

US EPA ARCHIVE DOCUMENT



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

OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

MEMORANDUM

DATE: 25-OCT-2001

SUBJECT: PP# 9F05092. **IMAZAPIC**. Additional Data to Amend HED's Residue Data and Analytical Methods Memorandum Concerning Pasture and Rangeland Grasses (D269038, W. Donovan, 12-JUN-2001). Barcode D278411. PC Codes 128943 & 129041. Case 291904. Submission S604551.

FROM: William H. Donovan, Ph.D., Chemist *William H. Donovan*
Registration Action Branch 1 (RAB1)
Health Effects Division (HED) (7509C)

THROUGH: G. Jeffrey Herndon, Branch Senior Scientist *G. Jeffrey Herndon*
RAB1/HED (7509C)

TO: Jim Tompkins/Stephanie Syslo, PM Team 25
Registration Division (7505C)

BASF Corporation submitted additional imazapic-related information in response to a memo identifying deficiencies in the residue chemistry database (D269038, W. Donovan, 12-JUN-2001). The following is HED's review of the additional data and summary of which deficiencies have been resolved and which remain outstanding.

The revised Section F of this petition proposes the establishment of the following permanent tolerances for residues of the herbicide imazapic [(±)-2-[4,5-dihydro-4-methyl-4-(1-methylethyl)-5-oxo-1H-imidazol-2-yl]-5-methyl-3-pyridinecarboxylic acid] and its metabolite (±)-2-[4,5-dihydro-4-methyl-4-(1-methylethyl)-5-oxo-1H-imidazol-2-yl]-5-hydroxymethyl-3-pyridinecarboxylic acid both free [CL 263284] and conjugated [CL 189215] in/on:

- Grass, forage 30 ppm
- Grass, hay 15 ppm

In addition, the petitioner has also proposed the following permanent tolerances for residues of imazapic and its metabolite CL 263284 in/on the commodities listed below:

Milk	0.10 ppm
Meat*	0.10 ppm
Fat*	0.10 ppm
Meat byproducts (except kidney)*	0.10 ppm
Kidney*	1.0 ppm

* Of cattle, goats, horses, and sheep

Executive Summary of Chemistry Deficiencies

- ▶ Agency validation of the grass and livestock analytical enforcement methods.
- ▶ Receipt and evaluation of the additional grass field trials BASF has agreed to conduct.

Detailed Considerations

1. Additional grass field trials.

Deficiency - Conclusions 10a - 10c from Memo, D269038, W. Donovan, 12-JUN-2001:

- 10a. The submitted grass field trial data are inadequate to support the proposed uses of imazapic on the crop group Grass Forage, Fodder, and Hay (Crop Group 17). The petitioner has not provided adequate residue data reflecting the maximum proposed use pattern of imazapic on grasses (a single postemergence application at 0.1875 lb ae/A with a 0-day PHI for forage and a 7-day PHI for hay). Only eight grass field trials were conducted according to the maximum proposed use pattern; the Agency (Table 5 of OPPTS 860.1500) requires a total of 12 trials (geographic distribution unspecified) for the establishment of tolerances for residues in/on grass commodities, with four trials each to be conducted on the representative cultivars of Bermuda grass, bluegrass, and bromegrass or fescue for establishment of crop group tolerances (Table 2 of OPPTS 860.1500). Also, no field trial data were submitted in support of the 0.0625 lb ai/packet WDG acid formulation, which represents a different formulation class as well as a different chemical form of imazapic; under current Agency policy, the results of trials reflecting a representative of each formulation type and/or major form of an active ingredient (e.g., the acid vs. salt) must be compared to determine if there is an effect of formulation type/chemical form on the relationship between application rate and residue level.
- 10b. In support of postemergence use of imazapic on grasses, the petitioner should conduct four additional field trials reflecting a single postemergence application of the 2 lb ae/gal ammonium salt SC formulation at 0.1875 lb ae/A. Because it appears that residues may be higher in trials conducted in late summer or fall, the petitioner is advised to conduct the required trials during these seasons, preferably in Regions 7 and 8.
- 10c. In support of the 0.0625 lb ai/packet WDG acid formulation, field trials reflecting a 25% reduction in the number of trials (i.e., 9 instead of 12) would be appropriate to support registration of the WDG acid formulation for use on grasses. **Should the petitioner choose to conduct these trials side-by-side with the maximum rate ammonium salt SC formulation trials, then only 4 side-by-side trials are necessary.**

Petitioner's Response

To support the use of PLATEAU® DG herbicide for the grass pasture/rangeland market, BASF agrees to conduct four (4) side-by-side trials of the WDG acid formulation with the maximum rate trials of the ammonium salt SC formulation.

BASF agrees to submit four (4) additional field trials reflecting the single postemergence application of the ammonium salt SC formulation at 0.1875 lb ae/A. The trials will be conducted in late summer or fall in Regions 7 and 8.

HED's Conclusion

Upon receipt of the results of these studies and determination of their adequacy, this deficiency will be resolved. **This deficiency remains outstanding.**

2. Goat metabolism study/bovine feeding study.

Deficiency - Conclusion 4c from Memo, D269038, W. Donovan, 12-JUN-2001:

- 4c. Because CL 263284 is a significant grass metabolite and may be consumed by ruminants, a goat metabolism study using ¹⁴C-labeled CL 263284 is needed to adequately delineate the nature of the residue in ruminants. Alternatively, a bovine feeding study where cattle are fed CL 263284 at 1x, 3x, and 10x the maximum theoretical dietary burden (MTDB) may be conducted.

Petitioner's Response

A goat metabolism study using ¹⁴C-labeled CL 263284 was previously submitted (MRID 433203-19). The review of that study concludes that "the metabolic fate of radiolabeled CL 263284, the hydroxylated metabolite of CL 263222, was determined in lactating goats." [D207019, J. Garbus, 18-SEP-1995].

Lactating goats were orally treated with 0, 2.33, or 14.5 ppm daily doses of [6-pyridine-¹⁴C] CL 263284 for seven consecutive days. The maximum residue levels of CL 263284 measured in the residue studies conducted at the maximum proposed use pattern of imazapic on grasses (a single postemergence application at 0.1875 lb ae/A with a 0-day PHI for forage and a 7-day PHI for hay) were 3.0 ppm for forage and 6.0 ppm for hay at a 7-day PHI or longer. Because no grass silage data are available, the maximum residue level from grass forage was used as recommended in 860.1000. The calculation of the maximum theoretical dietary burden (MTDB) based on these residue levels is presented in Table 1 below.

Feed Item	Maximum residue level ¹	%DM ²	% in Diet ²	MTDB ³ (ppm)
			Beef and Dairy Cattle	Beef and Dairy Cattle
Grass Forage	3.0	25	60	7.2
Grass Silage ⁴	3.0	40	40	3.0
TOTAL			100	10.2

¹ From Table 15 (D269038, W. Donovan, 12-JUN-2001).

² The % dry matter (%DM) and % in diet values for each feed item were based on information contained in Table 1 of OPPTS Test Guidelines Series 860.1000.

³ The maximum theoretical dietary burden for each feed item is calculated by multiplying (Tolerance/%DM) by the % of the feed item in the diet. The total MTDB is the sum of the individual feed item dietary burdens.

⁴ Because no grass silage data were provided, the tolerance level from grass forage was translated as recommended by 860.1000.

Using this MTDB of 10.2 ppm for CL 263284, the maximum dose rate of 14.5 ppm of the goat metabolism study represents 1.4x the maximum potential residue of CL 263284.

The results of this lactating goat study showed that CL 263284 was excreted without retention or accumulation in milk. After 7 days, radioactivity in blood, milk, liver, muscle, and fat was less than 0.01 ppm at all feeding rates. Of the edible tissues only kidney showed detectable residues (0.03 ppm at the 14.5 ppm dose rate) and these were identified as CL 263284 and a labile salt of CL 263284 which readily reverted to CL 263284 in aqueous media. The study director concluded that ruminants fed commodities containing CL 263284 residues would not produce secondary metabolites as tissue residue, and that elimination of CL 263284 via urine and feces is rapid and efficient.

HED's Conclusion

The submitted goat metabolism study did not show significant uptake of CL 263284 in any tissue matrix and did not find the presence of any other metabolites. Because the HED Metabolism Assessment Review Committee (MARC) determined that the residues of concern in livestock commodities consist of imazapic and CL 263284 (D275136, W. Donovan and W. Dykstra, 07-JUN-2001), and the bovine feeding study analyzed for both compounds, HED concludes that the recommended tolerance levels for imazapic residues in livestock commodities (D269038, W. Donovan, 12-JUN-2001) are adequate at this time. This conclusion should be reviewed upon receipt of the requested additional grass field trial data. **This deficiency is now resolved.**

3. Rotational Crop Intervals

Deficiency - Conclusion 13e from Memo, D269038, W. Donovan, 12-JUN-2001:

- 13e. The submitted rotational crop data reflecting the grass use rate support establishment of a 6-month PBI for small grains, an 11-month PBI for root and tuber crops, and a 12-month PBI for leafy vegetables. The proposed 4-month PBI for rye and wheat and 9-month PBI for legume vegetables are not currently supported by rotational crop data. If the petitioner wishes to establish PBIs less than those reflected in the current confined rotational crop study, limited field rotational crop studies or additional confined rotational crop studies making use of the grass application rate *and* desired PBI are recommended. Alternatively, the petitioner may increase the rye and wheat PBIs from 4 to 6 months, and increase the PBI for legume vegetables to 12 months. **The petitioner should submit additional rotational crop data or a revised Section B with updated rotational crop intervals for rye, wheat, and legume vegetables.**

Petitioner's Response

BASF accepts the revised PBIs as minimum rotational crop intervals and will submit revised PBI wording on the label (Section B) with other required label changes as agreed with J. Stone of PM Team 23.

HED's Conclusion

This deficiency is now resolved.

4. Revised Section F.

Deficiency - Conclusions 10h and 11d from Memo, D269038, W. Donovan, 12-JUN-2001:

- 10h. The available field trial data support tolerance levels for residues of imazapic and its metabolites CL 263284 and CL 189215 in/on grass forage at 30 ppm and grass hay at 15 ppm. However, these levels may be adjusted as necessary when the requested additional data have been submitted and evaluated. In the tolerance expression, HED recommends that the petitioner remove references to the form of imazapic applied. **A revised Section F should be submitted.**
- 11d. Based on the information presently available, the appropriate tolerance level for meat, fat, milk and meat byproducts (except kidney) is 0.10 ppm. For kidney, the appropriate tolerance level is 1.0 ppm. However, these levels may be adjusted as necessary when the requested additional grass field trial data have been submitted and evaluated. **A revised Section F should be submitted.**

Petitioner's Response

Submission of a revised Section F consistent with HED's request.

HED's Conclusion

This deficiency is now resolved.

cc: W. Donovan, D. Vogel
RDI: G. Kramer (25-OCT-2000), RAB1 Chemists (25-OCT-2001)
W. Donovan:806R:CM#2:(703)-305-7330:MC 7509C