

DIETARY EXPOSURE BRANCH, HED
DATA REVIEW QUICK FORM

Date: NOV 18 1988

MEMORANDUM

SUBJECT: Petition Review for Establishment
of Tolerance(s).
Evaluation of Analytical Method(s)
and Residue Data.

FROM: Stephanie H. Willett, Chemist SHW
Tolerance Petition Section
Dietary Exposure Branch
Health Effects Division, TS-769C

THRU: Charles L. Trichilo, Ph.D., Chief
Dietary Exposure Branch
Health Effects Division, TS-769C

TO: Robert Taylor PM 25
Registration Division, TS-767C

and

Toxicology Branch - HFA Support
Health Effects Division, TS-769C

1. Petition No(s): 8F3672/8H5562
2. DEB No(s): 4357, 4358
3. MRID No(s): 405026-02, -04, -05
4. Pesticide(s): glyphosate
5. Tolerance Proposal (RACs & Levels): Sorghum grain, Fodder,
and Storage at 5, 20 and 20 ppm respectively; sorghum
milling fractions (excluding grits) - 25 ppm
6. Petitioner: Monsanto

- * 7. Tolerance Expression: glyphosate
Established tolerances are for glyphosate and its metabolite
AMPA (N-aminomethylphosphonic acid)
8. Established Pesticide Tolerances: 40 CFR 180.364
at levels ranging from 0.1 to 200 ppm on various AACs
9. Established Food Additive Tolerances: 21 CFR 193.235
sugarcane (molasses) - 30 ppm; palm oil - 0.1 ppm; olives
(imported) - 0.1 ppm; dried tea - 1.0 ppm; instant tea - 4.0 ppm
10. Established Feed Additive Tolerances: 21 CFR 561.253
0.4 ppm - citrus pulp
20 ppm - soybean hulls
11. Is Pesticide a Registration Standard Chemical? (Yes/No) Yes
If yes, date Guidance Document issued: June 1986
12. Letter(s) of Authorization (if applicable): _____
13. Formulation(s): Roundup Herbicide, EPA Reg. No.
S24-308-AA, contains 3 lb glyphosate acid equiv/gal.
14. Inerts Status: cleared under 40 CFR 180.1001
15. Manufacturing Process: Adequately described for the purposes
of this petition. See PP# 6E338/FAP# 6H5502,
MRID # 401558-01, -02. Levels of N-nitrosoglyphosate
in technical product and nitrosamines in Roundup are
not of concern (see memos of W. Dykstra, 2/11/88 and W.
Clin, 2/25/88, PP # 6E3424).

16. Proposed Use(s): To be added to the preharvest section of the current label

- Preharvest applications - When applied as directed under the conditions described, this product will control or suppress annual and perennial weeds prior to the harvest of grain sorghum (milo).
- Apply up to but no more than 1 quart per acre of this product plus 0.5 to 1 percent nonionic surfactant by total spray volume in 3 to 20 gallons of water per acre.
- For ground applications, use this product in 3 to 20 gallons of water per acre. For aerial applications, use this product in 3 to 10 gallons of water per acre.
- Apply this product after maximum head fill or seed set is complete and the crop is physiologically mature. Make applications when the moisture content of the milo is 30 percent or less. Allow a minimum of 7 days between application and harvest.

17. Plant Metabolism Data on: Citrus, coffee, pome fruits, alfalfa, grapes, sugarcane, soy beans, nuts, cotton, wheat, corn, string beans, peas, carrots, cabbage. See Residue Chemistry Chapter of Reg. Std. No new metabolism studies were submitted with this petition.

18. Plant Residues Comprised of: parent glyphosate, AMPA and other minor metabolites. See Residue Chemistry Chapter of Reg. Std (5/31/85).

19. Plant Metabolism Data Translatable Here: all

20. Nature of Plant Metabolism on the Subject RAC(s) of This Petition is/is not adequately defined.

The Residue of Concern is: parent glyphosate and its AMPA (N-aminomethylphosphonic acid) metabolite

21. Animal Metabolism Data on: rats, fish, rabbits and
cattle. (see Reg Std). No additional metabolism data
submitted here.

22. Animal Residues Comprised of: parent, AMPA and MAMPA
in rats; parent and AMPA in fish. Residues
were not characterized in the ruminant metabolism
study

23. Animal Metabolism Data Applicable Here: none

* 24. Nature of Animal Metabolism Data is/~~is not~~ adequately defined.
The Residue of Concern is: not adequately understood.
Additional metabolism studies were requested in the
Reg. Std. dated 7/15/85.

25. Analytical Method(s) (Give Reference and/or Brief Description).
Analytical Residue Method For N-Phosphonomethyl Glycine,
and AMPA in Raw Agricultural Commodities and Water
MRID No. 405026-02

Glyphosate and AMPA can be isolated from various matrix extracts
and water by elution through Chalex 100 resin in the Fe (III) form.
Glyphosate and AMPA are eluted from the resin with HCl and
the iron is removed using an anion exchange resin. After
concentration to dryness to remove the HCl, samples are
analyzed using HPLC equipped with a o-phthalaldehyde
post-column reactor and a fluorescence detector.

26. Has there been a Method Trial? (Yes, No) Yes

If yes, provide details: GLC method in support of PP#s 4G1444, SF1536 and 6G1679; HPLC method in conjunction with PP#152455

If no, is a Method Trial needed? _____

27. Residues Determined by Method(s): glyphosate and its metabolite, AMPA

28. Method Validation (RACs/"spike chemical"/fortification level(s)/recovery range/average recovery): (HPLC method)

<u>Matrix</u>	<u>% Recovery glyphosate</u>	<u>% Recovery AMPA</u>
<u>milo Grain</u>	<u>84.8 ± 15.3</u>	<u>94.0 ± 14.9</u>
<u>milo Fodder</u>	<u>77.6 ± 8.7</u>	<u>76.1 ± 9.1</u>

Recoveries performed with each analytical set

29. Method Validation (limit of detection and/or sensitivity in ppm):

Parent: 0.05 ppm

Metabolite(s) (specify): AMPA - 0.05 ppm

30. Method Validation (state crops and control values reported):

milo grain: parent, < 0.05 - 0.29 ppm; AMPA - < 0.05 ppm

milo Fodder: parent, < 0.05 - 0.28 ppm; AMPA - < 0.05 ppm

*31. Adequate Analytical Method(s) are are not Available for Enforcement

Purposes unless additional methodology is needed for quantitation of other significant metabolites in animal commodities

These Method(s) are located: PAM II, method 3 (HPLC method)

32. PAM I Multiresidue Methods Data are available for parent pesticide tested via Protocols I II III IV (circle, as applicable). Additional multiresidue test information for parent compound that is needed: Glyphosate has not been tested via the multiresidue method protocols.

* 33. PAM I Multiresidue Methods Data are available for metabolite(s) tested via Protocols I II III IV (circle, as applicable). Additional multiresidue test information for metabolite(s) that is needed: MRM testing has not been conducted for AMPA. See # 32

* 34. Residue Data (RAC(s) and Processed Commodities)
 Field trials were conducted in New Mexico, Kentucky, Arkansas, Missouri, Kansas, Texas, Mississippi and Illinois. Glyphosate was applied by either ground or aerial equipment at 0.38 and 0.75 lb ai/A (0.5 and 1K 7 days prior to harvest. Grain and Sodder were harvested and stored frozen prior to analysis (≤ 15 months). Samples analyzed contained the following residue levels:

Sample	Treatment Rate (lb ai/A)	ppm parent Sound	ppm AMPA Sound
grain	0.38	<0.05 - 1.67	<0.05 (all)
	0.75	<0.05 - 3.21	<0.05 - 0.06
* Sodder	0.38	0.09 - 25.2	<0.05 - 0.25
	0.75	<0.05 - 20.7	<0.05 - 0.24

Grain samples treated at the 1K rate and having the highest residue levels (2-3 ppm) were processed into coarse grits, fine grits, germ-rich grits, bran, germ and flour. The following residue levels were detected (harvest to analysis time ≤ 16 months):

Sample	ppm parent Sound	ppm AMPA Sound
coarse grits	0.73, 1.0	< 0.05 (2 samples)
fine grits	0.89, 1.35	< 0.05 "
germ rich grits	1.06, 1.81	< 0.05 "
bran	3.07, 6.35	< 0.05, 0.07
germ	4.59, 7.79	< 0.05, 0.11
flour	8.57, 16.1	< 0.05, 0.24

All samples were analyzed by methodology previously described (see # 25).

35. Frozen Storage Stability Data are are not Available.

If yes, give RACs/fortification levels/length of storage/recovery range/conditions of storage (°C): corn grain, soybean Storage, sorghum straw, clover, tomatoes (MRLD #405026-05). Reanalysis of field trial samples indicated glyphosate and AMPA are stable for 10-44 months at 50°F. See also Residue Chemistry Chapter of Reg. Std. Residue levels in various crops spiked with glyphosate remained stable for 7 months.

36. Regional Registration is is not involved.

If yes, list States in which use is sought: _____

If yes, indicate/explain (see 51 FR 11341, 4/2/86 - Policy on Minor Uses) if a bona fide "Minor Use" is involved: N/A

37. Geographic Representation is is not adequate. If no, list RAC(s) and States from which additional data are needed: _____

*38. Residues will not exceed proposed tolerance(s) on (commodities) sorghum grain and sorghum milling fractions (excluding grits) but may exceed proposed tolerance(s) on (commodities) sorghum Storage and Feeder

39. Livestock Feeding Studies on (species): poultry, swine and dairy cattle (see Reg. Std). No additional studies were submitted here.

40. Animal Feeding Levels: 10, 30 and 100 ppm. *No detectable residues in milk, eggs, muscle or fat of cattle, swine or poultry from 100 ppm feeding level. Validity questioned since no storage stability data were submitted. Animal metabolism questions also have yet to be answered.*

41. Animal Residue Ingestion Levels from Proposed RAC Tolerance(s)
Levels (proposed tolerance level x percent in diet): 5 ppm in beef cattle; 10 ppm in dairy cattle/goats; 5 ppm in hogs; N/A ppm in horses; N/A ppm in sheep; 3 ppm in poultry.

*42. Livestock Tolerances are Adequate in (species) _____

but not adequate in animal commodities; conclusions will be made after review of metabolism, storage stability and residue data requested in Reg. Std (see Residue Chemistry Chapter, p289.)

43. Livestock Tolerances Need to be Established: Yes/No. If yes, species/levels: _____

*44. Other Comments: No data were submitted on probable residue levels in sorghum starch. See Cultural Practice file and memo of C.L. Trichilo dated 3/21/85. See attached memo.

45. *Note* ----- The main product of dry milling is flour, and of wet milling is starch. Both are primarily utilized in the food processing industry (e.g., as binders, thickening agents, in prepared breakfast foods, in brewing, et al.), but some starch may also be utilized for other industrial purposes (i.e., laundering, adhesives, pharmaceuticals, etc.).

46. Additional Information Needed: _____

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47. Additional Data Needed: 1) revise Section 5 to include AMPA in tolerance expression and increase proposed tolerance on Sockeye/Sorage to ≥ 30 ppm 2) animal metabolism data 3) animal feeding study data to insure adequacy of animal commodity tolerances 4) additional processing study data on sorghum starch from wet milling
*Note: Residue data must be supported by storage stability data.

48. RECOMMENDATIONS: Against the establishment of the proposed tolerances. See #'s 7, 24, 31, 32, 33, 34, 38, 42 and 44.

49. Other Comments Under Recommendations: Additional analytical methodology and feeding studies may be needed if the requested metabolism studies identify additional residues of concern.

50. Compatibility with Codex Tolerances? (Explain) The Codex and proposed US tolerances for sorghum and not compatible. The Canadian IRL is 0.1 ppm (negligible) for residues of glyphosate per se on all food crops. See attachment.

ATTACHMENT(S): (1) International Residue Limits Status Sheet
(2) memo - C. L. Trichulo, 3/21/85

cc: RF, Circ, Reviewer, PP# 8F 3672/845562

PMSD/ISB, FDA.

Approved: J. Onley, J. Onley, 11/15/88; RDSchmitt R. D. Schmitt, 11/12/88

INTERNATIONAL RESIDUE LIMIT STATUS

J. Jones
11/20/88

CHEMICAL Glyphosate

CODEX NO. 158

CODEX STATUS:

No Codex Proposal
Step 6 or above

Residue(if Step 8):
glyphosate (parent only)

PROPOSED U.S. TOLERANCES:

Petition No. 8F3672/8H5562

RCB Reviewer S.H. Willett ¹¹⁻⁹⁻⁸⁸

Residue: N-(phosphonomethyl)
glycine and its metabolite AMPA*

<u>Crop(s)</u>	<u>Limit (mg/kg)</u>
sorghum	0.05 **
straw and fodder (dry) of cereal grains	100

<u>Crop(s)</u>	<u>Limit (mg/kg)</u>
Sorghum grain	5
" Fodder	20
" Forage	20

CANADIAN LIMITS:

No Canadian limit

Residue: _____
parent only

MEXICAN LIMITS:

No Mexican limit

Residue: _____

<u>Crop(s)</u>	<u>Limit (mg/kg)</u>
all food crops	0.1

<u>Crop(s)</u>	<u>Limit (mg/kg)</u>
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NOTES:

* AMPA - aminomethylphosphonic acid
** At or near the limit of determination
4 Negligible Residue from limit


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

MAR 21 1985

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Definition of milled products for various grains.

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

TO: RCB Staff

As a result of the publication of the Residue Chemistry Guidelines, the Branch has received requests for definitions of the commodities designated as milled products for various grains. Unless there is information indicating that other milled products should be considered, the following products should be included in processing studies.

<u>Crop</u>	<u>Milled Products</u>
barley	hulls, bran, flour, pearl barley
buckwheat	hulls, middlings, flour
field corn	wet milling-starch, crude + refined oils
	dry milling-grits, meal, flour, crude + refined oils
guar	meal, gum
millet	hulls, flour, meal
oats	hulls, flour, rolled oats
rice	hulls, bran, polished rice
rye	flour, rye feed (mix of bran, red dog flour, and middlings)
grain sorghum	flour, starch
wheat	bran, flour, middlings, shorts

If an adequate processing study has been conducted on wheat, it would satisfy the requirement for studies on barley, buckwheat, millet, oats and rye. Guar, field corn, rice and grain sorghum would each require their own processing study.

cc: RF, Cultural practices files (corn, grain, guar, oats, rice, sorghum, wheat), Petition Review Aids File