1-15-93

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

JAN 15 1993

MEMORANDUM

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

SUBJECT: The HED Chapter of the Reregistration Eligibility Document (RED) for Glyphosate, Case #0178

FROM: Jane Smith, Chemist
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Health Effects Division (H7509C)

THRU: Esther Saito, Branch Chief
Chemical Coordination Branch 1/15/93
Health Effects Division (H7509C)
and
Penelope Fenner-Crisp, Ph.D, Director
Health Effects Division (H7509C) 1/15/93

TO: Lois Rossi, Chief
Reregistration Branch
Special Review and Reregistration Branch (H7508W)

Attached is the Human Health Assessment for the Glyphosate Reregistration Eligibility Document. This chapter includes the Hazard Assessment from Krystyna Locke in TBI, the Occupational/Residential Exposure Assessment from Jeff Evans in OREB, the Dietary Exposure from R. B. Perfetti in CBRS and the Dietary Risk Analysis from Steve Schaible in SAB.

Glyphosate is a non-selective, post-emergent herbicide applied to terrestrial food and non-food crops, turf, greenhouse crops and non-crop areas where total vegetation control is desired. Glyphosate must be translocated throughout the target plants for effective control. The sodium salt of glyphosate is used as a plant growth regulator. The ammonium salt of glyphosate is used as an herbicide and plant growth regulator. Tolerances for residues of glyphosate in or on food/feed and in processed commodities have been established. These tolerances and the residues of glyphosate to be regulated have been reassessed. The reassessment

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also considers CODEX harmonization. The details of this extensive reassessment can be found in the Product and Residue Chemistry Chapter (memo dated 10/27/92, R. B. Perfetti, CBRS#10665 and addendum date 1/12/93, R. B. Perfetti). This reassessment is not included in the HED Chapter since, according to the format provided by D. Campt (memo dated 3/18/92), it should appear under IV Risk Management, B. Regulatory Position of the RED compiled by SRRD.

There are some confirmatory data required resulting from the generation of the HED RED Chapter. These data include:

1) the data required in the product chemistry summary tables of the Product and Residue Chemistry Chapter (memo dated 10/27/92, R.Perfetti, CBRS#10665) for the unregistered trisodium salt technical, the 94% IPA FI, and the 75% IPA FI, and either certifcation of the suppliers of starting materials and the manufacturing process for the glyphosate technical products and manufacturing products have not changed since the last comprehensive product chemistry review or submission of a complete updated product chemistry data package.

2) an acute delayed neurotoxicity study (guideline 81-7) in the hen is required to confirm that phosphonates without leaving groups, like glyphosate, do not result in delayed neurotoxic effects.

3) additional field trial/residue chemistry requirements pending the Agency's final disposition of the Craven data.

Human health risks from exposure to glyphosate are considered to be minimal due to its low toxicity (acute category III, Group E [non-carcinogenic to humans]). Considering the worst case scenario, the chronic dietary risk posed by glyphosate for the general population is minimal. Protective clothing (including eye wear) is recommended for mixer/loader/applicators.

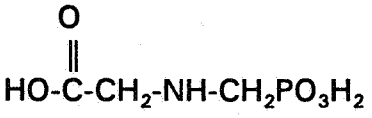
cc: Karl Baetcke
Larry Dorsey
Bill Burnum
Ed Zager

Attachments

A. Product Chemistry

1. Identification of the Active Ingredient

Glyphosate (N-phosphonomethyl glycine) is a nonselective herbicide and plant growth regulator.



Empirical Formula: $C_3H_8NO_5P$
Molecular Weight: 169.07
CAS Registry No.: 38641-94-0
Shaughnessy No.: 103601 (isopropylamine salt, IPA)
103603 (sodium salt)

The technical isopropylamine salt (IPA) is a white crystalline solid with a melting point of 200°C and a bulk density of 1.74 lb/ft^3. It is 1% soluble in water at 25°C and insoluble in ethanol, acetone, or benzene. The technical sodium salt is a white crystalline solid which decomposes at 140°C with a bulk density of 30 lb/ft^3.

2. Other Product Chemistry Issues

There are five manufacturing-use products (MP); the 53.5% IPA formulation intermediate (FI) and end-use product (EP), the 41% IPA FI and EP, the 62% IPA FI and MP, the 94% IPA FI and MP, and the 75% IPA technical and MP. All pertinent data requirements are satisfied for the unregistered IPA acid technical and the 62% IPA FI. Provided that the registrant submits the data required in the summary tables of the Product and Residue Chemistry Chapter (memo dated 10/27/92, R.Perfetti, CBRS#10665) for the unregistered trisodium salt technical, the 94% IPA FI, and the 75% IPA FI, and either certifies that the suppliers of beginning materials and the manufacturing process for the glyphosate technical products and manufacturing products have not changed since the last comprehensive product chemistry review or submits a complete updated product chemistry data package, Health Effects Division (HED) has no objections to the reregistration of glyphosate with respect to product chemistry data requirements.

B. Human Health Assessment

1. Toxicology Assessment

a. Acute Toxicity

The table below summarizes the toxicity results and categories for technical grade glyphosate. The acute inhalation study was waived by the Agency since glyphosate technical is a nonvolatile solid and adequate inhalation studies were conducted on the end-use product formulations.

Acute Toxicity

Test	Result	Category
Acute Oral (rat) (1)	> 4320 mg/kg	III
Acute Dermal (rabbit)(1)	> 2 g/kg	III
Acute Inhalation	Not Required	N/A
Eye Irritation (2)	mild irritation, clears in 7 days	III
Dermal Irritation (3)	slight irritation	IV
Skin Sensitization (4)	negative	N/A

Other studies submitted to the Agency give similar results. They are acceptable for reregistration (5,6)

b. Subchronic Toxicity

In a 90-day feeding study (7) Sprague-Dawley rats were fed diets containing 0, 1000, 5000 or 20000 ppm of glyphosate for three months. These doses were equivalent to 0, 63, 317 and 1267 mg/kg/day, respectively (males) and 0, 84, 404 and 1623 mg/kg/day, respectively (females). The following findings were regarded as possibly treatment-related: (1) increased serum phosphorus and potassium in all treated groups, males and females; (2) increased serum glucose in the mid-dose and high-dose males; (3) increased blood urea nitrogen (BUN) and serum alkaline phosphatase in the high-dose males; and (4) occurrence of pancreatic lesions in the high-dose males (pancreas was not examined in the low-dose and mid-dose groups). Based on these findings, the systemic NOEL is < 1000 ppm (not determined definitively) for both sexes.

In a second 90-day feeding study (8) CD-1 mice were fed diets containing 0, 250, 500 or 2500 mg/kg/day of glyphosate for three months. Body weight gains

of the high-dose males and females were about 24% and 18% lower, respectively, than those of the controls. Body weight gains of the low-dose and mid-dose groups were comparable to those of the controls. Based on the reduced body weight gains in both sexes, the NOEL for systemic toxicity is 500 mg/kg and the LOEL is 2500 mg/kg.

In a 21-day dermal study (9) glyphosate was applied to the skin of New Zealand white rabbits using 10 rabbits/sex/dose (5 with intact and 5 with abraded skin). The levels of glyphosate tested were 10, 1000 or 5000 mg/kg/day. The rabbits were exposed for three consecutive weeks, 6 hours/day, 5 days/week. Treatment-related effects observed only in the high dose groups included: (1) very slight erythema and edema in intact and abraded skin of both sexes; (2) decreased food consumption in males; and (3) decreased serum lactic dehydrogenase in both sexes. Based on these effects, the NOEL for males and females is 1000 mg/kg/day and the LOEL is 5000 mg/kg/day.

The required 90-day feeding study in dogs is satisfied by the one-year dog feeding study (10).

c. Chronic Feeding

A chronic feeding/carcinogenicity study (11) was conducted using male and female Sprague-Dawley rats which were fed diets containing 0, 30, 100 or 300 ppm of glyphosate for 26 months. These levels were equivalent to 0, 3, 10 and 31 mg of glyphosate/kg/day, respectively, for the males and 0, 3, 11 and 34 mg of glyphosate/kg/day, respectively, for the females. There were no effects based on any of the parameters examined (toxic signs, mortality, body weights, food consumption, hematology, clinical chemistry, urinalysis, organ weights and organ/tissue pathology). Therefore, the NOEL for systemic toxicity is $\geq$ 300 ppm (HDT; males: 31 mg/kg/day and females: 34 mg/kg/day).

A second chronic feeding/carcinogenicity study (12) was conducted using male and female Sprague-Dawley rats which were fed diets containing 0, 2000, 8000 or 20000 ppm of glyphosate for 2 years. These levels were equivalent to 0, 89, 362 or 940 mg/kg/day, respectively, for the males and 0, 113, 457 or 1183 mg/kg/day, respectively, for the females. Treatment-related effects observed only in the high-dose group included: (1) In the females: decreased body weight gains; and (2) In the males: increased incidence of cataracts and lens abnormalities, decreased urinary pH, increased absolute liver weight and increased liver weight/brain weight ratio (relative liver weight). No significant systemic effects were observed in the low-dose and mid-dose male and female groups. Therefore, the NOEL for systemic toxicity is 8000 ppm (males: 362 mg/kg/day and females: 457 mg/kg/day) and the LOEL is 20000 ppm (HDT; males: 940 mg/kg/day and females: 1183 mg/kg/day).

A chronic study (13) was conducted using male and female beagle dogs which were given glyphosate in gelatin capsules containing 0, 20, 100 or 500 mg/kg/day for one year. There were no effects based on all parameters examined, in all groups. Therefore, the NOEL for systemic toxicity is ≥ 500 mg/kg/day, for both sexes.

d. Carcinogenicity

A chronic feeding/carcinogenicity study (11) was conducted using Sprague-Dawley rats which were fed diets containing glyphosate (males: 0, 3, 10 or 31 mg/kg/day and females: 0, 3, 11 or 34 mg/kg/day) for 26 months. The following findings were observed in the high-dose groups when compared with the concurrent controls: (1) increased incidence of thyroid C-cell carcinomas in females; and (2) increased incidence of interstitial cell (Leydig cell) testicular tumors. However, the HED Carcinogenicity Peer Review Committee concluded that these neoplasms were not treatment-related and glyphosate was not considered to be carcinogenic in this study because the incidence of thyroid carcinomas was not statistically significant and the incidence of testicular tumors was within the historical incidence. The Committee also concluded that this study was not conducted at high enough dose levels for an adequate negative carcinogenicity.

A chronic feeding/carcinogenicity study (12) was conducted using Sprague-Dawley rats fed diets containing glyphosate (males: 0, 89, 362 or 940 mg/kg/day and females: 0, 113, 457 or 1183 mg/kg/day) for 2 years. The study showed a slightly increased incidence of (1) pancreatic islet cells adenomas in the low-dose and high-dose males; (2) hepatocellular (liver) adenomas in the low-dose and high-dose males; and (3) thyroid C-cells adenomas in the mid-dose and high-dose males and females. The HED Carcinogenicity Peer Review Committee concluded that these adenomas were not treatment-related and glyphosate was not considered to be carcinogenic in this study. With respect to pancreatic islet cells adenomas, there was no statistically significant positive dose-related trend in their occurrence; there was no progression to carcinomas; and the incidence of pancreatic hyperplasia (non-neoplastic lesion) was not dose-related. With respect to hepatocellular adenomas, the increased incidence of these neoplasms was not statistically significant in comparison with the controls; the incidence was within the historical control range; there was no progression to carcinomas; and the incidence of hyperplasia was not compound-related. With respect to thyroid C-cell adenomas, there was no statistically significant dose-related trend in their occurrence; the increased incidence was not statistically significant; there was no progression to carcinomas; and there was no significant dose-related increase in severity or incidence of hyperplasia in either sex.

A carcinogenicity study (14) in mice was conducted with CD-1 mice fed diets containing 0, 150, 750 or 4500 mg/kg/day of glyphosate for 18 months. No effects were observed in the low-dose and mid-dose groups. The following findings were observed in the high-dose group: (1) decreased body weight gain in males and females; (2) increased incidence of hepatocellular hypertrophy, hepatocellular necrosis and interstitial nephritis in males; (3) increased incidence of proximal tubule epithelial basophilia and hypertrophy in females; and (4) slightly increased incidence of renal tubular adenomas, a rare tumor, in males. Based on these effects, the systemic NOEL and LOEL were 750 mg/kg/day and 4500 mg/kg/day, respectively. The HED Carcinogenicity Peer Review Committee concluded that the occurrence of these adenomas was spontaneous rather than compound-induced because the incidence of renal tubular adenomas in males was not statistically significant when compared with the concurrent controls. An independent group of pathologists and biometricians also conducted extensive evaluations of these adenomas and reached the same conclusion. Therefore, glyphosate was not considered to be carcinogenic in this study.

On June 26, 1991, the HED Carcinogenicity Peer Review Committee classified glyphosate in Group E (evidence of non-carcinogenicity for humans), based on a lack of convincing evidence of carcinogenicity in adequate studies with two animal species, rat and mouse.

e. Developmental Toxicity

A developmental toxicity study (15) was conducted with pregnant Charles River COBS CD rats which were administered 0, 300, 1000 or 3500 mg/kg/day of glyphosate by gavage during gestation days 6 through 19. Treatment-related effects observed only in the high-dose dams included: (1) diarrhea; (2) decreased mean body weight gain; (3) breathing rattles; (4) inactivity; (5) red matter around the nose and mouth, and on forelimbs and dorsal head; (6) decreases in total implantations/dam and inviable fetuses/dam; and (7) deaths (6/25 or 24% of the group). Treatment-related developmental effects observed only in the high-dose group included: (1) increased number of litters and fetuses with unossified sternebrae; and (2) decreased mean fetal body weights. Therefore, the NOEL and LOEL for maternal toxicity are 1000 mg/kg/day and 3500 mg/kg/day, respectively. The NOEL and LOEL for developmental toxicity are 1000 mg/kg/day and 3500 mg/kg/day, respectively.

In a second study (16), pregnant Dutch Belted rabbits were administered 0, 75, 175 or 350 mg/kg/day of glyphosate by gavage during gestation days 6 through 27. Treatment-related findings were observed only in the high-dose group and included: (1) diarrhea; (2) nasal discharge; and (3) death (10/16 or 62.5% of does died by gestation day 21). Developmental toxicity was not observed at any dose tested. Therefore, the NOEL and LOEL for maternal toxicity are 175

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mg/kg/day and 350 mg/kg/day, respectively. The NOEL for developmental toxicity is ≥ 175 mg/kg/day. Due to high maternal mortality at the 350 mg/kg/day dose level, too few litters (only 6) were available to assess adequately developmental toxicity at that level.

f. Reproduction

A three-generation reproduction study (17) was conducted with male and female Sprague-Dawley rats which were administered 0, 3, 10 or 30 mg/kg/day of glyphosate continuously in the diet for three successive generations. The only effect observed was an increased incidence of focal tubular dilation of the kidney (both unilateral and bilateral combined) in the high-dose male F_{3b} pups. Therefore, the NOEL for systemic and reproductive toxicity is ≥ 30 mg/kg/day (HDT). The NOEL and LOEL for developmental toxicity are 10 mg/kg/day and 30 mg/kg/day, respectively.

A two-generation reproduction study (18) was conducted with Sprague-Dawley rats which were administered 0, 100, 500 or 1500 mg/kg/day of glyphosate continuously in the diet for two successive generations. Treatment-related effects observed only in the high-dose group included: (1) soft stools, very frequent, in the F_o and F_1 males and females; (2) decreased food consumption and body weight gain of the F_o and F_1 males and females during the growth (premating) period; and (3) decreased body weight gain of the F_{1a}, F_{2a} and F_{2b} male and female pups during the second and third weeks of lactation. Focal tubular dilation of the kidneys, observed in the previous study (17), was not observed at any dose level in this study. Based on the above findings, the systemic NOEL and LOEL is 10000 ppm (500 mg/kg/day) and 30000 ppm (1500 mg/kg/day), respectively. The reproductive NOEL is 30000 ppm (1500 mg/kg/day; HDT); and the developmental NOEL and LOEL is 10000 ppm (500 mg/kg/day) and 30000 ppm (1500 mg/kg/day), respectively.

Since the focal tubular dilation of the kidneys was not observed at the 1500 mg/kg/day level (HDT) in the 2-generation rat reproduction study (18) but was observed at the 30 mg/kg/day level (HDT) in the 3-generation rat reproduction study (17), the Office of Pesticide Programs (OPP) Developmental Peer Review Committee concluded that the latter was a spurious rather than glyphosate-related effect.

g. Mutagenicity

A Gene Mutation Assay in Ames Test (19) was conducted using glyphosate, both with and without metabolic activation. The strains of Salmonella typhimurium used were TA98, TA100, TA1535 and TA1537. No increases in reverse mutations were observed at any concentration.

A Gene Mutation Assay in Mammalian Cells (20) was conducted using glyphosate in the Chinese hamster ovary (CHO) cells/hypoxanthine - guanine - phosphoribosyl transferase (HGPRT) assay, with and without metabolic activation. No mutagenic response was observed either with or without metabolic activation up to the limit of cytotoxicity (10 mg/mL).

A Structural Chromosomal Aberration Assay (21) was conducted using a single dose of glyphosate administered intraperitoneally (i.p.) to male and female Sprague-Dawley rats. The dose used was 1 g/kg of body weight and the bone marrow cells were examined for clastogenic (chromosome-damaging) effect. No significant clastogenic effects were observed.

In a fourth study (22), glyphosate was tested in two assays: the rec-assay using B. subtilis H17 (rec^+) and M45 (rec^-); and the reverse mutation assays using E. coli WP2 hcr and Salmonella typhimurium strains TA98, TA100, TA1535, TA1537 and TA1538, with and without metabolic activation. No increases in mutations were observed in either study.

h. Metabolism

Two metabolism studies with rats are available. In the first study (23), single or repeated doses of radiolabeled ^{14}C-glyphosate were administered orally to male and female Sprague-Dawley rats. Following a single oral dose of ^{14}C-glyphosate, 30 to 36% of the dose was absorbed and less than 0.27% of the dose was eliminated as CO_2. Ninety-seven point five percent of the administered dose was excreted in the urine and feces as the parent compound, glyphosate. Amino methyl phosphonic acid (AMPA) was the only metabolite found in urine (0.2-0.3% of the administered dose) and feces (0.2-0.4% of the administered dose). Less than 1.0% of the absorbed dose remained in tissues and organs, primarily in bone tissue. Repeated dosing at 10 mg/kg did not significantly change the metabolism, distribution or excretion of glyphosate.

In a second study (24), male and female Sprague-Dawley rats received single intraperitoneal injections of radiolabeled ^{14}C-glyphosate. The dose level of glyphosate used for male and female rats was 1150 mg/kg. Blood samples were collected 0.25, 0.50, 1, 2, 4, 6 and 10 hours after injection. Femoral bone marrow samples were collected from one third of the male and female rats sacrificed at 0.5, 4, or 10 hours after injection. Thirty minutes after injection of glyphosate, the concentration of radioactivity in the bone marrow of male and female rats was equivalent to 0.0044% and 0.0072%, respectively, of the administered dose. Assuming first order kinetics, the decrease in radioactivity in bone marrow occurred with a half-life of 7.6 and 4.2 hours for males and females, respectively. Similarly, the half-lives of the radioactivity in plasma were

approximately 1 hour for both sexes. These findings indicate that very little glyphosate reaches bone marrow, that it is rapidly eliminated from bone marrow and that it is even more rapidly eliminated from plasma.

i. Neurotoxicity

The acute and 90-day neurotoxicity screening battery in the rat (guidelines 81-8-SS, 82-7) is not being required now since there was no evidence of neurotoxicity seen in any of the existing studies at very high doses and this chemical lacks a leaving group; therefore, it would not seem likely to inhibit esterases (the presumptive neurotoxic mechanism of concern for all organophosphates). However, the acute delayed neurotoxicity study (guideline 81-7) in the hen is required to confirm that phosphonates without leaving groups, like glyphosate, do not result in delayed neurotoxic effects.

j. Other Toxicological Considerations

A dermal penetration study (guideline 85-2) with technical grade glyphosate is not required because there are no toxicological endpoints to indicate this study is necessary.

Domestic Animal Safety Studies (86-1) are not required for the use patterns of glyphosate (a plant growth regulator herbicide).

Technical grade glyphosate contains N-nitrosoglyphosate (NNG) as a contaminant. Carcinogenicity testing of nitroso contaminants is normally required only in those cases in which the level of nitroso compounds exceeds 1.0 ppm (26). Analyses showed that greater than 92% of the individual technical glyphosate samples contained less than 1.0 ppm (1000 ppb) of NNG. HED concluded that the NNG content of glyphosate was not toxicologically significant.

k. Reference Dose

On August 27, 1992, the HED Reference Dose (RfD) Peer Review Committee recommended that the RfD for glyphosate be established at 2 mg/kg/day. This value was based on the maternal NOEL of 175 mg/kg/day from the rabbit developmental toxicity study (16) and an uncertainty factor (UF) of 100. This RfD has not yet been confirmed by the Agency RfD Work Group.

2. Exposure Assessment

a. Dietary Exposure

The qualitative nature of the residue in plants is adequately understood. Studies with a variety of plants including corn, cotton, soybeans, and wheat indicate that the uptake of glyphosate or its metabolite AMPA from soil is limited. The material which is taken up is readily translocated. Foliarly applied glyphosate is readily absorbed and translocated throughout the trees or vines to the fruit of apples, coffee, dwarf citrus (calamondin), pears and grapes. Metabolism via N-methylation yields N-methylated glycines and phosphonic acids. For the most part, the ratio of glyphosate to AMPA is 9 to 1 but can approach 1 to 1 in a few cases (e.g., soybeans and carrots). Much of the residue data for crops reflects a detectable residue of parent (0.05 - 0.15 ppm) along with residues below the level of detection (<0.05 ppm) of AMPA. The terminal residue to be regulated in plants is glyphosate per se.

The qualitative nature of the residue in animals is adequately understood. Studies with lactating goats and laying hens fed a mixture of glyphosate and AMPA indicate that the primary route of elimination was by excretion (urine and feces). These results are consistent with metabolism studies in rats, rabbits, and cows. The terminal residues in eggs, milk, and animal tissues are glyphosate and its metabolite AMPA; there was no evidence of further metabolism. The terminal residue to be regulated in livestock is glyphosate per se.

An adequate enforcement method is available for analysis of residues of glyphosate and its metabolite AMPA in or on plant commodities and in water. This method utilizes GLC (Method I of PAM Vol. II; limit of detection is 0.05 ppm). For enforcement of tolerances in animal commodities, an HPLC method with fluorescence detection is available; the reported limits of detection are 0.01 ppm for glyphosate and 0.012 ppm for AMPA.

The available storage stability data indicate that residues of glyphosate and its metabolite AMPA are stable under frozen storage conditions (-20°C): in or on plant commodities for a period of 1 year, in animal commodities for 2 years, and in water for 1 year. No additional storage stability data are needed.

All data requirements for magnitude of the residue in plants have been evaluated and deemed adequate. *[Note: The registrant has also committed to providing new potato and sorghum processing studies.]* All data requirements for magnitude of the residue in plants as a result of irrigation with glyphosate-treated water have also been submitted and are adequate to support registered use and applicable tolerances. No additional data are required for magnitude of the residue in animals, potable water, and fish.

The conclusions regarding the reregistration eligibility of glyphosate on the crops listed in Table A of the Product and Residue Chemistry Chapter (memo dated 10/27/92, R.Perfetti, CBRS# 10665) are based on the use patterns registered by the primary producer, Monsanto Agricultural Chemical Company, as reflected in the LUIS report for glyphosate (BEAD memo dated 9/22/92, M. Cogdell). All end-use product labels (e.g. MAI labels, SLNs, and products subject to the generic data exemption) may not be consistent with the basic producer labels at this time. Because Craven Laboratories data were used to support the reregistration of certain crops (See memo of 10/21/91, M. Metzger, CBRS # 8367, Barcode No. D167350) additional requirements may be levied pending the Agency's final disposition of the Craven data.

b. Occupational and Residential Exposure

Occupational and residential exposure can be expected based on the currently registered uses of products containing glyphosate. However, due to the low toxicity (acute category III) of glyphosate and the lack of other toxicological concerns (i.e carcinogenicity) occupational and residential exposure data are not required. Glyphosate is a non-selective herbicide applied to terrestrial food and non-food crops, turf, greenhouse crops, and non-crop areas where total vegetation control is desired. Glyphosate, when applied at lower rates, is also a plant growth regulator.

The IPA salt of glyphosate is a non-selective, post-emergent herbicide that must be translocated throughout the target plants for effective control. Since all forms of glyphosate can injure any plant if the green plant material is contacted, care regarding drift, and accuracy of the herbicide placement is essential. As a result of these efficacy criteria, there are a wide variety of treatment methods available to users. These include common application methods such as broadcast, aerial, spot, and directed spray applications and specialized application methods such as control droplet application (CDA); injection application; frill application; the use of recirculating sprayers, and wiper/wick type applicators.

The sodium salt of glyphosate is used as a plant growth regulator for sugarcane (to increase sugar production), peanuts (to shorten internodal length), and turfgrass grown in industrial locations (to suppress growth and seedhead development). While this chemical is applied to actively growing crops in low dosages, sprays drifting to other crops may cause injury.

The ammonium salt of glyphosate is used as an herbicide and plant growth regulator for turf grown in right-of-ways and in industrial, commercial, and residential locations. Formulations for these sites are water-soluble powders packaged in water-soluble bags. The liquid formulation is applied to agricultural crops.

Although glyphosate meets the Agency's exposure criteria for post-application/reentry and/or mixer/loader/applicator exposure monitoring data, glyphosate does not meet the Agency's toxicity criteria for these data requirements. Acute oral and dermal toxicity data for the technical material are in Toxicity Category III and IV. In addition, glyphosate is poorly absorbed dermally. The acute inhalation toxicity study for the technical material was waived because glyphosate is non-volatile and because there were adequate inhalation studies with end-use products showing low toxicity. Therefore, occupational and residential exposure data are not required to support the reregistration of glyphosate. (For these same reasons, these data were not required in the 1986 Registration Standard.)

Some glyphosate end-use products are in Toxicity Category I and II for primary eye irritation and dermal irritation. In California, where physicians are required to report pesticide poisonings, glyphosate was ranked third out of the 25 leading causes of illnesses or injury due to pesticides used between 1980 and 1984. These mixer/loader/applicator reported incidents consisted of eye and skin irritation. In reports issued by California since then (1987 and 1988), glyphosate continued to be a leading cause of illnesses or injuries (primarily eye and skin irritation). In the 1986 Registration Standard, the Agency recommended protective clothing (which includes protective eye wear) for mixer/loader/applicators using end-use products that could cause eye or skin irritation. At that time, it was determined that mixer/loaders were at risk of eye or skin injury from splashes during mixing and loading. The Agency did not recommend protective clothing for users of "homeowner" products (containing up to 10% glyphosate) because of the low concentration of glyphosate and the products are "ready-to-use", requiring no mixing; therefore, the potential for eye or dermal exposure is minimized.

HED recommends the continued use of protective clothing for products in Toxicity Category I and II for dermal skin and eye irritation. Existing and future protective clothing statements should be further refined via the Worker Protection Standards.

3. Risk Characterization

The chronic dietary risk analysis used tolerance level residues and assumed all acreage, of the crops considered, were treated with glyphosate to estimate the Theoretical Maximum Residue Contribution (TMRC) for the overall U.S. population and 22 DRES population subgroups. These exposures (TMRCs) were then compared to the RfD for glyphosate to estimate chronic dietary risk. A summary of the TMRCs and their representations as percentages of the RfD are attached as Table 2 in the Dietary Risk Evaluation Memo (dated 12/15/92, S. Schaible, DRES/SAB Caswell #661A).

The TMRC for the overall U.S. population from food uses of glyphosate is 0.028 mg/kg bwt/day, which represents 1.4% of the Reference Dose. Around half of this exposure comes from the recommended tolerance on wheat. None of the subgroups has an exposure that exceeds 5% of the RfD; the subgroup most highly exposed, non-nursing infants less than one year old, has an exposure of 0.060 mg/kg bwt/day, or 3% of the RfD. The proposed *wheat milling fractions (except flour)* was reduced from 40 ppm to 20 ppm in the addendum to the Product and Residue Chemistry Chapter (dated 1/12/93 by R. Perfetti). For this reason, a second DRES analysis was performed (dated 1/13/93, S. Schaible, DRES/SAB Caswell #661A). With the exception of the new residue value used for *wheat milling fractions (except flour),* the assumptions were the same in this analysis as in the previous analysis. The calculated TMRC for the overall U.S. population from food uses of glyphosate is 0.025 mg/kg bwt/day, which represents 1.2% of the RfD. The subgroup most highly exposed, non-nursing infants less than one year old, has a TMRC of 0.058 mg/kg bwt/day, or 2.9% of the RfD. Over one third of the dietary exposure and risk from glyphosate is due to the proposed tolerances on wheat.

This analysis was meant to be a "worst case" scenario of risk. The inclusion of recommended tolerances for reregistration as well as tolerances recommended for revocation; the use of the highest existing, pending, or recommended residue value for each commodity; and the assumptions of tolerance level residues and treatment of 100 percent of the crops for every commodity considered result in an overestimation of exposure and risk values for glyphosate (though there is also an underestimation due to the lack of consumption information for some of the commodities in the CFR to which glyphosate is expected to be applied). Nonetheless, given the risk values arrived at by this analysis, it seems that the chronic dietary risk posed by this pesticide on these food uses is minimal.

4. Occupational and Residential Risk

As discussed above in the occupational exposure assessment, exposure to humans from proper application of glyphosate to terrestrial food and non-food crops as well as greenhouses, turf, and non-crop areas can result in injury (primarily eye and skin irritation) from splashes during mixing and loading. HED continues to recommend protective clothing (including protective eye wear) for mixer/loader/applicators using end-use products that may be in toxicity category I or II for primary eye and dermal irritation.

GLYPHOSATE: TOXICOLOGY CHAPTER FOR RED

Barcode No.: D183195 Submission No.: S436271

Prepared by: Krystyna K. Locke, Toxicologist Date: 10/19/92

Reviewed by: Roger L. Gardner, Section Head Date: 10/27/92

Karl P. Baetcke, Branch Chief Date: 10/28/92
Toxicology Branch I
Health Effects Division

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ACUTE TOXICITY

Test	Results	Category
81-1 Acute Oral Toxicity in Rats; Study No.: Y-70-90; Date:9/18/70 MRID No.: 00067039	LD_{50}: 4320 mg/kg (both sexes). Study is Acceptable. Toxic signs: Reduced activity and appetite, lethargy, diarrhea, increasing weakness, collapse and death. Hemorrhagic lungs and liver, and gastrointestinal inflammation were observed at necropsy.	III
81-1 Acute Oral Toxicity in Rats; Study No.: 4885-88; Date: 9/20/88 MRID No.: 41400601	LD_{50}: > 5000 mg/kg (only dose tested in both sexes). Study is Acceptable. Toxic signs: Wet rales during the first 2 days after dosing. No abnormalities were noted at necropsy. There were no deaths.	IV
81-2 Acute Dermal Toxicity in Rabbits; Study No.: Y-70-90; Date: 9/18/70 MRID No.: 00067039	LD_{50}: > 2 g/kg (both sexes; limit dose). Study is Acceptable. Toxic signs: None observed and no abnormalities were noted at necropsy. There were no deaths.	III
81-2 Acute Dermal Toxicity in Rabbits; Study No.:4886-88; Date: 9/20/88 MRID No.: 41400602	LD_{50}: > 5 g/kg (both sexes). Study is Acceptable. Toxic signs: None observed and no abnormalities were noted at necropsy. There were no deaths.	IV
81-3 Acute Inhalation Toxicity in Rats.	The requirement for this study has been waived. The Agency accepted the argument that technical glyphosate is a non-volatile solid and that adequate inhalation studies were conducted on formulations. These studies showed low toxicity from this route of	

Test	Results	Category
81-4 Primary Eye Irritation in Rabbits; Study No.: 4888-88; Date: 9/20/88 MRID No.: 41400603	Study is Acceptable. <u>Toxic signs:</u> Corneal opacity, iritis, conjuncival redness, chemosis and discharge were observed initially in most or all animals, but eyes were clear in 7 days. Eyes were rinsed following a 24-hour exposure.	III
81-5 Primary Dermal Irritation in Rabbits; Study No.: 4887-88; Date: 9/20/88 MRID No.: 41400604	Primary Irritation Index (PII): 0.625 (both sexes). Study is Acceptable. <u>Toxic signs:</u> Following a 4-hour exposure, slight irritation was observed at 72 hours (last scoring time).	IV
81-6 Dermal Sensitization in Guinea Pigs; Study No.:BD-83-008; Date: 7/22/83 MRID No.: Not given Acc. No.: 252142	Technical glyphosate was not a sensitizer in this study. Study is Acceptable.	

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SUBCHRONIC TOXICITY

Three toxicity studies are available, as follows: **(1)** 90-Day Feeding in Rats (82-1a; No.: ML-86-351/EHL86128; Date: 11/30/70; MRID No.: 40559401); **(2)** 90-Day Feeding in Mice (82-1a; No.: 77-211; Date: 12/31/79; MRID No.: 00036803); and **(3)** 21-Day Dermal Toxicity in Rabbits (82-2; No.: 401-168; Date: 3/10/82; MRID No.: 00098460). The first study (MRID No.: 40559401) is actually a range-finding study for the subsequent chronic feeding/carcinogenicity study (MRID No.: 00093879) and is classified as Acceptable. The requirement for a 90-Day Feeding Study in Rats has been satisfied by that chronic feeding/carcinogenicity study. The second study (MRID No.: 00036803) is classified as Core-Supplementary because not all of the required parameters have been examined or adequately examined. Since only one 82-1a feeding study in rodents is required and this requirement has already been satisfied, a new 90-Day Feeding Study in Mice is not required. The third study (MRID No.: 00098460) is classified as Core-Guideline.

In the first study (MRID No.: 40559401), Sprague-Dawley rats were fed diets containing 0, 1000, 5000 or 20000 ppm of glyphosate for three months. These doses were equivalent to 0, 63, 317 and 1267 mg/kg/day, respectively (males) and 0, 84, 404 or 1623 mg/kg/day, respectively (females). The following findings were regarded as possibly treatment-related: **(1)** Increased serum phosphorus and potassium in all treated groups, males and females; **(2)** Increased serum glucose in the mid-dose and high-dose males; **(3)** Increased blood urea nitrogen (BUN) and serum alkaline phosphatase in the high-dose males; and **(4)** Occurrence of pancreatic lesions in the high-dose males (pancreas was not examined in the low-dose and mid-dose groups). Based on these findings, the systemic NOEL is < 1000 ppm (not determined definitively) for both sexes.

In the second study (MRID No.: 00036803), CD-1 mice were fed diets containing 0, 250, 500 or 2500 mg/kg/day of glyphosate for three months. Body weight gains of the high-dose males and females were about 24% and 18% lower, respectively, than those of the controls at study termination. Body weight gains of the low-dose and mid-dose groups were comparable to those of the controls. Based on the reduced body weight gains in both sexes, the NOEL for systemic toxicity is 500 mg/kg and the LOEL is 2500 mg/kg.

In the third study (MRID No.: 00098460), glyphosate was applied to the skin of New Zealand white rabbits, using 10 rabbits/sex/dose (5 with intact and 5 with abraded skin). The levels of glyphosate tested were 10, 1000 or 5000 mg/kg/day. The rabbits were exposed for three consecutive weeks, 6 hours/day, 5 days/week. Treatment-related effects, observed only in the high-dose groups, included **(1)** Very slight erythema and edema in

intact and abraded skin of both sexes; (2) Decreased food consumption in males; and (3) Decreased serum lactic dehydrogenase in both sexes. Based on these effects, the NOEL for males and females is 1000 mg/kg/day and the LOEL is 5000 mg/kg/day.

The 90-Day Feeding Study in Dogs (82-1b) is missing, but this requirement is satisfied by the one-year dog feeding study (MRID No.: 00153374). Other subchronic toxicity studies, 90-Day Dermal (82-3) and 90-Day Inhalation (82-4), are also missing, but, considering the use patterns of glyphosate, these studies are not required.

CHRONIC FEEDING

Three chronic feeding studies are available, as follows: (1) Combined Chronic Feeding Carcinogenicity in Rats (83-5; No.: 77-2062; Date: 12/23/81; MRID No.: 00093879); (2) Combined Chronic Feeding Carcinogenicity in Rats (83-5; No.: MSL-10495; Date: 9/26/90; MRID No.: 41643801; and (3) Chronic Feeding in Dogs (83-1b; NO.: 830116 and ML- 83-137; Date: 8/22/85; MRID No.: 00153374). The first study (MRID No.: 00093879) is classified as Core-Minimum and the two remaining studies (MRID No.: 41643801 and 00153374) as Core-Guideline.

In the first study (MRID No.: 00093879), male and female Sprague-Dawley rats were fed diets containing 0, 30, 100 or 300 ppm of glyphosate for 26 months. These levels were equivalent to 0, 3.05, 10.3 and 31.39 mg of glyphosate/kg/day, respectively, for the males and 0, 3.37, 11.22 and 34.02 mg of glyphosate/kg/day, respectively, for the females. Glyphosate had no effect on any of the parameters examined (toxic signs, mortality, body weights, food consumption, hematology, clinical chemistry, urinalysis, organ weights and organ/tissue pathology). Therefore, the NOEL for systemic toxicity is $\geq$ 300 ppm (HDT; males: 31.39 mg/kg/day and females: 34.02 mg/kg/day).

In the second study (MRID No.: 41643801), male and female Sprague-Dawley rats were fed diets containing 0, 2000, 8000 or 20000 ppm of glyphosate for 2 years. These levels were equivalent to 0, 89, 362 and 940 mg/kg/day, respectively, for the males and 0, 113, 457 and 1183 mg/kg/day, respectively, for the females. Treatment-related effects, observed only in the high-dose group, included: (1) In the females: decreased body weight gains, in comparison with the concurrent controls; and (2) In the males: increased incidence of cataracts and lens abnormalities, decreased urinary pH, increased absolute liver weight and increased liver weight/brain weight ratio (relative liver weight), each in comparison with the concurrent controls. No significant systemic effects were observed in the low-dose and mid-dose male and female groups. Therefore, the NOEL for systemic toxicity is 8000 ppm (males: 362 mg/kg/day and females:

457 mg/kg /day) and the LOEL is 20000 ppm (HDT; males: 940 mg/kg/day and females: 1183 mg/kg/day).

In the third study (MRID No.: 00153374), male and female beagle dogs were given glyphosate in gelatin capsules daily for one year at the following dose levels: 0, 20, 100 or 500 mg/kg/day. Glyphosate had no effect on all parameters examined, in all groups. Therefore, the NOEL for systemic toxicity is ≥ 500 mg/kg/ day, for both sexes.

CARCINOGENICITY

Three studies are available as follows: **(1)** Combined Chronic Feeding/Carcinogenicity in Rats (83-5; No.: 77-2062; Date: 12/23/81; MRID No.: 00093879); **(2)** Combined Chronic Feeding Carcinogenicity in Rats (83-5; No.: MSL-10495; Date: 9/26/90; MRID No.:41643801); and **(3)** Carcinogenicity in Mice (83-2b; No.: 77-2061; Date: 7/21/83; MRID No.: 00130406 and 00150564). The Core classification of studies **(1)** and **(2)** as carcinogenicity studies is Supplementary (MTD was not reached) and Guideline, respectively. The classification of the mouse study is Core-Minimum.

In the first study (MRID No.: 00093879), Sprague-Dawley rats were fed diets containing glyphosate (males: 0, 3.05, 10.3 or 31.39 mg/kg/day and females: 0, 3.37, 11.22 or 34.02 mg/kg/day) for 26 months. The following findings were observed in the high-dose groups when compared with the concurrent controls: **(1)** Increased incidence of thyroid C-cells carcinomas in females; and **(2)** Increased incidence of interstitial cells (Leydig cells) testicular tumors. However, because the incidence of thyroid carcinomas was statistically insignificant and the incidence of testicular tumors was within the historical incidence, the Health Effects Division (HED) Carcinogenicity Peer Review Committee concluded that these neoplasms were treatment-unrelated and, therefore, **glyphosate was not carcinogenic in this study.** Because the Maximally Tolerated Dose (MTD) was not reached in this study, the Committee also concluded that this study did not qualify as a carcinogenicity study* and should be repeated. (* The dose levels tested were inadequate for the assessment of the carcinogenic potential of glyphosate).

In the second study (MRID No.: 41643801), in which the MTD was reached, Sprague-Dawley rats were fed diets containing glyphosate (males: 0, 89, 362 or 940 mg/kg/day and females: 0, 113, 457 or 1183 mg/kg/day) for 2 years. Compared with the concurrent controls, there was a slightly increased incidence of **(1)** Pancreatic islet cells adenomas in the low-dose and high-dose males; **(2)** Hepatocellular (liver) adenomas in the low-dose and high-dose males; and **(3)** Thyroid C-cells adenomas in the mid-dose and high-dose males and females. However, the HED Carcinogenicity Peer Review Committee concluded that these adenomas were treatment-unrelated and, therefore, **glyphosate was**

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not carcinogenic in this study. In the case of pancreatic islet cells adenomas, there was no statistically significant positive dose-related trend in their occurrence; there was no progression to carcinomas; and the incidence of pancreatic hyperplasia (non-neoplastic lesion) was dose-unrelated. In the case of hepatocellular adenomas, the increased incidence of these neoplasms was statistically insignificant in comparison with the controls; the incidence was within the historical control range; there was no progression to carcinomas; and the incidence of hyperplasia was compound-unrelated. In the case of thyroid C-cell adenomas, there was no statistically significant dose-related trend in their occurrence; the increased incidence was statistically insignificant; there was no progression to carcinomas; and there was no significant dose-related increase in severity or incidence of hyperplasia in either sex.

In the third study (MRID No.: 00130406 and 00150564), CD-1 mice were fed diets containing 0, 1000, 5000 or 30000 ppm (0, 150, 750 and 4500 mg/kg/day) of glyphosate for 18 months. No effects were observed in the low-dose and mid-dose groups. Relative to the concurrent controls, the following findings were observed in the high-dose group: (1) Decreased body weight gain in males and females; (2) Increased incidence of hepatocellular hypertrophy, hepatocellular necrosis and interstitial nephritis in males; (3) Increased incidence of proximal tubule epithelial basophilia and hypertrophy in females; and (4) Slightly increased incidence of renal tubular adenomas, a rare tumor, in males. Based on these effects, the systemic NOEL and LOEL were 5000 ppm (750 mg/kg/day) and 30000 ppm (4500 mg/kg/day), respectively. Because the incidence of renal tubular adenomas in males was statistically insignificant when compared with the concurrent controls and because of the additional extensive evaluations of these adenomas by several independent pathologists and biometricians, the HED Carcinogenicity Peer Review Committee concluded (along with the pathologists and biometricians) that the occurrence of these adenomas was spontaneous rather than compound-induced. Therefore, glyphosate was not carcinogenic in this study.

On June 26, 1991, the HED Carcinogenicity Peer Review Committee classified glyphosate into Group E (evidence of non-carcinogenicity for humans), based on a lack of convincing evidence of carcinogenicity in adequate studies with two animal species, rat and mouse.

DEVELOPMENTAL TOXICITY

Two studies are available, as follows: (1) Developmental Toxicity in Rats (83-3a; No.: IRDL 401-054; Date: 3/21/80; MRID No.: 00046362); and (2) Developmental Toxicity in Rabbits (83-3b; No.: IRDC 401-056; Date: 2/29/80; MRID No.: 00046363). The study with rats is classified as Core-Guideline. The study with

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rabbits is classified as Core-Supplementary, due to the high death rate of the does in the high-dose group. However, the study is considered to have fulfilled the regulatory requirements for a developmental toxicity study in rabbits because a Developmental NOEL can still be determined.

In the first study (MRID No.: 00046362), pregnant Charles River COBS CD rats were administered single oral daily doses of glyphosate by gavage during gestation days 6 through 19. The fol- lowing dose leves were tested: 0, 300, 1000 or 3500 mg/kg/day. Treatment-related effects, observed only in the high-dose dams, included **(1)** Diarrhea; **(2)** Decreased mean body weight gain; **(3)** Breathing rattles; **(4)** Inactivity; **(5)** Red matter around the nose and mouth, and on forelimbs and dorsal head; **(6)** Decreases in total implantations/dam and in viable fetuses/dam; and **(7)** Deaths (6/25 or 24% of the group). Treatment-related developmental effects, observed only in the high-dose group, included **(1)** Increased number of litters and fetuses with unossified sternebrae; and **(2)** Decreased mean fetal body weights. Therefore, the NOEL and LOEL for maternal toxicity are 1000 mg/kg/day and 3500 mg/kg/day, respectively. The NOEL and LOEL for developmental toxicity are 1000 mg/kg/day and 3500 mg/kg/day, respectively.

In the second study (MRID No.: 00046363), pregnant Dutch Belted rabbits were administered single oral daily doses of glyphosate by gavage during gestation days 6 through 27. The following dose levels were used: 0, 75, 175 or 350 mg/kg/day. Treatment-related findings were observed only in the high-dose group and included **(1)** Diarrhea; **(2)** Nasal discharge; and **(3)** Death (10/16 or 62.5% of does died by gestation day 21). Developmental toxicity was not observed at any dose tested. Therefore, the NOEL and LOEL for maternal toxicity are 175 mg/kg/day and 350 mg/kg/day, respectively. The NOEL for developmental toxicity is $\geq$ 175 mg/kg/day. Due to high maternal mortality at the 350 mg/kg/day dose level, too few litters (only 6) were available to assess adequately developmental toxicity at that level.

REPRODUCTION

Two studies are available, as follows: **(1)** Three-Generation Reproduction Study with Rats (83-4; No.: 77-2063 and BDN-77-417; Date: 7/31/81; MRID No.: 00105995); and **(2)** Two-Generation Reproduction Study with Rats (83-4; No.: MSL-10387; Date: 8/27/90; MRID No.: 41621501). The first study is classified as Core-Minimum and the second as Core-Guideline.

In the first study (MRID No.; 00105995), male and female Sprague-Dawley rats were administered glyphosate continuously in the diet for three successive generations at the following dose levels: 0, 3, 10 or 30 mg/kg/day. The only effect observed was

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an increased incidence of focal tubular dilation of the kidney (both unilateral and bilateral combined) in the high-dose male F_{3b} pups. Therefore, the NOEL for systemic and reproductive toxicity is ≥ 30 mg/kg/day (HDT). The NOEL and LOEL for developmental toxicity are 10 mg/kg/day and 30 mg/kg/day, respectively.

In the second study (MRID No.: 41621501), Sprague-Dawley rats were administered glyphosate continuously in the diet for two successive generations at the following dose levels: 0, 2000, 10000 or 30000 ppm (0, 100, 500 and 1500 mg/kg/day, respectively). Treatment-related effects were observed only in the high-dose group and included (1) Soft stools, very frequent, in the F_0 and F_1 males and females; (2) Decreased food consumption and body weight gain of the F_0 and F_1 males and females during the growth (premating) period; and (3) Decreased body weight gain of the F_{1a}, F_{2a} and F_{2b} male and female pups during the second and third weeks of lactation ("weighing days" 14 and 21; F_{1b} litter was not produced in this study). Focal tubular dilation of the kidneys, observed in the high-dose F_{3b} male pups in the 3-generation rat reproduction study (MRID No.: 00105995), was not observed at any dose level in this study. Therefore, based on the above findings, the NOELs and LOELs are as follows: **Systemic NOEL** and **LOEL**: 10000 ppm (500 mg/kg/day) and 30000 ppm (1500 mg/kg/day), respectively; **Reproductive NOEL**: ≥ 30000 ppm (1500 mg/kg/day; HDT); and **Developmental NOEL** and **LOEL**: 10000 ppm (500 mg/kg/day) and 30000 ppm (1500 mg/kg/day), respectively.

Since the focal tubular dilation of the kidneys was not observed at the 1500 mg/kg/day level (HDT) in the 2-generation rat reproduction study (MRID No.: 41621501) but was observed at the 30 mg/kg/day level (HDT) in the 3-generation rat reproduction study (MRID No.: 00105995), the Office of Pesticide Programs (OPP) Mini Peer Review Committee concluded that the latter was a spurious rather than glyphosate-related effect.

MUTAGENICITY

Four studies are available, as follows: (1) Gene Mutation Assay in Ames Test (84-2a-1; No.: LF-78-161; Date: 6/16/78; MRID No.: 00078620; (2) Gene Mutation Assay in Mammalian Cells (84-2a-2; No.: ML-83-155 and HEL 830079; Date: 10/20/83; MRID No.: 00132681); (3) Structural Chromosomal Aberration Assay (In vivo cytogenetic assay; 84-2b; No.: ML-83-236; Date: 10/20/83; MRID No.: 00132683); and (4) Other Genotoxic Effects Assay (Rec-assay and reverse mutation assay; 84-4; No study number; Date: 7/20/78; MRID No.: 00078619). Each study is classified as Acceptable and glyphosate was negative for mutagenicity in each study.

In the first study (MRID No.: 00078620), glyphosate was tested both with and without metabolic activation (rat liver microsomal fraction commonly known as S-9 fraction) at concentra-

tions ranging from 0.1 to 1000 μg/plate. The strains of Salmonella typhimurium used were TA98, TA100, TA1535 and TA1537. No increases in reverse mutations were observed at any concentration. Positive results were obtained with standard reference mutagens (positive controls).

In the second study (MRID No.: 00132681), glyphosate was tested in the Chinese hamster ovary (CHO) cells/hypoxanthine - guanine - phosphoribosyl transferase (HGPRT) assay, with and without metabolic activation. The concentrations of glyphosate tested ranged from 2 to 25 mg/mL. No mutagenic response was observed either with or without metabolic activation up to limit of cytotoxicity (10 mg/mL; concentrations of glyphosate > 10 mg/mL were cytotoxic to CHO cells). Positive results were obtained with standard reference mutagens.

In the third study (MRID No.: 00132683), a single dose of glyphosate was administered intraperitoneally (i.p.) to male and female Sprague-Dawley rats. The dose used was 1 g/kg of body weight and the bone marrow cells were examined for clastogenic (chromosome-damaging) effect. No significant clastogenic effects were observed in the glyphosate-treated rats, but a highly significant number of chromosomal aberrations was observed in the bone marrow cells of rats treated with cyclophosphamide, a standard reference mutagen.

In the fourth study (MRID No.: 00078619), glyphosate was tested in two assays: in the rec-assay using B. subtilis H17 (rec^+) and M45 (rec^-); and in the reverse mutation assays using E. coli WP2 hcr and Salmonella typhimurium strains TA98, TA100, TA1535, TA1537 and TA1538, with and without metabolic activation. The concentrations of glyphosate tested in the rec-assay ranged from 20 to 2000 μg/disk and in the E. coli/S. typhimurium assays, from 10 to 5000 μg/plate. No increases in mutations were observed at any concentration tested in either study.

METABOLISM

Two metabolism studies with rats are available: (1) 85-1; No.: MSL-7215 and MSL7206; Date: 3/23/88; MRID No.: 40767101 and 40767102; and (2) 85-1; No.: 830109 and ML-83-218; Date: 10/24/83; MRID No.: 00132685. Each study is classified as Acceptable. Glyphosate, essentially unchanged, is rapidly eliminated from the body in the urine and feces.

In the first study (MRID No.: 40767101 and 40767102), single or repeated doses of ^{14}C-glyphosate were administered orally to male and female Sprague-Dawley rats, and the excretion and distribution of radioactivity was determined. Following a single oral dose of ^{14}C-glyphosate, 30 to 36% of the dose was absorbed and less than 0.27% of the dose was eliminated as CO_2. Unchanged glyphosate was the highest radiolabeled material found in the

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urine and feces. The minimum amount of unchnged glyphosate extracted from the urine and feces was 97.5% of the administered dose. Amino methyl phosphonic acid (AMPA) was the only metabolite found in urine (0.2-0.3% of the administered dose) and feces (0.2-0.4% of the administered dose). Less than 1.0% of the absorbed dose remained in tissues and organs, primarily in bone. Repeated dosing at 10 mg/kg did not significantly change the metabolism, distribution and excretion of glyphosate.

In the second study (MRID No.: 00132685), male and female Sprague-Dawley rats received single intraperitoneal injections of radiolabled ^{14}C-glyphosate. The dose level of glyphosate used for male and female rats was 1150 mg/kg. Blood samples were collected 0.25, 0.50, 1, 2, 4, 6 and 10 hours after injection. Femoral bone marrow samples were collected from one third of the male and female rats sacrificed at 0.5, 4, or 10 hours after injection. Thirty minutes after injection of glyphosate, the concentration of radioactivity in the bone marrow of male and female rats was equivalent to 0.0044% and 0.0072%, respectively, of the administered dose. Assuming first order kinetics, the decrease in radioactivity in bone marrow occurred with a half-life of 7.6 and 4.2 hours for males and females, respectively. Similarly, the half-lives of the radioactivity in plasma were approximately 1 hour for both sexes. These findings indicate that very little glyphosate reaches bone marrow, that it is rapidly eliminated from bone marrow and that it is even more rapidly eliminated from plasma.

NEUROTOXICITY

The acute and 90-day neurotoxicity screening battery in the rat (81-8-SS, 82-7) is not being required now since there was no evidence of neurotoxicity seen in any of the existing studies at very high doses and this chemical lacks a leaving group; therefore, it would not seem likely to inhibit esterases (the presumptive neurotoxic mechanism of concern for all organophosphates). However, the acute delayed neurotoxicity study (81-7) in the hen is required to confirm that phosphonates without leaving groups, like glyphosate, do not result in delayed neurotoxic effects.

STUDIES NOT REQUIRED FOR TECHNICAL GRADE GLYPHOSATE

A Dermal Penetration/Absorption Study (85-2) is frequently required for the registration of a pesticide. This study is not required because there are no toxicological endpoints to indicate the study is necessary.

Domestic Animal Safety Studies (86-1) are also required for the registration of some pesticides. However, considering the use patterns of glyphosate (a plant growth regulator herbicide), these studies are not required.

REFERENCE DOSE

On August 27, 1992, the Health Effects Division Reference Dose (RfD)/Peer Review Committee recommended to the Agency RfD Work Group that the RfD for glyphosate be established at 1.8 mg/kg/day. This value was calculated by using the maternal NOEL of 175 mg/kg/day from the rabbit developmental toxicity study (83-3b; MRID No.: 00046363) and an uncertainty factor (UF) of 100. This RfD has not yet been presented to the Agency RfD Work Group.

TOXICOLOGICAL SIGNIFICANCE OF N-NITROSOGLYPHOSATE, A CONTAMINANT IN TECHNICAL GLYPHOSATE

The Agency has determined that carcinogenicity testing of nitroso contaminants will normally be required only in those cases in which the level of nitroso compounds exceeds 1.0 ppm ["Pesticides Contaminated with N-nitroso Compounds, proposed policy 45 FR 42854 (June 25, 1980)"]. The levels of N-nitrosoglyphosate (NNG) in technical glyphosate have been examined by Toxicology Branch I, Health Effects Division. The overall NNG content in individual samples of technical glyphosate analyzed at production plants is shown below.

Number of Samples Analyzed	NNG Observed (ppb)	Percent of Samples
2035	< 1000	92.6
124	1000 - 1500	5.6
24	1500 - 2000	1.1
13	2000 - 3000	0.6
2	> 3000	0.1

The above data show that 92.6% of the individual glyphosate samples analyzed contain less than 1.0 ppm (1000 ppb) of NNG. Toxicology Branch I, therefore, concluded that the NNG content of glyphosate is not toxicologically significant.

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

NOV 18 1992

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: OCCUPATIONAL AND RESIDENTIAL EXPOSURE ASSESSMENT AND RECOMMENDATIONS FOR THE REREGISTRATION ELIGIBILITY DOCUMENT FOR GLYPHOSATE

FROM: Jeff Evans, Biologist
Reregistration Section
Occupational and Residential Exposure Branch
Health Effects Division (H7509C)

TO: Jane Smith, Acting Chemical Coordinator
Chemical Coordination Branch
Health Effects Division (H7509C)

THRU: Alan P. Nielsen, Section Head
Reregistration Section

Larry C Dorsey, Acting Chief
Occupational and Residential Exposure Branch
Health Effects Division (H7509C)

Please find the OREB review of ....

DP Barcode: D183196

Pesticide Chemical Codes: 103601, 103603, and 103604

EPA Reg. No.: N/A

EPA MRID No.: N/A

Review Time: 5 days

PHED: No

This memorandum presents the OREB science chapter review for the Glyphosate Reregistration Eligibility Document (RED). Occupational and residential exposure data requirements to support the reregistration of the isopropylamine salt (IPA) of glyphosate (103601), the sodium salt of glyphosate (103603), and the ammonium salt of glyphosate (103604) are discussed in this chapter. Precautionary label language recommendations regarding personal protective equipment are also addressed.

Occupational and Residential Exposure

Occupational and residential exposure can be expected based on the currently registered uses of these chemicals. Glyphosate is a non-selective herbicide applied to terrestrial food and non-food crops, turf, greenhouse crops, and non-crop areas where total vegetation control is desired. Glyphosate, when applied at lower rates, is also a plant growth regulator.

The IPA salt of glyphosate is a non-selective, post-emergent herbicide that must be translocated throughout the target plants for effective control. Since all forms of glyphosate can injure any plant if the green plant material is contacted, care regarding drift, and accuracy of the herbicide placement is essential. As a result of these efficacy criteria, there are a wide variety of treatment methods available to users. These include common application methods such as broadcast, aerial, spot, and directed spray applications and specialized application methods such as control droplet application (CDA); injection application; frill application; the use of recirculating sprayers, and wiper/wick type applicators.

The sodium salt of glyphosate is used as a plant growth regulator for sugarcane (to increase sugar production), peanuts (to shorten internodal length), and turfgrass grown in industrial locations (to suppress growth and seedhead development). While this chemical is applied to actively growing crops in low dosages, sprays drifting to other crops may cause injury.

The ammonium salt of glyphosate is used as an herbicide and plant growth regulator for turf grown in right-of-ways and in industrial, commercial, and residential locations. Formulations for these sites are water soluble powders packaged in water soluble bags. The liquid formulation is applied to agricultural crops.

Although glyphosate meets EPA's exposure criteria for postapplication/reentry and/or mixer/loader/applicator exposure monitoring data, glyphosate does not meet the Agency's toxicity criteria for these data requirements. Acute oral and dermal toxicity data for the technical material are in Toxicity Category III and IV. In addition, glyphosate is poorly absorbed dermally. The acute inhalation toxicity study for the technical material was waived because glyphosate is non-volatile and because there were adequate inhalation studies with end-use products showing low toxicity. Therefore, as in the 1986 Registration Standard, occupational and residential exposure data are not required to support the reregistration of glyphosate.

Some glyphosate end-use products are in Toxicity Category I and II for primary eye irritation and dermal irritation. In California, where physicians are required to report pesticide

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

OCT 27 1992

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Glyphosate: List A Reregistration Case No. 0718: Product and Residue Chemistry Chapters For The Reregistration Eligibility Document (RED). CBRS No. 10,665, DP Barcode No. D183202.

FROM: R. B. Perfetti, Ph.D., Chemist
Reregistration Section I
Chemistry Branch II: Reregistration Support
Health Effects Division (H7509C)

THRU: Edward Zager, Chief
Chemistry Branch II: Reregistration Support
Health Effects Division (H7509C)

TO: L. Rossi, Chief
Reregistration Branch
Special Review and Reregistration Division (H7508W)

and

J. Ellenberger, Chief
Acclerated Reregistration Branch
Special Review and Reregistration Division (H7508W)

For your information, please find attached the Glyphosate Product and Residue Chemistry Chapters for the Glyphosate RED. Future CBRS RED chapters will be prepared using this format. The Chemical Coordination Branch will combine this input along with chapters from TOX and OREB and provide SRRD with the HED risk assessment for glyphosate.

Attachments 1 and 2: Glyphosate Product and Residue Chemistry RED Chapters.

poisonings, glyphosate was ranked third out of the 25 leading causes of illnesses or injury due to pesticides between 1980 and 1984. These mixer/loader/applicator illnesses consisted of eye and skin irritation. In reports issued by California since then (1987 and 1988), glyphosate continued to be a leading cause of illnesses or injuries (primarily eye and skin irritation). In the 1986 Registration Standard, EPA recommended protective clothing for mixer/loaders using end-use products that could cause eye or skin irritation. At that time, it was determined that mixer/loaders were at risk of eye or skin injury from splashes during mixing and loading.

EPA did not recommend protective clothing for users of "homeowner" products (containing up to 10% glyphosate) because those products did not cause eye or dermal irritation.

OREB recommends the continued use of protective clothing for products in Toxicity Category I and II for dermal skin and eye irritation. Existing and future protective clothing statements should be further refined via the Worker Protection Standards.

cc: J. Evans, OREB
Correspondence File
Chemical File (103601, 103603, and 103604)
Circulation

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

OCT 27 1992

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Glyphosate: List A Reregistration Case No. 0718: Product and Residue Chemistry Chapters For The Reregistration Eligibility Document (RED). CBRS No. 10,665, DP Barcode No. D183202.

FROM: R. B. Perfetti, Ph.D., Chemist
Reregistration Section I
Chemistry Branch II: Reregistration Support
Health Effects Division (H7509C)

THRU: Edward Zager, Chief
Chemistry Branch II: Reregistration Support
Health Effects Division (H7509C)

TO: J. Smith and E. Saito, Acting Chief
Science Analysis and Coordination Branch
Health Effects Division (H7509C)

Attached are the Glyphosate Product and Residue Chemistry Chapters for the Glyphosate RED. These chapters were completed by Dynamac Corporation under supervision of CBRS, HED. They have undergone undergone secondary review in the branch and have been revised to reflect Agency policies.

There is currently a question regarding Craven Laboratories data for certain crops having glyphosate uses (See memo of 10/21/91, M. Metzger, CBRS # 8367, Barcode No. D167350.). Additional requirements may be levied pending the final disposition of the Craven data question.

If you need additional input please advise.

Attachments 1 and 2: Glyphosate Product and Residue Chemistry RED Chapters.

cc (With Attachments 1 and 2): RBP, Glyphosate Reregistration Standard File, Glyphosate Subject File, Circ. and Dynamac.

cc (Without Attachments): RF.

DYNAMAC
CORPORATION
Environmental Services

Final Report

GLYPHOSATE
Shaughnessy Nos. 103601 & 103603
Case No. 0178

Task 2A - Reregistration Eligibility Document: Product Chemistry Considerations

October 22, 1992

Contract No. 68-D2-0053

Submitted to:
U.S. Environmental Protection Agency
Arlington, VA 22202

Submitted by:
Dynamac Corporation
The Dynamac Building
2275 Research Boulevard
Rockville, MD 20850-3268

GLYPHOSATE

REREGISTRATION ELIGIBILITY DOCUMENT:

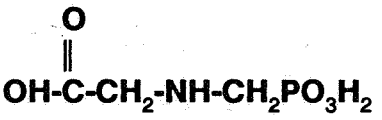
PRODUCT CHEMISTRY CONSIDERATIONS

(Shaughnessy Nos. 103601 and 103603; Case No. 0178)

TASK 2A

DESCRIPTION OF CHEMICAL

Glyphosate (N-phosphonomethyl glycine) is a nonselective herbicide and plant growth regulator.



Empirical Formula:	$C_3H_8NO_5P$
Molecular Weight:	169.07
CAS Registry No.:	38641-94-0
Shaughnessy No.:	103601 (isopropylamine salt, IPA)
	103603 (sodium salt)

IDENTIFICATION OF ACTIVE INGREDIENT

The technical isopropylamine salt (IPA) is a white crystalline solid with a melting point of 200 C and a bulk density of 1.74. It is 1% soluble in water at 25 C and insoluble in ethanol, acetone, or benzene. The technical sodium salt is a white crystalline solid which decomposes at 140 C with a bulk density of 30 lb/ft^3.

MANUFACTURING-USE PRODUCTS

A search of the Reference Files System (REFS) conducted 7/20/92 identified four glyphosate manufacturing-use products (MPs) registered to Monsanto Agricultural Company under Shaughnessy No. 103601. There are no registered MPs under Shaughnessy No. 103603. We note that according to the Glyphosate Registration Standard Update dated 4/26/90, two of the products identified as MPs in REFS, the 53.5% IPA formulation intermediate (FI; EPA Reg. No. 524-318) and the 41% IPA FI (EPA Reg. No. 524-339) are actually end-use products (EPs). A list of the Monsanto MPs subject to a reregistration eligibility decision is presented below. Data pertaining to the unregistered IPA acid technical (formerly referenced as the unregistered IPA salt

technical in the Science Chapter) and the unregistered trisodium salt technical are also required to satisfy data requirements for reregistration.

Formulation	EPA Reg. No.
62% IPA FI[a]	524-333
94% IPA FI	524-420
75% IPA T	524-421

a. This product is identified as an EP in REFS; an Agency review (CBRS Nos. 2346 and 2347, 9/1/87), concluded that it would be more appropriately designated a technical product.

REGULATORY BACKGROUND

The regulatory background for glyphosate products in terms of comprehensive product chemistry reviews is presented below.

Products	July 1986 Guidance Document		April 1990 Update	
	Data required	Data submitted in response	Data required	Data submitted in response
Unregistered trisodium salt technical	61-2, -3 62-1, -2*, -3* 63-4, -7, -8, -9, -11, -12, -13	none	none; not addressed in the Update	n/a[a]
Unregistered IPA acid technical	61-2, -3 62-1, -2*, -3* 63-4, -7, -8, -9, -11, -12, -13	61-2, -3 62-1 63-2 through -13	none	n/a

Products	July 1986 Guidance Document		April 1990 Update	
	Data required	Data submitted in response	Data required	Data submitted in response
62% IPA FI	61-2, -3 62-1, -2, -3 no 63 series; not reviewed for MPs in G.D.	61-1, -2, -3 62-1, -2, -3 63-2, -3, -4, -7, -12, -14, -15, -16, -18	63-17, -20	63-20
94% IPA FI 75% IPA T	none; not registered in 1986	n/a	n/a	n/a

a. n/a = not applicable
* Data pertaining to this guideline are not required for unregistered TGAIs.

The current status of the product chemistry data requirements for Monsanto glyphosate products is presented in the attached data summary tables. Please refer to these tables for a listing of the outstanding product chemistry data requirements. In addition, three MRIDs which have not yet been reviewed, but which may contain data pertinent to the reregistration of Monsanto glyphosate technical products and MPs, are included in the Product Chemistry Citations.

CONCLUSIONS

All pertinent data requirements are satisfied for the unregistered IPA acid technical and the 62% IPA FI. Provided that the registrant submits the data required in the attached data summary tables for the unregistered trisodium salt technical, the 94% IPA FI, and the 75% IPA FI, and either certifies that the suppliers of beginning materials and the manufacturing process for the glyphosate technical products and MPs have not changed since the last comprehensive product chemistry review or submits a complete updated product chemistry data package, CBRS has no objections to the reregistration of glyphosate with respect to product chemistry data requirements.

AGENCY MEMORANDA CITED IN THIS DOCUMENT

CBRS No(s).:	1686 and 1687
Subject:	PP#6F3380/6H5502. Glyphosate (Roundup®) in or on Soybeans. Amendment of 9/18/86.
From:	W. Chin
To:	R. Taylor and Toxicology Branch
Dated:	7/6/87
MRID(s):	00161333

CBRS No(s).:	2346 and 2347
Subject:	PP#6F3380/FAP#6H5502. Glyphosate in/on Soybeans Glyphosate Registration Standard. Product chemistry for isopropylamine and sodium sesqui salts; nitrosamines.
From:	J. Stokes
To:	R. Taylor and Toxicology Branch
Dated:	9/1/87
MRID(s):	40155801, 41055802, 40155803

CBRS No(s).:	3007
Subject:	PP#6E3424: Re-evaluation of nitrosamine contaminants in glyphosate products.
From:	W. Chin
To:	H. Jamerson and Toxicology Branch
Dated:	2/25/88
MRID(s):	40405401

CBRS No(s).:	7742
Subject:	Isopropylamine (IPA) Glyphosate. Product Chemistry Data (Storage Stability and Vapor Pressure) for Monsanto Products.
From:	K. Dockter
To:	E. Feris
Dated:	5/31/91
MRID(s):	41096101

PRODUCT CHEMISTRY CITATIONS

Bibliographic citations include only MRIDs containing data which fulfill data requirements. Three additional MRIDs which have not yet been reviewed, but which may contain data pertinent to the reregistration of Monsanto glyphosate MPs, are included in bold type at the end of this section.

References (cited):

00051977 Monsanto Company (1976) The Name, Chemical Identity, Physical Composition of the Pesticide: [Roundup]. Rev. (Unpublished study received Jun 3, 1976 under 524-308; CDL:096177-A)

00065754 Monsanto Company (1977) Roundup® Herbicide Analyses. (Unpublished study, including letter dated Mar 23, 1977 from L.H. Hannah to Robert J. Taylor, received May 12, 1977 under 524-308; CDL:229787-F)

00072227 Monsanto Agricultural Products Company (1978) Test for % Glyphosate. Method no. AQC-163-78 dated Oct 25, 1978. (Unpublished study received Apr 25, 1979 under 524-330; CDL:238240-E)

00076490 Monsanto Company (19??) Analytical Method--H_2SO_4/H_3PO_4 in Roundup Technical. (Unpublished study received Nov 9, 1973 under 524-308; CDL:120640-A)

00084121 Monsanto Company (1972) The Name, Chemical Identity, Physical Composition of the Pesticide Chemical: [Roundup]. (Unpublished study received on unknown date under 4G1444; CDL:098324-B)

00108160 Monsanto Co. (1978) Environmental Chemistry--Glyphosate: Summary of Data in EPA Files as of 1/9/78. (Unpublished study received Jan 16, 1978 under 524-308; CDL:096758-A)

00108202 Monsanto Co. (1978) The Name, Chemical Identity, Physical Composition of the Pesticide: [Glyphosate]. (Compilation; unpublished study received Jul 11, 1978 under 524-308; CDL:234319-A)

00161333 Hammon, J. (1986) Product Chemistry Data To Suppport the Continued Registration of Glyphosphate (N-phosphonomethyl-glycine): Report No. MSL-5066 (Revised): Project No. 7663. Unpublished study prepared by Monsanto Co. 172 p.

40154801 Barclay, J. (1986) Product Chemistry To Support the Registration of Sodium Sesqui-N-phosphonomethyl Glycinate: Product Identity and Composition: Laboratory Project No. MSL-6265. Unpublished study prepared by Monsanto Co. 41 p.

40154802 Barclay, J. (1986) Product Chemistry To Support the Registration of Sodium Sesqui-N-phosphonomethyl Glycinate: Analysis and Certification of Product Ingredients: Lab. Project No. MSL-6266. Unpublished study prepared by Monsanto Co. 48 p.

40155801 Barclay, J. (1986) Product Chemistry To Support the Registration of the Isopropylamine Salt of N-phosphonomethylglycine (62% Solution): Product Identity and Composition: Laboratory Project No. MSL-6196. Unpublished study prepared by Monsanto Co. 37 p.

40155802 Barclay, J. (1986) Product Chemistry To Support the Registration of the Isopropylamine Salt of N-phosphonomethylglycine (62% Solution). Analysis and Certification of Product Ingredients: Laboratory Project No. MSL-6197. Unpublished study prepared by Monsanto Co. 61 p.

40155803 Barclay, J. (1986) Product Chemistry To Support the Registration of the Isopropylamine Salt of N-phosphonomethylglycine (62% Solution). Physical and Chemical Characteristics: Laboratory Project No. MSL-6198. Unpublished study prepared by Monsanto Co. 16 p.

40405401 Hirsch, R.; Augustin, D. (1987) Nitrosamine Analyses of Roundup Herbicide, Rodeo Herbicide, MON 0139 and Polado Technical: Laboratory Project ID R. D. No. 835. Unpublished study prepared by Monsanto Agricultural Company. 212 p.

41096101 Leiber, M. (1988) Vapor Pressure Determinations for Glyphosate and MON-7200/15100: Project No. MSL-7642; R.D. No. 924. Unpublished study prepared by Monsanto Agricultural Co. 59 p.

References (not yet reviewed):

Data contained in the following MRID pertain to the trisodium salt TGAI, and may fulfill the remaining data requirements for this product. These data will be considered prior to issuance of the RED.

40154803 Barclay, J. (1986) Product Chemistry to Support the Registration of Sodium Sesqui-N-phosphonomethyl Glycinate: Physical and Chemical Characteristics: Lab. Proj. No. MSL-6267. Unpublished study prepared by Monsanto Co. 14 p.

Data contained in the following MRIDs pertain to the 62% IPA FI (EPA Reg. No. 524-333). These data will be considered prior to issuance of the RED.

41228401 Beasley, R.; Brockman, T.; Rogers, P. (1989) Product Chemistry to Support the Registration of the Isopropylamine Salt of N-Phosphonomethylglycine (62 percent

Solution): R. D. No. 954. Unpublished study prepared by Monsanto Agricultural Co. 50 p.

41228402 Beasley, R.; Brockman, T.; Rogers, P. (1989) Product Chemistry to Support the Registration of Isopropylamine Salt of (N-Phosphonomethylglycine) (62 percent Solution): R. D. No. 954. Unpublished study prepared by Monsanto Agricultural Co. 45 p.

Case No. 0178
Chemical No. 103601

Case Name: Glyphosate
Registrant: Monsanto
Product(s): IPA acid TGAI (unregistered)

PRODUCT CHEMISTRY DATA SUMMARY

Guideline Number	Requirement	Are Data Requirements Fulfilled? [a]	MRID Number [b]
61-1	Product Identity and Disclosure of Ingredients	N/A [c]	00161333, 40155801 [d]
61-2	Starting Materials and Manufacturing Process	Y	00051977, 00084121, 00108202, 00161333, 40155801 [d]
61-3	Discussion of Formation of Impurities	Y	00084121, 00161333, 40155801 [d]
62-1	Preliminary Analysis	Y	00161333, 40155802 [d]
62-2	Certification of Ingredient Limits	N/A [c]	00161333, 41055802 [d]
62-3	Analytical Methods to Verify the Certified Limits	N/A [c]	00065754, 00072227, 00076490, 00084121, 00108202, PP#6F1758, 00161333, 40155802 [d]
63-2	Color	Y	00051977, 00161333 [e]
63-3	Physical State	Y	00051977, 00161333 [e]
63-4	Odor	Y	00161333 [e]
63-5	Melting Point	Y	00051977, 00161333 [e]
63-6	Boiling Point	N/A	00161333 [e]
63-7	Density, Bulk Density or Specific Gravity	Y	00051977, 00161333 [e]
63-8	Solubility	Y	00051977, 00161333 [e]
63-9	Vapor Pressure	Y	00161333 [e], 41096101 [f]
63-10	Dissociation Constant	Y	00108160, 00161333 [e]
63-11	Octanol/Water Partition Coefficient	Y	00161333 [e]
63-12	pH	Y	00161333 [e]
63-13	Stability	Y	00161333 [e]

[a] Y = Yes; N = No; N/A = Not Applicable.

[b] References were reviewed in the Product Chemistry Science Chapter of the Registration Standard dated 7/15/85 unless otherwise noted.

[c] Data concerning this guideline are not required for the TGAI.

[d] CBRS Nos. 2346 and 2347, 9/1/87, J. Stokes.

[e] CBRS Nos. 1686 and 1687, 7/6/87, W. Chin.

[f] CBRS No. 7742, 5/31/91, K. Dockter.

Case No. 0178
Chemical No. 103603

Case Name: Glyphosate
Registrant: Monsanto
Product(s): Trisodium salt TGAI (unregistered)

PRODUCT CHEMISTRY DATA SUMMARY

Guideline Number	Requirement	Are Data Requirements Fulfilled? [a]	MRID Number [b]
61-1	Product Identity and Disclosure of Ingredients	N/A [c]	40154801 [d]
61-2	Starting Materials and Manufacturing Process	Y	40154801 [d]
61-3	Discussion of Formation of Impurities	Y	40154801 [d]
62-1	Preliminary Analysis	Y	40154802 [d]
62-2	Certification of Ingredient Limits	N/A [c]	41054802 [d]
62-3	Analytical Methods to Verify the Certified Limits	N/A [c]	00065754, 00072227, 00076490, 00084121, 00108202, PP#6F1758, 40154802 [d]
63-2	Color	Y	PP#8E2122
63-3	Physical State	Y	PP#8E2122
63-4	Odor	N	
63-5	Melting Point	Y	PP#8E2122
63-6	Boiling Point	N/A	
63-7	Density, Bulk Density or Specific Gravity	Y	PP#8E2122
63-8	Solubility	N	
63-9	Vapor Pressure	N	
63-10	Dissociation Constant	Y	PP#8E2122
63-11	Octanol/Water Partition Coefficient	N	
63-12	pH	N	
63-13	Stability	N	

[a] Y = Yes; N = No; N/A = Not Applicable.

[b] References were reviewed in the Product Chemistry Science Chapter of the Registration Standard dated 7/15/85 unless otherwise noted.

[c] Data concerning this guideline are not required for the TGAI.

[d] CBRS Nos. 2346 and 2347, 9/1/87, J. Stokes.

Case No. 0178
Chemical No. 103601

Case Name: Glyphosate
Registrant: Monsanto
Product(s): 62% IPA FI (EPA Reg. No. 524-333)

PRODUCT CHEMISTRY DATA SUMMARY

Guideline Number	Requirement	Are Data Requirements Fulfilled? [a]	MRID Number [b]
61-1	Product Identity and Disclosure of Ingredients	Y	40155801 [c]
61-2	Starting Materials and Manufacturing Process	Y	40155801 [c]
61-3	Discussion of Formation of Impurities	Y	40155801 [c]
62-1	Preliminary Analysis	Y	40155802 [c], 40405401 [d]
62-2	Certification of Ingredient Limits	Y	41055802 [c]
62-3	Analytical Methods to Verify the Certified Limits	Y	00065754, 00072227, 00076490, 00084121, 00108202, PP#6F1758, 40155802 [c]
63-2	Color	Y	00161333 [e], 40155803 [f]
63-3	Physical State	Y	00161333 [e], 40155803 [f]
63-4	Odor	Y	00161333 [e], 40155803 [f]
63-5	Melting Point	Y	00161333 [e]
63-6	Boiling Point	N/A	00161333 [e]
63-7	Density, Bulk Density or Specific Gravity	Y	00161333 [e], 40155803 [f]
63-8	Solubility	Y	00161333 [e]
63-9	Vapor Pressure	Y	00161333 [e], 41096101 [g]
63-10	Dissociation Constant	Y	00161333 [e]
63-11	Octanol/Water Partition Coefficient	Y	00161333 [e]
63-12	pH	Y	00161333 [e], 40155803 [f]
63-13	Stability	Y	00161333 [e]

[a] Y = Yes; N = No; N/A = Not Applicable.

[b] References were reviewed in the Product Chemistry Science Chapter of the Registration Standard dated 7/15/85 unless otherwise noted.

[c] CBRS Nos. 2346 and 2347, 9/1/87, J. Stokes.

[d] CBRS No. 3007, 2/25/88, W. Chin

[e] CBRS Nos. 1686 and 1687, 7/6/87, W. Chin.

[f] Glyphosate Reregistration Standard Update, dated 4/26/90.

[g] CBRS No. 7742, 5/31/91, K. Dockter.

Case No. 0178
Chemical No. 103601

Case Name: Glyphosate
Registrant: Monsanto
Product(s): 94% IPA FI (EPA Reg. No. 524-421)

PRODUCT CHEMISTRY DATA SUMMARY

Guideline Number	Requirement	Are Data Requirements Fulfilled? [a]	MRID Number
61-1	Product Identity and Disclosure of Ingredients	N	
61-2	Starting Materials and Manufacturing Process	N	
61-3	Discussion of Formation of Impurities	N	
62-1	Preliminary Analysis	N	
62-2	Certification of Ingredient Limits	N	
62-3	Analytical Methods to Verify the Certified Limits	N	
63-2	Color	N	
63-3	Physical State	N	
63-4	Odor	N	
63-5	Melting Point	N	
63-6	Boiling Point	N	
63-7	Density, Bulk Density or Specific Gravity	N	
63-8	Solubility	N	
63-9	Vapor Pressure	N	
63-10	Dissociation Constant	N	
63-11	Octanol/Water Partition Coefficient	N	
63-12	pH	N	
63-13	Stability	N	

[a] Y = Yes; N = No; N/A = Not Applicable.

Case No. 0178
Chemical No. 103601

Case Name: Glyphosate
Registrant: Monsanto
Product(s): 75% IPA T (EPA Reg. No. 524-421)

PRODUCT CHEMISTRY DATA SUMMARY

Guideline Number	Requirement	Are Data Requirements Fulfilled? [a]	MRID Number
61-1	Product Identity and Disclosure of Ingredients	N	
61-2	Starting Materials and Manufacturing Process	N	
61-3	Discussion of Formation of Impurities	N	
62-1	Preliminary Analysis	N	
62-2	Certification of Ingredient Limits	N	
62-3	Analytical Methods to Verify the Certified Limits	N	
63-2	Color	N	
63-3	Physical State	N	
63-4	Odor	N	
63-5	Melting Point	N	
63-6	Boiling Point	N	
63-7	Density, Bulk Density or Specific Gravity	N	
63-8	Solubility	N	
63-9	Vapor Pressure	N	
63-10	Dissociation Constant	N	
63-11	Octanol/Water Partition Coefficient	N	
63-12	pH	N	
63-13	Stability	N	

[a] Y = Yes; N = No; N/A = Not Applicable.

DYNAMAC
CORPORATION
Environmental Services

Final Report

GLYPHOSATE
Shaughnessy Nos. 103601 & 103603
Case 0178

TASK 2B: RED
RESIDUE CHEMISTRY

October 16, 1992

Contract No. 68-D2-0053

Submitted to:
U.S. Environmental Protection Agency
Arlington, VA 22202

Submitted by:
Dynamac Corporation
The Dynamac Building
2275 Research Boulevard
Rockville, MD 20850-3268

GLYPHOSATE

REREGISTRATION ELIGIBILITY DOCUMENT

RESIDUE CHEMISTRY CONSIDERATIONS

(Shaughnessy Nos. 103601 & 103603; Case 0178)

TASK 2B

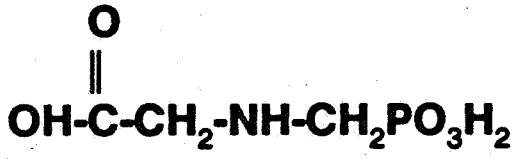
INTRODUCTION

Glyphosate (N-phosphonomethyl glycine) is a nonselective herbicide and plant growth regulator that includes isopropylamine salt (Chemical Code 103601) and the sodium salt (Chemical Code 103603). It is registered for use on a variety of food and feed crops; refer to Table A for a comprehensive list. Glyphosate is typically applied on these crops as postemergence spray to foliage of the vegetation controlled before planting, and after planting but prior to crop emergence, or as directed spray in established crops. In addition, glyphosate may be used in and around aquatic sites; treated water from aquatic sites may be used to irrigate crops *(Source: LUIS General Chemical Draft Report for Glyphosate, 7/20/92)*.

The Reregistration Standard Guidance Document for glyphosate was issued 6/86. The Glyphosate Product and Residue Chemistry Reregistration Standard Update was completed 4/26/90. The information contained in this document outlines the Residue Chemistry Science Assessments with respect to the reregistration of glyphosate.

Tolerances for residues of glyphosate in or on food/feed and in processed commodities are currently expressed in terms of the combined residues of glyphosate and its metabolite aminomethylphosphonic acid (AMPA), expressed as glyphosate *[Source: 40 CFR §180.364 (a)(b)(c), 185.3500, and 186.3500]*. The tolerances listed in 40 CFR §180.364(a) are for the combined residues resulting from application of the isopropylamine salt of glyphosate and/or the monoammonium salt of glyphosate. The majority of these tolerances are set at 0.2 ppm. The tolerances listed in 40 CFR §180.364(b) are for the combined residues resulting from application of the glyphosate isopropylamine salt and/or glyphosate monoammonium salt for herbicidal and plant growth regulator purposes and/or the sodium sesqui salt for plant regulator purposes. The tolerances listed in 40 CFR §180.364(c) are for the combined residues resulting from the use of irrigation water containing residues of 0.5 ppm following applications on or around aquatic sites. Adequate enforcement methods are available for the residue determination of these regulated compounds in or on plant and animal commodities, and in water. The HED Metabolism Committee has determined that aminomethyl-phosphonic acid (AMPA), the metabolite of glyphosate, no longer needs to be regulated and therefore this compound will be dropped from the tolerance regulation.

The structure of glyphosate is given below;



SUMMARY OF SCIENCE FINDINGS

§171-4 (a): Plant Metabolism: The qualitative nature of the residue in plants is adequately understood. Studies with a variety of plants including corn, cotton, soybeans, and wheat indicate that the uptake of glyphosate or its metabolite AMPA from soil is limited, but the residues which are taken up are readily translocated. Foliarly applied glyphosate is readily absorbed and translocated throughout apples, coffee, dwarf citrus (calamondin), grapes, and pears. Metabolism occurs via N-methylation and ultimately yields N-methylated glycines and phosphonic acids. For the most part, the ratio of glyphosate to AMPA is 9 to 1 but can approach 1 to 1 in a few cases (e.g., soybeans and carrots). Much of the residue data for crops reflects a detectable residue of parent (0.05-0.15 ppm) along with a nondetectable residue (<0.05 ppm) of AMPA. The terminal residue to be regulated in plants is glyphosate per se.

§171-4 (b): Animal Metabolism: The qualitative nature of the residue in animals is adequately understood. Studies involving lactating goats and laying hens fed a mixture of glyphosate and AMPA indicate that the primary route of elimination was by excretion (urine and feces) and that the results are consistent with the metabolism studies in rats, rabbits, and cows. The terminal residues in eggs, milk, and animal tissues are glyphosate and its metabolite AMPA; there was no evidence of further metabolism. The terminal residue to be regulated in livestock is glyphosate per se.

§171-4 (c) and (d): Residue Analytical Methods - Plants and Animals: Adequate enforcement methods are available for analysis of residues of glyphosate and its metabolite AMPA in or on plant commodities and in water. These methods include GLC (Method I of PAM Vol. II; limit of detection is 0.05 ppm) and HPLC with fluorometric detection. Use of the GLC method, however, is being discouraged due to lengthiness of the procedure. The HPLC method has undergone successful Agency validation (method tryout) and was recommended for inclusion in PAM Vol. II; the limit of detection is 0.0005 ppm. For enforcement of tolerances in animal commodities, an HPLC method with fluorescence detector is available; the reported limits of detection are 0.01 ppm for glyphosate and 0.012 ppm for AMPA.

§171-4 (e): Storage Stability: The available storage stability data indicate that residues of glyphosate and its metabolite AMPA are stable under frozen (-20 C) storage conditions: in or on plant commodities for a period of 1 year, in animal commodities for 2 years, and in water for 1 year. No additional storage stability data are needed.

§171-4 (f-l): Magnitude of the Residue in Plants, Animals, Potable Water, and Fish:

The conclusions regarding the reregistration eligibility of glyphosate on the crops listed in Table A are based on the use patterns registered by the basic producer, Monsanto Agricultural Chemical Company as reflected in the LUIS report for glyphosate, 7/20/92. When end-use product DCIs are developed (e.g. at issuance of the RED), RD should require that all end-use product labels (e.g. MAI labels, SLNs, and products subject to the generic data exemption) be amended such that they are consistent with the basic producer labels.

All data requirements for magnitude of the residue in plants have been evaluated and deemed adequate. *[Note: The registrant has also committed to providing new potato and sorghum processing studies.]* All data requirements for magnitude of the residue in plants as a result of irrigation with glyphosate-treated water have also been submitted and are adequate to support registered use and applicable tolerances. No additional data are required for magnitude of the residue in animals, potable water, and fish.

TABLE A. RESIDUE CHEMISTRY SCIENCE ASSESSMENTS FOR REREGISTRATION OF GLYPHOSATE.

Data Requirements	Tolerances, ppm [40 CFR]	Must Additional Data Be Submitted?	References[1]
§171-4 (a): Plant Metabolism	N/A	No	00038771, 00039141, 00051983, 00065753, 00108097, 00108129, 00108133, 00108140, 00108151, 00111945, PP4G14444, PP5F1560, PP7F2016, GS0178-003
§171-4 (b): Animal Metabolism	N/A	No	00094971, 00108098, 00108099, 00108100, 00108101, 00108116, 00108099, 00108200, PP4G1444, PP9F2163, GS0178-004, 40541301-40541302[2]

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TABLE A. *(Continued).*

Data Requirements	Tolerances, ppm [40 CFR]	Must Additional Data Be Submitted?	References[1]
§171-4 (c) and (d): Residue Analytical Methods	N/A	No	00028853, 00036222, 00036223, 00036231, 00037688, 00038770, 00038979, 00044423, 00051982, 00053002, 00053005, 00060108, 00061559, 00063714, 00065751, 00065752, 00067425, 00076805, 00078823, 00078824, 00108133, 00108144, 00108149, 00108151, 00108175, 00108176, 00108186, 00108231, 00111945, 00111949, 00122715, 00159419, PP4G1444, PP5F1536, PP6G1679, PP0F2329, PP9F2163, PP1F2455, GS0179-017, GS0178-019, GS0178-020, GS0178-021, GS0178-022, GS0178-23, GS1278-014, 00164729,[3] 40502601,[4] 40541304[2]
§171-4 (e): Storage Stability	N/A	No	00039142, 00040083, 00051980, 00053002, 00061553, 00061555, 00108129, 00108132, 40502605,[2,4,4] 40532004,[2,4,4] 41940701[5]
§171-4 (k) (l): Magnitude of the Residue in Plants			
Root and Tuber Vegetables Group			
- Artichokes, Jerusalem	0.2 [§180.364(a)]	No	N/A[6]
- Beets, garden	0.2 [§180.364(a)]	No	00108159
- Carrots	0.2 [§180.364(a)]	No	PP7F2016, 00108159
- Chicory	0.2 [180.364(a)]	No	N/A
- Horseradish	0.2 [§180.364(a)]	No	N/A
- Parsnips	0.2 [§180.364(a)]	No	N/A
- Potatoes	0.2 [§180.364(a)]	No	00108151, 41947001[7]

(Continued; footnotes follow)

TABLE A. *(Continued).*

Data Requirements	Tolerances, ppm [40 CFR]	Must Additional Data Be Submitted?	References[1]
(processed commodities)		No[8]	**40785302**
- Radish	0.2 [§180.364(a)]	No	00108159
- Rutabagas	0.2 [§180.364(a)]	No	N/A
- Salsify	0.2 [§180.364(a)]	No[9]	N/A
- Sugar beets	0.2 [§180.364(a)]	No	00039381, 00108151
(processed commodities)		No	**40785304**
- Sweet potato	0.2 [§180.364(a)]	No	00108151
- Turnips	0.2 [§180.364(a)]	No	40835201[10]
Leaves of Root and Tuber Vegetables Group	0.2 [§180.364(a)][11]		
- Beets, greens		No	N/A
- Chicory leaves		No	N/A
- Sugar beet tops		No	00039381, 00108151
- Turnip tops		No	40835201[10]
Bulb Vegetables Group	0.2 [§180.364(a)]		
- Garlic		No	N/A
- Onions (green and dry bulb)		No	40783101[12]
Leafy Vegetables (except Brassica) Group	0.2 [§180.364(a)]		
- Celery		No	N/A
- Lettuce (head and leaf)		No	00108159, PP7F2016
- Spinach		No	N/A
Brassica Leafy Vegetables Group	0.2 [§180.364(a)]		
- Broccoli		No	40802801, 40802801[13]
- Cabbage		No	00108159, PP7F2016
- Cauliflower		No	N/A
- Kale		No	N/A
- Mustard greens		No	40802801, 40802801[13]

(Continued; footnotes follow)

TABLE A. *(Continued).*

Data Requirements	Tolerances, ppm [40 CFR]	Must Additional Data Be Submitted?	References[1]
Legume Vegetables (Succulent/Dried) Group	0.2 [§180.364(a)][14]		
- Beans (succulent and dried)		No	00108159, PP7F2016
- Lentils		No	00108159
- Peas (succulent and dried)		No	00108159, PP7F2016
- Soybeans	20 [§180.364(a)][15]	No	00015759, 00015760, 00015761, 00015762, 00015763, 00015764, 00015765, 00015766, 00015767, 00024503, 00033954, 00038908, 00040084, 00061555, 00108153, 00108203, PP7F1971
(processed commodities)	100 (hulls) [§186.3500][16]	No	00061555, 00108153, 00156793[17]
Foliage of Legume Vegetables (Succulent/Dried) Group	0.2 [§180.364(a)][18]		
- Bean vines and hay		No	00108159, PP7F2016
- Lentil forage and hay		No	00108159
- Pea vines and straw		No	PP7F2016
- Soybean forage and hay	15 [§180.364(a)][19]	No	00015759, 00015760, 00015761, 00015762, 00015763, 00015764, 00015765, 00015766, 00015767, 00033954, 00038908, 00040084, 00061555, 00108153, 00108203, PP7F1971
Fruiting Vegetables Group	0.1 [§180.364(a)]	No	PP3E2893
Cucurbit Vegetables Group	0.5 [§180.364(a)]	No	PP3E2845
Citrus Fruits Group	0.2 [§180.364(a)]	No	00039142

(Continued; footnotes follow)

TABLE A. *(Continued).*

Data Requirements	Tolerances, ppm [40 CFR]	Must Additional Data Be Submitted?	References[1]
(processed commodities)	1.0 (dried pulp) 1.0 (molasses) [§186.3500][15]	No	PP8H5568[20], 40159401[21]
Pome Fruits Group	0.2 [§180.364(a)]	No	00108129
Stone Fruits Group	0.2 [§180.364(a)]	No	00111949
- Plums (fresh prunes)		No	00111949
(processed commodities)		No	**40785301**
Small Fruits and Berries Group	0.2 [§180.364(a)][22]		
- Blackberries		No	PP3E2930
- Blueberries		No	PP3E2930
- Cranberries		No	00053002
- Grapes		No	00038770, 00108132
(processed commodities)		No	**40785303**
- Raspberries		No	PP3E2930
Tree Nuts Group	0.2 [§180.364(a)]	No	00111945
- Almond hulls	1 [§180.364(a)]	No	00111945
Cereal Grains Group	0.1 [§180.364(a)]		
- Barley		No	00038908, 00040087, 00044422, 00108203
(processed commodities)		No	N/A
- Corn (field and fresh)		No	00023336, 00023512, 00037687, 00038908, 00040085, 00048284, 00108203, 40502602[4,17]
(processed commodities)		No	40502604,[4] 41478101[23]
- Oats		No	00038908, 00040087, 00044422, 00108203
(processed commodities)		No	N/A
- Rice		No	00038908, 00040087, 00044422
(processed commodities)		No[24]	N/A

(Continued; footnotes follow)

TABLE A. *(Continued).*

Data Requirements	Tolerances, ppm [40 CFR]	Must Additional Data Be Submitted?	References[1]
- Rye		No	N/A
(processed commodities)		No	N/A
- Sorghum		No	00038908, 00040087, 00044422, 00108203, 00109271, 40502601[25]
(processed commodities)		No[8]	40502603[25,26]
- Wheat		No[27]	00038908, 00040086, 00044426, 00108203, 00122715, 41484301[28,29]
(processed commodities)		No[30]	00150835[28,29,31]
Forage, Fodder, and Straw of Cereal Grains Group	0.2 [§180.364(a)][32]		
- Barley forage, hay, and straw		No	00038908, 00040087, 00044422, 00108203
- Corn forage and fodder		No	00023336, 00023512, 00037687, 00038908, 00040085, 00048284, 00108203, 40502602
- Oat forage, hay, and straw		No	00038908, 00040087, 00044422, 00108203
- Rice straw		No	00038908, 00040087, 00044422
- Rye forage and straw		No	N/A
- Sorghum forage and fodder		No	00038908, 00040087, 00044422, 00108203, 00109271, 40502601[25]
- Wheat forage and straw		No[33]	00038908, 00040086, 00044426, 00108203, 00122715, PPOF3865/FAP2H5635[29]
Grass Forage, Fodder, and Hay Group	0.2,[34] 200[35] [§180.364(a)]	No	00076805, 00108147
Non-grass Animal Feeds (forage, fodder, straw, and hay) Group	0.2,[36] 0.4,[37] 200[38] [§180.364(a)]	No	00076805, 00108147
- Alfalfa seed		No	**40541304**

(Continued; footnotes follow)

TABLE A. *(Continued).*

Data Requirements	Tolerances, ppm [40 CFR]	Must Additional Data Be Submitted?	References[1]
Miscellaneous Commodities			
- Acerola	0.2 [§180.364(a)]	No	PP3E2929
- Atemoya	0.2 [§180.364(a)]	No	PP6E3424[39]
- Asparagus	0.5 [§180.364(a)]	No	00108144, 40642401[40]
- Avocados	0.2 [§180.364(a)]	No	00108149
- Bananas	0.2 [§180.364(a)]	No	00108175
- Breadfruit	0.2 [§180.364(a)]	No[9]	40149401[41]
- Canistel	0.2 [§180.364(a)]	No[9]	40149401[41]
- Carambola	0.2 [§180.364(a)]	No	PP6E3424[39]
- Cherimoya	0.2 [§180.364(a)]	No[9]	PP0E3881[42]
- Cocoa beans	0.2 [§180.364(a)]	No[9]	PP0E3857[43]
- Coconut	0.1 [§180.364(a)]	No[9]	
- Coffee beans	1 [§180.364(a)]	No	00051980, 00051981[44]
- Cotton	15 (cottonseed, forage, & hay) [§180.364(a)]	No	00060103, 00061553, 00108176, 00108153, 00108203, PP7F1971
(processed commodities)		No	00061553, 00108176, 00108153
- Dates	0.2 [§180.364(a)]	No[9]	40149401[41]
- Figs	0.2 [§180.364(a)]	No	PP3E2929
- Genip	0.2 [§180.364(a)]	No[9]	PP0E3873[45]
- Guavas	0.2 [§180.364(a)]	No	00059050, PP1E2443
- Jaboticaba	0.2 [§180.364(a)]	No[9]	40149401[41]
- Jackfruit	0.2 [§180.364(a)]	No[9]	40149401[41]
- Kiwi fruit	0.2 [§180.364(a)]	No	PP3E2929
- Litchi Nut (Lychee)	0.2 [§180.364(a)]	No	PP9E3715[46,47]
- Longan	0.2 [§180.364(a)]	No	PP9E3715[46,47]
- Mamey Sapote (Mammee Apple)	0.2 [§180.364(a)]	No	PP9E3715[46,47]
- Mangoes	0.2 [§180.364(a)]	No	**40580401**
- Okra	0.2 [§180.364(a)]	No	N/A
- Olives	0.2 [§180.364(a)]	No	00108175, PP9F2223, FAP0H5255, 42398401[48]

(Continued; footnotes follow)

TABLE A. *(Continued).*

Data Requirements	Tolerances, ppm [40 CFR]	Must Additional Data Be Submitted?	References[1]
(processed commodities)	0.1 (imported olives) [§185.3500]	No	00108175, PP9F2223, FAPOH5255, 42398401[48]
- Palm oil	0.1 [§185.3500]	No	FAP6H5144
- Papayas	0.2 [§180.364(a)]	No	00063713
- Passion Fruit	0.2 [§180.364(a)]	No	PP9E3715[46,47]
- Peanuts	0.1 (peanuts) [§180.364(c)]; 0.5 (forage, hay, & hulls) [§180.364(a)(c)];	No	00144341, 00028852, 40750702
(processed commodities)		No	00144341[49], 00028852
- Persimmons	0.2 [§180.364(a)]	No[9]	40149401[41]
- Pineapple	0.1 [§180.364(a)]	No[50]	N/A
- Pistachio	0.2 [§180.364(a)]	No	00111945
- Sapodilla	0.2 [§180.364(a)]	No	PP9E3715[46,47]
- Sapote (black and white)	0.2 [§180.364(a)]	No[9]	40149401[41]
- Soursop	0.2 [§180.364(a)]	No[9]	40149401[41]
- Sugar apple	0.2 [§180.364(a)]	No	PP6E3424[39]
- Sugarcane	2.0 [§180.364(b)]	No[51]	00108140, PP8E2122, PP9H5196, PP8F2122
(processed commodities)	30.0 (molasses) [§185.3500]	No	00108168[17]
- Tamarind	0.2 [§180.364(a)]	No[9]	40149401[41]
- Tea	1.0 (dried tea), 7.0 (instant tea)[15] [§185.3500]	No	00078823, 00078824, PP8H5568[20]
- Watercress	0.2 [§180.364(a)][52]	No	N/A
§171-4 (h): Magnitude of the Residue in Plants Resulting from the Use of Irrigation Water	0.1 [§180.364(a)][53]	No	00039381, **40541305**
§171-4 (j): Magnitude of the Residue in Meat, Milk, Poultry, and Eggs	0.5[54]	No	00108115, PP5F1536, 40532001-03[2]

(Continued; footnotes follow)

TABLE A. *(Continued).*

Data Requirements	Tolerances, ppm [40 CFR]	Must Additional Data Be Submitted?	References[1]
§171-4 (g): Magnitude of the Residue in Fish	0.25 (fish) 3 (shellfish) [§180.364(b)]	No	00036229, 00076491, PP6G1679, PP6H5106, 00154311, 00155120[55]
§171-4 (f): Nature and Magnitude the Residue in Drinking and Irrigation Water	0.7[56]	No	00039377, 00039381, 00077227, 00077228, 00077229, 00077230, 00077231, 00077232, 00077233, 00077234, 00077235, 00077236, 00077237, 00077238, 00077301, 00108173, PP9F2163, PP6G1679/FAP6H5106, PP9F2163/FAP9H5024
§171-4 (i): Magnitude of the Residue in Food Handling Establishment		Not Required	
§171-5: Reduction of Residues		Not Required	

1. **Bolded** references were reviewed in the Update of 4/26/90. Unbolded references were reviewed in the Residue Chemistry Science Chapter of the Reregistration Standard dated 7/15/85. Otherwise, reviewed as noted.

2. CBTS Nos. 4285 & 4286, 1/30/89, W. Chin.

3. CBRS Nos. 2731, 2733, & 2734, 9/25/87, F. Griffith.

4. CBTS No. 4289, 2/1/89, M. Flood.

5. CBRS No. 8337, 4/2/92, R. Perfetti.

6. N/A = Not available because data from other crop group members were used to satisfy data requirements via translation.

7. CBRS No. 8367, 10/21/91, M. Metzger.

8. The available data were generated by Craven Laboratories; the registrant has committed to providing a new study (CBRS No. 10124, 8/26/92, R. Perfetti).

TABLE A. *(Continued).*

9. Not currently registered.

10. CBTS No. 4503, 2/10/89, M. Nelson.

11. A crop group tolerance of 0.2 ppm (negligible residue) has been established for the combined residues of glyphosate and its metabolite AMPA in or on "leafy vegetables", which is now considered to be an obsolete crop group classification (40 CFR §180.34).

12. CBTS No. 4284, 10/20/88, M. Nelson.

13. CBTS No. 4361, 12/9/88, F. Toghrol.

14. A crop group tolerance of 0.2 ppm (negligible residue) has been established for the combined residues of glyphosate and its metabolite AMPA in or on "seed and pod vegetables", which is now considered an obsolete crop group classification (40 CFR §180.34). In addition, an individual tolerance of 20 ppm has been established for the combined residues of glyphosate and its AMPA metabolite in or on soybeans (FR 42701, 9/16/92).

15. FR 42701, 9/16/92.

16. FR 42701, 9/16/92.

17. CBRS Nos. 8196 & 8220, 2/3/92, R. Perfetti.

18. A crop group tolerance of 0.2 ppm (negligible residue) has been established for the combined residues of glyphosate and its metabolite AMPA in or on the "forage and hay of seed and pod vegetables", which is now considered an obsolete crop group classification (40 CFR §180.34). In addition, individual tolerances of 15 ppm have been established for the combined residues of glyphosate and its metabolite AMPA in or on soybean forage and hay.

19. In addition, a tolerance of 200 ppm has been established for the combined residues of glyphosate and AMPA in or on soybean straw (FR 42701, 9/16/92). This tolerance should be deleted and the soybeans, hay tolerence level raised to 200 ppm to cover this dessicant use.

20. CBTS No. 4685, 3/22/89, M. Nelson.

21. CBTS Nos. 2369-2371, 7/20/87, M. Nelson.

22. A crop group tolerance of 0.2 ppm has been established for the combined residues of glyphosate and its metabolite AMPA in or on small fruits and berries. In addition, individual tolerances of 0.2 ppm have been established for the combined residues of glyphosate and its AMPA metabolite in or on grapes and cranberries.

23. CBTS Nos. 6745 & 6746, 7/13/90, F. Griffith.

24. Data requirements for rice processed commodities were waived (Residue Chemistry Science Chapter of the Reregistration Standard).

25. CBTS Nos. 4357 & 4358, 11/18/88, S. Willet.

26. CBTS Nos. 6740-6742, 9/5/90, S. Willet.

TABLE A. *(Continued).*

27. CBTS recommends for the establishment of a 4 ppm tolerance for combined residues of glyphosate and its metabolite AMPA in or on wheat grain (CBTS Nos. 9686-9690, 5/26/92, R. Cook).

28. CBTS Nos. 6748-6750, 1/29/91, R. Cook.

29. CBTS Nos. 9686-9690, 5/29/92, R. Cook.

30. CBTS recommends for the establishment of Monsanto's proposed 12-ppm FAT for combined residues of glyphosate and its metabolite AMPA in wheat milling fractions (except flour) (CBTS Nos. 9686-9690, 5/26/92, R. Cook).

31. CBTS Nos. 537 & 538, 4/18/85, R. Cook.

32. A crop group tolerance of 0.2 ppm has been established for the combined residues of glyphosate and its metabolite AMPA in or on "forage grasses", which is now considered an obsolete crop group classification (40 CFR §180.34).

33. CBTS recommends for the establishment of an 85-ppm tolerance for combined residues of glyphosate and its metabolite AMPA in or on wheat straw (CBTS Nos. 9686-9690, 5/26/92, R. Cook).

34. Tolerances have been established for the combined residues of glyphosate and its metabolite AMPA in or on forage grasses at 0.2 ppm; and on grasses, forage, at 0.2 ppm.

35. Tolerances have been established for the combined residues of glyphosate and its metabolite AMPA in or on individual grasses (bahiagrass, bluegrass, bromegrass, fescue, orchardgrass, ryegrass, timothy, and wheatgrass) at 200 ppm.

36. Tolerances have been established for the combined residues of glyphosate and its metabolite AMPA in or on alfalfa fresh and hay at 0.2 ppm

37. A crop group tolerance of 0.4 ppm has been established for the combined residues of glyphosate and its metabolite AMPA in or on "forage legumes (except soybeans and peanuts)", which is now considered an obsolete crop group classification (40 CFR §180.34).

38. Individual tolerances of 200 ppm have been established for the combined residues of glyphosate and its metabolite AMPA in or on alfalfa and clover.

39. CBTS No. 1528, 9/30/86, M. Firestone.

40. CBTS No. 3967, 9/8/88, R. Cook.

41. CBTS No. 5196, 9/19/89, W. Chin.

42. CBTS No. 6938, 9/5/90 and CBTS No. 7275, 11/10/90.

43. CBTS No. 6827, 7/24/90 and CBTS No. 7915, 4/23/91.

44. CBRS No. 9674, 7/9/92, D. McNeilly.

TABLE A. *(Continued).*

45. CBTS No. 6828, 7/20/90 and CBTS No. 6935, 9/5/90.

46. CBTS No. 4907, 4/5/89, M. Nelson.

47. CBTS No. 5327, 6/8/89, M. Nelson.

48. CBRS No. 10256, 10/8/92, R. Perfetti.

49. CBRS No. 10124, 8/26/92, R. Perfetti.

50. Data requirements for pineapples were waived (Residue Chemistry Science Chapter of the Reregistration Standard) based on the built-in 21-month preharvest interval.

51. Data for sugarcane are no longer required (CBRS Nos. 8196 & 8220, 2/3/92, R. Perfetti). Data for sugarcane forage are no longer required as the registrant has imposed a feeding restriction (CBRS Nos. 2372-2374, 9/25/87, F. Griffith).

52. A tolerance of 0.2 ppm (negligible residues) has been established for the combined residues of glyphosate and its metabolite AMPA in or on watercress as a member of the "leafy vegetables group" which is now considered an obsolete crop group classification.

53. Tolerances of 0.1 ppm have been established for the combined residues of glyphosate and its metabolite AMPA in or on the crop groups citrus, cucurbits, forage grasses, forage legumes, fruiting vegetables, grain crops, leafy vegetables, nuts, pome fruits, root crop vegetables, seed and pod vegetables, stone fruit, and the individual commodities cotton seed, hops, and avocados resulting from the use of irrigation water containing residues of 0.5 ppm following applications on or around aquatic sites.

54. Tolerances of 0.5 ppm have been established for the combined residues of glyphosate and its metabolite AMPA in the liver and kidney of cattle, goats, hogs, horses, poultry, and sheep.

55. CBRS No. 409, 4/10/86, E. Haeberer.

56. A maximum contaminant level (MCL) of 0.7 ppm in drinking water has been established by the Office of Ground Water and Drinking Water. The maximum expected concentration of the combined residues of glyphosate and AMPA in irrigation water has been determined to be 0.5 ppm.

TOLERANCE REASSESSMENT SUMMARY

The HED Metabolism Committee has determined that aminomethylphosphonic acid (AMPA), the metabolite of glyphosate, no longer needs to be regulated and therefore this compound will be dropped from the tolerance expression.

Tolerances Listed Under 40 CFR §180.364(a):

The tolerances listed in 40 CFR §180.364(a) are for the combined residues of glyphosate and its metabolite AMPA resulting from application of the isopropylamine salt of glyphosate and/or the monoammonium salt of glyphosate.

Sufficient data are available to ascertain the adequacy of the established tolerances listed in 40 CFR §180.364(a) for: acerola; alfalfa, forage, seed, and hay; almonds, hulls; artichokes, Jerusalem; asparagus; atemoya; avocados; Bahiagrass; bananas; beets, garden, roots; Bermudagrass; bluegrass; Brassica leafy vegetables group; bromegrass; bulb vegetables group; carambola; carrots; cereal grains group; citrus fruits group; coffee beans, green; clover; cotton forage; cotton hay; cottonseed; cranberries; cucurbit vegetables group; fescue; figs; foliage of legume vegetables group; fruiting vegetables group; grapes; grass forage, fodder, and hay group; guavas; horseradish; kiwifruit; leafy vegetables group; leaves of the root and tuber vegetables group; legume vegetables group; longan fruit; lychee; mangoes; non-grass animal feeds group, forage and hay; orchardgrass; papayas; parsnips; passion fruit; peanuts; peanuts, vines; pineapple; pistachio; pome fruits group; potatoes; radishes; rutabagas; ryegrass; sapodilla; sapote; small fruits and berries group; soybeans; soybean, forage; stone fruits group; sugar apple; sugar beets; sweet potatoes; timothy; tree nuts group; turnip roots; wheatgrass; and yams. Certain commodity definitions of the above tolerances are not in accordance with the definitions listed in Table II of Subdivision O; see Table B for modifications in commodity definitions.

The data for the present potato and sorghum processing studies were generated by Craven Laboratories, however, the registrant has committed to providing new studies.

The established crop group tolerances for the now-obsolete "seed and pod vegetables" (0.2 ppm) and "seed and pod vegetables, forage and hay" (0.2 ppm) are inappropriate and should be replaced with "legume vegetables group (except soybeans)" and "legume vegetables group, foliage of (except soybean forage and hay)", respectively. Soybeans must be excluded from the crop group tolerances because the use pattern for soybeans is different from other legume vegetables, and the established tolerance for soybeans and soybean forage and hay differ by a factor $>5x$ from other legume vegetables. To achieve compatibility with Codex MRLs for selected commodities, the following actions must be taken (see Table C): (i) increase U.S. tolerance for legume vegetables group (except soybeans) from 0.2 ppm to 5 ppm; and (ii) increase U.S. tolerance for soybean hay from 15 ppm to 20 ppm.

The individual tolerances for cranberries (0.2 ppm) and grapes (0.2 ppm) should be revoked since these fruits are covered by the crop group tolerance (0.2 ppm) for small fruits and berries. The tolerance for cotton hay should also be revoked since this is not a raw agricultural commodity of cotton.

Tolerances for wheat, grain and wheat, straw at 4 and 85 ppm, respectively, have been proposed (PP0F3865/FAP2H5635). When these tolerances have been established, the tolerances for the cereal grains group and the cereal grains group, forage, fodder, and straw should be modified to "cereal grains group (except wheat)" and "cereal grains group, forage, fodder, and straw (except wheat straw)", respectively. To achieve compatibility with the Codex MRL for wheat grain, the U.S. tolerance should be established at 5 ppm (see Table C).

The existing and conflicting tolerances for alfalfa (200 ppm), alfalfa fresh and hay (0.2 ppm), clover (200 ppm), and forage legumes (except soybeans and peanuts; 0.4 ppm) should be deleted. Concomitant with the deletion of these tolerances, a tolerance of 100 ppm for residues in or on the non-grass animal feeds group, forage and hay, should be established. The available data from alfalfa, lespedeza, and trefoil will support this crop group tolerance.

The established tolerances for "forage grasses" (0.2 ppm), "grasses, forage" (0.2 ppm), Bahiagrass (200 ppm), Bermudagrass (200 ppm), bluegrass (200 ppm), bromegrass (200 ppm), fescue (200 ppm), orchardgrass (200 ppm), ryegrass (200 ppm), timothy (200 ppm), and wheatgrass (200 ppm) should be deleted. Concomitant with the deletion of these tolerances, a tolerance for residues in on or on the grass forage, fodder, and hay group should be established at 100 ppm. The available data indicate that following registered use, residues in or on the grass forage, fodder, and hay group will not exceed 100 ppm.

Individual tolerances exist for residues in or on salsify and the following tropical/subtropical crops:breadfruit; canistel; cherimoya; cocoa beans; coconut; dates; genip; jaboticaba; jackfruit; persimmons; sapote (black and white); soursop; and tamarind. There are currently no registered uses of glyphosate on these crop sites. Unless an interested party declares intent to include these crop sites on a product label and submit appropriate, supporting residue data, we recommend that these individual tolerances be revoked.

A tolerance of 200 ppm has recently been established for residues in or on soybean straw (FR 42701, 9/16/92). However, this tolerance should be revoked since this is not a raw agricultural commodity of soybeans. The tolerance for soybeans, hay should be raised to cover this dessicant use.

The expression negligible residues (N) should be deleted. For a complete listing of appropriate commodity definition changes and recommendations, see Table B.

Tolerances Listed Under 40 CFR §180.364(b):

The tolerances listed in 40 CFR §180.364(b) are for the combined residues of glyphosate and its metabolite AMPA resulting from application of the glyphosate isopropylamine salt and/or glyphosate monoammonium salt for herbicidal and plant growth regulator purposes and/or the sodium sesqui salt for plant regulator purposes.

Sufficient data are available to ascertain the adequacy of the established tolerances listed in 40 CFR §180.364(b) for: liver and kidney of cattle, goats, hogs, horses, poultry, and sheep; peanuts; peanuts, hay; peanuts, hulls; sugarcane; fish; and shellfish. See Table B for modifications in commodity definitions.

Tolerances Listed Under 40 CFR §180.364(c):

The tolerances listed in 40 CFR §180.364(c) are for the combined residues of glyphosate and its metabolite AMPA resulting from the use of irrigation water containing residues of 0.5 ppm following applications on or around aquatic sites, and are established at 0.1 ppm.

Sufficient data are available to ascertain the established tolerances listed in 40 CFR §180.364(c) for the crop groupings Brassica leafy vegetables group; bulb vegetables group; cereal grains group; citrus fruits group; cucurbit vegetables group; foliage of legume vegetables group; forage, fodder, and straw of the cereal grains group; fruiting vegetables group; grass forage, fodder and hay group; leafy vegetables group; leaves of the root and tuber vegetables group; legume vegetables group; non-grass animal feeds group, forage and hay; pome fruits group; root and tuber vegetables group; stone fruits group; tree nuts group; and the individual commodities avocados, cottonseed, and hops. See Table B for modifications in commodity definitions.

Tolerances Listed Under 40 CFR §185.3500:

The tolerances listed in 40 CFR §185.3500(1) are for the combined residues of glyphosate and its metabolite AMPA resulting from the application of the glyphosate for herbicidal purposes and/or the sodium sesqui salt for plant regulator purposes.

Sufficient data are available to ascertain the adequacy of the established food additive tolerances listed in 40 CFR §185.3500(1) for sugarcane, molasses. See Table B for modifications in commodity definitions.

The tolerances listed in 40 CFR §185.3500(2) are for the combined residues of glyphosate and its metabolite AMPA resulting from the application of the isopropylamine salt of glyphosate for herbicidal purposes.

Sufficient data are available to ascertain the adequacy of the established food additive tolerances listed in 40 CFR §185.3500(2) for olives (imported), palm oil, dried tea and instant tea. See Table B for modifications in commodity definitions.

A 12-ppm food additive tolerance for wheat milling fractions (except flour) has been proposed (FAP2H5635). To achieve compatibility with the Codex MRL for wheat bran, unprocessed, the U.S. tolerance should be established at 40 ppm (see Table C).

Food additive tolerances must be proposed for residues of glyphosate in potatoes, chips and potatoes, granules (1 ppm each). The available processing data indicate that combined residues of glyphosate concentrate ca. 4-5x in potato chips and granules.

Tolerances Listed Under 40 CFR §186.3500:

The tolerances listed in 40 CFR §186.3500(a) are for the combined residues of glyphosate and its metabolite AMPA.

Sufficient data are available to ascertain the adequacy of the established feed additive tolerances listed in 40 CFR §186.3500(a) for dried citrus pulp and soybean hulls. See Table B for modifications in commodity definitions.

A tolerance has recently been established at 1.0 ppm for the combined residues of glyphosate and AMPA in citrus, molasses (FR 42701, 9/16/92).

Feed additive tolerances must be proposed for combined residues of glyphosate and AMPA in potatoes, waste from processing (1.0 ppm). The available processing data indicate that combined residues of glyphosate concentrate ca. 4-5x in dry peel and 2.4x in wet peel.

Table B. Tolerance Reassessment Summary

Commodity	Current Tolerance (ppm)	Tolerance Reassessment (ppm)	Comment/*Correct Commodity Definition*
Tolerances listed under 180.364(a):			
Acerola	0.2		
Alfalfa Alfalfa, fresh and hay Clover Forage legumes (except soybeans and peanuts)	200.0 0.2 200.0 0.4	Revoke and establish at 100	*Non-grass animal feeds group, forage and hay*
Almond hulls	1		*Almonds, hulls*
Artichokes, Jerusalem	0.2		
Asparagus	0.5		
Atemoya	0.2		
Avocados	0.2		
Bahiagrass Bermudagrass Bluegrass Bromegrass Fescue Forage grasses Grasses, forage Orchardgrass Ryegrass Timothy Wheatgrass	200.0 200.0 200.0 200.0 200.0 0.2 0.2 200.0 200.0 200.0 200.0	Revoke and establish at 100	*Grass forage, fodder, and hay group*
Bananas	0.2		
Beets	0.2		*Beets, garden, roots*
Beets, sugar	0.2		*Sugar beets*
Breadfruit	0.2	Revoke	No registered uses
Canistel	0.2	Revoke	No registered uses
Carambola	0.2		
Carrots	0.2		
Cherimoya	0.2	Revoke	No registered uses
Chickory	0.2		*Chicory, roots*
Citrus fruits	0.2		*Citrus fruits group*
Cocoa beans	0.2	Revoke	No registered uses
Coconut	0.1	Revoke	No registered uses
Coffee beans	1		*Coffee beans, green*
Cotton, forage	15		
Cotton, hay	15	Revoke	Not in Table II, Subdivision O, PAG
Cottonseed	15		

(continued)

Table B *(Continued).*

Commodity	Current Tolerance (ppm)	Tolerance Reassessment (ppm)	Comment/*Correct Commodity Definition*
40 CFR §180.364(a) continued:			
Cranberries	0.2	Revoke	Covered under small fruits and berries group
Dates	0.2	Revoke	No registered uses
Figs	0.2		
Forage grasses Grasses, forage	0.2 0.2	0.2	*Forage, fodder, and straw of cereal grains group (except wheat straw)*
Fruits, small and berries	0.2		*Small fruits and berries group*
Genip	0.2	Revoke	No registered uses
Grain crops	0.1		*Cereal grains group (except wheat)*
Grapes	0.2	Revoke	Covered under small fruits and berries group
Guavas	0.2		
Horseradish	0.2		
Jaboticaba	0.2	Revoke	No registered uses
Jackfruit	0.2	Revoke	No registered uses
Kiwifruit	0.2	0.1	Codex harmonization (see Table C)
Leafy vegetables	0.2		*Leafy vegetables (except Brassica) group* and *Leaves of root and tuber vegetables group*
Longan	0.2		*Longan fruit*
Lychee	0.2		
Mamy sapote	0.2		*Sapote*
Mangoes	0.2		
Nuts	0.2		*Tree nuts group*
Olives	0.2		
Papayas	0.2		
Parsnips	0.2		*Parsnips, roots*
Passion fruit	0.2		
Peanut, forage	0.5		*Peanuts, vines*
Persimmons	0.2	Revoke	No registered uses
Pineapple	0.1		*Pineapples*
Pistachio nuts	0.2		*Pistachios*

(continued)

Table B *(Continued).*

Commodity	Current Tolerance (ppm)	Tolerance Reassessment (ppm)	Comment/*Correct Commodity Definition*
40 CFR §180.364(a) continued:			
Pome fruits	0.2		*Pome fruits group*
Potatoes	0.2		
Radishes	0.2		*Radishes, root*
Rutabagas	0.2		*Rutabagas, root*
Salsify	0.2	Revoke	No registered uses
Sapodilla	0.2		
Sapote, black	0.2	Revoke	No registered uses
Sapote, white	0.2	Revoke	No registered uses
Seed and pod vegetables	0.2	5	Codex harmonization (see Table C); *Legume vegetables group (except soybeans)*
Seed and pod vegetables, forage Seed and pod vegetables, hay	0.2 0.2	0.2	*Foliage of legume vegetables group (except soybean forage and hay)*
Soursop	0.2	Revoke	No registered uses
Soybeans	20		
Soybeans, forage	15		
Soybeans, hay	15	200	Raised to cover dessicant use.
Soybeans, straw	200	Revoke	Not in Table II, Subdivision O, PAG
Stone fruit	0.2		*Stone fruits group*
Sugar apple	0.2		
Sweet potatoes	0.2		
Tamarind	0.2	Revoke	No registered uses
Turnips	0.2		*Turnips, roots*
Vegetables, bulb	0.2		*Bulb vegetables group*
Vegetables, cucurbit	0.5		*Cucurbit vegetables group*
Vegetables, fruiting (except cucurbits) group	0.1		*Fruiting vegetables group*
Vegetables, leafy, Brassica (cole)	0.2		*Brassica leafy vegetables group*
Yams	0.2		
Wheat, grain	N/A	5.0	Codex harmonization; see Table C
Wheat, straw	N/A	85 (proposed)	

(continued)

Table B *(Continued).*

Commodity	Current Tolerance (ppm)	Tolerance Reassessment (ppm)	Comment/*Correct Commodity Definition*
Tolerances listed under 40 CFR §180.364(b):			
Cattle, kidney	0.5	2.0	Codex harmonization (see Table C)
Cattle, liver	0.5	2.0	Codex harmonization (see Table C)
Fish	0.25		
Goats, kidney	0.5		
Goats, liver	0.5		
Hogs, kidney	0.5	1.0	Codex harmonization (see Table C)
Hogs, liver	0.5	1.0	Codex harmonization (see Table C)
Horses, kidney	0.5		
Horses, liver	0.5		
Peanuts	0.1		
Peanut, hay	0.5		*Peanuts, hay*
Peanut, hulls	0.5		*Peanuts, hulls*
Poultry, kidney	0.5		
Poultry, liver	0.5		
Sheep, kidney	0.5		
Sheep, liver	0.5		
Shellfish	3.0		
Sugarcane	2.0		
Tolerances listed under 40 CFR 180.364(c):			
Avocados	0.1		
Citrus	0.1		*Citrus fruits group*
Cottonseed	0.1		
Cucurbits	0.1		*Cucurbit vegetables group*
Forage grasses	0.1		*Grass forage, fodder, and hay group*
Forage legumes	0.1		*Non-grass animal feeds group, forage and hay*
Fruiting vegetables	0.1		*Fruiting vegetables group*
Grain crops	0.1		*Cereal grains group* and *Forage, fodder, and straw of cereal grains group*

(continued)

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Table B *(Continued).*

Commodity	Current Tolerance (ppm)	Tolerance Reassessment (ppm)	Comment/*Correct Commodity Definition*
40 CFR 180.364(c) continued:			
Hops	0.1		
Leafy vegetables	0.1		*Leafy vegetables (except Brassica) group* and *Brassica (cole) leafy vegetables group*
Nuts	0.1		*Tree nuts group*
Pome fruits	0.1		*Pome fruits group*
Root crop vegetables	0.1		*Root and tuber vegetables group* and *Leaves of root and tuber vegetables group* and *Bulb vegetables group*
Seed and pod vegetables	0.1		*Legume vegetables group* and *Foliage of legume vegetables group*
Stone fruit	0.1		*Stone fruits group*
Tolerances listed under 40 CFR §185.3500(a)(1):			
Molasses, sugarcane	30.0		*Sugarcane, molasses*
Tolerances listed under 40 CFR §185.3500(a)(2):			
Oil, palm	0.1		*Palm oil, refined*
Olives, imported	0.1		
Potatoes, chips	N/A	1.0	New tolerance needed
Potatoes, granules	N/A	1.0	New tolerance needed
Tea, dried	1.0		
Tea, instant	7.0	Revoke	Not in Table II, Subdivision O, PAG
Wheat milling fractions (except flour)	N/A	40	Codex harmonization; see Table C
Tolerances listed under 40 CFR §186.3500(a):			
Citrus, pulp, dried	1.0		
Citrus molasses	1.0		*Citrus, molasses*
Potatoes, waste from processing	N/A	1.0	New tolerance needed
Soybean hulls	100		*Soybeans, hulls*

CODEX HARMONIZATION

Several maximum residue limits (MRLs) for glyphosate have been established by Codex in various commodities. The Codex MRLs (currently expressed in terms of glyphosate per se) and applicable U.S. tolerances (expressed in terms of the combined residues of glyphosate and its metabolite AMPA) are listed in Table C. The HED Metabolism Committee has determined that AMPA no longer needs to be regulated and therefore will be deleted from the tolerance expression. Based on the Committee's determination, the expression of the U.S. tolerances and the Codex MRLs will be harmonized, and both will now be expressed in terms of glyphosate per se.

Table C. Codex MRLs and applicable U.S. tolerances. Recommendations for compatibility are based on conclusions following reassessments of U.S. tolerances (see Table B).

Commodity	MRL (Step) (mg/kg)	U.S. Tolerance (ppm)	Recommendation
Barley	20 (CXL)	0.1 (Cereal grains group, except wheat)	
Beans (dry)	2 (CXL)	0.2 (Legume vegetables group, except soybeans)	
Cattle meat	0.1(CXL)		
Cattle milk	0.1(CXL)		
Cattle, edible offal	2 (CXL)	0.5 (Cattle, liver & kidney)	increase U.S. tolerances
Cottonseed	0.5(CXL)	15	
Eggs	0.1(CXL)		
Hay or fodder (dry) of grasses	50 (CXL)	100 (Grass forage, fodder, and hay group)	
Kiwifruit	0.1(CXL)	0.2	decrease U.S. tolerance
Maize	0.1(CXL)	0.1	
Oats	20 (CXL)	0.1 (Cereal grains group, except wheat)	
Peas (dry)	5 (CXL)	0.2 (Legume vegetables group, except soybeans)	increase U.S. tolerance
Pig meat	0.1(CXL)		
Pig, edible offal	1 (CXL)	0.5 (Hogs, liver & kidney)	increase U.S. tolerances
Poultry meat	0.1(CXL)		
Rape seed	10 (CXL)		
Rice	0.1(CXL)	0.1 (Cereal grains group, except wheat)	
Sorghum	0.1(CXL)	0.1 (Cereal grains group, except wheat)	
Soya bean fodder	20 (Step 8)	15 (Soybeans, hay)	
Soya bean forage (green)	5 (Step 8)	15 (Soybeans, forage)	
Soya bean (dry)	5 (Step 8)	20 (Soybeans)	
Soya bean (immature seeds)	0.2(CXL)		
Straw and fodder (dry) of cereal grains	100 (CXL)	0.2 (Forage, fodder, and straw of cereal grains group, except wheat straw)	
Sweet corn (corn-on-the-cob)	0.1(CXL)	0.1 (Cereal grains group, except wheat)	
Wheat	5 (CXL)	4 (proposed)	increase U.S. tolerance proposal
Wheat bran, unprocessed	40 (Step 6)	12 (proposed)	increase U.S. tolerance proposal
Wheat flour	0.5(Step 8)		
Wheat wholemeal	5 (Step 8)	12 (proposed)	

The following conclusions can be made regarding efforts to harmonize the U.S. tolerances with the Codex MRLs:

- Compatibility between the U.S. tolerances and permanent Codex MRLs exists in or on: corn (field and sweet); rice; and sorghum.

- The levels of U.S. tolerances should be increased, toxicological and DRES considerations permitting, to achieve compatibility with the Codex MRLs in or on the following commodities: (i) liver and kidney of cattle (from 0.5 to 2.0 ppm); (ii) liver and kidney of hogs (from 0.5 to 1.0 ppm); and (iii) legume vegetables group (except soybeans) (from 0.2 to 5 ppm);

- The level of the U.S. tolerance should be decreased to achieve compatibility with the Codex MRLs in or on kiwifruit (from 0.2 to 0.1 ppm).

- The U.S. tolerances in or on the following commodities were based on registered use patterns in the U.S. and cannot be lowered to achieve compatibility with the Codex MRLs: (i) grass forage, fodder, and hay group; (ii) soybeans; and (iii) soybeans, forage.

- Wheat grain and wheat bran tolerances of 4 and 12 ppm, respectively, have been proposed. To achieve compatibility with Codex, these tolerance levels should be increased, toxicological and DRES considerations permitting, to 5 and 40 ppm, respectively.

- Wide differences ($>5x$) exist between the U.S. tolerances and permanent Codex MRLs in or on the following commodities: barley; beans (dry); soybeans, hay; cottonseed; oats; forage, fodder, and straw of cereal grains. The decision to harmonize residue levels in or on these commodities cannot be made at this time.

- No questions of compatibility exist with respect to commodities where: (i) no Codex MRLs have been established, but U.S. tolerances exist; and (ii) Codex MRLs have been established, but U.S. tolerances do not exist.

AGENCY MEMORANDA CITED IN THIS DOCUMENT

CBRS No.:	398
Subject:	EPA Reg. No. 524-308. Glyphosate ropewick wiper on sorghum. Additional data received 10/12/84. Accession No. 255024.
From:	K. Dockter
To:	Robert Taylor
Dated:	8/8/85
MRID(s):	None

CBRS No.:	409
Subject:	PP#3F2956, Glyphosate on Shellfish. Evaluation of Supplemental Data Submission of December 13, 1985 (Accession Numbers 260534, 260497; RCB No. 409).
From:	E. Haeberer
To:	Robert Taylor & Toxicology Branch
Dated:	4/10/86
MRID(s):	00155120 and 00154311

CBTS Nos.	537 and 538
Subject:	PP3F2809/FAP5H5450: Glyphosate in or on Wheat Grain and Wheat Straw. Amended Section F and D, letter of 11/13/84 and new Food Additive Petition.
From:	R. Cook
To:	R. Taylor & Toxicology Branch
Dated:	4/18/85
MRID(s):	00150835

CBTS Nos.	546
Subject:	PP#5F3170. (RCB #546) Glyphosate on sugar cane and animal commodities. Evaluation of analytical method and residue data (Amendment to 40 CFR 180.364). Accession No. 073023.
From:	C. Deyrup
To:	R. Taylor & Toxicology Branch
Dated:	2/14/85
MRID(s):	None

CBTS Nos.	564 and 565
Subject:	5F3157/5H5446: Glyphosate on peanuts. Evaluation of analytical methods and residue data. Accession No. 072983.
From:	M. Bradley
To:	R. Taylor & Toxicology Branch
Dated:	5/1/85
MRID(s):	None

CBTS Nos.	889 and 890
Subject:	PP#6F3380/6H5502: Glyphosate (Roundup) in or on Soybeans. Evaluation of Analytical Method and Residue Data. (Acc. #261638; RCB #889 and #890).
From:	W.T. Chin
To:	R. Taylor & Toxicology Branch
Dated:	10/24/86
MRID(s):	None

CBTS No.:	1325
Subject:	PP#5F3170 (RCB #1325) Glyphosate on sugar cane and animal commodities. Amendment of 8/16/85. No Accession No.
From:	C. Deyrup
To:	Robert Taylor & Toxicology Branch
Dated:	9/2/86
MRID(s):	None

CBRS No.:	1342
Subject:	PP#3F2956, Glyphosate on Shellfish. Revised Label Submission (No Accession Number; RCB No. 1342).
From:	E. Haeberer
To:	Robert Taylor & Toxicology Branch
Dated:	10/16/86
MRID(s):	00155120 and 00154311

CBTS No.: 1528
Subject: PP#6E3424 (RCB#1528) - Glyphosate on Atemoya, Carambola and Sugar Apple - Evaluation of Analytical Methodology and Residue Data (Accession No. 263498).
From: M. Firestone
To: H. Jamerson
Dated: 9/30/86
MRID(s): None

CBTS No.: 2344 and 2345
Subject: PP5F2809/FAP5H5450. Glyphosate on wheat from wiper application. Amended Section F and letter dated Dec. 12, 1986.
From: R. W. Cook
To: R. Taylor & Toxicology Branch
Dated: 7/24/87
MRID(s): None

CBRS No.: 2346 and 2347
Subject: PP#6F3380/FAP#6H5502 - Glyphosate in/on Soybeans (RCB#'s 2346 and 2347). Amendment from Monsanto dated 2/20/87.
Glyphosate Registration Standard. Product chemistry for isopropylamine and sodium sesqui salts; nitrosamines.
Response by Monsanto (letter dated 3/24/87) to the 3(c)2(B) letter of 8/11/86. (MRID#'s 401548-01, -02, -03, -01C, -02C, -03C, and Acc# 263795).
From: J. Stokes
To: R. Taylor & Toxicology Branch
Dated: 9/1/87
MRID(s): 40154801-40154803.

CBRS Nos.: 2356
Subject: Glyphosate on Shellfish, PP#3F2956, Revised Section B Submission of March 1987, (No Accession No., RCB#2356).
From: E.T. Haeberer
To: R. Taylor & Toxicology Branch
Dated: 7/8/87
MRID(s): None

CBTS Nos.: 2357
Subject: PP#6F3408 (RCB No. 2357) - Glyphosate on Sunflower Seeds - Amendment dated January 29, 1987 (No Accession Number).
From: N. Dodd
To: R. Taylor & Toxicology Branch
Dated: 7/29/87
MRID(s): None

CBTS Nos.: 2369-2371
Subject: Glyphosate on citrus fruits.
From: M. Nelson
To:
Dated: 7/20/87
MRID(s): 40159401

CBRS Nos.: 2372-2374
Subject: EPA Registration Nos. 524-318, -333, and -339 Glyphosate. Comparison of Analytical Methods and Response to Registration Standard. (Accession Nos. 265985 and 262896).
From: F. Griffith
To: R. Taylor & Toxicology Branch
Dated: 9/25/87
MRID(s): 00164729

CBTS No.: 3841
Subject: PP#8E3631. (RCB# 3841) Glyphosate on Leafy Vegetables (except Brassica). Evaluation of the Analytical Method and the Residue Data.
From: C. Deyrup
To: H. Jamerson & Toxicology Branch
Dated: 7/5/88
MRID(s): 40578000 through 40578003.

CBTS No.: 3967
Subject: PP8E3648. Glyphosate on Asparagus. Evaluation of Analytical Methods and Residue Data.
From: R. Cook
To: H. Jamerson & Toxicology Branch
Dated: 9/8/88
MRID(s): 40642400-40642401

CBTS No.: 4284
Subject: Petition Review for Establishment of Tolerance(s).
Evaluation of Analytical Method(s) and Residue Data. PP#8E3676.
From: M. Nelson
To: H. Jamerson & Toxicology Branch
Dated: 10/20/88
MRID(s): 40783101

CBTS Nos.: 4285 and 4286
Subject: PP#6F3380/6H5502. Glyphosate (Roundup (R)) in or on Soybeans.
Amendment of 7/22/88 and Registration Standard Data Follow-up.
From: W. Chin
To: R. Taylor & Toxicology Branch
Dated: 1/30/89
MRID(s): 40532001-40532004 and 40541301-40541303

CBTS No: 4287
Subject: PP8F3665. Glyphosate on Peanuts. Evaluation of Analytical Methods and Residue Data. RCB No. 4287. No. 407507-02. RCB Project #8-1086A.
From: R. Cook
To: R. Taylor & Toxicology Branch.
Dated: 11/22/88
MRID(s): 40750702

CBTS No.: 4289
Subject: PP#8F3673/EPA Registration No. 524-308 - Glyphosate for Use In or On Field Corn - MRID Nos. 405026-01, -03, and -05 - Evaluation of Analytical Method and Residue Data.
From: M. Flood
To: R. Taylor & Toxicology Branch
Dated: 2/1/89
MRID(s): 40502601, 40502603, and 40502605

CBTS Nos.: 4357 and 4358
Subject: Petition Review for Establishment of Tolerance(s). Evaluation of Analytical Method(s) and Residue Data. PP8F3672 and PP8H5562.
From: S. Willet
To: R. Taylor & Toxicology Branch
Dated: 11/18/88
MRID(s): 40502602, 40502604, and 40502605

CBTS No: 4361
Subject: PP8E3682. Glyphosate (Roundup) in or on Brassica (Cole) Leafy Vegetables Crop Group. EPA Reg. No. 524-308. IR-4 Response to the Registration Standard Data Call-In, June, 1986.
From: F. Toghrol
To: H. Jamerson
Dated: 12/9/88
MRID(s): 40802800-40802802

CBRS No.: None
Subject: Glyphosate. PP#6F3380/FAP#6H5502. Withdraw of Request for a Petition Validation of a HPLC Method (Acc#262896).
From: J. Stokes
To: D. A. Marlow
Dated: 2/9/89
MRID(s): None

CBTS No.: 4503
Subject: Petition Review for Establishment of Tolerance(s). Evaluation of Analytical Method(s) and Residue Data. PP#8E3696.
From: M. Nelson
To: H. Jamerson & Toxicology Branch
Dated: 2/10/89
MRID(s): 40835200-01

CBTS No.: 4685
Subject: PP#8H5568. Glyphosate in or on Dried Citrus Pulp, Citrus Molasses, and Instant Tea. Tolerance Revisions Pursuant to the Glyphosate Registration Standard.
From: M. Nelson
To: R. Taylor/V. Walters & Toxicology Branch
Dated: 3/22/89
MRID(s): None

CBTS No.: 4907
Subject: Petition Review for Establishment of Tolerance(s). Evaluation of Analytical Method(s) and Residue Data. PP#9E3715.
From: M. Nelson
To: H. Jamerson
Dated: 4/5/89
MRID(s): None

CBTS No.: 5057
Subject: PP8F3665. Glyphosate (sodium sesqui salt) on peanuts. Letter 2/1/89. No MRID No., DEB No. 5057.
From: R. W. Cook
To: R. J. Taylor & Toxicology Branch
Dated: 3/31/89
MRID(s): None

CBTS No.: 5196
Subject: PP#9E3754: Glyphosate in/on Some Tropical and Sub-tropical Minor Tree Crops. Evaluation of Analytical Methods and Residue Data.
From: W. Chin
To: H. Jamerson & Toxicology Branch
Dated: 9/19/89
MRID(s): 40149400-01

CBTS No.: 5327
Subject: PP#9E3715. Glyphosate in or on Longan, Lychee, Mamey Sapote, Sapodilla, and Passion Fruit. Amendment of April 20, 1989.
From: M. Nelson
To: H. Jamerson & Toxicology Branch
Dated: 6/8/89
MRID(s): None

CBTS Nos.: 6740-6742
Subject: PP8F3672/8H5562 - Glyphosate on Grain Sorghum.
From: S. Willet
To: R. Taylor and Toxicology Branch
Dated: 9/5/90
MRID(s): 41472002

CBRS Nos.: 6745 and 6746
Subject: PP8F6373 - Glyphosate on Field Corn.
From: F. Griffith
To: R. Taylor
Dated: 7/13/90
MRID(s): 41478101

CBTS Nos.: 6748-6750
Subject: PPOF3865. Glyphosate on Wheat Grain and Straw. Evaluation of Analytical Methods and Residue Data.
From: R. Cook
To: R. Taylor & Toxicology Branch
Dated: 1/29/91
MRID(s): 41488301

CBTS No.: 6827
Subject: PP#0E3857 Glyphosate on cocoa beans.
From:
To:
Dated: 7/24/90
MRID(s): None

CBTS No.: 6828
Subject: PP#3E3873 Glyphosate on genip.
From:
To:
Dated: 7/20/90
MRID(s): None

CBTS No.: 6935
Subject: PP#0E3873 Glyphosate on genip.
From:
To:
Dated: 9/5/90
MRID(s): None

CBTS No.: 6938
Subject: PP#0E3881 Glyphosate on cherimoya.
From:
To:
Dated: 9/5/90
MRID(s): None

CBTS No.: 7275
Subject: PP#0E3881 Glyphosate on cherimoya.
From:
To:
Dated: 11/10/90
MRID(s): None

CBTS No.: 7915
Subject: PP#0E3857 Glyphosate on cocoa beans.
From:
To:
Dated: 4/23/91
MRID(s): None

CBRS Nos.: 8196 and 8220
Subject: Monsanto Company: Response to the Glyphosate Reregistration Standard: Product and Residue Chemistry Data.
From: R. Perfetti
To:
Dated: 2/3/92
MRID(s): 00156793

CBRS No.: 8337
Subject: Monsanto Agricultural Chemical Corp.: Response to the Glyphosate Reregistration Standard: Storage Stability Data.
From: R. Perfetti
To: W. Burnam and L. Rossi
Dated: 4/2/92
MRID(s): 41940701

CBRS No.: 8367
Subject: Glyphosate on Potatoes, Corn, Sorghum, Grapes, Plums/Prunes, Sugar Beets, and Peanuts. Impact of Craven Analytical Data on Registrations.
From: M. Metzger
To: P. Bagley
Dated: 10/21/92
MRID(s): 41947001-41947006

CBRS No.: 9674
Subject: Glyphosate: Monsanto Response to the Registration Standard and data waiver requests: coffee, peanuts, sugarcane, wheat processed fractions.
From: D. McNeilly
To: E. Feris
Dated: 7/9/92
MRID(s): None

CBTS Nos.: 9686-9690
Subject: PP#0F3865/FAP#2H5635. Glyphosate on Wheat Grain and Straw and Wheat Milling Fractions. Letter of 2/28/92.
From: R. Cook
To: R. Taylor and Toxicology Branch
Dated: 5/29/92
MRID(s): None

CBRS No.: 10105
Subject: Glyphosate: Storage Stability Data.
From: R. Perfetti
To:
Dated:
MRID(s):

CBRS No.: 10124
Subject: Response to the Glyphosate reregistration Standard: Product and Residue Chemistry.
From: R. Perfetti
To: L. Rossi and E. Saito
Dated: 8/26/92
MRID(s): 00144301, 41573601, and 41940701

CBRS No.: 10256
Subject: Glyphosate: Olives and olive-processing studies.
From: R. Perfetti
To: L. Rossi and E. Saito
Dated: 10/8/92
MRID(s): 42398401

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

DEC 18 1992

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Glyphosate: List A Reregistration Case No. 0718: Addendum To the Residue Chemistry Chapter For The Reregistration Eligibility Document (RED). No CBRS No., No DP Barcode No., No MRID #.

FROM: R. B. Perfetti, Ph.D., Chemist
Reregistration Section I
Chemistry Branch II: Reregistration Support
Health Effects Division (H7509C)

THRU: Edward Zager, Chief
Chemistry Branch II: Reregistration Support
Health Effects Division (H7509C)

TO: J. Smith and E. Saito, Acting Chief
Science Analysis and Coordination Branch
Health Effects Division (H7509C)

Please replace the "171-4 (c) and (d): Residue Analytical Methods - Plants and Animals" Section of the Residue Chemistry Chapter (Memo dated 10/27/92) with the following section;

§171-4 (c) and (d): Residue Analytical Methods - Plants and Animals: An adequate enforcement method is available for analysis of residues of glyphosate and its metabolite AMPA in or on plant commodities and in water. This method utilizes GLC (Method I of PAM Vol. II; limit of detection is 0.05 ppm). For enforcement of tolerances in animal commodities, an HPLC method with fluorescence detection is available; the reported limits of detection are 0.01 ppm for glyphosate and 0.012 ppm for AMPA.

(Note To SRRD): There is currently a question regarding Craven Laboratories data for certain crops having glyphosate uses (See memo of 10/21/91, M. Metzger, CBRS # 8367, Barcode No. D167350.). Additional requirements may be levied pending the final disposition of the Craven data question.

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If you need additional input please advise.

cc: RBP, Glyphosate Reregistration Standard File, Glyphosate Subject File, Circ. and RF.

cc (Without Attachments): RF.

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

JAN 12 1993

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

MEMORANDUM

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FROM: R. B. Perfetti, Ph.D., Chemist
Reregistration Section I
Chemistry Branch II: Reregistration Support
Health Effects Division (H7509C)

THRU: Edward Zager, Chief
Chemistry Branch II: Reregistration Support
Health Effects Division (H7509C)

TO: J. Smith and E. Saito, Acting Chief
Science Analysis and Coordination Branch
Health Effects Division (H7509C)

In order to align U. S. tolerances with CODEX MRLS our original recommendation for the *wheat milling fractions (except flour)* tolerance was 40 ppm in the Residue Chemistry RED chapter. The CODEX MRL for *wheat* is 5 mg/kg. The proposed U.S. tolerance for *wheat* is 4 ppm. In order to harmonize with CODEX MRLs we recommended that a tolerance for *wheat* of 5 ppm be established. The concentration factor of glyphosate from *wheat* to *wheat milling fractions (except flour)* is 3X based on U.S. processing data and 4X based on CODEX processing data. Therefore, **the recommended tolerance for *wheat milling fractions (except flour)* should be reduced from 40 ppm to 20 ppm.** These changes should be made to TABLE B on page 23, to TABLE C on page 24 and on page 25 of the RED chapter. The current CODEX MRL of 40 mg/kg may be changed in the future to harmonize with the U. S. tolerance.

cc: RBP, Glyphosate Reregistration Standard File, Glyphosate Subject File, Circ. and RF.

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

DEC 15 1992

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

SUBJECT: Dietary Exposure Analysis for Glyphosate in Support of the Reregistration Eligibility Document

FROM: Stephen A. Schaible
Dietary Risk Evaluation Section
Science Analysis Branch/ HED (H7509C)

TO: Jane Smith
Chemical Coordination Branch
Health Effects Division (H7509C)

THROUGH: James P. Kariya, Chief
DRES/SAB
Health Effects Division

Action Requested

Provide a Dietary Risk Evaluation System analysis to estimate the worst case chronic dietary exposure and risk from glyphosate food uses that are either published, pending, or being supported through reregistration.

Discussion

1. Toxicological Endpoint: The Dietary Risk Evaluation System (DRES) chronic analysis used a Reference Dose (RfD) of 2 mg/kg body weight/day, based on a No Observed Effect Level (NOEL) of 175 mg/kg bwt/day and an uncertainty factor of 100. The NOEL was taken from a developmental toxicity study in rabbits which demonstrated increased incidence of soft stool, diarrhea, nasal discharge, and death as effects (G. Ghali memo to J. Kariya, 12/8/92, personal communication w/ G. Ghali, 12/8/92). The Reference Dose was determined by the HED RfD Peer Review Committee on August 27, 1992.

Glyphosate has been classified as a Group E human carcinogen by the HED Carcinogenicity Peer Review Committee (Second Peer Review of Glyphosate, W. Dykstra and G. Ghali, 10/30/91).

2. Residue Information: Food uses evaluated in this analysis are the published and/or recommended tolerances being supported in the reregistration of glyphosate, as listed in Table B of the Residue Chemistry Chapter of the Reregistration Eligibility Document (RED) (R.B. Perfetti, 10/27/92). Published tolerances for glyphosate are listed in 40 CFR 180.364, 185.3500, and 186.3500. Pending tolerances for glyphosate in/on field corn and

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the kidney and liver of cattle, goats, hogs, horses, poultry, and sheep are included in the DRES analysis as well. These tolerances are to expire three years after the date of issuance of the Federal Register notice for this petition (F.D. Griffith, Jr. memo dated 7/13/90).

Feed items listed in Table B were not included in the DRES analysis, and any proposed increases, decreases, or revocations in tolerances for feed items (e.g. alfalfa, soybean hay, forage grasses) are reflected in the DRES analysis only through changes in the tolerances for meat and poultry. Glyphosate residues do not transfer to fat and therefore are not present in milk and eggs (personal communication, J. Smith, R.B. Perfetti, 11/30/92).

This DRES analysis portrays a "worst case" scenario; it includes commodities for which tolerances have been recommended for reregistration, even though registrants have not yet petitioned for such tolerances; tolerances for which revocation has been recommended but which have not yet been revoked; and tolerances pending registration. The recommended tolerances in Table B were the residue levels used in the analysis except where an existing tolerance in the file (published or pending) was greater than the residue level recommended in Table B. For instance, the existing tolerance of 0.2 ppm for kiwifruit was used in the analysis instead of the tolerance of 0.1 ppm recommended for reregistration.

In the DRES glyphosate file, if a pending or recommended tolerance for a raw agricultural commodity (RAC) was greater than the existing published tolerance, the information about the published tolerance was preserved by entering multiple listings for that commodity. For instance, in the file under "mung beans (sprouts)" there are two entries; one at 0.2 ppm which reflects the published tolerance for "seed and pod vegetables" in CFR 180.364 and the other at 4.8 ppm, reflecting the difference between the tolerance recommended as part of reregistration of 5 ppm and the existing tolerance (the sum of these two entries is equal to the recommended tolerance of 5 ppm). This was done for the commodities in the legume vegetables crop group (formerly the seed and pod vegetables crop group), the pending tolerance on field corn, and the secondary residues in the kidney and liver of cattle, goats, hogs, horses, and sheep.

There are several glyphosate tolerances existing on crop groups which are being supported through reregistration. It should be noted that in some cases the crop groups in DRES do not match the crop groups listed in 40 CFR 180.34; many of the commodities listed as being members of crop groups in the CFR do not have consumption reported in the 1977-78 USDA Nationwide Food Consumption Survey (NFCS) from which DRES consumption estimates are derived, and do not appear in DRES (e.g., arrugula or chrysanthemum, which are members of the "leafy vegetables (except Brassica) group" in the CFR). To the extent that these commodities are not included in the DRES analysis but are capable of having glyphosate residues on them and being consumed, underestimation of exposure is possible. However, most of the commodities in the CFR crop groups but not in DRES are food items normally considered as having low consumption.

(2) 2

In general, there are more instances where a commodity is present in a CFR crop group and not in the DRES equivalent group than the other way around, but there are a few instances where a commodity is considered as belonging to a crop group in DRES but not in CFR 180.34. For the purpose of this analysis, members of crop groups in DRES were included only if they were also present in the equivalent crop group in the CFR (e.g., "watercress", which is a member of the "leafy vegetables (excl. Brassica)" crop group in DRES, but is not a member of the equivalent group in the CFR, was not included in the analysis). It should also be noted that the commodities "dill" and "okra", which are presently in the DRES file by virtue of belonging to the old "seed and pod vegetable" group (for which a tolerance of 0.1 ppm exists in 40 CFR 180.364), do not belong to the "legume vegetables" crop group which is recommended to replace the seed and pod vegetable group in the CFR, and would need individual tolerances if glyphosate use was to continue on those sites.

Though the existing tolerance of "mamey sapote" (Calocarpum sapota) is being supported through reregistration, it is incorrectly reported in Table B of the Residue Chemistry Chapter of the RED that the correct commodity definition to apply this tolerance to is "sapote". The fruit referred to in the market place as "sapote" is usually "white sapote" (Casimiroa edulis) (B. Schneider note to S. Schaible dated 12/1/92), which no longer is registered for use on the glyphosate label, and is recommended for tolerance revocation in Table B. Mamey sapote and sapote are not the same fruit. In addition, the DRES file had previously mapped the tolerance of mamey sapote to the DRES commodity "maney (mammee apple)", which is also incorrect according to B. Schneider's note. There is presently no DRES commodity listing for mamey sapote and this tolerance was left out of the analysis for lack of consumption information to apply the residue to. Other food commodities having glyphosate tolerances but not represented in DRES are canistel, jackfruit, and jaboticaba (revocation recommended for these three); atemoya, sapodilla, and tamarind.

The DRES commodities "horseradish" and "wine and sherry" were added to the glyphosate file for this analysis; the first directly through the published tolerance for horseradish and the second indirectly through the published tolerance on grapes. Incorrect tolerances for cane sugar, passion fruit, lychee, mamey, and longan fruit (in the DRES file prior to this analysis) were corrected to reflect the proper tolerances of the CFR (cane sugar from 0.2 ppm to 2.0 ppm, the rest from 0.01 ppm to 0.2 ppm).

A summary of the residue information used in this analysis is attached as Table 1.

3. Exposure Analysis: The DRES chronic analysis used tolerance level residues and 100 percent crop treated to estimate the Theoretical Maximum Residue Contribution (TMRC) for the overall U.S. population and 22 DRES population subgroups. These exposures were then compared to the RfD for glyphosate to get estimates of chronic dietary risk. A summary of the TMRCs and

their representations as percentages of the RfD are attached as Table 2.

The TMRC for the overall U.S. population from food uses of glyphosate is 0.027746 mg/kg bwt/day, which represents 1.4% of the Reference Dose. Around half of this exposure comes from the recommended tolerance on wheat. None of the subgroups has an exposure that exceeds 5% of the RfD; the subgroup most highly exposed, non-nursing infants less than one year old, has an exposure of 0.060115 mg/kg bwt/day, or 3% of the RfD.

This analysis was meant to be a "worst case" scenario of risk. The inclusion of recommended tolerances for reregistration as well as tolerances recommended for revocation; the use of the highest existing, pending, or recommended residue value for each commodity; and the assumptions of tolerance level residues and 100 percent of crop treated for every commodity result in overestimation of exposure and risk values for glyphosate (though there is also underestimation due to the lack of consumption information for some of the commodities in the CFR to which glyphosate is expected to be applied). None the less, given the risk values arrived at by this analysis, it seems that the chronic dietary risk posed by this pesticide on these food uses is minimal.

Attachments

cc: DRES, CBRS, Tox 1, Caswell # 661A

TABLE 1

CHEMICAL INFORMATION FOR CASWELL NUMBER 661A DATE: 12/14/92 PAGE: 1

CHEMICAL	STUDY TYPE	EFFECTS	REFERENCE DOSES	DATA GAPS/COMMENTS	STATUS
Glyphosate (+ salts) Caswell #661A CAS No. 1071-83-6 A.I. CODE: 417300 CFR No. 180.364	developmental-rabbit NOEL= 175.0000 mg/kg 0.00 ppm LEL= 350.0000 mg/kg 0.00 ppm ONCO: D (SAP); E (HED)	increased incidence of soft stool, diarrhea, nasal discharge, and death	ADI UF -->100 OPP RfD= 2.000000 EPA RfD= 2.000000	Temporary PRODVOL heading based on G.Ghali memo to J. Kariya, 12/8/92 (old RfD 0.1 mg/kg/day)	HED RfD Peer Review Comm meeting 8/27/92 WHO last reviewed 1986. On IRIS.

FOOD CODE	FOOD NAME	PETITION NUMBER	TOLERANCE (PPM) NEW	PENDING	PUBLISHED
01002AA	BLACKBERRIES	3E2930			0.200000
01003AA	BOYSENBERRIES	3E2930			0.200000
01004AA	DEWBERRIES	3E2930			0.200000
01005AA	LOGANBERRIES	3E2930			0.200000
01006AA	RASPBERRIES	3E2930			0.200000
01007AA	YOUNGBERRIES	3E2930			0.200000
01009AA	BLUEBERRIES	3E2930			0.200000
01010AA	CRANBERRIES	0E2421			0.200000
01010JA	CRANBERRIES-JUICE	0E2421			0.200000
01011AA	CURRANTS	3E2930			0.200000
01012AA	ELDERBERRIES	3E2930			0.200000
01013AA	GOOSEBERRIES	3E2930			0.200000
01014AA	GRAPES-FRESH	5F1560			0.200000
01014DA	GRAPES-RAISINS	5F1560			0.200000
01014JA	GRAPES-JUICE	5F1560			0.200000
01015AA	HUCKLEBERRIES (GAYLUSSACIA)	3E2930			0.200000
01016AA	STRAWBERRIES	3E2930			0.200000
02001AA	CITRUS CITRON	6F1733			0.200000
02002AA	GRAPEFRUIT-UNSPECIFIED	6F1733			0.200000
02002AB	GRAPEFRUIT-PULP	6F1733			0.200000
02002JA	GRAPEFRUIT-JUICE	6F1733			0.200000
02003AA	KUMQUATS	6F1733			0.200000
02004AA	LEMONS-UNSPECIFIED	6F1733			0.200000
02004AB	LEMONS-PULP	6F1733			0.200000
02004HA	LEMONS-PEEL	6F1733			0.200000
02004JA	LEMONS-JUICE	6F1733			0.200000
02005AA	LIMES-UNSPECIFIED	6F1733			0.200000
02005AB	LIMES-PULP	6F1733			0.200000
02005HA	LIMES-PEEL	6F1733			0.200000
02005JA	LIMES-JUICE	6F1733			0.200000
02006AA	ORANGES-UNSPECIFIED	6F1733			0.200000
02006AB	ORANGES-PULP	6F1733			0.200000
02006HA	ORANGES-PEEL	6F1733			0.200000
02006JA	ORANGES-JUICE	6F1733			0.200000
02007AA	TANGELOS	6F1733			0.200000
02008AA	TANGERINES	6F1733			0.200000
02008JA	TANGERINE-JUICE	6F1733			0.200000
03001AA	ALMONDS	7F1893			0.200000
03002AA	BRAZIL NUTS	7F1893			0.200000
03003AA	CASHEWS	7F1893			0.200000

CHEMICAL	STUDY TYPE	EFFECTS	REFERENCE DOSES	DATA GAPS/COMMENTS	STATUS
Glyphosate (+ salts) Caswell #661A CAS No. 1071-83-6 A.I. CODE: 417300 CFR No. 180.364	developmental-rabbit NOEL= 175.0000 mg/kg 0.00 ppm LEL= 350.0000 mg/kg 0.00 ppm ONCO: D (SAP); E (HED)	increased incidence of soft stool, diarrhea, nasal discharge, and death	ADI UF -->100 OPP RfD= 2.000000 EPA RfD= 2.000000	Temporary PRODVOL heading based on G.Ghali memo to J. Kariya, 12/8/92 (old RfD 0.1 mg/kg/day)	HED RfD Peer Review Comm meeting 8/27/92 WHO last reviewed 1986. On IRIS.

FOOD CODE	FOOD NAME		PETITION NUMBER	NEW	TOLERANCE (PPM) PENDING	PUBLISHED
03004AA	CHESTNUTS		7F1893			0.200000
03005AA	FILBERTS & HAZELNUTS		7F1893			0.200000
03006AA	HICKORY NUTS		7F1893			0.200000
03007AA	MACADAMIA NUTS (BUSH NUTS)		7F1893			0.200000
03008AA	PECANS		7F1893			0.200000
03009AA	WALNUTS		7F1893			0.200000
03010AA	BUTTER NUTS		7F1893			0.200000
03011AA	PISTACHIO NUTS		7F1893			0.200000
03013AA	BEECHNUTS		7F1893			0.200000
04001AA	APPLES-FRESH		6F1861			0.200000
04001DA	APPLES-DRIED		6F1861			0.200000
04001JA	APPLES-JUICE		6F1861			0.200000
04002AA	CRABAPPLES		6F1861			0.200000
04003AA	PEARS-FRESH		6F1861			0.200000
04003DA	PEARS-DRIED		6F1861			0.200000
04004AA	QUINCES		6F1861			0.200000
05001AA	APRICOTS-FRESH		260044			0.200000
05001DA	APRICOTS-DRIED		260044			0.200000
05002AA	CHERRIES-FRESH		260044			0.200000
05002DA	CHERRIES-DRIED		260044			0.200000
05002JA	CHERRIES-JUICE		260044			0.200000
05003AA	NECTARINES		260044			0.200000
05004AA	PEACHES-FRESH		260044			0.200000
05004DA	PEACHES-DRIED		260044			0.200000
05005AA	PLUMS(DAMSONS)-FRESH		260044			0.200000
05005DA	PLUMS-PRUNES(DRIED)		260044			0.200000
05005JA	PLUMS/PRUNE-JUICE		260044			0.200000
06001AA	AVOCADOS		8F2021			0.200000
06002AA	BANANAS-UNSPECIFIED		9F2223			0.200000
06002AB	BANANAS-FRESH		9F2223			0.200000
06002DA	BANANAS-DRIED		9F2223			0.200000
06003AA	COCONUT-FRESH	(REVOKE)	2F2680			0.100000
06003DA	COCONUT-COPRA	(REVOKE)	2F2680			0.100000
06003JA	COCONUT-WATER	(REVOKE)	2F2680			0.100000
06004AA	DATES	(REVOKE)	9E3754			0.200000
06005AA	FIGS		3E2929			0.200000
06006AA	GUAVA		1E2443			0.200000
06007AA	MANGOES		1E2490			0.200000
06009AA	OLIVES		3E2929			0.200000
06010AA	PAPAYAS-UNSPECIFIED		1E2443			0.200000

CHEMICAL	STUDY TYPE	EFFECTS	REFERENCE DOSES	DATA GAPS/COMMENTS	STATUS
Glyphosate (+ salts) Caswell #661A CAS No. 1071-83-6 A.I. CODE: 417300 CFR No. 180.364	developmental-rabbit NOEL= 175.0000 mg/kg 0.00 ppm LEL= 350.0000 mg/kg 0.00 ppm ONCO: D (SAP); E (HED)	increased incidence of soft stool, diarrhea, nasal discharge, and death	ADI UF -->100 OPP RfD= 2.000000 EPA RfD= 2.000000	Temporary PRODVOL heading based on G.Ghali memo to J. Kariya, 12/8/92 (old RfD 0.1 mg/kg/day)	HED RfD Peer Review Comm meeting 8/27/92 WHO last reviewed 1986. On IRIS.

FOOD CODE	FOOD NAME	PETITION NUMBER	NEW	TOLERANCE (PPM) PENDING	PUBLISHED
06010AB	PAPAYAS-PULP	1E2443			0.200000
06010DA	PAPAYAS-DRIED	1E2443			0.200000
06010JA	PAPAYAS-JUICE	1E2443			0.200000
06012AA	PERSIMMONS (REVOKE)	9E3754			0.200000
06013AA	PINEAPPLE-FRESH/PULP	2F2634			0.100000
06013DA	PINEAPPLE-DRIED	2F2634			0.100000
06013JA	PINEAPPLE-FRESH/JUICE	2F2634			0.100000
06014AA	PASSION FRUIT (GRANADILLA)	9E3715			0.200000
06015AA	POMEGRANATES	1E03978			0.200000
06016AA	PLANTAINS	9F2223			0.200000
06017AA	LYCHEES (LITCHI)	9E3715			0.200000
06017DA	LYCHEE-DRIED	9E3715			0.200000
06018AA	KIWI (0.1 PPM TOL IN REREG)	3E2929			0.200000
06020AA	ACEROLA	3E2929			0.200000
06024AA	SOURSOP (ANNONA MURICATA) (REVOKE)	9E3754			0.200000
06025AA	SUGAR APPLES (SWEETSOP)	6E3424			0.200000
06026AA	BREAD FRUIT (REVOKE)	9E3754			0.200000
06028AA	SAPOTE (REVOKE)	9E3754			0.200000
06029AA	CARAMBOLA	6E3424			0.200000
06030AA	CHERIMOYA (REVOKE)	0E3881			0.200000
06031AA	LONGAN FRUIT	9E3715			0.010000
06033AA	GENIP (SPANISH LIME) (REVOKE)	0E3873			0.200000
07001FA	COCOA BUTTER (REVOKE)	0E3857			0.200000
07001SA	CHOCOLATE (REVOKE)	0E3857			0.200000
07002AA	COFFEE	6E1809			1.000000
07003AA	TEA (1 PPM DRIED)	1H5310			1.000000
07003AA	TEA (7 PPM INSTANT- REVOKE)	8H5568			6.000000
07006AA	CHICORY	7F2016			0.200000
08015AA	DILL (SEED & POD VEG-REVOKE)	7F2016			0.200000
08020AA	HOPS				0.100000
08022AA	HORSERADISH	8E3676			0.200000
10002AA	CANTALOUPES-UNSPECIFIED	3E2845			0.500000
10002AB	CANTALOUPES-PULP	3E2845			0.500000
10003AA	CASABAS	3E2845			0.500000
10004AA	CRENSHAWS	3E2845			0.500000
10005AA	HONEYDEW MELONS	3E2845			0.500000
10007AA	PERSION MELONS	3E2845			0.500000
10008AA	WATERMELON	3E2845			0.500000
10010AA	CUCUMBERS	3E2845			0.500000
10011AA	PUMPKIN	3E2845			0.500000

CHEMICAL INFORMATION FOR CASWELL NUMBER 661A DATE: 12/14/92 PAGE: 4

CHEMICAL	STUDY TYPE	EFFECTS	REFERENCE DOSES	DATA GAPS/COMMENTS	STATUS
Glyphosate (+ salts) Caswell #661A CAS No. 1071-83-6 A.I. CODE: 417300 CFR No. 180.364	developmental-rabbit NOEL= 175.0000 mg/kg 0.00 ppm LEL= 350.0000 mg/kg 0.00 ppm ONCO: D (SAP); E (HED)	increased incidence of soft stool, diarrhea, nasal discharge, and death	ADI UF -->100 OPP RfD= 2.000000 EPA RfD= 2.000000	Temporary PRODVOL heading based on G.Ghali memo to J. Kariya, 12/8/92 (old RfD 0.1 mg/kg/day)	HED RfD Peer Review Comm meeting 8/27/92 WHO last reviewed 1986. On IRIS.

FOOD CODE	FOOD NAME	PETITION NUMBER	TOLERANCE (PPM) NEW	PENDING	PUBLISHED
10013AA	SQUASH-SUMMER	3E2845			0.500000
10014AA	SQUASH-WINTER	3E2845			0.500000
10017AA	BITTER MELON	3E2845			0.500000
10020AA	TOWELGOURD	3E2845			0.500000
11001AA	EGGPLANT				0.100000
11003AA	PEPPERS (SWEET/GARDEN)				0.100000
11003AB	CHILI PEPPERS				0.100000
11003AD	PEPPERS-OTHER				0.100000
11004AA	PIMIENTOS				0.100000
11005AA	TOMATOES-WHOLE				0.100000
11005JA	TOMATOES-JUICE				0.100000
11005RA	TOMATOES-PUREE				0.100000
11005TA	TOMATOES-PASTE				0.100000
11005UA	TOMATOES-CATSUP				0.100000
13001AA	BEETS-TOPS(GREENS)	8E2122			0.200000
13002AA	CELERY	8E2122			0.200000
13003AA	CHICORY (FRENCH OR BELGIAN ENDIVE)	8E2122			0.200000
13005AA	BROCCOLI	8E2122			0.200000
13006AA	BRUSSEL SPROUTS	8E2122			0.200000
13007AA	CABBAGE-GREEN AND RED	8E2122			0.200000
13008AA	CAULIFLOWER	8E2122			0.200000
13009AA	COLLARDS	8E2122			0.200000
13010AA	CABBAGE-CHINESE/CELERY(INC. BOK CHOY)	8E2122			0.200000
13011AA	KALE	8E2122			0.200000
13012AA	KOHLRABI	8E2122			0.200000
13013AA	LETTUCE-LEAFY VARIETIES	8E2122			0.200000
13014AA	DANDELION	8E2122			0.200000
13015AA	ENDIVE (CURLEY) AND ESCAROLE	8E2122			0.200000
13016AA	FENNEL	8E2122			0.200000
13017AA	CRESS (GARDEN/FIELD)	8E2122			0.200000
13020AA	LETTUCE-UNSPECIFIED	8E2122			0.200000
13021AA	MUSTARD GREENS	8E2122			0.200000
13022AA	PARSLEY	8E2122			0.200000
13023AA	RHUBARB	8E2122			0.200000
13024AA	SPINACH	8E2122			0.200000
13025AA	SWISS CHARD	8E2122			0.200000
13026AA	TURNIPS-TOPS	8E2122			0.200000
13034AA	TARO-GREENS				0.200000
13039AA	CRESS (UPLAND)	8E2122			0.200000
13045AA	LETTUCE-HEAD VARIETIES	8E2122			0.200000

CHEMICAL	STUDY TYPE	EFFECTS	REFERENCE DOSES	DATA GAPS/COMMENTS	STATUS
Glyphosate (+ salts) Caswell #661A CAS No. 1071-83-6 A.I. CODE: 417300 CFR No. 180.364	developmental-rabbit NOEL= 175.0000 mg/kg 0.00 ppm LEL= 350.0000 mg/kg 0.00 ppm ONCO: D (SAP); E (HED)	increased incidence of soft stool, diarrhea, nasal discharge, and death	ADI UF -->100 OPP RfD= 2.000000 EPA RfD= 2.000000	Temporary PRODVOL heading based on G.Ghali memo to J. Kariya, 12/8/92 (old RfD 0.1 mg/kg/day)	HED RfD Peer Review Comm meeting 8/27/92 WHO last reviewed 1986. On IRIS.

FOOD CODE	FOOD NAME		PETITION NUMBER	TOLERANCE (PPM) NEW	PENDING	PUBLISHED
14001AA	BEETS-ROOTS		7F2016			0.200000
14003AA	CARROTS		7F2016			0.200000
14007AA	GARLIC		8E3676			0.200000
14009AA	ARTICHOKES-JERUSALEM		7F2016			0.200000
14010AA	LEEKS		8E3676			0.200000
14011AA	ONIONS-DRY-BULB (CIPOLLINI)		8E3676			0.200000
14011DA	ONIONS-DEHYDRATED OR DRIED		8E3676			0.200000
14013AA	POTATOES(WHITE)-WHOLE		7F2016			0.200000
14013AB	POTATOES(WHITE)-UNSPECIFIED		7F2016			0.200000
14013AC	POTATOES(WHITE)-PEELED		7F2016			0.200000
14013AC	POTATOES(WHITE)-PEELED		REREG	0.800000		
14013DA	POTATOES(WHITE)-DRY		7F2016			0.200000
14013HA	POTATOES(WHITE)-PEEL ONLY		7F2016			0.200000
14014AA	RADISHES-ROOTS		7F2016			0.200000
14014AB	RADISHES-TOPS					0.200000
14015AA	RUTABAGAS-ROOTS		7F2016			0.200000
14015AB	RUTABAGAS-TOPS					0.200000
14016AA	SALSIFY(OYSTER PLANT)	(REVOKE)	7F2016			0.200000
14017AA	SHALLOTS		8E3676			0.200000
14018AA	SWEETPOTATOES (INCLUDING YAMS)		7F2016			0.200000
14019AA	TURNIPS-ROOTS		7F2016			0.200000
14021AA	PARSNIPS		7F2016			0.200000
14030AA	PARSLEY ROOTS		7F2016			0.200000
15001AA	BEANS-DRY-GREAT NORTHERN		REREG	4.800000		
15001AA	BEANS-DRY-GREAT NORTHERN		7F2016			0.200000
15001AB	BEANS-DRY-KIDNEY		REREG	4.800000		
15001AB	BEANS-DRY-KIDNEY		7F2016			0.200000
15001AC	BEANS-DRY-LIMA		REREG	4.800000		
15001AC	BEANS-DRY-LIMA		7F2016			0.200000
15001AD	BEANS-DRY-NAVY (PEA)		REREG	4.800000		
15001AD	BEANS-DRY-NAVY (PEA)		7F2016			0.200000
15001AE	BEANS-DRY-OTHER		REREG	4.800000		
15001AE	BEANS-DRY-OTHER		7F2016			0.200000
15001AF	BEANS-DRY-PINTO		REREG	4.800000		
15001AF	BEANS-DRY-PINTO		7F2016			0.200000
15002AA	BEANS-SUCCULENT-LIMA		REREG	4.800000		
15002AA	BEANS-SUCCULENT-LIMA		7F2016			0.200000
15003AA	BEANS-SUCCULENT-GRFEN		REREG	4.800000		
15003AA	BEANS-SUCCULENT-GREEN		7F2016			0.200000
15003AB	BEANS-SUCCULENT-OTHER		REREG	4.800000		

CHEMICAL	STUDY TYPE	EFFECTS	REFERENCE DOSES	DATA GAPS/COMMENTS	STATUS
Glyphosate (+ salts) Caswell #661A CAS No. 1071-83-6 A.I. CODE: 417300 CFR No. 180.364	developmental-rabbit NOEL= 175.0000 mg/kg 0.00 ppm LEL= 350.0000 mg/kg 0.00 ppm ONCO: D (SAP); E (HED)	increased incidence of soft stool, diarrhea, nasal discharge, and death	ADI UF -->100 OPP RfD= 2.000000 EPA RfD= 2.000000	Temporary PRODVOL heading based on G.Ghali memo to J. Kariya, 12/8/92 (old RfD 0.1 mg/kg/day)	HED RfD Peer Review Comm meeting 8/27/92 WHO last reviewed 1986. On IRIS.

FOOD CODE	FOOD NAME	PETITION NUMBER	TOLERANCE (PPM) NEW	PENDING	PUBLISHED	
15003AB	BEANS-SUCCULENT-OTHER	7F2016			0.200000	
15003AC	BEANS-SUCCULENT-YELLOW/WAX	REREG	4.800000			
15003AC	BEANS-SUCCULENT-YELLOW,WAX	7F2016			0.200000	
15004AA	CORN (POP)	8E2122			0.100000	
15005AA	CORN (SWEET)	8E2122			0.100000	
15006AA	PEANUTS-WHOLE	0F2329			0.100000	
15007AA	PEAS(GARDEN)-MATURE SEEDS/DRY	REREG	4.800000			
15007AA	PEAS(GARDEN)-MATURE SEEDS,DRY	7F2016			0.200000	
15009AA	PEAS(GARDEN)-GREEN IMMATURE	REREG	4.800000			
15009AA	PEAS(GARDEN)-GREEN IMMATURE	7F2016			0.200000	
15011AA	LENTILES-WHOLE	REREG	4.800000			
15011AA	LENTILES-WHOLE	7F2016			0.200000	
15011AB	LENTILES-SPLIT	REREG	4.800000			
15011AB	LENTILES-SPLIT	7F2016			0.200000	
15013AA	MUNG BEANS (SPROUTS)	REREG	4.800000			
15013AA	MUNG BEANS (SPROUTS)	7F2016			0.200000	
15015AA	OKRA (SEED & POD VEG-REVOKE)	7F2016			0.200000	
15022AA	BEANS-DRY-BROADBEANS(MATURE SEED)	REREG	4.800000			
15022AA	BEANS-DRY-BROADBEANS(MATURE SEED)	7F2016			0.200000	
15022AB	BEANS-SUCCULENT-BROADBEANS(IMMATURE SEED	REREG	4.800000			
15022AB	BEANS-SUCCULENT-BROADBEANS(IMMAT. SEED)	7F2016			0.200000	
15023AA	BEANS-DRY-PIGEON BEANS	REREG	4.800000			
15023AA	BEANS-DRY-PIGEON BEANS	7F2016			0.200000	
15027AA	BEANS-UNSPECIFIED	REREG	4.800000			
15027AA	BEANS-UNSPECIFIED	7F2016			0.200000	
15029AA	SOYBEANS-SPROUTED SEEDS	6F3380			20.00000	
15030AA	BEANS-DRY-HYACINTH(MATURE SEEDS)	REREG	4.800000			
15030AA	BEANS-DRY-HYACINTH(MATURE SEEDS)	7F2016			0.200000	
15030AB	BEANS-SUCCULENT-HYACINTH(YOUNG PODS)	REREG	4.800000			
15030AB	BEANS-SUCCULENT-HYACINTH(YOUNG PODS)	7F2016			0.200000	
15031AA	BEANS-DRY-BLACKEYE PEAS(COWPEAS)	REREG	4.800000			
15031AA	BEANS-DRY-BLACKEYE PEAS(COWPEAS)	7F2016			0.200000	
15032AA	BEANS-DRY-GARBANZO(CHICK PEA)	REREG	4.800000			
15032AA	BEANS-DRY-GARBANZO(CHICK PEA)	7F2016			0.200000	
16002AA	ASPARAGUS	8E3648			0.500000	
16004AA	ONIONS-GREEN	8E3676			0.200000	
24001AA	BARLEY	8E2122			0.100000	
24002EA	CORN (GRAIN-ENDOSPERM)	8E2122			0.100000	
24002EA	CORN,GRAIN-ENDOSPERM (3yr tol)	8F3673		1.900000		T
24002HA	CORN (GRAIN-BRAN)	8E2122			0.100000	

CHEMICAL	STUDY TYPE	EFFECTS	REFERENCE DOSES	DATA GAPS/COMMENTS	STATUS
Glyphosate (+ salts) Caswell #661A CAS No. 1071-83-6 A.I. CODE: 417300 CFR No. 180.364	developmental-rabbit NOEL= 175.0000 mg/kg 0.00 ppm LEL= 350.0000 mg/kg 0.00 ppm ONCO: D (SAP); E (HED)	increased incidence of soft stool, diarrhea, nasal discharge, and death	ADI UF -->100 OPP RfD= 2.000000 EPA RfD= 2.000000	Temporary PRODVOL heading based on G.Ghali memo to J. Kariya, 12/8/92 (old RfD 0.1 mg/kg/day)	HED RfD Peer Review Comm meeting 8/27/92 WHO last reviewed 1986. On IRIS.

FOOD CODE	FOOD NAME		PETITION NUMBER	TOLERANCE (PPM) NEW	PENDING	PUBLISHED	
24002HA	CORN,GRAIN-BRAN	(3yr tol)	8F3673		1.900000		T
24002SA	CORN SUGAR		8E2122			0.100000	
24002SA	CORN SUGAR	(3yr tol)	8F3673		1.900000		T
24003AA	OATS		8E2122			0.100000	
24004AA	RICE-ROUGH		8E2122			0.100000	
24004AB	RICE-MILLED		8E2122			0.100000	
24005AA	RYE-ROUGH		8E2122			0.100000	
24005GA	RYE-GERM		8E2122			0.100000	
24005WA	RYE-FLOUR		8E2122			0.100000	
24006AA	SORGHUM (INCLUDING MILO)		8E2122			0.100000	
24007AA	WHEAT-ROUGH		REREG	40.00000			
24007GA	WHEAT-GERM		REREG	40.00000			
24007HA	WHEAT-BRAN		REREG	40.00000			
24007WA	WHEAT-FLOUR		REREG	5.000000			
24012AA	MILLET		8E2122			0.100000	
25002SA	BEET SUGAR					0.200000	
25003SA	CANE SUGAR					2.000000	
25003SB	SUGAR-MOLASSES		9H5196			30.00000	
26001AA	BUCKWHEAT		8E2122			0.100000	
27002OA	CORN/GRAIN-OIL		8E2122			0.100000	
27002OA	CORN,GRAIN-OIL	(3yr tol)	8F3673		1.900000		
27003OA	COTTONSEED-OIL		8E2122			15.00000	
27003WA	COTTONSEED-MEAL		8E2122			15.00000	
27007OA	PEANUTS-OIL		0F2329			0.100000	
27010OA	SOYBEANS-OIL		6F3380			20.00000	
27015OA	COCONUT-OIL	(REVOKE)	2F2680			0.100000	
27016OA	OLIVE OIL		3E2929			0.200000	
27019OA	PALM OIL		6H5115			0.100000	
28023AA	SOYBEANS-UNSPECIFIED		6F3380			20.00000	
28023AB	SOYBEANS-MATURE,SEEDS DRY		6F3380			20.00000	
28023WA	SOYBEANS-FLOUR, FULL FAT		6F3380			20.00000	
28023WB	SOYBEANS-FLOUR, LOW FAT		6F3380			20.00000	
28023WC	SOYBEANS-FLOUR,DEFATTED		6F3380			20.00000	
43058AA	WINE AND SHERRY		3E2930			0.200000	
53001KA	BEEF(ORGAN MEATS)-KIDNEY		0F2329			0.500000	
53001KA	BEEF(ORGAN MEATS)-KIDNEY	(3yr tol)	8F3673		0.500000		
53001KA	BEEF(ORGAN MEATS)-KIDNEY		REREG	1.000000			
53001LA	BEEF(ORGAN MEATS)-LIVER		0F2329			0.500000	
53001LA	BEEF(ORGAN MEATS)-LIVER	(3yr tol)	8F3673		0.500000		
53001LA	BEEF(ORGAN MEATS)-LIVER		REREG	1.000000			

CHEMICAL	STUDY TYPE	EFFECTS	REFERENCE DOSES	DATA GAPS/COMMENTS	STATUS
Glyphosate (+ salts) Caswell #661A CAS No. 1071-83-6 A.I. CODE: 417300 CFR No. 180.364	developmental-rabbit NOEL= 175.0000 mg/kg 0.00 ppm LEL= 350.0000 mg/kg 0.00 ppm ONCO: D (SAP); E (HED)	increased incidence of soft stool, diarrhea, nasal discharge, and death	ADI UF -->100 OPP RfD= 2.000000 EPA RfD= 2.000000	Temporary PRODVOL heading based on G.Ghali memo to J. Kariya, 12/8/92 (old RfD 0.1 mg/kg/day)	HED RfD Peer Review Comm meeting 8/27/92 WHO last reviewed 1986. On IRIS.

FOOD CODE	FOOD NAME		PETITION NUMBER	NEW	TOLERANCE (PPM) PENDING	PUBLISHED
53002KA	GOAT(ORGAN MEATS)-KIDNEY		0F2329			0.500000
53002KA	GOAT(ORGAN MEATS)-KIDNEY	(3yr tol)	8F3673		0.500000	
53002LA	GOAT(ORGAN MEATS)-LIVER		0F2329			0.500000
53002LA	GOAT(ORGAN MEATS)-LIVER	(3yr tol)	8F3673		0.500000	
53003AA	HORSE		0F2329			0.500000
53005KA	SHEEP(ORGAN MEATS)-KIDNEY		0F2329			0.500000
53005KA	SHEEP(ORGAN MEATS)-KIDNEY	(3yr tol)	8F3673		0.500000	
53005LA	SHEEP(ORGAN MEATS)-LIVER		0F2329			0.500000
53005LA	SHEEP(ORGAN MEATS)-LIVER	(3yr tol)	8F3673		0.500000	
53006KA	PORK(ORGAN MEATS)-KIDNEY		0F2329			0.500000
53006KA	PORK(ORGAN MEATS)-KIDNEY	(3yr tol)	8F3673		0.500000	
53006LA	PORK(ORGAN MEATS)-LIVER		0F2329			0.500000
53006LA	PORK(ORGAN MEATS)-LIVER	(3yr tol)	8F3673		0.500000	
53010AA	FISH-UNSPECIFIED		9F2163			0.250000
53013AA	FISH-SHELLFISH		3F2956			3.000000
53016AA	FISH-FRESHWATER FINFISH		9F2163			0.250000
53017AA	FISH-SALTWATER FINFISH		9F2163			0.250000
53017DA	FISH-FINFISH-SALTWATER-DRIED		9F2163			0.250000
55008LA	TURKEY-GIBLETS (LIVER)		0F2329			0.500000
55008LA	TURKEY-GIBLETS (LIVER)	(3yr tol)	8F3673		0.500000	
55013LA	POULTRY/OTHER-GIBLETS(LIVER)		0F2329			0.500000
55013LA	POULTRY,OTHER-GIBLETS(LIVER)	(3yr tol)	8F3673		0.500000	
55015LA	CHICKEN-GIBLETS(LIVER)		0F2329			0.500000
55015LA	CHICKEN-GIBLETS(LIVER)	(3yr tol)	8F3673		0.500000	

TABLE 2

TOLERANCE ASSESSMENT SYSTEM ROUTINE CHRONIC ANALYSIS DATE: 12/14/92 PAGE: 1

CHEMICAL INFORMATION	STUDY TYPE	EFFECTS	REFERENCE DOSES	DATA GAPS/COMMENTS	STATUS
Glyphosate (+ salts) Caswell #661A CAS No. 1071-83-6 A.I. CODE: 417300 CFR No. 180.364	developmental-rabbit NOEL= 175.0000 mg/kg 0.00 ppm LEL= 350.0000 mg/kg 0.00 ppm ONCO: D (SAP); E (HED)	increased incidence of soft stool, diarrhea, nasal discharge, and death	ADI UF -->100 OPP RfD= 2.000000 EPA RfD= 2.000000	Temporary PRODVOL heading based on G.Ghali memo to J. Kariya, 12/8/92 (old RfD 0.1 mg/kg/day)	HED RfD Peer Review Comm meeting 8/27/92 WHO last reviewed 1986. On IRIS.

POPULATION SUBGROUP	TOTAL TMRC (MG/KG BODY WEIGHT/DAY) CURRENT TMRC*	NEW TMRC**	NEW TMRC AS PERCENT OF RFD	DIFFERENCE AS PERCENT OF RFD	EFFECT OF ANTICIPATED RESIDUES ARC	%RFD
U.S. POPULATION - 48 STATES	0.011220	0.027745	1.387259	0.826236		
U.S. POPULATION - SPRING SEASON	0.011006	0.027186	1.359299	0.808980		
U.S. POPULATION - SUMMER SEASON	0.011338	0.027247	1.362334	0.795415		
U.S. POPULATION - FALL SEASON	0.011375	0.028546	1.427315	0.858584		
U.S. POPULATION - WINTER SEASON	0.011149	0.027987	1.399362	0.841913		
NORTHEAST REGION	0.010681	0.025930	1.296518	0.762493		
NORTH CENTRAL REGION	0.011226	0.028161	1.408036	0.846732		
SOUTHERN REGION	0.011193	0.026780	1.338981	0.779335		
WESTERN REGION	0.011970	0.031247	1.562360	0.963857		
HISPANICS	0.011310	0.027448	1.372424	0.806917		
NON-HISPANIC WHITES	0.011316	0.028136	1.406784	0.840973		
NON-HISPANIC BLACKS	0.010483	0.025272	1.263596	0.739433		
NON-HISPANIC OTHERS	0.011641	0.028304	1.415204	0.833137		
NURSING INFANTS (< 1 YEAR OLD)	0.011764	0.020275	1.013738	0.425545		
NON-NURSING INFANTS (< 1 YEAR OLD)	0.040595	0.060115	3.005733	0.975972		
FEMALES (13+ YEARS, PREGNANT)	0.007799	0.020075	1.003733	0.613761		
FEMALES 13+ YEARS, NURSING	0.009986	0.030043	1.502126	1.002809		
CHILDREN (1-6 YEARS OLD)	0.022320	0.058679	2.933935	1.817925		
CHILDREN (7-12 YEARS OLD)	0.016242	0.041039	2.051972	1.239895		
MALES (13-19 YEARS OLD)	0.011379	0.028735	1.436746	0.867777		
FEMALES (13-19 YEARS OLD, NOT PREG. OR NURSING)	0.009734	0.022798	1.139916	0.653208		
MALES (20 YEARS AND OLDER)	0.008717	0.022193	1.109643	0.673786		
FEMALES (20 YEARS AND OLDER, NOT PREG. OR NURS)	0.008164	0.019976	0.998779	0.590601		

*Current TMRC does not include new or pending tolerances.
**New TMRC includes new, pending, and published tolerances.

TOLERANCE ASSESSMENT SUMMARY FOR Glyphosate (+ salts) DATE: 12/14/92
CASWELL #661A

ANALYSIS FOR POPULATION SUB-GROUP: U.S. POPULATION - 48 STATES

EXISTING TOLERANCES (PUBLISHED ONLY)		
RESULT IN A TMRC OF:	0.011221	MG/KG/DAY
THE EXISTING TMRC IS EQUIVALENT TO:	0.561	% OF THE ADI.
PROPOSED NEW TOLERANCES (CURRENT PETITION ONLY)		
RESULT IN A TMRC OF:	0.015875	MG/KG/DAY
THESE NEW TOLERANCES WILL OCCUPY:	0.794	% OF THE ADI.
IF THE NEW TOLERANCES (CURRENT PETITION ONLY)		
ARE APPROVED THE RESULTANT TMRC WILL BE:	0.027095	MG/KG/DAY
THE NEW TMRC WILL OCCUPY	1.355	% OF THE ADI.
OTHER PENDING TOLERANCES EXCLUDING THE		
CURRENT NEW PETITION HAVE A TMRC OF:	0.000651	MG/KG/DAY
THIS TMRC WILL OCCUPY	0.033	% OF THE ADI.
IF ALL PENDING TOLERANCES (INCLUDING THE		
CURRENT NEW PETITION) ARE GRANTED		
THE RESULTANT TMRC WILL BE:	0.027746	MG/KG/DAY
THE TOTAL TMRC WILL OCCUPY	1.387	% OF THE ADI.

ANALYSIS FOR POPULATION SUB-GROUP: NON-NURSING INFANTS (< 1 YEAR OLD)

EXISTING TOLERANCES (PUBLISHED ONLY)		
RESULT IN A TMRC OF:	0.040596	MG/KG/DAY
THE EXISTING TMRC IS EQUIVALENT TO:	2.030	% OF THE ADI.
PROPOSED NEW TOLERANCES (CURRENT PETITION ONLY)		
RESULT IN A TMRC OF:	0.017632	MG/KG/DAY
THESE NEW TOLERANCES WILL OCCUPY:	0.882	% OF THE ADI.
IF THE NEW TOLERANCES (CURRENT PETITION ONLY)		
ARE APPROVED THE RESULTANT TMRC WILL BE:	0.058227	MG/KG/DAY
THE NEW TMRC WILL OCCUPY	2.911	% OF THE ADI.
OTHER PENDING TOLERANCES EXCLUDING THE		
CURRENT NEW PETITION HAVE A TMRC OF:	0.001888	MG/KG/DAY
THIS TMRC WILL OCCUPY	0.094	% OF THE ADI.
IF ALL PENDING TOLERANCES (INCLUDING THE		
CURRENT NEW PETITION) ARE GRANTED		
THE RESULTANT TMRC WILL BE:	0.060115	MG/KG/DAY
THE TOTAL TMRC WILL OCCUPY	3.006	% OF THE ADI.

ANALYSIS FOR POPULATION SUB-GROUP: CHILDREN (1-6 YEARS OLD)

EXISTING TOLERANCES (PUBLISHED ONLY)		
RESULT IN A TMRC OF:	0.022321	MG/KG/DAY
THE EXISTING TMRC IS EQUIVALENT TO:	1.116	% OF THE ADI.
PROPOSED NEW TOLERANCES (CURRENT PETITION ONLY)		
RESULT IN A TMRC OF:	0.034691	MG/KG/DAY
THESE NEW TOLERANCES WILL OCCUPY:	1.735	% OF THE ADI.
IF THE NEW TOLERANCES (CURRENT PETITION ONLY)		
ARE APPROVED THE RESULTANT TMRC WILL BE:	0.057011	MG/KG/DAY
THE NEW TMRC WILL OCCUPY	2.851	% OF THE ADI.
OTHER PENDING TOLERANCES EXCLUDING THE		
CURRENT NEW PETITION HAVE A TMRC OF:	0.001669	MG/KG/DAY
THIS TMRC WILL OCCUPY	0.083	% OF THE ADI.
IF ALL PENDING TOLERANCES (INCLUDING THE		
CURRENT NEW PETITION) ARE GRANTED		
THE RESULTANT TMRC WILL BE:	0.058679	MG/KG/DAY
THE TOTAL TMRC WILL OCCUPY	2.934	% OF THE ADI.

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

JAN 13 1993

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

SUBJECT: Addendum to DRES Analysis for Glyphosate Reregistration Eligibility Document

FROM: Stephen A. Schaible
Dietary Risk Evaluation Section
Science Analysis Branch/ HED (H7509C)

TO: Jane Smith
Chemical Coordination Branch
Health Effects Division (H7509C)

THROUGH: James P. Kariya, Head
DRES/SAB
Health Effects Division

A Dietary Risk Evaluation System (DRES) analysis estimating the worst case chronic dietary exposure and risk posed by glyphosate food uses was performed and written up in a S. Schaible memo dated 12/15/92. In that analysis, a residue value of 40 ppm for "wheat milling fractions (except flour)" (hereafter in this memo referred to simply as "wheat milling fractions") was used, taken from Table B of the Residue Chemistry Chapter of the RED (R.B. Perfetti, 10/27/92). This tolerance was recommended as a means of harmonizing residue values with Codex maximum residue limits (MRLs) through reregistration (the proposed U.S. tolerance for wheat milling fractions being 12 ppm).

Since this analysis was performed, CBRS has taken the position that the 40 ppm Codex MRL is not supported by the data. Instead, CBRS recommends that a residue level of 20 ppm be adopted as the Codex MRL for wheat milling fractions and that this residue value also be adopted in the reregistration of glyphosate in an effort to harmonize with Codex. An addendum addressing this change has been issued by CBRS (R.B. Perfetti to J. Smith/ E. Saito, dated 1/12/93).

Though risk values for the overall population and the 22 DRES population subgroups were all minimal using the 40 ppm value (the highest subgroup had an exposure which represented only three percent of the RfD for glyphosate), wheat milling fractions contributed the largest risk to the overall population of any of the food uses of glyphosate. For this reason, a second DRES analysis was performed using the revised tolerance for wheat milling fractions of 20 ppm.

With the exception of the new residue value used for "wheat milling fractions (except flour)", residue inputs and assumptions

were the same in this analysis as in the previous analysis, as were the toxicological endpoints which exposure was compared to. The calculated Theoretical Maximum Residue Contribution (TMRC) for the overall U.S. population from food uses of glyphosate is 0.024674 mg/kg bwt/day, which represents 1.2% of the RfD. The subgroup most highly exposed, non-nursing infants less than one year old, has a TMRC of 0.057640 mg/kg bwt/day, or 2.9% of the RfD. Over one third of the dietary exposure and risk from glyphosate is due to the proposed tolerances on wheat.

These new risk values should be reported in the dietary risk characterization section of the Reregistration Eligibility Document instead of the values listed in the 12/15/92 memo.

cc: DRES, CBRS, Tox 1, Caswell # 661A

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