UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

Subject: Reregistration of Sodium Acifluorfen. BASF Corp. 90 Day Response to Phase 4 DCI. DP Barcode D169747. MRID No. None. CBRS No. 8741.

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Background

BASF Corp. has replied to the Phase 4 DCI (received 09/16/91) for sodium acifluorfen, or 5-[(2-chloro-4-trifluoromethyl)-phenoxy]-2-nitrobenzoic acid sodium salt. Each Guideline DCI data requirement addressed by the registrant, the registrant's response to the data requirement, and the CBRS evaluation of the response follow.

Discussion

Guideline No. 171-4(a): Nature of the Residue- Plants

Requirement-
Radiolabeled plant metabolism studies are required for a legume vegetable (soybeans), a cereal grain (rice), and peanuts.

Response-
BASF submitted a summary of a soybean metabolism study purchased

from Rhone-Poulenc Ag Co. as part of an Amended Phase 3 Response (10/31/90), MRID No. 41688504. The Agency did not acknowledge the study.

The former registrant of sodium acifluorfen was not requested to supply rice and peanut metabolism studies (in support of the original tolerances for these particular crops). BASF will now commit to perform the studies, but requests a due date of 06/93, two years from the date of receipt of the relevant DCI. This position was stated in a letter of 08/23/91 to the Chemical Review Manager.

CBRS Evaluation-
The soybean metabolism study was included in the Phase 4 review by CBRS. It was found to be unacceptable (CBRS Phase 4 Review, S. Funk, 02/14/91). The submission (MRID No. 41688504) is a summary of three studies (Rhone-Poulenc, Inc. and Mobil Chemical Co.) used in support of PP #9F2158. In report PME-81.47, six plants were treated with ^{14}C-labeled (trifluoromethylphenyl ring) sodium acifluorfen by application with a microsyringe to the leaflets at a rate equivalent to 0.5 lb. a.i./acre. The plants were analyzed (top section, treated section, bottom section) at 3, 7, 14, and 28 days after treatment. The sections of the forage samples were homogenized with methanol and filtered. The total radioactivity in the extract and in the residue was determined. The methanol extract was analyzed by TLC, revealing the parent and seven metabolites at 3, 7, and 14 days. No data are reported for 28 days. The upper and lower plant portions contained no radioactivity (3 - 28 days). Total radioactivity recovery ranged from 100% to 88%. Unextracted radioactivity ranged from 4% after 3 days to 23% after 28 days. No further characterization was made.

In reports 81/020 and 349, ^{14}C-labeled (trifluoromethylphenyl ring) sodium acifluorfen was sprayed on plants grown under natural conditions at the V-3 to V-4 growth stage at a rate of 0.19 lb. a.i./acre (0.4X). Forage samples were analyzed up to 8 weeks after treatment; straw, pods, and grain samples were taken and analyzed 12 weeks after treatment. Total radioactivity was measured in the samples, in acetonitrile-water extracts, and in the extraction residue. No additional characterization was attempted. Total radioactivity in forage decreased from 32 ppm (as sodium acifluorfen) from time zero to 0.02 ppm at week eight. TRR in straw, pods, and grain was <0.05 ppm, < 0.03 ppm, and < 0.02 ppm, respectively.

In report 82/049, application of a ^{14}C-labeled (trifluoromethyl ring) sodium acifluorfen was made to plants under natural growing conditions at a rate of 0.5 lb.a.i./acre (1X). Only forage samples were analyzed. The TRR declined from 103 ppm at day 0 to 0.19 ppm on day 28. Acifluorfen (14% TRR) and the amino analog of acifluorfen (2% TRR) were identified from seven day forage samples

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(TRR 23.4 ppm). A chloroform extract contained at least 10 unidentified metabolites (36% TRR). An ethyl acetate extract contained 11 unidentified metabolites (19% TRR). The marc (residue) contained 36% TRR.

These radiolabeled studies on soybeans are not acceptable for purposes of reregistration. Only parent and one metabolite were identified, the total of the two being < 20% of TRR (seven days, soybean forage). Unextractable radioactivity in soybean forage ranged from 4% (day 0) to 40% (day 28). Major metabolites were detected by TLC but not identified. Efforts must be made to extract most (90%) of the radiolabel and to identify each metabolite comprising ≥ 10% of the TRR. Application rates in excess of 0.5 lb. a.i./acre may be needed to obtain individual components of adequate concentration for identification purposes.

CBRS recommends against a time extension to 06/93 to submit the soybean, peanut, and rice metabolism studies. The registrant committed in the Phase 3 response (05/90) to generate new studies, but rescinded the commitment upon acquiring the Rhone-Poulenc Ag Co. soybean study. The registrant recognized the data gap, and appropriate studies should be underway.

The registrant should be cognizant that the discovery of new metabolites of toxicological significance in the new nature of the residue in plants studies may create additional data requirements under Guidelines 171-4(c), 171-4(e), 171-4(j), and 171-4(k/l).

Guideline 171-4(e): Storage Stability

Requirement-
Storage stability studies are required for peanuts (nutmeat, hulls) peanut processed commodities (meal, crude oil, refined oil, soapstock), rice grain, rice processed commodities (grain dust, polished rice, hulls, bran), processed soybean fractions (meal, hulls, soapstock, crude oil, refined oil), and animal commodities (egg, milk, muscle tissue, liver, cattle kidney).

Response-
(1) Soybeans and peanuts are both oilseeds and both undergo similar processing. Therefore, storage stability studies for one should suffice for both.
(2) No weathered residues are anticipated in/on crop matrices treated with sodium acifluorfen. Only laboratory-fortified samples will be studied.
(3) The required rac's and processed commodities will be spiked with the parent and amine metabolite and analyzed by the residue analytical method.
(4) Proposed schedule (time extension):

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Commodity	Study Initiation	Final Report Submission
Peanuts (incl. processed commodities)	11/91	06/94
Livestock	06/93[1]	10/95

[1] After final report on nature of residue in animals, run in parallel with magnitude of the residue studies in livestock.

(5) A waiver is requested for storage stability studies on meat, milk, poultry, and eggs. No detectable residues (lod 0.05 ppm) are expected, even at exaggerated feeding rates. See 171-4(j).

CBRS Evaluation-

(1) CBRS agrees. An adequate storage stability study for peanuts and the processed fractions will suffice for both peanuts and soybeans, including the processed commodities.

(2) If crop field trials have revealed (or will reveal) no detectable residues of the active ingredient and/or its regulated metabolites, then laboratory-fortified samples may be used. It is imperative that time 0 (day of preparation) fortified samples be promptly analyzed. Fortifications should be made slightly above the limit of quantitation and near the established tolerance concentration.

(3) Samples are to be fortified with the active ingredient and all regulated metabolites. Currently, this is the parent and the corresponding acid, methyl ester, and amino analogue in both plants and animals (40CFR180.383). Fortification with sodium acifluorfen and the amine analog only, as proposed, will not suffice. Fortification with the methyl ester is also required. The free acid need not be tested. The regulatory method converts sodium acifluorfen to the free acid during the initial extraction and determines sodium acifluorfen and the acid as the methyl ester. Therefore, methyl ester fortification will need to be conducted in separate trials from the amine/sodium acifluorfen fortification.

(4) CBRS has no objection to the proposed schedule and requested time extension, but time frames are in the purview of SRRD. The SRRD 24 month time period for peanut/peanut commodity storage stability studies does not provide adequate time to complete a 2 year storage stability study for peanuts. For animal commodities, the animal metabolism study (171-4(b)) must be completed before the storage stability study is initiated, if required (see (5)). The DCI allots 24 months for conducting the nature of the residue in animal study. The storage stability and magnitude studies would not, therefore, start until 06/93.

(5) CBRS recommends that this requirement be reserved, pending outcome of the new 171-4(b) studies. The registrant claims that existing studies show no residue accumulation in eggs, milk, or tissues. That study measured only total radioactive levels and did not determine the parent and individual metabolites. The storage stability study will need to be conducted simultaneously with the feeding study, per the registrant's proposed schedule, if the reserved feeding study is found to be necessary.

Guideline 171-4(j): Magnitude of the Residue in Meat, Milk, Poultry, and Eggs

Requirement-
Sodium acifluorfen must be fed to ruminants and poultry at levels corresponding to 1X, 3X, and 10X the anticipated dietary burden. Parent and regulated metabolites are to be determined in milk, eggs, poultry tissue (fat, muscle, liver), and cattle tissue (fat, muscle, liver, kidney).

Response-
A waiver is requested. The registrant argues that the maximum anticipated residue in soybeans, peanuts, and rice is 0.01 ppm, the method detection limit. The maximum dietary burden would be 0.01 ppm for ruminants and poultry. A radiolabeled feeding study at 0.1 ppm (10X) revealed radioactivity in ruminant liver only (0.007 ppm, as acifluorfen) and in poultry meat (0.03 ppm), gizzard (0.03 ppm), liver (0.01 ppm), fat (0.03 ppm), kidney (0.01 ppm), heart (0.01 ppm), and eggs (0.02 ppm). Anticipated residue levels in animal commodities would be below the regulatory method limit of detection (0.05 ppm).

CBRS Evaluation-
The tolerances for soybeans, peanuts, and rice are established as 0.1 ppm. Using the tolerance values, the animal dietary burden could be 0.1 ppm. The radiolabeled feeding study at 1 ppm (10X tolerance) showed residues in ruminant liver (0.06 ppm), kidney (0.05 ppm), heart (0.03 ppm), and tongue (0.03 ppm) and in poultry meat (0.05 ppm), bone (0.05 ppm), gizzard (0.04 ppm), liver (0.15 ppm), skin (0.09 ppm), fat (0.10), kidney (0.15 ppm), heart (0.08 ppm), and egg (0.16 ppm). There may exist a potential for bioaccumulation, but CBRS will reserve the requirement for magnitude of the residue in meat, milk, poultry, and eggs pending an evaluation of the results of the nature of the residue studies (171-4(a), (b)).

Guideline 171-4(k): Magnitude of the Residue- Soybeans

Requirement-
Additional field trials must be conducted in IL or IN, IA, and MN.

Response-
Studies cannot be started until the 1992 growing season, because the DCI was not received until June 3, 1991. A time extension for report submission from 06/93 to 06/24/94 is requested.

Evaluation-
CBRS recommends against extension of the report submission due date. Analyses and report generation within 9 or 10 months of crop harvest is not an unrealistic requirement. However, time extensions are within the purview of SRRD.

Guideline 171-4(l): Magnitude of the Residue in Processed Commodities- Peanuts

Requirement-
A processing study must be conducted for peanuts. Peanuts with detectable residues of the parent and the regulated metabolites must be processed into meal, crude oil, refined oil, and soapstock.

Response-
A waiver is requested. The maximum label (Blazer, 7969-79) rate has been lowered (09/05/91) to 0.5 lb. a.i./acre/season from the former 2.0 lbs. a.i./acre/season. Data (MRID No. 92168052) from a 3.3 lbs. a.i./acre application (6X), 70 day PHI, show no residues on nuts (<0.01 ppm) or hulls (<0.02 ppm). Applications somewhat above this rate will kill the crop (no data submitted).

Should the waiver be denied, a time extension is requested to perform the processing study.

Evaluation-
The new label (Blazer, 7969-79) limits use to 0.5 lb. a.i./acre, preemergence/cracking/postemergence application The new Storm label (7969-76) also limits total annual sodium acifluorfen use to 0.5 lb. a.i./acre. The 3.3 lbs. a.i./acre application represents 6.6X the new maximum seasonal rate. The 70 day PHI is less than the label 75 day PHI.

CBRS will not accept the 6.6X data as evidence of the lack of residues on the processed commodities. The crop bearing detectable residues of sodium acifluorfen and any regulated metabolites must be processed into the commodities meal, crude oil, soapstock, and refined oil. The requirement may be waived only if treatment of the crop at an exaggerated rate equal to or greater than the maximum theoretical concentration factor due to processing results in no detectable residues on the rac. A 6.6X rate is less than the maximum theoretical concentration factor due to processing. If phytotoxicity occurs at exaggerated rates less than the maximum theoretical concentration factor, then the registrant must treat the crop at the maximum rate that does not produce significant phytotoxic effects, must submit proof of the phytotoxicity at greater rates than that used, and must perform a processing study

on the rac, regardless of the presence or absence of residues.

Field trials to produce the crop for processing cannot be started until the 1992 growing season. An extension to 07/94 for report submission is reasonable, but the granting of such extensions is in the purview of SRRD.

Guideline 171-4(l): Magnitude of the Residue in Processed Commodities- Soybeans

Requirement-
A processing study must be conducted for soybeans. Soybeans with detectable residues of the parent and the regulated metabolites must be processed into hulls, meal, crude oil, refined oil, and soapstock.

Response-
A waiver is requested. The maximum label (Blazer, 7969-79) rate has been lowered (09/02/91) to 0.5 lb. a.i./acre/season from the former 1.0 lb. a.i./acre/season. Data (MRID No. 92168053) from 11 trials at 1.0 lb. a.i./acre application (2X), 17 - 49 day PHI, show no residues on the grain (<0.01 ppm). A single trial with 2 applications totaling 1.3 lbs. a.i./acre showed no residues (<0.01 ppm), PHI 46 days. Total seasonal applications of about 1.5 lbs. a.i./acre will kill the crop (no data submitted).

Should the waiver be denied, a time extension is requested to perform the processing study.

Evaluation-
The 1.0 lbs. a.i./acre applications do represent 2X the new maximum seasonal rate for Storm (7969-76 09/16/91) and Galaxy (7969-77, 09/16/91), but not for Blazer (7969-79, 09/05/91). Total seasonal application under the Storm label is 0.875 lb. a.i./acre, consisting of a maximum preplant application rate of 0.375 lb. a.i./acre and a soybean postemergence application rate of 0.5 lb. a.i./acre. The 17 - 49 day PHI's are less than the label 50 day PHI.

CBRS will not accept the 1.1X - 2X data as evidence of the lack of residues on the processed commodities. The crop bearing detectable residues of sodium acifluorfen and any regulated metabolites must be processed into the commodities meal, hulls, soapstoack, crude oil, and refined oil. The requirement may be waived only if treatment of the crop at an exaggerated rate equal to or greater than the maximum theoretical concentration factor due to processing results in no detectable residues on the rac. A 2X rate is less than the maximum theoretical concentration factor due to processing. If phytotoxicity occurs at exaggerated rates less than the maximum theoretical concentration factor, then the registrant must treat the crop at the maximum rate that does not produce significant phytotoxic effects, must submit proof of the

phytotoxicity at greater rates than that used, and must perform a processing study on the rac, regardless of the presence or absence of residues.

Field trials to produce the crop for processing cannot be started until the 1992 growing season. An extension to 07/94 for report submission is reasonable, but the granting of such extensions is in the purview of SRRD.

Conclusion and Recommendation

The conclusions and new/additional requirements for the Subdivision O Residue Chemistry Guidelines are summarized in Table 1. CBRS assumes that DCI requirements for sodium acifluorfen not addressed by BASF Corporation in the 90 day response are agreeable.

Table 1: CBRS Recommendations on Issues of the Registrant 90 Day Response to Phase 4 Reregistration DCI

Guideline	Parameter	Registrant Reply/Request	Requirement/ Comment	Waiver/ Reserve Recom-mendation	Time Extension Recom-mendation
171-4(a)	Nature of Residue-soybeans, rice, peanuts	(1) Acknowledge/review previously submitted soybean study. (2) Time extension for rice and peanut studies (06/93).	(1) Study is rejected, not upgradeable. Major metabolites (≥ 10% TRR) must be identified; 90% TRR must be extracted. (2) Requirement has been known to registrant. Extension not warranted.	N/A	No[1]
171-4(e)	Storage Stability-soybeans, peanuts, rice	(1) Storage stability for peanuts and peanut processed commodities should suffice for peanuts and soybeans. (2) Laboratory-fortified samples to be used. (3) Fortify with amine metabolite and parent. (4) Time extension for peanut (06/94) and livestock study (10/95) . (5) Waive studies for meat, milk, poultry, eggs.	(1) Accept. (2) Accept, if field samples contain no detectable residues. (3) Reject. Must fortify with methyl ester, as well as parent and amine metabolite. (4) Justified to complete 2 yr. peanut storage stability study. Livetock reserved. (5) Results of new nature of residue in animals studies needed to determine if this requirement applicable.	(5) Reserve	Yes[1] (peanuts)

Table 1: CBRS Recommendations on Issues of the Registrant 90 Day Response to Phase 4 Reregistration DCI

Guideline	Parameter	Registrant Reply/Request	Requirement/ Comment	Waiver/ Reserve Recom-mendation	Time Extension Recom-mendation
171-4(j)	Magnitude of the residue-meat, milk, poultry, eggs	Waiver, based on lack of residues in animal studies to date.	Results of nature of the residue studies (in progress) may indicate need for magnitude study.	Reserve	N/A[2]
171-4(k)	Magnitude of the residue-soybeans	Time extension (06/94)	Current deadline provides 6 - 9 mos. for analysis after crop harvest.	N/A	No[1]
171-4(l)	Magnitude of the residue-peanuts processed	(1) Waiver, based on lack of residues on rac at near phytotoxic 6X rate field trial. (2) Time extension (06/94).	(1) Processing study required unless treatment at rate $\geq$ maximum theoretical processing conc. factor produces no residues. (2) Time extension reasonable.	No	Yes[1]
171-4(l)	Magnitude of the residue-soybeans processed	(1) Waiver, based on lack of rac residues at near phytotoxic 2X rate field trials. (2) Time extension (06/94).	(1) Processing study required unless treatment at rate $\geq$ maximum theoretical processing conc. factor produces no residues. (2) Time extension reasonable.	No	Yes[1]

[1] Granting of time extensions is in the purview of SRRD. [2] CBRS will be amenable to a time extension request if this requirement is imposed.

cc: RF, List B Sodium Acifluorfen File, Circ., S. Funk, C.Furlow (PIB, FOD).

RDI: A. Rathman:12/04/91: D.Edwards:12/04/91: E. Zager:12/04/91:

H7509C:CBRS:S.Funk:305-5430:CM#2:RM803-A:SF(1191.2):12/03/91.