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

(25)

NOV 23 1981

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

#661A

Memorandum

SUBJECT: PP#9F2163/FAP#9H5204. Glyphosate on various crops and water. Amendment of 6/25/81.

FROM: R. B. Perfetti, 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
Herbicide/Fungicide Branch
Registration Division (TS-767)
and
Toxicology Branch
Hazard Evaluation Division (TS-769)

This amendment is in response to our memo of 9/24/80 in which several deficiencies in the subject petition were outlined. These deficiencies, the petitioners response to them along with certain revisions in other aspects of this use are discussed below.

Deficiencies:

1. The following modifications are needed in the proposed regulation for irrigated crops:

   The words "negligible" and "poultry" should be deleted and the phrase "and the individual crops" should be inserted after "stonefruit." The revised regulation should be submitted in a Section F.

2. While we are cognizant of the difficulties encountered in identifying small amounts of material, further identification of the residue in fish is needed. The petitioner was informed of this requirement for a permanent tolerance as early as 1976. In lieu of new metabolism study, however, reanalysis of previous catfish samples containing the highest levels of radioactivity may be submitted. We suggest that proteins be removed from the sample extracts via dialysis rather than precipitation. In order to keep the volume of the samples low, an ultrafiltration system such as made by Amicon using an Amicon Diaflow membrane could be used. The eluate from the ultrafiltration system should contain the protein-free radioactive residue. Also, if the petitioner feels that the glyphosate residues are being catabolized into small fragments and reincorporated into bio-molecules, he should attempt to isolate labeled amino acids (except glycine), sugars, carbohydrates, proteins, etc. If no catfish samples are available, a new metabolism study will be needed.

3. "Cold" residue fish experiments will be more informative at such time as the metabolism situation in fish is clarified.

4. The label restriction prohibiting use of glyphosate on banks of tidewater areas and flooded rice paddies or rice levees is acceptable and must remain on the label until such time as satisfactory shellfish residue studies using "non-aged" residues of glyphosate are submitted.

5. No label restrictions specifying a maximum application rate of 4.0 lb acid equivalent/acre per treatmen of a bank or limiting treatment to 1 mile of shoreline in any 24 hour period appear on the revised label. The 24 hour limitation was discussed in our conference of January 30, 1980, in which it was agreed that the restriction could be kept off the label only if a good case, showing that treating lengths longer than 1 mile would not change the residue picture, could be made. Either such a case for removal of the requirement or submission of a revised Section B containing both label instructions discussed above must be submitted.

6. Removal of the direct application to moving water use until such time as the additional residue studies required by RCB, discussed and agreed to in our conference of May 19, 1980, are completed and submitted, is acceptable.

   Also, when and if the use involving direct application to the surface on non-moving waters is re-proposed, the raw data for the Florida study for this use should be submitted.

7. Until such time as the direct application to moving water residue studies discussed above are submitted, the proposed 0.5 ppm tolerance level for potable water is adequate. If the additional data for direct application to moving water indicates a higher tolerance level is needed, the higher level should be proposed for potable water for all aquatic uses.

8. The available data are adeqate to show that, provided the tolerance level in potable water is 0.5 ppm, residues in the irrigated crops and crop groupings listed in 40 CFR 180. 34 will not be expected to exceed 0.1 ppm, with the exception of the crop grouping small fruits and the individual crop hops. At the very least, irrigated crop residue data is needed for 1 crop in the grouping small fruits and on hops. This data should reflect appropriate irrigation systems and exaggerated application rates.

9. No estimation of an appropriate tolerance level in fish can be made until such time as the metabolism and residue (especially re-proposal of additional aquatic uses) questions discussed in the conclusions above are resolved. No toleance for residues of glyphosate in potable water can be established until tolerances for fish are also established.

10. Secondary residues of glyphosate in meat, milk, poultry and eggs, resulting from feeding of irrigated crops or drinking of water treated with this herbicide, will be covered under present tolerances. If a higher tolerance level for potable water is needed when, for example, the direct application to moving water use or another aquatic use is re-proposed, this conclusion may require modification.

Response to 1:

The petitioner has submitted a revised Section F including these revisions. We consider this deficiency resolved.

Response to 2, 3 and 9:

The petitioner has made no formal response to these deficiencies in this submission. He has however indicated to us in an earlier conference that additional fish metabolism work is being performed at this time and will be completed and submitted presently (See memo of conference 6/29/81, K.H. Arne). We do not consider these deficiencies resolved.

Response to 4:

This restriction has been retained on the label. We consider this deficiency resolved.

Response to 5:

The petitioner has submitted a rationale as to why there is no need to limit the length of treatment of shoreline during any 24 hour period. We are inclined to accept this argument. The petitioner has also submitted a revised Section B incorporating a statement limiting the treatment rate for an application to 3.75 lb acid equivalent/acre. We consider this deficiency resolved.

Response to 6 and 7:

The petitioner has submitted additional residue data for direct application of glyphosate to flowing water. This data reflected one application via ground or air (one study) of 3.75 lb acid equivalent/acre to streams or irrigation canals in Utah, Maryland, Tennessee, Louisiana, Alabama, Texas, Michigan, New York and Florida (one study in each state.) Instantaneous residues (samples taken within 50 ft of application.) of parent ranged from <5 ppb to 1.95 ppm with residues in excess of 0.5 ppm occuring in three of the nine experiments. Residues of aminomethylphosphonic acid ranged from <5 ppb to 15.37 ppb. N-nitroso-N-(phosphomethyl)-glycine residues were all given as <2 ppb. No significant difference in residue levels between ground vs aerial application were observed.

The analyses above were performed using a method other than the one discussed in our original review of this petition. It is found on page 68 of Section D of this amendment (6/28/81). Briefly, the method involves filtration of water samples, dilution with deionized water and clean-up on an anion exchange resin which also separates glyphosate and aminomethylphosphonic acid from N-nitroso-N-(phosphomethyl)-glycine (NNG). The samples are evaporated and further cleaned-up on separate cation-exchange columns. The cation exchange chromatography separates parent form aminomethylphophonic acid. After cation exchange chromatography NNG is analyzed via hplc using a Griess post-column reactor system and measurement of absorbance at 546 nm. The parent and aminomethyl-phosphonic acid samples are derivitized using O-methyl-N, N'-dicyclohexyl pseudourea and quantitated via glc using a phosphorous specific flame photometric detector. Additional clean-up procedures (if needed) involving a Florisil column for glyphosate, an alumina column for aminomethylphosphonic acid or a methanol procedure for NNG are also described.

Validation data reflected fortification of water samples with 5 to 100 ppb of glyphosate or aminomethylphosphonic acid and recoveries ranged form 51.6 to 81.5% and from 51.1 to 76.9% respectively. Blank values for parent and metabolite were <5 ppb to 62.54 ppb and <5 ppb respectively. Water samples fortified with 1 to 16 ppb of NNG gave recoveries of 50.9 to 133.4% with all blank values given as <2 ppb. Sample chromatograms were submitted.

Based on the additional residue data submitted above and in light of the 0.5 mile treatment restriction for potable water intakes we conclude that the proposed 0.5 ppm food-additive tolerance level for this food is appropriate for direct application of glyphosate to moving waters as well as all aquatic uses proposed previously. The correct method of enforcement remains the PAM II procedure as opposed to the new method discussed above. We again request that the raw data for the Florida study involving direct application to non-moving waters be submitted for our files. This information was missing from the original petition.

We consider these deficiencies resolved.

Response to 8:

The petitioner has obtained a 0.2 ppm tolerance for grapes and presents an argument that irrigation of hops would occur such that water would not come in contact with the r.a.c. Based on this we conclude that an 0.1 ppm tolerance for irrigated small fruits and hops is adequate.

We consider this deficiency resolved.

Response to 10:

The petitioner did not need to respond directly to this deficiency. It is our judgement that since the 0.5 ppm tolerance level in water is deemed adequate for all proposed aquatic uses that any secondary residues resulting in meat, milk, poultry or eggs from these aquatic uses will be covered under present tolerances for these commodities. We consider this deficiency resolved.

INERT INGREDIENT INFORMATION Deleted

Other Considerations:

Because of TOX Branch objections the petitioner has modified his formulation of glyphosate for use in aquatic sites. Of the four formulations proposed two have all inerts cleared under Section 180.1001. Two other formulations however contain the [redacted] which is not cleared as an inert ingredient. The petitioner should be informed that this inert must be cleared under §180.1001 before these formulations can be used on food or raw agricultural commodities.

INERT INGREDIENT INFORMATION Deleted

Conclusions:

1. The major remaining questions (see conclusions 2, 3 and 9 in our memo or 9/24/80) with regard to this aquatic use involve the submission of an acceptable fish metabolism study and proposing an appropriate tolerance level in fish. The petitioner has informed us that this metaoblism study is being performed. We await submission of this information.

2. The rice paddy and estruarial treatment restrictions must remain on the label until the shellfish residue studies using "non-aged" residues required earlier are submitted and an appropriate tolerance for shellfish is established.

3. The 0.5 ppm tolerance for potable water is appropriate for this aquatic use.

4. We request that the raw data for the Florida study involving direct application to non-moving waters be submitted for our files. This information was missing from the original petition.

5. A 0.1 ppm toelrance for residues of glyphosate in small fruits and hops is adequate.

6. Secondary residues in meat, milk, poultry or eggs resulting from this aquatic use will be covered under existing tolerances for these commodities.

7. The inert ingredient, [redacted] which is found in two of the new formulations proposed must be cleared under §180.1001 before any tolerances for this aquatic use can be established.

Recommendation

We recommend that the proposed tolerances not be established for the reasons given in conclusions 1, 4 and 7 above. The requirements for resolution of these deficiencies are also discussed in the appropriate conclusions above. The petitioner should also be reminded of our requirement regarding shellfish tolerances discussed in conclusion 2 above.

Attachment

INTERNATIONAL RESIDUE LIMIT STATUS

CHEMICAL N-Phosphonomethylglycine (Glyphosate)

PETITION 9F2163/9H5204

CCPR NO.

Codex Status

[✓] No Codex Proposal Step 6 or above

Residue (if Step 9):

Crop(s)	Limit (mg/kg)
None	

CANADIAN LIMIT

Residue: glyphosate

Crop	Limit (ppm)
Negligible residue of 0.1 ppm on cereals, corn, forage legumes, grasses, potatoes, soybeans, sugar beets.	

Notes:

Proposed U.S. Tolerances

N-phosphonomethylglycine and its metabolite aminomethylphosphonic acid aquatic uses

Residue: See above

Crop(s)	Total (ppm)
Irrigated crops	.1
Fish	.2
Potable Water	.5

MEXICAN TOLERANCIA

Residues:

Crop	Tolerance (ppm)
	none

Chem 100.364 Glyphosate Roundup 8/31/81

File last updated 8/31/81

ACCEPTABLE DAILY INTAKE DATA

RAT, Older	NOEL		S.F.	ADI	MPI
mg/kg	ppm			mg/kg/day	mg/day(60kg)
5.000	100.00		100	0.0500	3.0000

Published Tolerances

CROP	Tolerance	Food Factor	mg/day(1.5kg)
Cottonseed(41)	6.000	0.15	0.01350
Grain Crops(64)	0.100	13.79	0.02069
Avocados(6)	0.200	0.03	0.00009
Citrus Fruits(33)	0.200	3.81	0.01144
Coffee(36)	1.000	0.75	0.01119
Grapes, inc raisins(66)	0.100	0.49	0.00074
Leafy vegetables(60)	0.200	2.76	0.00828
Nuts(101)	0.200	0.10	0.00031
Pome Fruits(126)	0.200	2.79	0.00837
Root Crop Veg(136)	0.200	11.00	0.03299
Seed&Pod Veg(143)	0.200	3.66	0.01098
Soybeans(140)	6.000	0.02	0.00263
Palm Oil(202)	0.100	0.03	0.00005
Kidney(203)	0.100	0.03	0.00005
Pistachio nuts(210)	0.200	0.03	0.00009
Liver(211)	0.100	0.03	0.00005
Asparagus(5)	0.200	0.14	0.00043
Bananas(7)	0.200	1.42	0.00426
Olives(104)	0.100	0.06	0.00009
Stone Fruits(151)	0.200	1.25	0.00374
Sugar,cane&beet(154)	2.00	3.64	0.10915
Molasses(96)	20.000	0.03	0.00920
Cranberries(44)	0.200	0.03	0.00009

MPI	TMRC	% ADI
3.0000 mg/day(60kg)	0.3284 mg/day(1.5kg)	10.95

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Unpublished, Tox Approved 9F2103,2329,2455,9h5204,1E2443,2444,2490,1G2441

CROP	Tolerance	Food Factor	mg/day(1.5kg)
Cucurbits(49)	0.100	2.64	0.00426
Fruiting Vegetables(80)	0.100	2.99	0.00449
Small Fruit,Berries(140)	0.100	0.83	0.00124
Hops(73)	0.03	0.03	0.00005
Fish,Shellfish(59)	2.000	1.08	0.03250
Potable Water(190)	0.500	133.33	1.00000
Peanuts(115)	0.100	0.36	0.00054
Guava(104)	0.200	0.03	0.00009
Papayas(109)	0.200	0.03	0.00009
Cottonseed(41)	9.000	0.15	0.02025
Mangoes(88)	0.200	0.03	0.00009
Kidney(203)	0.400	0.03	0.00010
Liver(211)	0.400	0.03	0.00010

MPI	TMRC	% ADI