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

JAN 12 1984

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP #3F2904 (Accession No. 071661).
Poast® [BAS 9052H] in or on Soybeans
and Alfalfa (hay and forage).
Evaluation of analytical methodology
and residue.

FROM: John H. Onley, Ph.D., Chemist
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Hazard Evaluation Division (TS-769)

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

TO: Robert Taylor, Product Manager No. 25
Fungicide-Herbicide Branch
Registration Division (TS-767)

and
Toxicology Branch
Hazard Evaluation Division (TS-769)

The Agricultural Chemicals Group, BASF Wyandotte Corporation proposes that 40 CFR 180.412 be amended to establish tolerances for the combined residues of the herbicide 2-[1-(ethoxyimino)butyl]-5-[2-(ethylthio)propyl]-3-hydroxy-2-cyclohexen-1-one and its metabolites containing the 2-cyclohexen-1-one moiety (calculated as the herbicide) in or on the following raw agricultural commodities:

Soybeans, hay and forage	20 ppm
Alfalfa, hay and forage	20 ppm

At present, the following BAS 9052H tolerances have been established: cottonseed-5 ppm, cottonseed soapstock-15 ppm, soybean seeds-10 ppm, milk-0.05(N) ppm, eggs-0.5 ppm, and the fat, meat by-products, and meat of cattle, goats, hogs, horses, poultry, and sheep-0.2 ppm.

Conclusions

1a. Since a 90-day PHI is needed in order for field residues to decline to levels less than 10 ppm on soybeans, the

petitioner should reconsider his request for the establishment of a 20 ppm BAS 9052H tolerance on soybean forage, i.e., the grazing and feeding restrictions on soybean forage and ensilage should be returned to the present proposed label. For example, soybeans will grow to maturity between 126-158 days; it requires about 53 days for soybeans to grow from planting to the third-node stage. Therefore, when considering the necessary growth time and the necessary 90-day PHI, the proposed tolerance on soybean forage becomes impractical. However, the establishment of an appropriate tolerance on soybean hay would be practical in conjunction with the required 90-day PHI (see the Proposed Use section of this review).

1b. Under "Restrictions and Limitations" of the proposed alfalfa label we suggest that the following be used:

> Do not apply Poast within 7 days of feeding, grazing, or harvesting when used alone. Do not apply Poast and 2,4-DB as a tank mix unless the 60-day feeding, grazing, and harvesting restrictions on the 2,4-DB label can be observed.

2a. At this time, the nature of the residue in plants is not adequately understood (see the Nature of the Residue section of this review). The Laboratory Report No. PM-39 (Metabolism and Distribution of [4-^{14}C]-BAS 9052H in Soybean Plants) submitted in the present petition showed that about 60% of the applied radioactivity was not characterized in soybean plants harvested 7 days after application. The quantity of uncharacterized radioactivity increased with time. The petitioner should further attempt to release more of the bound or polar residues and thereafter identify the aglycones.

2b. At this time, we conclude that the nature of the residue in animals is not adequately understood for the establishment of more tolerances on crops involving feed items. The petitioner will need to carry out a new lactating animal metabolism study at a feeding level between 50-100 ppm ^{14}C-BAS 9052H (parent compound). The petitioner should also submit results from a poultry metabolism study carried out at a feeding level between 10-20 ppm ^{14}C-BAS 9052H (see Animal Metabolism section of this review).

3a. In the plant metabolism studies discussed in this review, methanol did not prove to be an effective solvent for the extraction of weathered residues from soybean plants. We now have some concern as to whether or not methanol is suitable for use as the extraction solvent in the analytical procedure already approved for regulatory purposes. In view of the preceding, we conclude that the analytical methodology for the determination of BAS 9052H residues in plant commodities needs

to be further investigated on samples containing weathered residues. For example, the petitioner may want to carry out his initial extraction of plant samples with a solvent mixture

of methanol plus acid, or he may want to apply ultrasonic treatments, enzymatic hydrolyses, etc., during any step of the sample preparation in an effort to release more of the bound residues from the plant matrices. In brief, we require the petitioner to validate the analytical methodology as part of the ^{14}C metabolism studies.

3b. Methanol is also used in the proposed analytical method for extracting metabolized residues from animal commodities; the methodology needs to be further investigated.

4. Storage Stability. The recoveries of BAS 9052H and its metabolites from stored samples are surprisingly much higher than the recoveries of standards/residues from samples that were fortified at time of analyses (see the Residue Data section of this review); the petitioner should explain this difference.

5a. We reserve our conclusion on the adequacy of the proposed 20 ppm tolerance on alfalfa forage and hay until those questions raised in the Nature of the Residue and Analytical Method sections of this review have been resolved.

5b. An alfalfa forage sample coded 503 (Illinois) had a residue of 38 ppm at the proposed PHI of 7-days; the petitioner states that this sample had been allowed to dry prior to analysis sample. Since alfalfa hay could be considered dried alfalfa forage, the sample would appear to be one for alfalfa hay. The petitioner should be able to submit a further explanation on the residue level in this sample.

5c. We need to know the mode of application (aerial and/or ground) on alfalfa plots.

6a. The petitioner should submit some residue data on his reserve soybean hay samples after those questions raised on the plant metabolism and analytical methodology have been resolved. At this time, we reserve our conclusion on the adequacy of the proposed BAS 9052H tolerances on soybean hay and forage (see the Residue Data section of this review). In view of the questions raised on the adequacy of the methodology for determining Poast residues in soybean forage and alfalfa forage and hay, we now question the adequacy of the established tolerance on soybean seeds. The petitioner should address this issue also. After the methodology question is resolved, we will also re-evaluate the residue data in light of the revised

use pattern for soybeans.

6b. We need to know the mode of application (aerial and/or ground) on soybean plots.

7. After reviewing the submitted residue data for supporting the new BAS 9052H uses on alfalfa and soybeans (with no forage, ensilage, and hay restrictions), we are unable to draw conclusions on the adequacy of the established meat, milk, poultry, and egg tolerances until those questions raised in the Animal Metabolism and Analytical Methods sections of this review have been resolved. After the resolution of the preceding questions, the petitioner may need to reanalyze some of his reserve meat, milk, poultry, and egg samples from his previous feeding studies.

8. An International Residue Limit Status sheet is attached to this review. No Codex, Canadian, or Mexican tolerances have been established for Poast® [BAS 9052H] in or on alfalfa and soybean forage and hay.

Recommendations

At this time, RCB recommends against the proposed 20 ppm Poast® [BAS 9052H] tolerances on alfalfa and soybean forage and hay for those reasons given in conclusions 1a, 1b, 2a, 2b, 3a, 3b, 4, 5a, 5b, 5c, 6a, 6b, and 7.

Detailed Consideration

Manufacture and Formulation

The manufacturing process for technical BAS 9052H was submitted in PP#0G2396, and it was discussed in our December 4, 1980 review.

The technical product is >94.9% pure. The associated impurities (listed in aforecited review) are not expected to pose a residue problem.

Technical BAS 9052H is formulated into an emulsifiable concentrate containing 20.0% by weight of ai. Process impurities (6) comprise 1.04% by weight of the formulation [redacted] comprise the remaining 78.96%. [redacted] the inerts are cleared for use under Sec. 180.1001(c).

The formulated product is known as Poast® Post-Emergence Grass Herbicide. It contains 1.53 lbs ai/gal.

Proposed Use

Alfalfa. For the control of several annual and perennial grass weeds in alfalfa, Poast® is to be applied (broadcast) at rates of 1 1/2 to 2 1/2

pts. (0.29-0.48 lb. a.i.)/A in the states of California, Arizona, New Mexico and at rates of 1 to 2 1/2 pts. (0.19-0.48 lb. a.i.)/A in states other than California, Arizona, and New Mexico. The product is to be applied in a minimum of 5 gallons of water/A by air or 10 gallons of water/A by ground equipment, and the mumber of applications depend upon the type of grass to be controlled and the growth of the grass; however, no more than a total of 5 pints (1 lb.) of Poast per acre will be used in one season. A PHI of 7 days is proposed. A nonphytotoxic oil concentrate, containing only EPA exempt ingredients, is to be added to the spray solution at 2 pints per acre for ground and aerial applications.

Poast is also proposed to be used with 2,4-DB [4-(2,4-dichlorophenoxy) butyric acid] in a tank mix; both products are included in the tank mix according to rates recommended on their respective labels.

However, we find that the 7-day PHI restriction and reference to feeding restrictions on the 2,4-DB label under "Restrictions and Limitations" of the proposed alfalfa label need to be defined better. We suggest that the following be used:

> Do not apply Poast within 7 days of feeding, grazing, or harvesting when used alone.
>
> Do not apply Poast and 2,4-DB as a tank mix unless the 60-day feeding, grazing, or harvesting restrictions on the 2,4-DB label can be observed.

Actually, the 2,4-DB label contains a 60-day feeding and grazing restriction; alfalfa forage or hay that has not been subject to the preceding 60-day restriction could contain illegal amounts of 2,4-DB. We foresee no residue problem with 2,4-DB residues if the above restrictions are written on the proposed alfalfa label.

Soybean. For the control of several annual perennial grass weeds in soybeans, Poast® is to applied in a similar manner as previously discussed in our (M. Nelson) 3/25/83 review of amendment 3/15/83 to PP #2F2670; the differences are as follows:

1. Perennial grasses - a second application is requested if regrowth occurs or new plants emerge. This application was not permitted previously so that the maximum applied a.i. of Poast® would not exceed 0.5 lb a.i./A/season (see our 3/8/83 review of amendment 2/1/83 to PP#2F2670). Now, depending on the desired grass control, the proposed rates for Poast® on soybean range from 1/2 to 4 pts (0.1 to 0.8 lb a.i.)/A/season.

2. The previously proposed grazing and feeding restriction on treated soybean forage, ensilage or hay to livestock has been deleted

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from the proposed label.

After resolution of the questions involving the validity of the analytical method, we will also re-evaluate the soybean residue data in light of the revised use pattern as noted above.

Residue data submitted previously in PP#2F2670 showed that a harvesting restriction of 90 days was needed in order for Poast residues to be at a level less than 10 ppm on soybean seeds. The growing period for soybean maturity range between 126 to 158 days. It requires about 53 days for soybeans to grow from planting to the third-node stage. Therefore, when considering the necessary growth time and the necessary 90-day PHI, it does not appear that the establishment of a tolerance on soybean forage would be feasible. The establishment of an appropriate tolerance on soybean hay would be practical in conjunction with the required 90-day PHI.

The petitioner should reconsider his request for the establishment of a BAS 9052H tolerance on soybean forage, i.e., the grazing and feeding restriction on soybean forage and ensilage should be returned to the present proposed label.

Nature of the Residue

Metabolism studies in plants (soybeans) and animals (rats and lactating goats) were submitted in PP#0G2396 and were discussed in our reviews dated December 4, 1980 and May 21, 1981.

Plants.

Metabolism data submitted in the present petition are found in Laboratory Report No. PM-39 (Metabolism and Distribution of [4-^{14}C]-BAS 9052H in Soybean Plants). Poast [4-^{14}C]-BAS 9052H was applied at a rate of 1.0 lb. a.i./A to soybean plants grown to the 2-3 trifoliate stage under natural environmental conditions. Whole plant samples (less roots) were harvested at 2 hours, 7, 14, 22, and 35 days after treatment. The radioactivity calculated as BAS 9052H equivalents decreased from 92.3 mg/kg at 2 hours to 1.2 mg/kg at 35 days after treatment.

Each sample was first extracted with methanol; a base was added to the extract; and then the extract (sample) was allowed to stand for 30 minutes. The alkaline methanolic solution was extracted with dichloromethane. The aqueous methanolic solution was adjusted to pH 2, and then it was extracted with dichloromethane. The results on the distribution of the radioactivity at 0, 7, and 35 days are summarized below (see the Metabolism Report in the present submission for a full account):

Fractions	Days After Treatment 0		7		35	
	ppm	%	ppm	%	ppm	%
Total radio-activity in forage	92.3	100	16.7	100	1.2	100
Total not ext. by MeOH	6.4	7	2.8	17	0.3	22
Total ext by MeOH	73.8	80	8.8	53	0.4	33
Total ext. after alkaline treatment	0.4	0.5	0.4	3	0.03	3
Final aqueous	6.6	7	4	25	0.4	30

The distribution of the above methanol extractable ^{14}C-residues (pH 2 + pH 11) at 0, 7, and 35 days are summarized below (see formulas and chemical names for the below abbreviated compounds in following Figure 1 from Metabolism Report No: PM-39 of PP#3F2904):

	0-day %	7-days %	35-days %
MS	0.2	-	-
MSO	55.6	24.4	14.3
MSO_2	0.9	2.7	2.2
M1S	0.4	0.04	0.06
M1SO	1.0	2.0	0.7
$M1SO_2$	0.1	1.1	0.6
M2S	0.2	-	-
M2SO	2.8	5.4	3.2
M2SO2	0.4	0.8	1.5
6-OH-$M2SO_2$	0.02	0.07	0.1
5-OH-MSO_2	0.3	0.2	0.5
Total ident. in MeOH ext.	61.92	36.67	23.16
Approx. amts of bound residues	38%	63%	76%

Metabolism studies on soybeans were also submitted in PP#0G2396. Poast was applied at a rate of 0.9 lb. a.i./A to 3 plots in New Jersey and 2 plots at Greenville, Mississippi. In New Jersey, whole plants (less roots) were harvested at 0, 6, 19, 41, and 69 days after treatment. At the Mississippi location, plants were harvested at 0, 3, 7, 14, 28, 56 days after treatment. At 0, 6-7, and 28 days after application, the following ppm of ^{14}C-Poast equivalents were observed in the soybean plants:

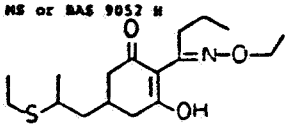
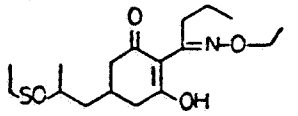
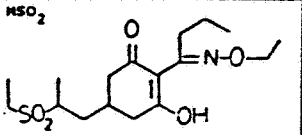
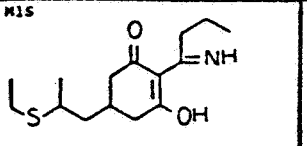
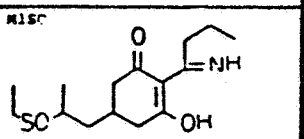
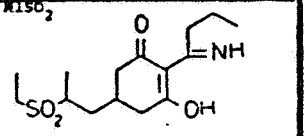
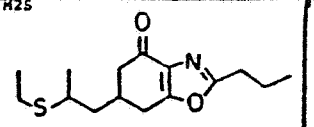
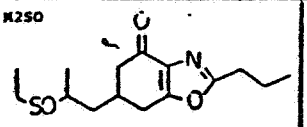
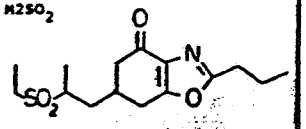
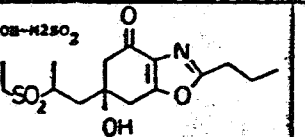
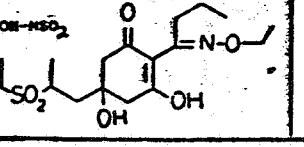
	ABBREVIATION AND STRUCTURAL FORMULA	MOLECULAR WEIGHT	CHEMICAL NAME
M TYPE	MS or BAS 9052 H 	327	2-[1-(ethoxyimino)butyl]-5-[2-(ethylthio)propyl]-3-hydroxy-2-cyclohexen-1-one
	MSO 	343	2-[1-(ethoxyimino)butyl]-5-[2-(ethylsulfinyl)propyl]-3-hydroxy-2-cyclohexen-1-one
	MSO_2 	359	2-[1-(ethoxyimino)butyl]-5-[2-(ethylsulfonyl)propyl]-3-hydroxy-2-cyclohexen-1-one
M1 TYPE	M1S 	283	2-[1-(imino)butyl]-5-[2-(ethylthio)propyl]-3-hydroxy-2-cyclohexen-1-one
	M1SO 	299	2-[1-(imino)butyl]-5-[2-(ethylsulfinyl)propyl]-3-hydroxy-2-cyclohexen-1-one
	$M1SO_2$ 	315	2-[1-(imino)butyl]-5-[2-(ethylsulfonyl)propyl]-3-2-cyclohexen-1-one
M2 TYPE	M2S 	281	6-[2-(ethylthio)propyl]-6,7-dihydro-2-propyl-4(5H)-benzoxazolone
	M2SO 	297	6-[2-(ethylsulfinyl)propyl]-6,7-dihydro-2-propyl-4(5H)-benzoxazolone
	$M2SO_2$ 	313	6-[2-(ethylsulfonyl)propyl]-6,7-dihydro-2-propyl-4(5H)-benzoxazolone
HYDROXY	6-OH-$M2SO_2$ 	329	6-[2-(ethylsulfonyl)propyl]-6-hydroxy-6,7-dihydro-2-propyl-4(5H)-benzoxazolone
	5-OH-MSO_2 	375	2-[1-(ethoxyimino)butyl]-5-[2-(ethylsulfonyl)propyl]-3,5-dihydroxy-2-cyclohexen-1-one

FIGURE 1: STRUCTURES AND ABBREVIATION OF BAS 9052 H AND ITS RELATED REFERENCE STANDARDS (reproduced from page 6 of Metabolism Report No: PM-39)

Days after treatment	ppm range
0	32-82
6-7	21-29
28	0.7-2.0

Our Comments/Conclusions on the Plant Metabolism.

At present, permanent Poast tolerances have been established on the grains of soybeans and cottonseed; however, before proceeding with the establishment of more permanent tolerances we will need to investigate further the bound [^{14}C]-BAS 9052H residues that were observed in the aforementioned metabolism studies. For example, its is shown that about 60% of the radioactivity in the 7-day samples was not characterized (see above results Lab. Report No. PM-39), and the quantity of uncharacterized radioactivity increased with time (see the above results at 35-days).

We need to know more about the above uncharacterized/bound radioactivity. We noticed that during an intermediate step in the sample preparation, acid more so than base did release some of the bound residues. Therefore, the petitioner may want to carry out his initial extraction of soybean samples using a solvent mixture of methanol and acid, and/or he may want to use ultrasonic treatments, enzymatic hydrolyses, etc., during any phase of the sample preparation in an effort to release the bound or polar residues and thereafter identify the aglycones.

In view of the above, we conclude that the nature of the residue in soybeans and alfalfa is not adequately understood at this time.

Animals. Metabolism studies for BAS 9052H in animals (rats and lactating goats) were submitted in PP#0G2396 and were discussed in our (E. Zager) reviews of December 4, 1980 and May 12, 1981.

With regards to animal metabolism, we said the following in our December 4, 1980 review:

"Four groups of rats; five male and five female rats in each group were administered ^{14}C labeled BAS 9052H as follows: group A, 10 mg/kg (i.v.); group B, 10 mg/kg (oral); group C, 10 mg/kg (oral); and group D, 325 mg/kg (oral). The rats in group C were preconditioned on unlabeled BAS 9052H for two weeks. Blood and excreta were collected for 2 days. Absorption, distribution and excretion of the radioactivity in rats were rapid. The major route of excretion was urine, with an average 78.5% of the administered activity being excreted via that route during the two days following administration. Approximately, 20.1% of the administered activity was excreted during the same period in feces. Less than 2% of the administered dose was associated with tissues. Highest levels were found in the liver reaching 0.6 ppm in groups A, B, and C and 13 ppm in group D. The major metabolites of BAS 9052H in the rat excreta were identified as MSO, M1SO, and M2SO; minor metabolites were MSO_2, $M1SO_2$,

$M2SO_2$ and 5-OH-MSO_2. The metabolites in the tissues were not identified. After extraction of the livers with polar solvents, approximately one half of the residues remained bound in groups A, B, and C and about one-third remained bound in group D.

Two lactating goats were fed an amount of ^{14}C-BAS 9052H (0.5 mg) equivalent to 1.25 ppm in the diet for eleven consecutive days.

Milk, urine, feces and blood samples were taken daily. #Twenty-four hours after the final dose, the goats were sacrificed and tissue samples were removed for analysis.

All of the administered ^{14}C-activity was found in the urine and feces. None of the tissues showed levels of activity above the limit of quantitation of the instruments used (0.003 ppm). Chromatographic examination of the urine indicated that the major metabolites were MSO (38%), M1SO (16%) and M2SO (15%).

The submitted metabolism studies are not considered adequate since only parent compound, BAS 9052H, was administered to animals, although essentially no residues of parent compound were present in treated soybean plants. For further consideration we will require metabolism studies involving administration to animals of plant substrates containing weathered residues of BAS 9052H. In particular, we are interested in the metabolism of MU, MU-1, and MU-2."

In our May 21, 1981 review of amendment March 3, 1981 to PP#0G2396, we concluded that metabolism/feeding studies involving the feeding of plant substrates containing weathered residues of BAS 9052H to livestock were needed.

Subsequently, in our (M. Nelson) Mar. 25, 1983 review of Amendment March 15, 1983 to PP#2F2670 and in our (J. Onley) March 16, 1983 review of Amendment March 1, 1983 to PP#2F2748, we recommended for the establishment of tolerances of 10, 5, and 15 ppm on soybeans (seeds), cottonseeds, and cottonseed soapstock, respectively, with grazing and feeding restrictions. However, our recommendations for establishing the preceding tolerances were made with the petitioner's understanding that he would submit a goat feeding study with hydroxy metabolites as a condition of registration. Accordingly, we received a protocol (amendment of February 9, 1983) for a goat feeding study, and on March 9, 1983 we recommended that the petitioner proceed with the lactating goat feeding study; the results from this study will be discussed under the Meat, Milk, Poultry and Eggs section of this review.

Although the above conditions were such wherein tolerances could be established on soybeans (seeds), cottonseed, cottonseed soapstock and animal commodities, there is still the need for further investigation on

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the nature of the residue in animals. As aforementioned, in the animal metabolism study, two lactating goats were fed an amount of ^{14}C-BAS 9052H (0.5 mg) equivalent to 1.25 ppm in the diet for eleven consecutive days; all of the administered radioactivity was found in the urine and feces. However, the "cold" animal feeding studies run at higher levels do indicate that some BAS 9052H residues are found in animal tissues. We are now considering proposed uses that could result in at least 20 to 40 ppm BAS 9052H equivalent being fed to some animals.

There is now a new goat metabolism/feeding study with weathered residues (see the Meat, Milk, Poultry, and Eggs section of this review). But the residues in the treated crop fed are also less than the feeding level possible from alfalfa (near 40 ppm) and in the treated crop plus gelatin capsule regime, the gelatin capsule ingredients don't really reflect weathered residues even though total residues in the larger regime (21 ppm) may approximate the total residue in the livestock diet.

What do these studies show? Maybe that the total residue in tissues from doses approximating that expected in the livestock diet are no higher than 0.06 ppm (provided we spiked the diet with the right residues and provided the method extracts the residue). Are the residues in the treated beans the same as those expected in the forage? (In other words, is the feeding of the residue on the weathered bean pertinent to forage?) There are several questions that still need to be resolved.

In view of the above, before any further consideration for tolerances on alfalfa and soybean forage and hay, the petitioner will need to carry out a new lactating animal metabolism study at a feeding level between 50-100 ppm ^{14}C-BAS 9052H (parent compound); the last metabolism study submitted was carried out at a level of 1.25 ppm.

The petitioner will also need to submit data from a poultry metabolism study carried out at a feeding level between 10-20 ppm ^{14}C-BAS 9052H.

Alfalfa containing residues at levels between 20-40 ppm would put about 1-2 ppm BAS 9052H residues in chicken diet and about 4-7 ppm BAS 9052H residues in turkey diet.

For both studies (animal and poultry), the petitioner should make all attempts (acid, base hydrolysis, etc.) to extract and characterize possible polar and bound residues. For example, methanol, the extraction solvent used in the analytical methodology for plant and animal commodities, extracted only about 33% of weathered residues on soybeans harvested 35 days after application (see Our Comments/Conclusions on Plant Metabolism above).

Analytical Methodology

The analytical method used to measure Poast® [BAS 9052H] and its

metabolites in soybean and alfalfa forage and hay is BWC Agricultural Chemicals Method 30B. This method is a derivation of Methods Nos. 30 and 30A which was submitted in the proposals for permanent tolerances (PP#2F2670) in or on soybeans, meat, milk, poultry and eggs commodities and for permanent tolerance/FAT in or on cottonseed/cottonseed soapstock (PP#2F2748).

In brief, the soybean forage and alfalfa forage, hay and seed were extracted with methanol, carried through precipitation, dichloromethane partition, oxidation, methylation, dichloromethane partition, and silica gel column clean-up steps (for alfalfa hay only, another dichloromethane partition step was used); then, the samples were analyzed by a gas chromatograph equipped with a sulfur specific FPD detector.

A summary of the recoveries of Poast® [BAS 9052H] and its metabolites using Method No. 30B is given below:

	Fortification Level, ppm	Range Percent Recovery
Soybean forage		
BAS 9052H	0.05-100	52-100
MSO	0.05-60	58-69
MSO_2	0.05-60	63-110
M2SO	0.05-60	44-64
$M2SO_2$	0.05-60	51-98
M1S	0.05-60	58-73
5-OH-MSO_2	0.05-100	59-118
Alfalfa forage		
BAS 9052H	0.05-20	75-102
MSO	0.05-30	79-103
MSO_2	0.05-1	76-103
M2SO	0.05-1	62-68
$M2SO_2$	1.0	68-70
M1SO	0.05-1	60-92
5-OH-MSO_2	0.05-30	70-99
Alfalfa Hay		
BAS 9052H	0.05-15	73-99
MSO	0.05-15	80-95
MSO_2	0.5 -1.0	84-97
M2SO	1.0	66-76
$M2SO_2$	1.0	75-80
M1SO	0.1 -1.0	59-92

Method No. 30B (continued)

5-OH-MSO_2	0.05-15	63-99
Alfalfa seed		
BAS 9052H	0.05	103
MSO	0.05	110
M2SO	0.05	88
M1SO	0.05	100
5-OH-MSO_2	0.05	83-97

Our Comments/Conclusions on the Analytical Methodology.

We (see memo of M. Nelson, April 22, 1983 PP#2F2670) concluded previously that adequate methodology was available for regulating BAS 9052H residues in/on soybean grain, cottonseed, cottonseed soapstock, and animal commodities. However, the plant metabolism data submitted in the present petition (see the Plant Metabolism section of this review) have caused some concern as to whether or not the aforementioned analytical methodology is suitable for regulating BAS 9052H/metabolites residues in raw agricultural commodities. Our reasons are given below.

The soybean metabolism study (Lab. Report No. PM-39) submitted in the present petition used methanol as the extraction solvent; methanol is also used as the extraction solvent in the proposed regulatory procedure (Method 30B). We noticed that at 0-day, methanol extracted 80% of the radioactivity; at a 7-day PHI, it extracted 53% of the radioactivity; and at a 35-day PHI, it extracted only 33% of the radioactivity. Therefore, methanol extracted less BAS 9052H (weathered) residues as the PHI increased.

We recognize that the preceding recoveries for BAS 9052H and its metabolites are within an acceptable range, but we interpret that these recoveries reflect the immediate extraction of added compounds (BAS 9052H, MSO, etc.) from soybean forage, and alfalfa forage, hay and seeds. Since, we observed in the soybean metabolism study that acid released much of the radioactivity from the plant matrix, we are suggesting to the petitioner that he may want to carry out his initial extraction of plant samples with a solvent mixture of methanol and acid, or he may want to apply ultrasonic treatments, enzymatic hydrolyses, etc., during any step of the sample preparation in an effort to release more of the bound residues from the plant matrices.

In view of the preceding, we conclude that the proposed regulatory method (No. 30B) needs to be further investigated for the extraction of weathered residues (BAS 9052H and metabolites) from soybean and alfalfa forage and hay. In brief, we require the petitioner to validate the analytical methodology as part of the ^{14}C metabolism studies.

Residue Data

Storage Stability. Two freezer storage stability studies were carried out. In the first study, control soybean forage samples were fortified with approximately 1 ppm BAS 9052H and approximately 1 ppm MSO standards. The samples were stored frozen at -15°C and analyzed at various intervals through 27 months of freezer storage. The recoveries for BAS 9052H ranged from 81 to 118%, and the recoveries for MSO ranged from 75 to 112%. However, when control samples were fortified and analyzed the same day as the stability samples, the recoveries for BAS 9052H were 67, 67, 76, 60, 69, and 68%, and the recoveries for MSO were 66, 63, 83, 71, 63, and 64%. In the second freezer storage study soybean seed samples were fortified with approximately 1 ppm BAS 9052H or with 0.5 ppm of each MSO_2, $M2SO_2$, and 5-OH-MSO_2. The samples were stored frozen at -15°C and analyzed at various intervals through 24 months of freezer storage. Control samples were also fortified and analyzed the same day as the stability samples; results are summarized below:

	Percent Recovered	
Compound	Stored samples	Samples Fortified at Time of Analyses
BAS 9052H	85-114	62-82
MSO_2	92-107	49-66
$M2SO_2$	92-108	49-56
5-OH-MSO_2	70-94	60-85

In the above studies, the recoveries of BAS 9052H and its metabolites from stored samples are surprisingly much higher than the recoveries of standards/residues from samples that were fortified at time of analyses; the petitioner should explain this difference.

Field residue data on alfalfa forage, hay and seed. Residue studies were carried out in the states of Illinois, Connecticut, Arizona, California, Washington, Michigan and Wisconsin. The alfalfa plots were treated with one or two (0.5 lb. a.i., 0.5 lb. a.i. plus 0.5 lb. a.i., 0.4 lb. a.i., 0.4 lb. a.i. plus 0.4 lb. a.i., or 1.0 a.i.)/A applications of Poast. The residue data do not indicate the mode (ground or air) of application; we will need this information.

Alfalfa forage samples were harvested at 5 to 130 days after the last treatments, and the total residue (parent + metabolites) values, except for one sample-coded 503, ranged from <0.05 to 14 ppm; the one sample aforementioned had been allowed to dry prior to analysis, and it contained a total residue of 38.0 ppm (BAS 9052H plus metabolites) at a 7-day PHI. Of those samples containing <0.05 to 14 ppm, the highest value 14 ppm was observed at a 7-day PHI. Residue values for the controls

ranged from <0.05 to 2.1 ppm.

Alfalfa hay samples were collected at 17 to 130 days after the last treatments, and the total residue (parent + metabolites) values ranged from <0.05 to 12.7 ppm. Residue values for the controls ranged from <0.05 to 1.5 ppm.

Alfalfa seed samples were also harvested in California at 67 days after the last treatment, and the total residue (parent + metabolites) values ranged from 0.21 to 0.48 ppm. A control value of 0.09 ppm was reported.

Our Comments/Conclusions on the Field Residue Data for Alfalfa Forage and Hay.

Referring to the soybean metabolism study (Lab. Report No. PM-39) in this review, we find that methanol, which is used as the extraction solvent, will extract about 53% of weathered residues in/on soybean plants harvested 7 days after treatment. Thus, we will have to reserve a conclusion on the adequacy of the proposed 20 ppm tolerance on alfalfa forage and hay until those questions raised in the Nature of the Residue and Analytical methodology sections of this review have been resolved.

Incidently, we noticed that alfalfa forage sample coded 503 (Illinois) had a residue of 38 ppm at 7 days after harvesting; the reason given was "Sample had been allowed to dry prior to analysis." Since alfalfa hay could be considered dried alfalfa forage, the petitioner's label contains a 7-day PHI, and the total residue values on alfalfa hay harvested 17 days (lowest sample interval submitted) after application ranged from 9.5 to 12.8 ppm, we ask the petitioner to expand on the preceding explanation.

Field Residue Data on Soybean Forage. Residue studies were carried out in the states of Iowa and Mississippi. The soybean plots were treated with one or two (0.75 lb. a.i., 0.75 lb. a.i. plus 0.75 lb. a.i., 0.84 lb. a.i., or 0.84 lb. a.i. plus 0.84 lb. a.i.)/A applications of Poast (the proposed application rate range from 0.1-0.8 lb. a.i./A/season). The residue data do not indicate the mode (ground or air) of application; we will need this information.

Soybean forage samples were harvested at 0 to 90 days after the last treatments, and the total residue (parent + metabolites) values ranged from <0.05 (PHI=90 days) to 78.5 ppm (ppm (PHI=0 day).

Our Comments/Conclusions on the Field Residue Data for Soybean Forage and Hay.

At this time, we reserve our conclusions on the adequacy of the proposed tolerances on soybean forage and hay until those questions relating to plant metabolism and analytical methodology have been resolved. Also, the petitioner should be informed that we will need residue data on

soybean hay after the aforementioned questions have been resolved.

In view of the questions, raised on the adequacy of the methodology for determining Poast® residues in soybean forage and alfalfa forage and hay, we now question the adequacy of the established tolerance on soybean seeds. The petitioner should address this issue also.

Meat, Milk, Poultry, and Eggs

The feed items asociated with the proposed use are soybeans, soybean hulls, meal, soapstock, ensiled, hay, straw, and forage; also, alfalfa forage, seed, hay, and meal. Soybean seed may comprise up to 50% of the diet of laying hens and up to 25% of the diet of other animals. Soybean hay and forage may comprise up to 40% of the diets of dairy cattle and sheep. Alfalfa forage and hay may comprise up to 100% and 80% of the diets of horses and dairy cattle, respectively. Alfalfa meal may comprise up to 5%, 50%, 60%, 80%, and 100% of the diets of poultry, swine, sheep, dairy cattle, and horses.

Feeding studies with lactating dairy cows (administered 0, 0.6, or 50.0 ppm BAS 9052H for 30 days) and laying hens (fed 0, 1, 10, or 100 ppm BAS 9052H for 30 days) were first reported in PP#0G2396 (see our December 4, 1980 review of PP#G2396 - E. Zager and our July 23, 1982 review of PP#2F2670 - M. Nelson).

Analyses of meat, milk, and egg samples were originally via Method 29 (described in aforecited review), which would not have detected any hydroxy metabolites present.

In a conference held June 11, 1981 re PP#0G2396, RCB agreed that the petitioner could reanalyze meat and poultry samples from these feeding studies by analytical methodology capable of determining hydroxylated metabolites (i.e., Method 30; see Analytical Methods section) for purposes of a permanent tolerance petition in lieu of conducting further feeding studies (see conference memo of June 17, 1981, PP#0G2396, for confirmation).

Subsequently in PP#2F2748, the petitioner submitted comparative analyses of meat (beef muscle, liver, and kidney), milk, and egg samples from the aforementioned studies. The results of these comparative analyses (conducted on samples from the highest feeding level of each study only) show that the data obtained by the two methods are in reasonable agreement since none of the reanalyzed samples contained detectable residues ($\geq$ 0.05 ppm) of hydroxylated metabolites.

In milk, no detectable residue ($\geq$ 0.05 ppm) of BAS 9052H equivalents was found in any sample at the 0.6 ppm (Method 29) or 50 ppm (Methods 29 and 30) dosing level. Also, no detectable radioactive residue ($\leq$ 0.003 ppm) could be found in the milk from the goat dosed at 1.25 ppm with ^{14}C-

BAS 9052H.

For milk, we therefore conclude that the proposed 0.05 ppm tolerance level for residues in milk is appropriate in conjunction with the proposed use (even taking recovery values averaging 72±8 or 70±11%, depending on the analytical method, into account; we are presuming the feeding study data is "raw," as the crop data is).

In beef muscle, no detectable residue (≤ 0.05 ppm) of BAS 9052H equivalents was reported in any sample from cows dosed at either the 0.6 ppm (Method 29) or 50 ppm (Methods 29 and 30) levels.

In beef kidney, no detectable residue (≤ 0.05 ppm) of BAS 9052H equivalents was reported in samples from cows dosed at the 0.6 ppm (Methods 29) level. However, cows dosed at the 50 ppm level showed residues in kidney samples ranging between <0.05-0.09 ppm (Method 29) and 0.07-0.10 ppm (Method 30).

In beef liver, as with kidney, NDR (<0.05 ppm) were reported in 0.6 ppm (Method 29) level samples. Cows dosed at the 50 ppm level showed residues in liver samples ranging between <0.05-0.12 ppm (Method 29) and <0.05-0.15 ppm (Method 30).

In poultry muscle, no detectable residue (<0.05 ppm) of BAS 9052H equivalents was found (Method 29) in any samples from the 1.0 ppm or 10 ppm (with one exception, 0.11 ppm, allegedly aberrant) feeding levels. Residue values of <0.05-0.19 ppm were found (Method 29; insufficient sample for reanalysis via Method 30) in muscle tissues from the 100 ppm level.

In poultry liver, NDR (<0.05 ppm) were reported (Method 29) in any samples from the 1.0 ppm feeding level. Residue levels of <0.05-0.17 ppm and 0.23-0.47 ppm were found (Method 29 only) in samples from the 10 and 100 ppm levels, respectively.

As for eggs, no credible (two reportedly aberrant values, however) detectable residues (>0.05 ppm) were found (Method 29) in samplings from the 1.0 ppm feeding level. Residue levels between <0.05 and 0.34 ppm were reported (Method 29) in egg samples from the 10 ppm level. And, residue levels of <0.05 to 1.88 ppm (Method 29) and 0.15 to 1.6 ppm (Method 30, limited sampling) were reported in eggs from the 100 ppm level.

The petitioner has submitted a feeding study entitled, "Determination of BAS 9052H and its Metabolites Residues in Goat Tissue (Kidney, Liver, Muscle) and Milk Samples Obtained From Goats Exposed to Twenty-Eight Consecutive Daily Doses of BAS 9052H Weathered Residues" in the present petition; this is a cold feeding study.

In brief, two control goats were individually fed a ration of 300 g

untreated cracked soybean seed plus 700g standard ration daily. One of the goats was also given an empty gelatin capsule by a ball gun. The goats used for treatment were divided into two groups; each group contained 3 goats. Group I goats were fed daily 1 kg of a mixture composed of 300 g treated cracked soybean seed plus 700g standard dairy ration. Group II goats were fed the same ration as Group I goats plus a gelatin capsule containing 15 mg MSO and 15 mg 5-OH-MSO_2.

The petitioner summarizes the residue contents in the cracked soybean seed, dairy ration mixture, and gelatin capsules as follows:

The goat feed (dairy ration mixture) was prepared from cracked soybean seed containing the following residue:

21.4 ± 1.8 ppm BAS 9052H equivalents from DME.
8.7 + 0.6 ppm BAS 9052H equivalents from DME-OH.
30.1 ± 2.3 ppm BAS 9052H equivalents total.

The goat feed (dairy ration mixture) prepared from cracked soybean seed contained the following residue:

8.2 ± 2.1 ppm BAS 9052H equivalents from DME.
3.1 + 0.8 ppm BAS 9052H equivalents from DME-OH.
11.2 ± 2.9 ppm BAS 9052 equivalents total.

The gelatin capsules contained the following residue:

10.1 ± 2.6 ppm BAS 9052H equivalents from DME.
11.0 + 0.8 ppm BAS 9052H equivalents from DME-OH (5-OH-MSO_2).
21.1 ± 2.5 ppm BAS 9052H equivalents total.

After making corrections for recovery efficiency of the analytical method and after making the assumption that 25% of the total dietary consumption of a lactating goat can be in the form of soybean seed, the petitioner calculated that goats in Group I were fed an average of 7 ppm BAS 9052H equivalents in their total diet, and those goats of Group II were fed an average of 21 ppm BAS 9052H equivalents.

All milk, kidney, liver, and muscle control samples of Groups I and II contained less than 0.05 ppm BAS 9052H residues. Of the treated goats, one kidney sample contained 0.06 ppm BAS 9052H equivalents; all of the remaining kidney samples, milk liver, and muscle samples of Groups I and II contained less than 0.05 ppm BAS 9052H equivalents. The duration of the feeding studies was 28 days.

Our Comments/Conclusions on Residues in Meat, Milk, Poultry and Eggs.

After considering the proposed uses and reviewing the residue data submitted in PP#2F2670 and 2F2748, FAP#3H5392, and subsequent amendments, we recommended for the meat, milk, poultry and egg tolerances established

in 40 CFR 180.412. However, with the new proposed uses on soybeans (with no forage, ensilage, and hay restrictions) and alfalfa, we are now unable to draw any conclusions on the adequacy of the established meat, milk, poultry, and eggs tolerances until those questions raised in the Animal Metabolism and Analytical Method sections of this review have been resolved.

Other Considerations.

An International Residue Limit Status sheet is attached to this review. No Codex, Canadian, or Mexican tolerances have been established for Poast® [BAS 9052H] in or on alfalfa and soybean forage and hay.

cc: R.F., Circu, J.H. Onley, TOX, EEB, EAB, FDA, PP#3F2904, Robert E. Thompson (RTP)
RDI:Section Head:R.D.Quick:Date:12/23/83:R.D.Schmitt:Date:12/23/83
TS-769:RCB:Reviewer:J.H.Onley: RAVEN:RM:1123:DCR-34335:1/9/84:J. Onley:1/5/83:
corrected by:LDT:1/10/84

INTERNATIONAL RESIDUE LIMIT STATUS

CHEMICAL sethoxydim

PETITION NO 3F2904

CCPR NO.

Reviewer: J. Onley

7.A 11/17/83

Codex Status

[✓] No Codex Proposal Step 6 or above

Proposed U. S. Tolerances

Residue (if Step 9):

Residue: Poast (Sethoxydim) and metabolites

Crop(s)	Limit (mg/kg)

Crop(s)	Tol. (ppm)
Soybeans, hay and forage	20.0
Alfalfa, hay and forage	20.0

CANADIAN LIMIT

Residue: presumably parent

MEXICAN TOLERANCIA

Residue:

Crop	Limit (ppm)
Soybeans	0.1 1/

Crop	Tolerancia (ppm)
none	

Notes: 1/ Negligible residue type tolerance

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