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

JUL 13 1990

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: PP#8F3673 - Glyphosate on Field Corn.
Review of the April 2, 1990 Amendment.
(MRID No. 414781-01) [DEB Nos. 6745 and 6746]
(HED Project No. 0-1393)

FROM: Francis D. Griffith, Jr., Chemist
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TO: Robert J. Taylor, PM 25
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and

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Health Effects Division (H7509C)

THRU: Richard D. Schmitt, Ph.D., Chief
Dietary Exposure Branch
Health Effects Division (H7509C)

Monsanto Company has submitted this amendment consisting of a revised Section B (revised directions for use for Roundup® use on corn), supplementary Section D (supplemental corn dry processing study and analytical residue method), and a revised Section F (changed tolerance expression and higher tolerance levels proposed) in response to deficiencies outlined and summarized in our review of February 1, 1989 by M.T. Flood. The deficiencies are listed and repeated in the body of this review in the order they appeared in the February 1, 1989 review, followed by the petitioner's responses, then DEB comments. Our conclusions and recommendation follow.

CONCLUSIONS

1. DEB Conclusion on **Directions for Use**

The petitioner proposed a label restriction on the use of ammonium sulfate as an adjuvant in preharvest

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application of Roundup® to corn. This deficiency is resolved.

The petitioner combined paragraphs and defined the number of gallons of water to mix with Roundup® in air or ground application. This deficiency is resolved.

2. DEB Conclusion on **Residue Analytical Method**

The petitioner has explained that glyphosate and aminomethylphosphonic (AMPA), being very polar and water-soluble compounds, cannot be recovered though FDA's multiresidue methods (MRM). DEB accepts this explanation and waives the requirement for MRM data for glyphosate and AMPA. This deficiency is resolved.

Due to the EPA lab's difficulty in obtaining the custom HPLC column in a timely manner and the lack of specifications for making this column for different matrices, DEB and Analytical Chemistry Branch (ACB)/BEAD terminated the petition method validation (PMV). The column is considered to be unique and exotic. While the HPLC method is not suitable to be an enforcement method, it is suitable to gather residue data. Since DEB and ACB terminated the PMV, the HPLC column issue has become moot.

There are adequate glyphosate residue analytical methods (GLC) available in PAM II to enforce the proposed tolerances.

3. DEB Conclusion on **Magnitude of the Residue - Crop Field Trials**

The petitioner's explanation that glyphosate residues are sometimes higher at 14 days than at 7 days because of senescent loss of plant moisture is plausible. This deficiency is resolved.

The petitioner's explanation that corn forage was not analyzed because Roundup® is applied close to harvest, when no green corn forage is available for sampling, is plausible. This deficiency is resolved.

4. DEB Conclusion on **Proposed Tolerances**

The petitioner confirmed that the proposed tolerances are for combined residues of glyphosate and AMPA. The petitioner has proposed the suggested glyphosate plus AMPA tolerance levels for corn grain, corn fodder and forage, and for livestock kidney and liver. These deficiencies are resolved.

DEB concludes that the proposed tolerances of glyphosate plus its metabolite AMPA on corn grain at 2 ppm, on corn fodder and forage at 35 ppm, and in livestock kidney and liver at 1 ppm are not expected to be exceeded when Roundup® is used as directed.

5. DEB Conclusion on **Magnitude of the Residue Food/Feed**

The petitioner has conducted an adequate supplemental corn dry processing study using treated corn bearing detectable residues. The dry processing closely simulates commercial corn dry processing. Residues of glyphosate plus AMPA did not concentrate in grits (average concentration factor 0.8X to 0.9X) or in corn flour (0.9X). Thus, food additive tolerances are not required for these corn dry processing commodities. The deficiency is resolved.

Glyphosate and AMPA residue data on corn grain dust are required as the proposed use is late season foliar with real residues detected. The petitioner is encouraged to submit a protocol prior to starting any tests.

Once the petitioner has generated the glyphosate and AMPA residue data on corn grain dust with a Food Additive Tolerance request as needed this will engender a review of livestock diets, adequacy of feeding studies and secondary tolerances, as corn grain dust can be 20 % of livestock diets.

In view that these data requirements were not part of our original deficiencies DEB will recommend for the glyphosate tolerances with a 3 year expiration from date of issuance. This will allow the petitioner time to generate the requested glyphosate on corn grain dust residue data.

6. DEB Conclusion on **Harmonization of Tolerances**

An International Residue Limit Status Sheet is attached to this review. However, residue levels of glyphosate from the proposed use are far in excess of those permitted by Codex and Canada, thus compatibility cannot be achieved at this time.

RECOMMENDATION

TOX and EFGWB considerations permitting, DEB recommends for the requested glyphosate tolerances of 2 ppm on field corn grain, 35 ppm on field corn forage and fodder, and 1 ppm in liver and kidney of cattle, goats, hogs, horses, poultry, and sheep **WITH A 3 YEAR EXPIRATION FROM DATE OF ISSUANCE**.

DETAILED CONSIDERATIONS

DIRECTIONS FOR USE

Deficiencies from our February 1, 1989 Review.

3a. A revised Section B is needed which combines the first two paragraphs of the proposed label to read as follows:

Apply up to . . . spray volume in 3 to 20 gallons of water per acre for ground applications or 3 to 10 gallons of water per acre for aerial applications.

3b. The label recommends use of ammonium sulfate as an adjuvant. Residue levels of glyphosate may be higher as a result of this use. If it was not used as an adjuvant in residue trials one of the following must be submitted:

a) A revised Section B which stipulates that ammonium sulfate not be used when glyphosate is applied to preharvest corn.

b) Additional residue data reflecting use of ammonium sulfate as an adjuvant in glyphosate (residue data from preharvest application of glyphosate to other crops may be acceptable if the data show no higher glyphosate residue when ammonium sulfate is present).

Petitioner's Response

The petitioner has submitted revised directions for use for Roundup® (EPA Registration No. 524-308 AA) use on field corn.

DEB Comments

The petitioner's revised Section B contains the revisions proposed by the Agency for spray volumes for ground and air applications. Deficiency 3a is resolved.

The revised Section B also contains a label restriction of not using ammonium sulfate when applying Roundup® preharvest to corn. Deficiency 3b is resolved.

The petitioner has now proposed an adequate set of directions for use of Roundup® on field corn.

RESIDUE ANALYTICAL METHOD

Deficiencies from our February 1, 1989 Review

5a. The HPLC method used to obtain residue data is undergoing EPA method validation. Tolerances will not be delayed pending completion of the validation trial.

5b. Neither glyphosate nor AMPA has been tested under FDA's multiresidue protocols. On the basis of FDA's "Decision Tree for MRM Testing" appropriate tests are needed for glyphosate and AMPA.

Petitioner's Response

In the cover letter of April 2, 1990 signed by E.J. Dorwood-King, Senior Registration Specialist of Monsanto Company, the petitioner provided an explanation why glyphosate and AMPA are not recovered thru FDA multiresidue methods.

DEB Comments

The petitioner points out that glyphosate and its metabolite AMPA are polar and water-soluble. Thus, recovery from Protocol I (or E), Protocol II, Protocol C, and Protocol III (or D) are not probable. Recovery of glyphosate through Protocol IV (or A) is also not probable due to lack of solubility in methanol and base hydrolysis to form a primary amine. Glyphosate can be oxidized to a primary amine; however, recovery is doubtful under present Protocol A instrument parameters. Recovery through Protocol B (acids/phenol) is also questionable due to solubility factors.

The petitioner's explanation as to why no FDA multiresidue method validation data need be presented is acceptable. DEB concludes that MRM data may be waived for glyphosate and its metabolite AMPA through Protocols I through IV or A through E. Deficiency 5b is resolved.

On January 25, 1989, in a memorandum from the Analytical Chemistry Section of ACB/BEAD, the EPA lab documented problems in obtaining the custom-packed HPLC column. While cost of the column was not a determining factor in rejecting this method, the lack of specifications for making the column for specific matrices, plus the time needed to procure the HPLC column once the sample matrix(ces) were known led the Agency to conclude the column was unique and exotic. The HPLC method is thus not suitable to be an enforcement method; however, it is suitable to gather residue data. DEB withdrew its request for a PMV trial for glyphosate on soybeans at that time (see memorandum dated February 28, 1989 from R.D. Schmitt to D.A. Marlow). The HPLC method issue is now moot.

There are adequate analytical residue methods (GLC) available in PAM-II to enforce the proposed tolerances. 5

MAGNITUDE OF THE RESIDUE - CROP FIELD TRIALS

Deficiencies from our February 1, 1989 Review

6b. Residue data on corn grain and fodder show significantly higher glyphosate levels at 14 days than at 7 days. An explanation for this is needed.

6c. Provide an explanation as to why forage was not analyzed.

Petitioner's Response

The petitioner provided the requested explanations in the cover letter of this amendment.

DEB Comments

The petitioner explained that glyphosate residues are higher at 14 days than at 7 days in corn forage and fodder due to senescent loss of plant moisture. Thus, while the amount of glyphosate remains the same, the loss of moisture in plant material leads to a higher residue level on a sample weight basis. This is a plausible explanation. Deficiency 6b is resolved.

The petitioner explained that Roundup® is to be applied when the corn is mature and just before harvest, thus no green corn plant forage as such is available for sampling and analysis. This is a plausible explanation. Deficiency 6c is resolved.

PROPOSED TOLERANCES

Deficiencies from our February 1, 1989 Review

1. You should confirm that the proposed tolerances refer to the combined residues of glyphosate and its metabolite AMPA.

7. The proposed tolerances are inadequate. A revised Section F is needed proposing tolerances for the combined residues of glyphosate and AMPA of 2.0 ppm for corn grain and 35 ppm for corn forage and fodder.

9. Glyphosate residue levels in kidney of cattle were significantly lower than levels found in an earlier study. Residue levels calculated using the earlier study on cattle can exceed the existing tolerance of 0.05 ppm in kidney, depending on the particular diet considered. Therefore, a revised Section F is needed proposing tolerances of 1.0 ppm for the liver and kidney of cattle, goats, swine, horses, poultry, and sheep.

Petitioner's Response

The petitioner submitted a revised section F proposing glyphosate tolerances be established in terms of glyphosate and its metabolite AMPA in or on corn grain at 2 ppm; corn forage and fodder at 35 ppm; and in kidney and liver of cattle, goats, hogs, horses, poultry, and sheep at 1 ppm.

DEB Comments

The petitioner confirmed the proposed tolerances are for combined residues of glyphosate and AMPA. Deficiency 1 is resolved.

The petitioner has proposed the suggested glyphosate plus AMPA tolerance level for corn grain, and corn fodder and forage. Deficiency 7 is resolved.

The petitioner has proposed the suggested higher glyphosate plus AMPA tolerance levels for livestock kidney and liver. Deficiency 9 is resolved.

MAGNITUDE OF THE RESIDUE - FOOD/FEED

Deficiency from our February 1, 1990 Review

8b. Corn grain was not dry-milled into either grits or flour. A new processing study should be carried out in which these commodities are prepared. There is no need to process the corn into the items that have already been analyzed.

Petitioner's Response (See MRID No. 414781-01)

The petitioner has presented additional glyphosate residue data in dry processed corn products in a study titled "Glyphosate Residues in or on Corn Grits and Flour Following Preharvest Application of Roundup® Herbicide to Corn" by U.S. Kunda, dated January 1990 and coded Laboratory Project No. MSL-9797.

DEB Comments

Two crop field trials on corn in Delaware and Wisconsin for the crop year 1984 were treated with Roundup® at rates of 0.38 pounds and 0.75 (1X) pounds glyphosate acid equivalent ai/acre, air application. Samples were harvested at 7 and 14 days, and shipped to Monsanto labs in St. Louis for analysis. Field trial history, crop information, pesticide treatment information, harvesting, shipping, and storage data have been previously submitted and reviewed (see review by M.T. Flood, February 1, 1989).

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Samples of corn grain bearing detectable glyphosate residues were shipped to Texas A&M University for processing. A control plot was planted, and samples were harvested and analyzed for comparison purposes. The glyphosate treated corn bearing detectable residues was processed at Texas A&M University by a dry corn processing technique that closely simulates current corn dry processing industrial practices.

In summary, before dry processing the raw agricultural commodity (RAC) corn grain is cleaned by screening and aspiration to remove dust, stones, insects, etc. Corn is tested for moisture content and adjusted to 15 percent before actual dry processing. For dry milling or processing of corn, the moisture content is adjusted to 22 percent and is tempered about 2 1/2 hours. The kernels are cracked on an impact mill (Entoleter Centrimill) then air-dried for 30 minutes at 140 to 160 °F (Proctor-Schwartz forced air oven). The sample is allowed to cool to 90 °F, then the corn is placed on a 1/8 inch shaker screen and shaken. The lighter hulls remain on top of the screen and are removed as the hulls fraction. The sample is next passed over an Oliver Gravity Separator to separate out germ from large grits. The germ is dried to a moisture content of 10 percent or less. To prepare the medium grits, fine grits, coarse meal, meal, and flour fractions the sample is passed through a series of sieves (Great Western).

Glyphosate residues in whole corn grain were 0.65 ppm (from Delaware) and 0.87 ppm (from Texas). When processed into large grits, glyphosate residues were 0.71 ppm (1.1X) and 0.64 ppm (0.7X). Glyphosate residues declined when processed into medium grits (0.59 ppm or 0.9X and 0.51 ppm or 0.6X, respectively) and remained at those levels in small grits. Glyphosate residues in corn flour were 0.56 ppm (0.9X) and 0.81 ppm (0.9X).

While there is a slight variability in the dry corn processing residues between the two sample sets, DEB concludes that glyphosate does not concentrate in corn grits or corn flour. Current Branch policy does not consider a concentration factor of <1.2X to be significant enough to warrant establishment of a food additive tolerance. Thus, the petitioner does not need to propose secondary food additive tolerances for glyphosate in these dry processing corn commodities.

DEB concludes the petitioner has conducted the required supplemental corn dry processing study using treated corn bearing detectable residues. This deficiency is now resolved.

However, since our original review DEB has issued its "Overview of Residue Chemistry Guidelines (10/10/89)." Table II has been clarified in that "milled products" are identified. For corn this includes grain dust. Glyphosate and AMPA residue data are required for corn grain dust as the proposed use is foliar late season with real glyphosate residues detected. The

petitioner is strongly encouraged to submit a protocol on how he plans to generate these data prior to starting any tests.

Once the petitioner has generated the glyphosate and AMPA on corn grain dust residue data with a Food Additive Tolerance request, as needed this will engender a review of potential livestock diets, adequacy of feeding studies and secondary glyphosate tolerances in meat, milk, poultry, and eggs as corn grain dust can be 20% of livestock diets.

In view that these data requirements were not part of our original deficiencies DEB will recommend for the glyphosate tolerances with a 3 year expiration from date of issuance. This will allow the petitioner time to generate the requested glyphosate on corn grain dust residue data.

Harmonization of Tolerances

An International Residue Limit Status Sheet is attached to this review. There is a Codex tolerance of 0.05 ppm for residues of glyphosate, per se, on maize. There is a Canadian negligible residue limit of 0.1 ppm for residues of glyphosate on all food crops. Residue levels of glyphosate from the proposed use are far in excess of those permitted by Canada and Codex, thus compatibility cannot be achieved at this time. The question of revising §180.364 to limit the tolerance expression to residues of glyphosate only will be considered as part of the reregistration process.

Attachment: International Residue Limit Status Sheet

cc: R.F., Circ (7), PP#8F3673, R.D. Schmitt, Reviewer (FDG), FDA, DRES/SACB(Kariya), PIB/FOD(Furlow).

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