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SUBJECT: PP#[illegible]. Glyphosate in or on bananas (plantains) and olives. Evaluation of analytical methodology and residue data.

FROM: M. Nelson, Chemist, RCB, HED (TS-769)

TO: Team 23 (R. Taylor), RD, FD (TS-767) and TOX, HED (TS-769)

THRU: Richard D. Schmitt, Acting Chief, RCB, HED (TS-769)

Monsanto Agricultural Products Company proposes the establishment of tolerances for combined residues of the herbicide glyphosate (N-(phosphonomethyl)glycine) and its metabolite aminomethylphosphonic acid (CP 50435) in or on the import crops bananas (plantains) at 0.2 ppm and olives at 0.1 ppm.

Tolerances are presently established (40 CFR 180.364; 21 CFR 561.253, 193.235) on a wide variety of raw agricultural and some processed commodities. A Section 18 exemption and a number of temporary tolerances have also been established, and a number of miscellaneous tolerances are co-pending. (For an updated listing, ref. Pesticide Chemical News Guide.)

__Conclusions__

1. The nature of the residue is adequately understood. Parent glyphosate will be the predominant residue; small quantities of the aminomethylphosphonic acid (CP 50435) metabolite may also be present.

2. N-nitrosoglyphosate is present as an impurity in the technical product and Roundup at levels of ≤0.4 ppm; this has been the subject of a favorable hazard assessment review by OPP, EPA.

3. Adequate analytical methodology for residues of glyphosate and CP 50435 is available for enforcement purposes.

4a. Combined residues in bananas will not exceed the proposed tolerance level of 0.2 ppm (provided significantly more liberal use patterns are not involved). Only detectable (≥0.05 ppm) residues of glyphosate per se were found, and these only in some of the pulp samples.

4b. Residues in table (processed) olives and olive oil were non-detectable (<0.05 ppm) under the conditions Roundup was used. The proposed tolerance level (0.1 ppm) reflects the combined method sensitivities of glyphosate plus CP 50435.

4c. The proposed tolerances on bananas and olives are to cover foreign usage. Fresh olives per se are not imported; the import commodities are processed olives and olive oil. Thus, a food additive tolerance rather than a pesticide tolerance should be proposed for olives. A revised Section F is needed for olives, and it should be expressed in terms of "imported processed olives."

5. No feed items for the RAC are associated with this foreign use. Secondary residues will thus not result in meat, milk, poultry, or eggs.

6. The petitioner has stated that actual use labels will be written in accordance with the regulations of those countries where registratioin is proposed, and that the rates and time of application will conform with the residue data submitted with this petition.

7. The petitioner has indicated that all of the foreign countries for which use on bananas and olives is contemplated have some level of pesticide registration and control.

8. There is no conflict between the proposed tolerance levels for bananas and olives and the current international residue limits for glyphosate residues (see attached sheet).

<u>Recommendations</u>

We recommend against the proposed tolerances for the reason cited in Conclusion 4c, which see.

Provided a revised Section F substituting a food additive tolerance proposal (at 0.1 ppm) for olives (to be expressed in terms of "imported processed olives") is received, and if toxicological considerations still permit, we can recommend for the establishment of tolerances for:

bananas (including plantains)	0.2 ppm
imported processed olives	0.1 ppm (food additive)

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Note: The petitioner should be advised that if, in future, he intends to extend the proposed use on imported processed olives to include domestically grown olives, residue data for fresh (non-processed) olives (the R.A.C. within the US) will be needed, and a pesticide tolerance will then need to be proposed to cover the domestic use.

<u>Detailed Considerations</u>

<u>Manufacture and Formulation</u>

The manufacturing process for technical glyphosate has previously been submitted (PP# [illegible], Sec. A) and detailed in our reviews (e.g., D. Duffy review of 11/30/76, PP# 6G1976/FAP 6H5140).

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INERT INGREDIENT INFORMATION Deleted

The technical product is formulated as an aqueous concentrate containing 41% of the isopropylamine salt of glyphosate as the active ingredient. The formulation, called Roundup (EPA Reg. No. 524-308-AA), contains 4 lbs of this isopropylamine salt per gallon; this corresponds to 3 lbs of glyphosate acid per gallon. (Since the petitioner expresses the treatment rates in terms of the acid, lbs ai/A refers to lbs glyphosate acid/A.)

The inert ingredients in the formulation consist of the surfactant [redacted] (cleared under 40 CFR 180.1001(d)); [redacted] small amounts of various manufacturing impurities [redacted] which are not expected to present any residue problem.

An additional impurity in the formulated product (and an impurity in the technical product as well) is N-nitrosoglyphosate (NNG) which has been reported in Roundup at levels of [redacted] NNG in glyphosate has been subjected to a hazard assessment review (see 8/24/78 memorandum of R. Taylor, FDB to TAS, CPB) with the result that OPP does not bar the establishment of glyphosate tolerances on NNG grounds (per 6/5/78 R. Taylor memorandum).

Proposed Uses

The petitioner states (Section B) that actual use labels will be written in accordance with the regulations of those countries where registration is proposed, and that the rates and time of application will conform with the residue data submitted in Section D of this petition. See Residue Data section for details.

The countries of interest have been indicated to be as follows:

Bananas (Plantains)

Honduras	Panama
Costa Rica	Colombia
Puerto Rico	Ecuador

Olives

Spain
Italy
Greece

Additionally, in Section F of this petition, the petitioner presents generalized directions for use for Roundup with bananas and olives. These proposed uses for site preparation (pre-plant) and for weed control (post-directed). For bananas, use of a 1% solution of Roundup herbicide in water is recommended (ca 3 lbs ai/100 gals. H_2O) and, for olives, 1-5 qts formulation (0.75-3.75 lbs ai)/A, depending on the weed species to be controlled. The residue data presented in Section D covers applications at approximately these—and even higher—rates, so either set of use directions (Section B's or F's) would seem acceptable. Multiple applications should not constitute a problem in view of the documented limited uptake of glyphosate from soil; the data on bananas supports this.

Nature of the Residue

Radiotracer plant metabolism studies (corn, soybeans, wheat, cotton, rice, barley, oats, sorghum, sugarbeets, sugarcane, potatoes, vegetable crops, grasses, coffee, citrus, orchard crops) have been submitted in conjunction with various previous glyphosate petitions and discussed in our reviews thereof.

In all cases, the major degradative pathway of glyphosate has been shown to entail C-N bond cleavage to form glyoxylate and the major metabolite, aminomethylphosphonic acid (CP 50435). Further metabolism involves significant incorporation of fragments of these compounds into natural plant products.

Tracer studies in rats, rabbits, and cows indicate that most of the radioactive dose is excreted (90% within 5-7 days), primarily in the feces. The major component of the residue is parent compound with only trace amounts of the CP 50435 metabolite being found.

We conclude that the metabolism of glyphosate in bananas/plantains and olives (based upon the metabolism studies in various diverse crops) and animals is adequately delineated.

Analytical Methodology

The analytical procedures submitted with this petition (one for banana pulp and peel and one for table olives and olive oil) were utilized for determining residues of glyphosate and CP 50435. In principle, they consist of the same basic methodology previously applied to various other r.a.c.'s and processed commodities for which such tolerances have been granted or sought. Additionally, by suitable separation and detection (LC) techniques, it is also possible for this methodology to measure residues, if any, of N-nitrosoglyphosate (NNG) which might be present.

Briefly, the methodology individually isolates and purifies glyphosate, CP 50435, and NNG residues from aqueous extracts of the subject crops by using ion exchange resins. Glyphosate and CP 50435 are then converted to their N-trifluoroacetyl methyl ester derivatives and quantitatively determined by phosphorus-sensitive FPD-GLC utilizing either a 10% DC-200 on 80-100 Chromosorb W (HP) or 3.8% OV-17 on 80-100 Gas Chrom Q column. The NNG fraction receives additional clean-up and is then determined using an HPLC interfaced with a Griess detector (specific for those compounds which hydrolyze in dilute acid to give nitrite). The claimed sensitivity of the methodology is 0.05 ppm for glyphosate and CP 50435 and 0.02 ppm for NNG; this is borne out by the sample chromatograms submitted.

Recovery data was submitted. For bananas, the percent recovery from fortified (0.05-0.2 ppm) pulp and peel samples averaged 83% for glyphosate, 72% for CP 50435, 48% for NNG, and 63% for glyphosate, 84% for CP 50435, and 82% for NNG, respectively. For olives, the percent recovery from fortified (0.05 - 0.1 ppm) table olive and olive oil samples averaged 97% for glyphosate, 54% for CP 50435 and, 63% for glyphosate, 54% for CP 50435, respectively. Control values for residues of glyphosate and CP 50435 were all below method sensitivity (i.e., <0.05 ppm), regardless of substrate; residues of NNG in bananas were ≤0.03 ppm, and were not reported for olives.

As a result of successful MTV's on soybeans and beef liver (PP# 5F1536), and after consultation with FDA, RCB has previously concluded (see memorandum of 1/6/77, J. E. Cummings) that the basic methodological procedure for glyphosate in various substrates, though subject to difficulties (exceedingly time consuming, variable recoveries), would be adequate for enforcement purposes. Our position remains unchanged.

Residue Data

Bananas. Residue data is available from studies conducted in Honduras, Panama, Colombia, and Ecuador in 1976 and 1977. The application of Roundup herbicide to banana plantations was in the form of bananacide, preplant, and/or post-directed treatments. The studies are summarized below.

(1) Bananacide. Bananacide treatment was applied by injections of a 25% solution of Roundup in water to various parts of the pseudostem (mother plant), bullhead (stump of harvested plant), and suckers of the selected plants to be removed.

In ca 4 weeks, the treated plants were discarded and ca one week later new rhizomes were planted (presumably on the same site). Bananas from these new plants were then sampled at harvest (357-420 days after the bananacide treatment to the old plants) for analysis of residues.

Glyphosate and aminomethylphosphonic acid (CP 50435) residues in pulp and peel samples were all <0.05 ppm (i.e., non-detectable); residues of nitrosoglyphosate (NNG) were non-detectable (<0.02 ppm) in pulp samples and ND to ≤0.03 ppm in the peels.

(2) Bananacide + Preplant + Post-Directed. Banana plants to be removed were treated with injections of Roundup, as described above.

In ca 4 weeks, the treated plants were removed and the preplant treatment was administered. It consisted of a single application of 3 or 6 lbs active acid (glyphosate) (this is equivalent to 1 and 2 gallons of Roundup, respectively) in 25-30 gallons of water per acre to cover the ground evenly, including the area where the new rhizomes were to be planted. Approximately one week later, the new rhizomes were planted.

Post-directed treatments [4 soil-directed applications of 3 or 6 lbs active acid (glyphosate) (i.e., 1 or 2 gallons of Roundup, respectively) in 25-30 gallons of water per acre] were applied at intervals

(3,3,3, and 1 month apart, respectively) during the growth cycle, and samples of bananas were taken for residue analysis at time of final harvest, some 21-78 days following the last treatment.

Glyphosate and CP 50435 residues in the peel were all <0.05 ppm, the sensitivity of the method. In the pulp, CP 50435 residues were also <0.05 ppm, but glyphosate residues per se ranged from ND to 0.19 ppm (reflecting the 6 lbs ai/A treatment rate; the highest reported value at the 3 lbs ai/A rate was 0.17 ppm). Both banana pulp and peel samples were screened for NNG, and reportedly no authentic residues were observed (background peaks representing up to 0.06 ppm NNG equivalent were present in some of both control and treated peel samples, but were not due to a true N-nitroso response).

(3) Post-directed. Banana plants received post-directed treatments only. The regimen consisted of 5 soil-directed applications of 3 or 6 lbs active acid (glyphosate) (i.e., 1 or 2 gallons of Roundup, respectively) in 25-30 gallons of water per acre applied at intervals (3,3,3,3, and 1 month apart, respectively) during the growth cycle. Samples of bananas were taken for residue analysis at varying intervals (as decline series, weekly, with PHI's of 1-22 days) following the final application.

In peel, ND (<0.05 ppm) of glyphosate or CP 50435 were found. In pulp, ND of CP 50435 were present, but glyphosate residues ranged from ND to 0.17 ppm (with one apparently aberrant and irreproducible value of 0.36 ppm which was subsequently discounted since it could not be confirmed by reanalysis). The 0.17 ppm value reflected a 6 lbs ai/A treatment rate; the highest value reported at a 3 lbs ai/A rate was 0.11 ppm. As discussed above, no authentic residues of NNG were observed.

Conclusions: The r.a.c. for bananas is the whole banana (excluding, for purposes of residue analyses, crown tissue and stalk). Based on the various data in this petition, and <u>provided</u> significantly different use patterns are not involved, we can conclude that a 0.2 ppm tolerance should be adequate to cover any combined residues of glyphosate plus CP 50435 residues which might be present in whole bananas. (Because of the nature of the proposed uses, we did not need data on bagged versus non-bagged bananas for this petition.)

<u>Olives</u>. Residue data is available from studies on 7 different varieties of olives conducted at several site locations in Spain in 1976 and 1977.

Roundup was applied as a single, directed, foliar post-emergent spray to the undesirable vegetative growth in Spanish olive yards. The recommended maximum rate of application was 10 liters of formulation per hectare, which was stated to be equivalent to 3.6 kg a.i./ha (and is also equivalent to 3.2 lbs ai/A; 1 gallon of formulation contains 3 lbs ai glyphosate acid). In actuality, however, the experimental rates used in the studies were 2.16 or 4.32 kg ai/ha (i.e., 1.9 or 3.8 lbs ai/A, or 2-1/2 or 5 qts of formulation/A). Olives were harvested 20-54 days after the above treatment.

After harvesting, the olives were processed into "table olives" (whether these were green, black, or both was not specified) and olive oil using standard commercial procedures. Residues of glyphosate and CP 76435 were subsequently analyzed for in these processed commodities; ND (<0.05 ppm) of either compound were detected. Unprocessed olives were not analyzed. Residues of [illegible] were not looked for.

Conclusions: The proposed tolerance for olives is 0.1 ppm, which is high enough to reflect the combined method sensitivities for glyphosate and CP 76435. Based on the residue data/use pattern discussed above, this proposed level appears adequate.

Even though residue data reflecting multiple applications in olive groves has not been provided, this type data from other crops, the known limited nature of glyphosate uptake from soil, and the fact that the crop is subjected to processing prior to importation, all combine to reassure us that ND would likely result from use of Roundup at the recommended rates to control weeds in olive groves, even if multiple applications were made.

Based on the petitioner's stated intent, only a tolerance on imported olives is being sought. The importation of fresh olives from the Mediterranean area (the petitioner has indicated Spain, Italy, and Greece as the likely countries for registration of a use for Roundup on olives) into the USA is forbidden because they are a host for the olive fruit fly (see Cultural Practices File). Thus, it is processed olives and olive oil which are the import items, and a food additive tolerance for "imported, processed olives" (and for olive oil if concentration has been shown to occur during processing) is appropriate rather than a pesticide tolerance, as currently proposed. A revised Section F is needed.

If, in future, the petitioner wishes to extend the proposed use to include domestically grown olives, residue data for fresh (unprocessed) olives (the r.a.c. within the USA) will be needed, and a pesticide tolerance will then need to be proposed to cover the domestic use.

Residues in Meat, Milk, Poultry, and Eggs

No feed items are associated with these import crops. Accordingly, there is no reasonable expectation of the presence of secondary residues in meat, milk, poultry, or eggs as a result of these proposed uses.

Other Considerations

There is no conflict between the proposed tolerance levels for bananas and olives and the current international residue limits for glyphosate residues; see attached sheet.

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The petitioner has stated that all of the foreign countries for which use on bananas and olives is contemplated have some level of pesticide registration and control, and that actual use labels will be written in accordance with regulations of those countries where registration is proposed.

Attachment

TS-762:PCP:M.Nelson:JP:X77324:FMR10:CK2:2-11-80
RPI:R.Quick:2-6-80:F.Schmitt:2-6-80

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