pesticide on peanuts. Since the registrant is pursuing a grazing/feeding restriction for peanut hay, peanut hulls will not appear as a livestock feed item in the

newly updated Table II (see Conclusion 9a), and no detectable residues occurred on peanut nutmeats from previous trials, data from a total of 9 field trials on peanut nutmeats (assuming no detectable residues are found in future trials as well) will have to be submitted **prior to a permanent tolerance request.** In the current submission, field trial data for both banded and broadcast applications from three different sites was submitted. Provided the questions concerning the field trial data of the original submission (see review of G.J. Herndon dated 6/19/92) are adequately resolved, these three additional field trial sites can be counted toward the 9 required. Based on the generally higher residues (in peanut hay and hulls) in the banded (rather than broadcast) side-by-side trials, if the registrant wants a registration for both uses, the additional 3 trial sites can be conducted using the **banded application only.** The location of these trials is outlined in the 6/2/94 Field Trial Document.

10a. The proposed label does not mention any rotational crops or plant-back intervals. For the purposes of this EUP and temporary tolerance request, the tolerance expression will include the parent compound, fluazinam, only. Therefore, based on the results of this confined rotational crop study showing that no parent compound was detected in any plant commodities, having no rotational crop restrictions seems appropriate. For a future, permanent tolerance request, these conclusions and their impact on any future requirements are subject to review by the HED Metabolism Committee.

10b. CBTS requests that the registrant explain the unusually long maturity times for some of crops sown 120 and 365 DAT (i.e. carrots requiring 235 days to mature and lettuce taking 124 days). This requirement can be deferred until a petition for a permanent tolerance is submitted.

11. Based on the results in Table 18, fluazinam residues concentrate in peanut crude oil and soapstock. The Agency sets tolerances on refined (not crude) oil, and residues do not concentrate in this fraction. Peanut soapstock is no longer recognized as a significant animal feed item. Therefore, no 409/701 tolerances are necessary for this proposed use.

12a. The results of the radiolabeled goat metabolism study, which was conducted at the equivalent of 11 ppm in the feed, showed that no fluazinam was detected in any goat commodities at levels of 0.01 ppm or greater. Changes are underway to eliminate peanut hulls as a livestock feed item in Table II and allow the grazing/feeding of peanut hay to be restricted (see Conclusion 9a). The only remaining feed item, peanut meal, exhibited non-detectable residues (taken from peanut nutmeat residue data). Therefore, no meat or milk tolerances will be needed for this proposed EUP/temporary tolerance request.

12b. No poultry metabolism or feeding studies have been submitted. Since the only peanut item fed to poultry is meal, which exhibited no detectable residues of fluazinam, no additional studies will be required and no poultry or egg tolerances will be established for the purposes of this EUP/temporary tolerance request.

12c. The registrant is advised to send in the requested final peanut metabolism report as soon as it is ready. These results will be needed before the metabolism data can be presented to the HED Metabolism Committee. The decision of the Committee will impact the need for ruminant and/or poultry feeding studies for any future Section 3/permanent tolerance requests.

**Recommendations**

Until the deficiencies outlined in Conclusion 7c (availability of a reference standard) is satisfactorily resolved, CBTS cannot recommend in favor of the proposed temporary tolerance and EUP. However, a DRES run can be initiated using a residue level of 0.02 ppm for peanuts.

The deficiencies outlined in Conclusions 3, 5b, 6b, 7a, 7b, 9b, 10b, and 12d are intended to aid the registrant in fulfilling the data requirements for a future, Section 3 registration.

**Note to P.M.:**

CBTS recommends that the petitioner be given a copy of this complete review.

## Detailed Considerations

**The conclusions drawn in this memo are based on the tolerance expression including only the parent compound, fluazinam, in the regulation of any plant and animal commodity. If the HED Metabolism Committee concludes that the tolerance should include additional and/or different metabolites, additional data will need to be generated for the other sections of this memo.**

**New Data and Changes Not Cited in the 6/19/92 Memo**

In the current submission, the petitioner has submitted a rotational crop study that was not under the purview of CBTS when the original package was submitted. In addition, the petitioner has submitted a new proposed label. Since there were no deficiencies associated with these actions (as cited in the 6/19/92 memo of G.J. Herndon, these changes/additions will be addressed in the first part of the memo, and the previous deficiencies in the later part of the memo.

Proposed Use

The original EUP request was for the Fluazinam 50 WP formulation. A proposed label for a Fluazinam 500F formulation (a flowable formulation containing 4.17 lbs.ai./gal.) was provided with the current EUP request.

For control of Scleotinia blight, Southern blight, and/or limb rot, apply Fluazinam 500F at a rate of 1 to 1.5 pints/A. (0.52 to 0.78 lb.ai./A.) in sufficient water to obtain through coverage of stems and soil surface below crop canopy. Begin applying at 45-70 days after planting or when conditions become conducive to disease development and make a repeat application 3-4 weeks later. If disease conditions remain favorable, a third application may be made 3-4 weeks after the second, **provided that no more than 3 pints of Fluazinam 500F are applied per acre per growing season (1.6 lbs.ai./A./season).** The minimum PHI is 30 days. Do not graze treated areas or feed hay or threshings from treated fields to livestock.

Under this EUP use, 1000 acres in Alabama, Florida, Georgia, North Carolina, Oklahoma, Texas, and Virginia will be treated in 1995 and 1996 (2000 total acres), requiring a total of 3120 lbs.ai.

Comments

Changes are underway to eliminate peanut hulls as a livestock feed item in Table II and allow the grazing/feeding of peanut hay to be restricted (see Conclusion 9a). Therefore, the proposed label, which includes a restriction against grazing/feeding peanut hay, is appropriate.

Rotational Crop

"Fluazinam Technical: Confined Rotational Crop: Part 1", R. Robinson and S. Hoffman, Xeno Biotic Laboratories, Inc., 12/16/94 (MRID# 435210-11).

A confined rotational crop study was conducted using barley, carrots, and lettuce sown 30, 120, and 365 days post application and grown to maturity. The study was conducted using fluazinam labelled separately with carbon-14 in the phenyl ring and at the 2,6-positions of the pyridine ring of the molecule, similar to the plant and animal metabolism studies.

The rotational crop study was conducted using outdoor test plots. For each label, 3 plots, each 2 feet by 10 feet, were used.0 A separate plot was used for each of the three planting intervals, and contained each of the 3 plant types. Each plot received two broadcast spray applications (28 days apart) of the test material (a combination of labeled and unlabeled fluazinam) at 1

lb.ai./A./application, for a total of 2 lb.ai./A. (1.25X the proposed seasonal rate).

No crops were grown in the soil during the ageing period. The 30 DAT barley crop failed and was replanted 68 DAT. The samples were harvested according to Table 1.

Table 1

Summary of Rotational Crop Sampling Times

| crop | ageing period (days after test substance application) | harvest | |
|---|---|---|---|
| | | days after test substance application | days after sowing |
| immature lettuce | 30 | 68 | 38 |
| | 120 | 174 | 54 |
| | 365 | 455 | 90 |
| lettuce | 30 | 89 | 59 |
| | 120 | 244 | 124 |
| | 365 | 477 | 112 |
| immature carrots (roots and tops) | 30 | 99 | 69 |
| | 120 | 320 | 200 |
| | 365 | 509 | 144 |
| carrots (roots and tops) | 30 | 155 | 125 |
| | 120 | 355 | 235 |
| | 365 | 534 | 169 |
| barley (forage) | 30 (68)* | 68 (99)* | 38 (31)* |
| | 120 | 174 | 54 |
| | 365 | 420 | 55 |
| barley (straw and grain) | 30 (68)* | 138 (174)* | 108 (106)* |
| | 120 | 355 | 235 |
| | 365 | 449 | 84 |

* - Because of crop failure, barley planted at 30 DAT in the plot treated with [$^{14}$C-Phenyl]Fluazinam was replanted at 68 DAT.

The edible portions of the plant samples were ground and

aliquots were combusted to determine total radioactivity. The results are shown in Table 2.

Table 2

Summary of the TRR Found in Rotational Crops

| | | TRR (in ppm parent equivalents) by planting interval | | |
|---|---|---|---|---|
| label | commodity | 30 DAT | 120 DAT | 365 DAT |
| phenyl | lettuce (immature) | 0.318 | 0.470 | 0.104 |
| | lettuce | 0.282 | 0.174 | 0.040 |
| | carrot (immature tops) | 0.429 | 0.164 | 0.056 |
| | carrot (tops) | 0.349 | 0.223 | 0.040 |
| | carrot (immature roots) | 0.101 | 0.066 | 0.015 |
| | carrot (root) | 0.070 | 0.066 | 0.012 |
| | barley (forage) | 0.135 | 0.934 | 0.529 |
| | barley (straw) | 0.093 | 0.256 | 0.273 |
| | barley (grain) | 0.054 | 0.155 | 0.296 |
| pyridine | lettuce (immature) | 0.119 | 0.036 | 0.049 |
| | lettuce | 0.065 | 0.034 | 0.039 |
| | carrot (immature tops) | 0.333 | 0.045 | 0.059 |
| | carrot (tops) | 0.222 | 0.034 | 0.057 |
| | carrot (immature roots) | 0.087 | 0.036 | 0.010 |
| | carrot (root) | 0.045 | 0.024 | < 0.010 |
| | barley (forage) | 0.327 | 0.075 | 0.138 |
| | barley (straw) | 1.249 | 0.105 | 0.266 |
| | barley (grain) | 0.234 | 0.065 | 0.228 |

Crop samples containing radioactive residues greater than 0.010 ppm fluazinam equivalents (all samples except 365 DAT pyridine labeled carrot roots) were extracted three times with methanol/acetone. The fractions were combined and concentrated, resulting in an aqueous fraction. This fraction was partitioned with methylene chloride, resulting in three separate phases (methylene chloride, aqueous and post extraction solids (PES)). The TRR was determined by HPLC/LSC (the PES fraction was combusted

prior to analysis). The results are shown in Tables 3 and 4.

Table 3

Concentrations of Radioactivity* in Various Fractions from Edible Crop Samples After Treatment of Soil with **[$^{14}$C-Phenyl]Fluazinam**

| | | 30 DAT | | 120 DAT | | 365 DAT | |
|---|---|---|---|---|---|---|---|
| commodity | fraction | ppm | % | ppm | % | ppm | % |
| lettuce | $CH_2Cl_2$ | < 0.001 | 0 | 0.003 | 2 | 0.002 | 6 |
| | aqueous | 0.267 | 95 | 0.163 | 94 | 0.025 | 62 |
| | PES | 0.015 | 5 | 0.008 | 5 | 0.013 | 32 |
| carrot (root) | $CH_2Cl_2$ | 0.007 | 10 | 0.006 | 9 | 0.003 | 28 |
| | aqueous | 0.057 | 82 | 0.052 | 78 | 0.006 | 48 |
| | PES | 0.006 | 8 | 0.008 | 13 | 0.003 | 29 |
| barley (grain) | $CH_2Cl_2$ | 0.004 | 8 | 0.004 | 2 | 0.011 | 4 |
| | aqueous | 0.023 | 41 | 0.117 | 75 | 0.175 | 59 |
| | PES | 0.027 | 51 | 0.034 | 22 | 0.110 | 37 |

* - expressed as $\mu$g fluazinam equivalents/g fresh weight

Table 4

Concentrations of Radioactivity* in Various Fractions from Edible Crop Samples After Treatment of Soil with **[$^{14}$C-Pyridine]Fluazinam**

| | | 30 DAT | | 120 DAT | | 365 DAT | |
|---|---|---|---|---|---|---|---|
| commodity | fraction | ppm | % | ppm | % | ppm | % |
| lettuce | $CH_2Cl_2$ | 0.006 | 9 | 0.003 | 10 | 0.003 | 8 |
| | aqueous | 0.031 | 49 | 0.014 | 43 | 0.017 | 43 |
| | PES | 0.028 | 43 | 0.013 | 38 | 0.019 | 49 |
| carrot (root) | $CH_2Cl_2$ | 0.006 | 14 | 0.003 | 14 | N/A | - |
| | aqueous | 0.025 | 55 | 0.015 | 60 | N/A | - |
| | PES | 0.014 | 31 | 0.006 | 26 | N/A | - |
| barley (grain) | $CH_2Cl_2$ | 0.009 | 4 | 0.003 | 4 | 0.011 | 5 |
| | aqueous | 0.012 | 5 | 0.017 | 27 | 0.046 | 20 |
| | PES | .213 | 91 | 0.045 | 69 | 0.171 | 75 |

* - expressed as $\mu$g fluazinam equivalents/g fresh weight

The registrant chose the aqueous fraction from the 174 phenyl-labeled DAT barley forage sample (due to the large amount of sample available and its relatively high radioactivity) to try to determine the nature of the polar residue. The fraction was subjected to C-18 solid-phase extraction and preparative HPLC using both reversed-phase and animo columns. Based on these analyses, the registrant believed that the $^{14}C$ residues appeared to be one compound. The registrant acidified the purified aqueous fraction, extracted it with ether, and analyzed by GC/MS and HPLC. These techniques indicated the presence of the single metabolite [$^{14}C$]trifluoroacetic acid ([$^{14}C$]-TFA).

Based on similar HPLC profiles, the registrant believes that the aqueous extracts from the phenyl-labeled lettuce, carrot and barley grain samples is also composed exclusively of [$^{14}C$]-TFA.

Comments

The results of the confined rotational crop study show that major degradation of the fluazinam molecule occurs in soil. **No fluazinam or any other metabolite with the intact fluazinam nucleus was detected in any of the rotational plant commodities, from even the shortest rotation interval**, suggesting that it is rapidly cleaved and/or not translocated.

In most cases, a majority of the radioactivity from the edible portion of the rotational crops (see Tables 3 and 4) was found in the aqueous fraction (some of the barley samples exhibited a high percentage of bound radioactivity). Very little radioactivity was found in the methylene chloride fraction (up to 8% in barley grain, 10% in lettuce, and 28% in carrot roots), where metabolites containing the intact fluazinam nucleus would be expected to be located.

Work-up of the phenyl-labeled aqueous fractions indicated that the radioactivity eluted early (4-5 minutes), the majority of which eluted in a single band, which was identified as [$^{14}C$]trifluoroacetic acid. The pyridine-labeled aqueous fractions exhibited late-eluting radioactivity (15-20 minutes), indicating different metabolism pathways between the two labels. No metabolites from the pyridine-labeled aqueous fractions were identified.

CBTS requests that the registrant explain the unusually long maturity times for some of crops sown 120 and 365 DAT (i.e. carrots requiring 235 days to mature and lettuce taking 124 days). This requirement can be deferred until a petition for a permanent tolerance is submitted.

The proposed label does not mention any rotational crops or

plant-back intervals. For the purposes of this EUP and temporary tolerance request, the tolerance expression will include the parent compound, fluazinam, only. Therefore, based on the results of this confined rotational crop showing that no parent compound was detected in any plant commodities, having no rotational crop restrictions seems appropriate. For a future, permanent tolerance request, these conclusions and their impact on any future requirements are subject to review by the HED Metabolism Committee.

**Previous Deficiencies**

The Deficiencies listed below were cited by CBTS in the 6/19/92 memo of G.J. Herndon concerning PP#2G04099.

Deficiency 2 from the 6/19/92 Memo

The product chemistry data submitted are not adequate to fulfill the requirements for this temporary tolerance request. For the purposes of this temporary tolerance request, the deficiencies cited in sections 61-1, 61-2, 61-3, 62-1, 62-2, and 62-3 (see Attachments III and IV) need to be addressed. The additional comments on the physical and chemical characteristics (sections 63-2 through 63-20), etc. are intended to aid the petitioner in fulfilling the requirements of a future, permanent tolerance.

Registrant's Response to Deficiency 2

The registrant has submitted additional data that addresses the Deficiencies outlined in 61-3, 63-12, 63-13, and 63-17.

CBTS's Comments and Conclusions to Deficiency 2

The submitted data are adequate to fulfill 61-3, 63-12, and 63-13.

For a future, permanent tolerance request, additional data will be needed to fulfill 61-1, 61-2, 62-2, 62-3, and 63-17.

For the purposes of this EUP/temporary tolerance request, **deficiency 2 has been resolved.**

Deficiencies 3a and 3b from the 6/19/92 Memo

The submitted plant metabolism data on potatoes were not adequate to define the nature of the residue in potatoes (nor in peanuts, or plants in general). A combination of a low dose of radioactivity in the applied fluazinam, and less than exhaustive attempts made at characterizing the residue, resulted in less than 3% of the TRR being identified. Therefore:

a). a plant metabolism study should be conducted on peanuts, using sufficiently high radioactivity levels in the

applied fluazinam (separate studies for nitrophenyl and pyridyl ring labeled material) to allow characterization of the total radioactive residue (TRR).

and

b). more thorough and definitive procedures must be employed to identify the individual components of the TRR.

Registrant's Response to Deficiencies 3a and 3b

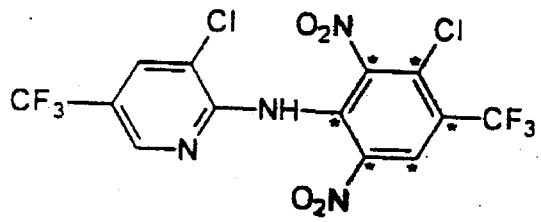
The registrant has submitted a **interim** peanut metabolism study.

"Fluazinam Technical: A Peanut Plant Metabolism Study", D.A. Hartman, 12/21/94, Ricerca, Inc., MRID# 435210-18.

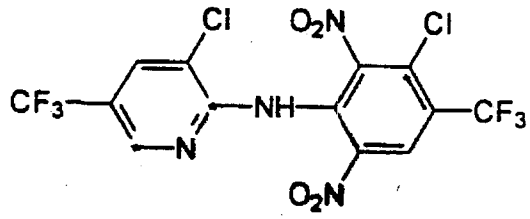
Set-up

A plant metabolism study on peanuts was submitted. Two different isotopically labeled forms of fluazinam (IKF-1216) were used to study the metabolic fate of each moiety: $^{14}$C-phenyl-labeled IKF-1216 (designated as $^{14}$C(B)-IKF-1216) and $^{14}$C-pyridyl-labeled IKF-1216 (designated as $^{14}$C(Py)-IKF-1216), as shown in Figure 1.

Figure 1




$^{14}$C(B)-IKF-1216




$^{14}$C(Py)-IKF-1216

The peanut plants (variety Florunner) were grown in troughs in a fences confine using a loamy sand soil. In 1992, eleven plants were grown in each of 3 troughs (1 control, 1 phenyl-labeled, and 1 pyridyl-labeled). In 1993 and 1994, twenty-seven were grown in each of 4 troughs (3 treated, 1 untreated). Due to cold weather (and resulting slow maturity) of the 1992 study, portable greenhouses were used in the 1993 and 1994 studies and supplemental

lighting was used in the 1994 study. The equivalent of a 40% F formulation of the test substance was made by combining labeled and unlabeled IKF-1216 with surfactant. The plants were covered with plastic sheeting prior to application of the test substance using an aerosol sprayer. The plastic sheeting was left on for one day after each treatment. The test substance was applied 4 times during the growing season at the rate of 0.44 lb.ai/A./application or 1.8 lb.ai./A./season (about 1X the proposed rate). In the 1992 trial, three intermediate harvests were made prior to the final, mature stage. The registrant claims this was done to develop methodology which could be used on the final samples. Other than the intermediate harvests made on the 1992 crop, the crops were harvested at maturity. Samples of peanut foliage, nutmeat, and shell were harvested and analyzed separately.

Initial Analysis

The foliage and shells were initially rinsed (methanol and water) before homogenization, and the rinsates analyzed. In most cases, the ground RAC's were combusted and analyzed by liquid scintillation counting (LSC).

Extraction, Fractionation, and Analysis of Radioactive Residues

Each of the sample matrices was initially extracted with aqueous acetonitrile. Then various solvents and reagents were used to separate the initial extract into different fractions (various acidic, neutral, and basic aqueous and organic layers). These fractions were then analyzed using HPLC and a liquid scintillation counter (LSC). The retention times of the various peaks were compared to those of standards, and confirmed using various instrumentation (HPLC/UV, HPLC/PIC, HPLC/MS, HPLC/RAD, FAB/MS, and GC/MS) and techniques such as methylation, ethylation, and acetylation, as well as acid and base hydrolysis. Some of the matrices containing enough unextracted radioactive residue were subjected to soxhlet extractions, acid hydrolysis, base hydrolysis, α-amylase, and/or cellulase.

Various solvent systems (80% acetonitrile/water, acetonitrile, water, hexane, and methylene chloride) were used to extract/fractionate the radioactivity from the three crop matrices. These fractions were then analyzed using HPLC ($C_8$, phenyl, and CN columns) and a liquid scintillation counter (LSC). The retention times of the various peaks were compared to those of standards, and confirmed using various instrumentation (HPLC/UV, NMR, LC/MS (both EI and CI), LC/MS/MS, and GC/FID) and techniques such as methylation, as well as acid, base, and enzyme hydrolysis. The results of the analyses are shown in Table 5.

Table 5

TRR Levels in Peanut Commodities

| Test Substance | Commodity | Year | Radioactivity (ppm of parent equivalents) |
|---|---|---|---|
| phenyl | foliage | 1992 | 9.43 |
| | | 1992* | 11.4 |
| | | 1993 | 25.6 |
| | shells | 1992 | 0.73 |
| | | 1992* | 0.86 |
| | | 1993 | 0.77 |
| | nuts | 1992 | 0.24 |
| | | 1992* | 0.26 |
| | | 1993 | 0.73 |
| pyridyl | foliage | 1992 | 8.82 |
| | | 1992* | 21.3 |
| | | 1994 | 30.7 |
| | shells | 1992 | 1.43 |
| | | 1992* | 1.13 |
| | | 1994 | 4.30 |
| | nuts | 1992 | 0.36 |
| | | 1992* | 0.50 |
| | | 1994 | 1.19 |

* - Sample taken from the interim harvest after the 3rd application (before normal maturity)

CBTS's Comments and Conclusions to Deficiencies 3a and 3b

While the submitted peanut metabolism study is only interim, the reviewer had questions concerning the presentation of the data. The registrant had not provided a complete residue profile outlining and tabulating (% and ppm) the identified, unidentified extractable, and unextractable radioactivity. A meeting with the registrant was held on 6/13/95. The registrant committed to providing this additional data, as well as a proposed degradation scheme outlining the speculated steps from parent compound to natural incorporation, in the final report.

No parent compound and related compounds were detected in the peanut nutmeats at levels of 0.01 ppm or greater. Radioactivity was tentatively shown to be incorporated into sucrose and fatty acids, and is also believed to incorporated into proteins. In the peanut hulls, the parent compound was identified only in the intermediate 1992 harvest from the pyridyl-labeled hulls. In the peanut foliage samples, the parent compound, AMPA, and TFA (trifluroacetic acid) were found.

For the purposes of this EUP and temporary tolerance request, the submitted peanut metabolism study is acceptable. The tolerance expression will include the parent compound, fluazinam, only. For a future, permanent tolerance request, the additional data/information listed above should be provided. For a permanent tolerance request, any conclusions drawn by CBTS are subject to review by the HED Metabolism Committee.

For the purposes of this EUP/temporary tolerance request, **Deficiencies 3a and 3b have been resolved.**

Deficiency 3c from the 6/19/92 Memo

The type of organic solvent used in the organic/aqueous partition in Procedure 2 was not specified. The petitioner should provide information on all the solvents used.

Registrant's Response to Deficiency 3c

No response was provided.

CBTS's Comments and Conclusions to Deficiency 3c

No response is necessary. The registrant has submitted a new plant metabolism study on peanuts (see Registrant's Response to Deficiencies 3a and 3b). **Deficiency 3c has been resolved.**

Deficiency 4 from the 6/19/92 Memo

No animal metabolism studies were submitted. In the absence of residue data on peanut hulls, CBTS cannot draw any conclusions on the need for tolerances for cattle meat and meat by-products (see section on Meat, Milk, Poultry, and Eggs), and therefore on the need for animal metabolism studies. For the purposes of this temporary tolerance request, a ruminant metabolism study may not be needed if no residues are detected in the peanut hulls. If measurable residues are found in the peanut hulls, the petitioner will need to perform an animal metabolism study on a representative lactating ruminant, and conducted using both nitrophenyl ring and pyridyl ring labeled $^{14}C$ fluazinam, separately.

Registrant's Response to Deficiency 4

The registrant has submitted two volumes of a ruminant metabolism study.

"Fluazinam Technical: Nature of the Residue in Lactating Goats: I", T. Cheng, 6/3/94, Hazleton Wisconsin, Inc., MRID# 435210-19.

and

"Fluazinam Technical: Nature of the Residue in Lactating Goats: II", T. Cheng, 12/14/94, Hazleton Wisconsin, Inc., MRID# 435210-20.

Set-up and Dosing

Two lactating goats were given capsules containing $^{14}C$-fluazinam orally for 4 consecutive days. Two different test materials were used; one containing phenyl ring-labeled $^{14}C$-fluazinam (57 mCi./mmole), and the other containing pyridyl ring-labeled $^{14}C$-fluazinam (47 mCi./mmole). Each of the test substances was dissolved into acetonitrile and checked for radioactive concentration. Enough of this solution was added to gelatin capsules in order to have 20 mg. of $^{14}C$-fluazinam in each capsule. Controls were prepared with acetonitrile only. In all cases, the acetonitrile was evaporated before the capsules were sealed.

The goats used were all at least 2 years old, in at least their second lactation, and weighed between 53 and 65 kg. each. Three total animals were used; one served as a control, one was fed phenyl-labeled test material, and one was fed pyridyl-labeled test material. The animals were fed a grain based diet at the rate of 1 kg./animal/day, and allowed to consume alfalfa grass hay and tap water ad libitum. The capsules were administered orally at the rate of 1 capsule per day for 4 consecutive days. Based on the average animal weight of 60 kg., this total dose is equivalent to about 1.3 mg./kg.body weight. In terms of feeds (animals fed labeled material consumed about 1.8 kg. of food per day), this dose is equivalent to about 11 ppm in the feed. All animals appeared healthy throughout the study.

Sample Collection

The animals were hand milked twice each day and the milk weighed after each milking. Total excretion of urine and feces was collected and weighed twice a day. Urine and feces produced after the Day 4 p.m. collection, but before sacrifice, were collected and labeled as Day 4 (sacrifice) collection.

At approximately 23 hours after the last dose, a sample of heparinized blood was taken from each animal by venipuncture. The animals were then sacrificed using a captive-bolt pistol and

exsanguination. The following samples were collected: muscle (round), liver (entire), kidneys (both), fat (renal and omental), bile (from the gallbladder), urine (from the bladder), and GI tract and contents (treated animals only).

Initial Analysis

The various samples were homogenized and either counted directly by liquid scintillation counting (LSC) or combusted, with the resulting $^{14}CO_2$ counted by LSC. The petitioner claimed a limit of detection by LSC of 0.001 ppm. The total recovery of radioactivity in the samples collected for analysis is summarized in Table 6.

Table 6

Percent of Total Radioactivity in Each Matrix of Lactating Goats

| | Percent of Radioactive Dose | | |
|---|---|---|---|
| Matrix | Control | Phenyl-Labeled Fluazinam | Pyridyl-Labeled Fluazinam |
| Blood | NA | < 0.01 | < 0.01 |
| Milk | NA | 0.31 | 0.59 |
| Tissues (includes bile) | NA | 1.80 | 2.40 |
| Feces | NA | 66.18 | 62.37 |
| GI tract contents | NA | 9.04 | 10.51 |
| Urine (includes cage wash and wipe) | NA | 8.91 | 11.55 |
| Total | NA | 86.24 | 87.42 |

NA : not applicable

Tables 7 and 8 list the results of the analysis of the milk (Table 7) and the blood, bile, and tissue (Table 8) samples in the goat studies.

Table 7

Concentrations of Radioactivity in Milk of Lactating Goats

| | μg equivalents $^{14}$C-fluazinam/g | | |
|---|---|---|---|
| Collection Time | Control | phenyl-labeled | pyridyl-labeled |
| Day 1 am | NA | NA | NA |
| Day 1 pm | NA | 0.046 | 0.060 |
| Day 2 am | NA | 0.018 | 0.018 |
| Day 2 pm | NA | 0.048 | 0.070 |
| Day 3 am | NA | 0.021 | 0.021 |
| Day 3 pm | NA | 0.062 | 0.071 |
| Day 4 am | NA | 0.020 | 0.022 |
| Day 4 pm | NA | 0.071 | 0.078 |
| Day 4 (sacrifice) | NA | 0.032 | 0.028 |

NA : not applicable

Table 8

Concentrations of Radioactivity in Blood, Bile, and Tissues of Lactating Goats

| | μg equivalents $^{14}$C-fluazinam/g | | |
|---|---|---|---|
| Matrix | Control | phenyl-labeled | pyridyl-labeled |
| Blood | NA | 0.015 | 0.049 |
| Bile | NA | 4.660 | 2.901 |
| Fat (omental and renal) | NA | 0.160 | 0.262 |
| GI tract | NA | 0.152 | 0.125 |
| Kidneys | NA | 0.034 | 0.060 |
| Liver | NA | 0.470 | 0.852 |
| Muscle (round) | NA | 0.035 | 0.025 |

NA : not applicable

Extraction, Cleanup, and Analysis of Radioactive Residues

Samples of liver, kidney, and muscle were homogenized with acetonitrile:water (1:1). The supernatant was partitioned with saturated aqueous sodium chloride. The organic phase was concentrated using nitrogen; the aqueous phase was lyophilized and reextracted with methanol containing 1% trichloroacetic acid. The two fractions were recombined before analysis.

Samples of fat were homogenized with acetonitrile:water (1:1) and hexane. The hexane and interface (containing the non-extractable solids) layers were removed and the acetonitrile:water phase was partitioned with saturated aqueous sodium chloride. Both the organic and aqueous fractions were concentrated before analysis. The hexane phase was heated, filtered, and concentrated prior to anaylsis.

Samples of milk were homogenized with acetonitrile and centrifuged. The resulting pellets were homogenized with acetonitrile:water (1:1) and centrifuged. Saturated aqueous sodium chloride was added to the combined supernatants, the mixture centrifuged, and the organic layer was concentrated before analysis.

Additional enzyme treatment (liver and kidney) and acid hydrolysis (liver) were performed on the non-extractable fractions of these matrices.

Analysis of samples was performed by HPLC using UV and LSC detectors, and confirmed by TLC. The results of these analyses are found in Tables 9 and 10 (refer to Attachment I for the names and structures of the compounds).

Table 9

Metabolites Detected by HPLC in Samples from Goats Using Phenyl-Labeled $^{14}$C-Fluazinam

| | Matrix (Total Radioactive Residue) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Liver | | Kidney | | Muscle | | Fat | | Milk | |
| Component | % of $^{14}$C | ppm | % of $^{14}$C | ppm | % of $^{14}$C | ppm | % of $^{14}$C | ppm | % of $^{14}$C | ppm |
| Fluazinam | ND | NA | ND | NA | ND | NA | ND | NA | ND | NA |
| DAPA | 12.5 | 0.059 | 15.3 | < 0.01 | 17.5 | < 0.01 | 49.2 | 0.078 | 30.3 | 0.021 |
| AMPA | ND | NA | 3.7 | < 0.01 | 20.1 | < 0.01 | 34.9 | 0.055 | 37.9 | 0.026 |
| DAPA Sulfamate 1 | 2.7 | 0.013 | 3.8 | < 0.01 | ND | NA | ND | NA | ND | NA |
| DAPA Sulfamate 2 | 2.7 | 0.013 | 6.5 | < 0.01 | ND | NA | ND | NA | 4.2 | < 0.01 |
| unk. DAPA conjugate | 3.6 | 0.017 | 20.1 | < 0.01 | 4.4 | < 0.01 | ND | NA | 3.8 | < 0.01 |
| AMPA sulfamate | 6.3 | 0.030 | 10.1 | < 0.01 | ND | NA | ND | NA | 11.5 | < 0.01 |
| **Subtotal** | **27.8** | **0.131** | **59.5** | **0.020** | **42.0** | **0.015** | **84.1** | **0.134** | **87.7** | **0.0576** |
| Uncharacterized Extractable | 8 | 0.038 | 5.1 | < 0.01 | 18.3 | < 0.01 | 8.4 | 0.013 | 3.5 | < 0.01 |
| Nonextractable | 64.2 | 0.302 | 35.4 | 0.012 | 39.7 | 0.014 | 7.5 | 0.012 | 8.8 | < 0.01 |
| TOTAL | 100 | 0.470 | 100 | 0.034 | 100 | 0.035 | 100 | 0.160 | 100 | 0.0657 |

ND : not detectable
NA : not applicable

Table 10

Metabolites Detected by HPLC in Samples from Goats Using Pyridyl-Labeled $^{14}$C-Fluazinam

| | Matrix (Total Radioactive Residue) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Liver | | Kidney | | Muscle | | Fat | | Milk | |
| Component | % of $^{14}$C | ppm | % of $^{14}$C | ppm | % of $^{14}$C | ppm | % of $^{14}$C | ppm | % of $^{14}$C | ppm |
| Fluazinam | ND | NA | ND | NA | ND | NA | ND | NA | ND | NA |
| DAPA | 8.7 | 0.074 | 8.8 | < 0.01 | 16.8 | < 0.01 | 28.3 | 0.074 | 26.4 | 0.019 |
| AMPA | 7.5 | 0.064 | 6.8 | < 0.01 | 26.3 | < 0.01 | 48.6 | 0.126 | 50.9 | 0.037 |
| DAPA Sulfamate 1 | 1.5 | 0.013 | 2.2 | < 0.01 | ND | NA | ND | NA | ND | NA |
| DAPA Sulfamate 2 | 3.1 | 0.026 | 8.4 | < 0.01 | ND | NA | ND | NA | 3.4 | < 0.01 |
| unk. DAPA conjugate | ND | NA | 15.9 | 0.010 | 5.7 | < 0.01 | ND | NA | 3.4 | < 0.01 |
| AMPA sulfamate | 5.5 | 0.047 | 19.0 | 0.011 | ND | NA | ND | NA | 13.7 | 0.01 |
| **Subtotal** | **26.3** | **0.224** | **61.1** | **0.037** | **48.8** | **0.012** | **76.9** | **0.201** | **97.8** | **0.061** |
| Uncharacterized Extractable | 15.4 | 0.131 | 4.2 | < 0.01 | 4.2 | < 0.01 | 18.6 | 0.049 | 0 | < 0.01 |
| Nonextractable | 58.3 | 0.497 | 34.7 | 0.022 | 47.0 | 0.012 | 4.5 | 0.012 | 3.0 | < 0.01 |
| TOTAL | 100 | 0.852 | 100 | 0.060 | 100 | 0.025 | 100 | 0.262 | 100.8 | 0.062 |

ND : not detectable
NA : not applicable

The non-extractable fraction of some of the liver and kidney samples were subjected to enzyme and acid hydrolysis, which released and additional 31-96% of the radioactivity.

CBTS's Comments and Conclusions to Deficiency 4

No fluazinam was detected in any goat commodities at levels of 0.01 ppm or greater. The major metabolites identified were DAPA, AMPA, and various sulfamated derivatives of these two compounds. Based on the metabolites identified, the metabolism of fluazinam appears to involve the reduction of the one or both of the two nitro groups attached to phenyl ring of the fluazinam molecule. The proposed pathway involves the formation of mono-amino derivatives (AMPA), which subsequently undergoes further reduction to di-amino derivatives (DAPA) and/or sulfamate conjugates. The initial degradation does not appear to involve cleavage of the pyridine and

phenyl rings (the metabolites detected all contained the intact fluazinam nucleus).

The nature of the residue in ruminants is adequately elucidated. For the purposes of this EUP/temporary tolerance request, the tolerance expression will include the parent compound, fluazinam, only. Pending review by the HED Metabolism Committee, other metabolites may need to be included in the tolerance expression for a future, permanent tolerance request.

For a future Section 3 registration, the registrant will need to submit a poultry metabolism study.

**Deficiency 4 has been resolved.**

Deficiency 5a from the 6/19/92 Memo

The submitted method recoveries were not validated by another laboratory. Independent lab validation is required prior to any approval of a temporary tolerance (PR 88-5). EPA laboratory validation of the method will be initiated upon receipt of the independent lab validation.

Registrant's Response to Deficiency 5a

The registrant has submitted 2 volumes:

"Fluazinam: Method for the Analysis in Peanut Nut Meat", R.G. Kenyon, 9/22/94, Ricerca, Inc. (MRID# 435210-16)

and

"Fluazinam: Independent Laboratory Validation of Method for the Analysis in Peanut Nut Meat", D.A. Thiem, 12/21/94, Colorado Analytical R&D Corp. (MRID# 435210-17)

The analytical method supplied with this submission is essentially the same as that reviewed in the previous submission (see memo of G.J. Herndon dated 6/19/92). The registrant has provided additional recovery data that is associated with new field trial data. Both the previous recoveries (reviewed in the 6/19/92 memo) and new ones are supplied in Table 11.

- Table 11

Recovery of Fluazinam from Fortified Peanut Nutmeats

| Submission | Spike level (ppm) | Recovery |
|---|---|---|
| original | 0.01 | 78% |
| | 0.01 | 90% |
| | 0.01 | 93% |
| | 0.01 | 119% |
| | 0.06 | 82% |
| | 0.10 | 84% |
| | 0.20 | 90% |
| | 0.30 | 90% |
| | 0.50 | 90% |
| | 1.0 | 95% |
| current | 0.01 | 88% |
| | 0.01 | 75% |
| | 0.01 | 91% |
| | 0.01 | 92% |
| | 0.05 | 72% |
| | 0.05 | 74% |
| | 0.05 | 82% |
| | 0.10 | 98: |
| | 1.0 | 107% |

The method has also undergone independent lab method validation at Colorado Analytical R&D Corporation. The results are shown in Table 12.

Table 12

Independent Lab Recoveries of Fluazinam from Peanut Nutmeats

| Spike level (ppm) | Recovery |
|---|---|
| 0.01 | 56% |
| 0.01 | 68% |
| 0.02 | 99% |
| 0.02 | 101% |
| 0.05 | 112% |
| 0.05 | 102% |

In their discussion of the method, Colorado Analytical R&D Corporation noted that the low recoveries for the 0.01 ppm fortification level were due to an interference peak, that also showed up in the controls at about 0.008 ppm. They claim that the method is not suited for the determination of fluazinam below 0.02 ppm in peanut nutmeat containing high levels of interfering peaks. They believe that the method can be improved in the Florisil cleanup step.

CBTS's Comments and Conclusions to Deficiency 5a

For the purposes of this EUP/temporary tolerance request, the proposed method is adequate. An independent laboratory validation (ILV) has ben submitted. The independent lab believes the method can be improved in the Florisil cleanup step. The registrant may wish to make any modifications/improvements to the method prior to the Beltsville lab validation.

The petitioner is reminded that, for a permanent tolerance on a food use chemical, data on whether the FDA/USDA multi-residue methodology will detect and identify fluazinam are required (see 40 CFR 158.240).

**Deficiency 5a has been resolved.**

Deficiency 6 from the 6/19/92 Memo

No storage stability data were provided with this petition. The residue samples were stored up to 42 days between harvest and extraction. Storage stability data should be provided corresponding to the total length of time the samples were stored (harvest to analysis).

Registrant's Response to Deficiency 6

The registrant has provided the following study:

"Fluazinam: Determination of Fluazinam in Treated Peanuts - 1991. Amendments to MRID# 42270614", R.G. Kenyon, 2/22/93, 5/5/93, Ricerca, Inc. (MRID# 435210-13)

Untreated control peanut nutmeat samples were spiked to yield a fortification level of 0.25 ppm. Samples were stored at temperatures of -10°F to 10°F and up to 190 days before analysis. The results of the study are shown in Table 13.

Table 13

Storage Stability Recoveries for Peanut Nutmeat Samples

| | Recoveries (%) | |
|---|---|---|
| Days in Storage | Uncorrected for Method Recovery | Corrected for Method Recovery |
| 0 | 92 | 100 |
| 29 | 80 | 105 |
| 60 | 84 | 91 |
| 88 | 80 | 80 |
| 102 | 84 | 81 |
| 190 | 80 | 77 |

CBTS's Comments and Conclusions to Deficiency 6

The data shown in Table 13 are adequate to show that fluazinam (parent compound only) is stable in the frozen peanut nutmeat matrix for periods up to 6⅓ months. For the purposes of this EUP request, the submitted storage stability data are adequate. Also, if the additional field trial samples requested are held more than 190 days between harvest and analysis, additional storage stability data covering this longer interval will be needed.

**Deficiency 6 has been resolved.**

Deficiency 7b from the 6/19/92 Memo

The dates of sample analyses were not listed, so CBTS does not know how much time the samples were held between extraction and analysis. These analysis dates should be provided, as well as storage stability data for the total length of time the RAC samples

and extracts were stored (see Conclusion 6).

Registrant's Response to Deficiency 7b

No response was provided.

CBTS's Comments and Conclusions to Deficiency 7b

Sample harvest and analysis dates were provided with the new field trial data in the current submission. The samples from the new field trials were stored up to 151 days from sampling to analysis. This time period is covered by the 190 day storage stability data on peanut nutmeats.

**Deficiency 7b has been resolved.**

Deficiency 7c from the 6/19/92 Memo

No residue data on peanut hulls were provided with this petition. A label restriction against feeding peanut hulls to cattle is not practical since hulls are not under grower control. In the absence of residue data on peanut hulls, CBTS cannot draw any conclusions on the need for tolerances for cattle meat and meat by-products (see Conclusion 8). The petitioner should provide residue data on peanut hulls.

Registrant's Response to Deficiency 7c

The registrant has provided the following study:

"Fluazinam: Magnitude of the Residue in Peanuts - 1993", P. Hayes and R. Kenyon, Ricerca Inc., 8/5/94 (MRID# 435210-15).

The registrant has provided new field trial residue data on peanut nutmeats, hulls, and hay conducted in three different sites in 1993. In all but the banded application from 1 trial, rates were approximately 0.7 lb.ai./A./application (0.90X the proposed rate) for a total of approximately 2.1 lb.ai./A./season (1.3X the proposed rate). The results are shown in Tables 14, 15, and 16.

Table 14

Residue Summary of Fluazinam Residues in/on Peanut **Nutmeats**

| location | method of application | # applications | rate (lbs.ai./A.) average | rate (lbs.ai./A.) final application | rate (lbs.ai./A.) total | PHI (days) | maximum total residues in ppm* Total |
|---|---|---|---|---|---|---|---|
| Waller County, TX | broadcast | 3 | 0.705 | 0.702 | 2.11 | 29 | < 0.01 |
| | | | | | | | < 0.01 |
| | banded | 3 | 0.712 | 0.711 | 2.14 | 29 | < 0.01 |
| | | | | | | | < 0.01 |
| Skippers, VA | broadcast | 3 | 0.676 | 0.705 | 2.03 | 30 | < 0.01 |
| | | | | | | | < 0.01 |
| | banded | 3 | 0.705 | 0.695 | 2.12 | 30 | < 0.01 |
| | | | | | | | < 0.01 |
| Shorterville, AL | broadcast | 3 | 0.697 | 0.694 | 2.09 | 28 | < 0.01 |
| | | | | | | | < 0.01 |
| | banded | 3 | 0.368 | 0.398 | 1.11 | 28 | < 0.01 |
| | | | | | | | < 0.01 |

* - uncorrected for method and storage recoveries

Table 15

Residue Summary of Fluazinam Residues in/on Peanut **Hulls**

| location | method of application | # applications | rate (lb.ai./A.) average | rate (lb.ai./A.) final application | rate (lb.ai./A.) total | PHI (days) | maximum total residues in ppm* Total |
|---|---|---|---|---|---|---|---|
| Waller County, TX | broadcast | 3 | 0.705 | 0.702 | 2.11 | 29 | 0.10 |
| | | | | | | | 0.09 |
| | banded | 3 | 0.712 | 0.711 | 2.14 | 29 | 0.17 |
| | | | | | | | 0.18 |
| Skippers, VA | broadcast | 3 | 0.676 | 0.705 | 2.03 | 30 | 0.04 |
| | | | | | | | 0.03 |
| | banded | 3 | 0.705 | 0.695 | 2.12 | 30 | 0.05 |
| | | | | | | | 0.05 |
| Shorterville, AL | broadcast | 3 | 0.697 | 0.694 | 2.09 | 28 | 0.02 |
| | | | | | | | 0.02 |
| | banded | 3 | 0.368 | 0.398 | 1.11 | 28 | 0.01 |
| | | | | | | | 0.01 |

* - uncorrected for method and storage recoveries

Table 16

Residue Summary of Fluazinam Residues in/on Peanut **Hay**

| location | method of application | # applications | rate (lb.ai./A.) average | rate (lb.ai./A.) final application | rate (lb.ai./A.) total | PHI (days) | maximum total residues in ppm* Total |
|---|---|---|---|---|---|---|---|
| Waller County, TX | broadcast | 3 | 0.705 | 0.702 | 2.11 | 29 | 0.29 |
| | | | | | | | 0.30 |
| | banded | 3 | 0.712 | 0.711 | 2.14 | 29 | 0.39 |
| | | | | | | | 0.45 |
| Skippers, VA | broadcast | 3 | 0.676 | 0.705 | 2.03 | 30 | 1.54 |
| | | | | | | | 1.46 |
| | banded | 3 | 0.705 | 0.695 | 2.12 | 30 | 1.77 |
| | | | | | | | 2.01 |
| Shorterville, AL | broadcast | 3 | 0.697 | 0.694 | 2.09 | 28 | 0.20 |
| | | | | | | | 0.22 |
| | banded | 3 | 0.368 | 0.398 | 1.11 | 28 | 0.07 |
| | | | | | | | 0.07 |
| | | | | | | | 0.23 |
| | | | | | | | 0.27 |

* - uncorrected for method and storage recoveries

CBTS's Comments and Conclusions to Deficiency 7c

Based on recent data the Agency has received, peanut hulls are no longer routinely fed to livestock and, based on current practices, a restiction against feeding peanut hay is practical. These changes will be incorporated into an updated Table II (to be released shortly). Therefore, the current Section F that proposes a temporary tolerance for peanut nutmeats at 0.020 ppm (no temporary tolerances are proposed for either peanut hulls or peanut hay) and Section B which includes a restriction against grazing/feeding peanut hay are appropriate.

Based on the 6/2/94 Field Trial Document, a total of 12 field trial sites (9 if no residues are detected) are required for the registration of a new pesticide on peanuts. Since the registrant is pursuing a grazing/feeding restriction for peanut hay, peanut hulls will not appear as a livestock feed item in the newly updated Table II (see Conclusion 9a), and no detectable residues occurred on peanut nutmeats from previous trials, data from a total of 9 field trials on peanut nutmeats (assuming no detectable residues are found in future trials as well) will have to be submitted **prior to a permanent tolerance request.** In the current submission, field

trial data for both banded and broadcast applications from three different sites was submitted. Provided the questions concerning the field trial data of the original submission (see review of G.J. Herndon dated 6/19/92) are adequately resolved, these three additional field trial sites can be counted toward the 9 required. Based on the generally higher residues (in peanut hay and hulls) in the banded (rather than broadcast) side-by-side trials, if the registrant wants a registration for both uses, the additional 3 trial sites can be conducted using the **banded application only.** The location of these trials is outlined in the 6/2/94 Field Trial Document.

For the purposes of the proposed EUP/temporary tolerance request, **Deficiency 7c has been resolved.**

Deficiency 7d from the 6/19/92 Memo

Chromatograms of the standards that were analyzed with the samples were not provided. Without the standard chromatograms, CBTS cannot verify the results found in the submitted sample chromatograms. These standard chromatograms should be provided.

Registrant's Response to Deficiency 7d

No response was provided.

CBTS's Comments and Conclusions to Deficiency 7d

Chromatograms have been provided with the new field trial data. **Deficiency 7d has been resolved.**

Deficiency 7e from the 6/19/92 Memo

The identity of the chromatogram in Figure 8 of the submission (spiked blank, sample 91-1105-3 from Georgia) is questionable. The matrix background in this sample is much cleaner than either the blank (sample 91-1105-1) or the treated sample (sample 91-1109-1). The petitioner should provide an explanation for this anomaly.

Registrant's Response to Deficiency 7e

No response was provided.

CBTS's Comments and Conclusions to Deficiency 7e

Chromatograms have been provided with the new field trial data. **Deficiency 7e has been resolved.**

Deficiency 8 from the 6/19/92 Memo

No peanut processing data were submitted with this petition. These data are required in order to determine whether there is any

concentration of residues in processed fractions (peanut meal, soapstock, and crude and refined oil), unless data from appropriate exaggerated application rates show no detectable residues in nutmeats.

Registrant's Response to Deficiency 8

The registrant has provided the following report:

"Fluazinam: Determination of Residues in Peanuts and Processing Fractions", R.G. Kenyon, Ricerca Inc., 5/26/94 (MRID# 435210-14).

Peanut plants were treated with 3 applications of 1 lb.ai./A./application and harvested 30 days after the last application. The peanuts were sent to the Food Protein Research and Development Center at Texas A and M University for processing. The processed fractions included whole peanuts, nutmeats, hulls, solvent extracted presscake (meal), crude oil, refined oil, and soaspstock. The processed samples were shipped to Ricerca for analysis. The samples were analyzed by "Analytical Methods for Fluazinam and Its Metabolites in Crops", Y. Ganse, S. Ogyu, and K. Ohyama; or "Analytical Methods for Fluazinam and Its Metabolites in Peanut Oil", Y. Ganse, S. Ogyu, and K. Ohyama. The method recoveries are listed in Table 17.

Table 17

Recovery of Fluazinam from Amended Peanuts and Processing Fractions

| | | % Recovery | |
|---|---|---|---|
| peanut matrix | fortification levels | range | mean |
| nutmeats | 0.01 - 0.30 | 74 - 108 | 94 ± 15 |
| hulls | 0.01 - 1.0 | 84 - 115 | 95 ± 13 |
| presscake | 0.01 - 1.0 | 88 - 116 | 100 ± 13 |
| crude oil | 0.01 - 1.0 | 76 - 96 | 88 ± 7 |
| refined oil | 0.01 - 1.0 | 91 - 113 | 100 ± 8 |
| soapstock | 0.01 - 0.50 | 85 - 110 | 95 ± 8 |

Table 18

Fluazinam Residues and Concentration Factors in Peanut Processed Fractions

| peanut fraction | mean fluazinam residue (ppm) | concentration factor |
|---|---|---|
| nutmeats (prior to processing - hand hulled) | < 0.01 | < 1X |
| nutmeats (mechanically dehulled) | 0.01 | 1X |
| hulls (prior to processing - hand hulled) | 0.55 | 55X |
| hulls (mechanically dehulled) | 0.36 | 36X |
| presscake (meal) | < 0.01 | < 1X |
| crude oil | 0.03 | 3X |
| refined oil | 0.01 | 1X |
| soapstock | 0.05 | 5X |

CBTS's Comments and Conclusions to Deficiency 8

The registrant believes that the higher residues in/on the mechanically (as opposed to hand) dehulled nutmeats are due to residue transfer/contamination from contact with the hulls. This is supported by the lower residues in/on the mechanically (as opposed to hand) hulled peanut hulls.

Based on the results in Table 18, fluazinam residues concentrate in peanut crude oil and soapstock. The Agency sets tolerances on refined (not crude) oil, and residues do not concentrate in this fraction. Peanut soapstock is no longer recognized as a significant animal feed item. Therefore, no 409/701 tolerances are necessary for this proposed use.

**Deficiency 8 has been resolved.**

Deficiency 9 from the 6/19/92 Memo

The feeding of hay and vines is under grower control, and therefore the feeding restrictions on the proposed label are appropriate. However, CBTS is concerned about the other three feed items (peanut meal, hulls, and soapstock), and especially peanut hulls for which no residue data were generated. In the absence of residue data on peanut hulls, CBTS cannot draw any conclusions on the need for tolerances for cattle meat and meat by-products. For the purposes of this temporary tolerance request, cattle tolerances may not be needed if no residues are detected in the peanut hulls. If required, however, these studies should not be initiated until the nature of the residue in animals is understood (see Conclusion 4) and the residue levels in the animal feed items are determined.

Registrant's Response to Deficiency 9

No response was provided.

CBTS's Comments and Conclusions to Deficiency 9

The results of the radiolabeled goat metabolism study, which was conducted at the equivalent of 11 ppm in the feed, showed that no fluazinam was detected in any goat commodities at levels of 0.01 ppm or greater. As noted under CBTS's Comments and Conclusions to Deficiency 7c, changes are underway to eliminate peanut hulls as a livestock feed item in Table II and allow the grazing/feeding of peanut hay to be restricted. The only remaining feed item, peanut meal, exhibited non-detectable residues (taken from peanut nutmeat residue data). Therefore, no meat or milk tolerances will be needed for this proposed EUP/temporary tolerance request.

No poultry metabolism or feeding studies have been submitted. Since the only peanut item fed to poultry is meal, which exhibited no detectable residues of fluazinam, no additional studies will be required and no poultry or egg tolerances will be established for the purposes of this EUP/temporary tolerance request.

The registrant is advised to send in the requested final peanut metabolism report as soon as it is ready. These results will be needed before the metabolism data can be presented to the HED Metabolism Committee. The decision of the Committee will impact the need for ruminant and/or poultry feeding studies for any future Section 3/permanent tolerance requests.

**Deficiency 9 has been resolved.**

Attachment I : Names and Structures of Fluazinam Metabolites

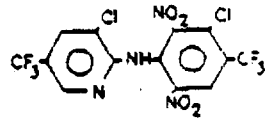
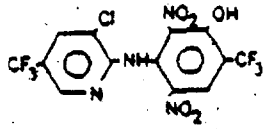
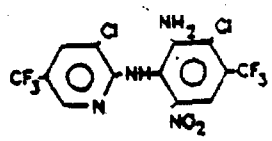
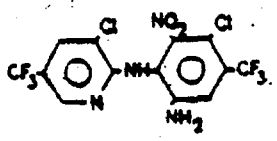
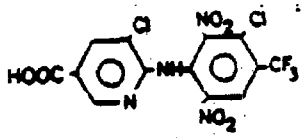
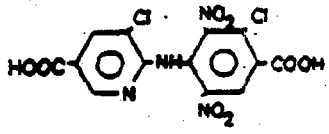
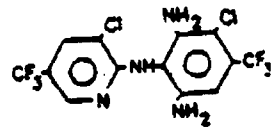
cc: circu., PP# 2G04099, RF, SF (fluazinam), G.J. Herndon, E. Haeberer (section head).

RDI: Section Head: E. Haeberer: 7/28/95,
Branch Senior Scientist: R.A. Loranger: 8/22/95,
Branch Chief: M. Metzger: 9/5/95.

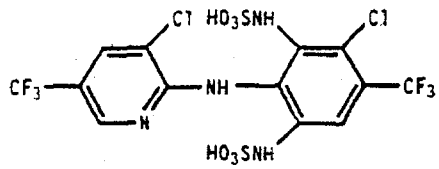
H7509C: CBTS: G.J. Herndon: 305-6362: CM#2, Rm. 804C: 7/20/95.

Attachment I

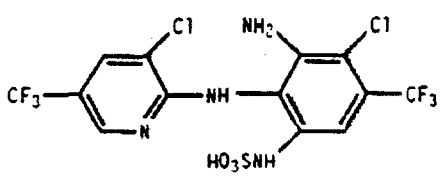
Names and Structures of Fluazinam Metabolites

| Code | Identity | Structure |
|---|---|---|
| P/Parent | 3-chloro-N-(3-chloro-5-trifluoromethyl-2-pyridyl)-α,α,α-trifluoro-2,6-dinitro-p-toluidine |  |
| HYPA | 5-(3-chloro-5-trifluoromethyl-2-pyridylamino)-α,α,α-trifluoro-4,6-dinitro-o-cresol |  |
| MAPA | 2-chloro-6-(3-chloro-5-trifluoromethyl-2-pyridylamino)-α,α,α-trifluoro-5-nitro-p-toluidine |  |
| AMPA | 4-chloro-6-(3-chloro-5-trifluoromethyl-2-pyridylamino)-α,α,α-trifluoro-5-nitro-o-toluidine |  |
| CAPA | 5-chloro-6-(3-chloro-α,α,α-trifluoro-2,6-dinitro-p-toluidine)-nicotinic acid |  |
| DCPA | 6-(4-carboxy-3-chloro-2,6-dinitroanilino)-5-chloronicotinic acid |  |
| DAPA | 4-chloro-2-(3-chloro-5-trifluoromethyl-2-pyridylamino)-5-trifluoromethyl-p-phenylenediamine |  |

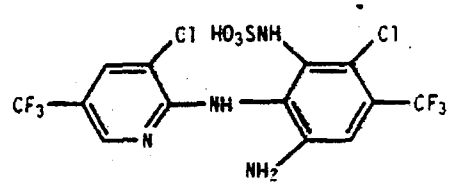
DAPA-bis-sulfamate



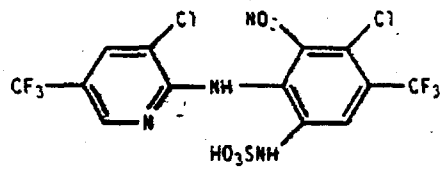

DAPA-sulfamate isomer




DAPA-sulfamate isomer




AMPA-sulfamate




AMPA isomer