

US EPA ARCHIVE DOCUMENT



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

FILE

OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

25-Feb-1999

MEMORANDUM

Subject: **PP#2F04886.** Glyphosate in/on Glyphosate-Tolerant Sugar Beets. **HED Risk Assessment.**

CAS #: 1071-83-6
Chemical #: 103601, 417300
Submission #: S557001
DP Barcode: D253421

Case #: 289071
Class: Herbicide
40 CFR: 180.364

From: Tom Bloem, Chemist *TB*
Registration Action Branch I
Health Effects Division (7509C)

Through: Melba Morrow, Branch Senior Scientist *MM*
Registration Action Branch I
Health Effects Division (7509C)

To: Jim Tompkins/Vickie Walters
Registration Division (7505C)

Monsanto Company proposes to establish the following tolerance for residues of the herbicide glyphosate (N-phosphonomethyl glycine) resulting from the preharvest application of the isopropylamine salt or the monoammonium salt of glyphosate to glyphosate tolerant sugar beets. There are 63 products containing glyphosate and 85 tolerances for various crops and crop groupings, including processed commodities and animal feed items.

commodity	tolerance (ppm)
sugar beet tops	10
sugar beet root	10
dried sugar beet pulp	25

I. EXECUTIVE SUMMARY

HED has reviewed the appropriate toxicology and chemistry databases provided by the petitioner, Monsanto Corporation, for the establishment of glyphosate tolerances in/on sugar beet tops, sugar beet root and dried sugar beet pulp. A HED glyphosate risk assessment document was recently submitted to the Registration Division (D252388, T. Bloem, 22-Jan-1999). This risk assessment did not incorporate the HED approved tolerances in/on sugar beet tops, sugar beet root and dried sugar beet pulp. This document addresses that oversight and includes only information pertaining to residue chemistry and dietary exposure (refer to HED Risk Assessment of 22-Jan-1999 for complete document)

Glyphosate was reviewed by the Hazard Identification Assessment Review Committee (HIARC, 26-Mar-1998) and the FQPA Safety Factor Committee to evaluate the toxicology database and to address sensitivity of infants and children from exposure to this chemical (see Attachment 1 & 2). The HIARC reassessed doses and endpoints for acute dietary, chronic dietary as well as occupational and residential risk assessments. The following dose/endpoint selections and risk assessment determinations were made:

- Acute dietary: An acute dietary dose and endpoint were not identified in the database. A risk assessment is not required.
- Chronic dietary: RfD = 2.0 mg/kg/day. (NOAEL = 175 mg/kg/day; Uncertainty Factor = 100);
- The carcinogenic potential of glyphosate has been evaluated by the HED Cancer Peer Review Committee (26-Mar-1998). Glyphosate has been classified as a Group E chemical -- no evidence of carcinogenicity for humans in two acceptable animal studies. Thus, a cancer risk assessment is not required.
- Short-, intermediate-, and long-term dermal and inhalation: Doses and endpoints were not identified for these routes of exposure. These risk assessments are not required.
- The FQPA Safety Factor Committees recommended that no additional factors were required to address sensitivity of infants and children.
- No developmental neurotoxicity study was required.

For the U.S. population, 1.5% of the RfD (0.029960 mg/kg body wt/day) is occupied by dietary (food) exposure. For the most highly exposed subgroup, non-nursing infants <1 year old, 3.3% of the RfD (0.065430 mg/kg body wt/day) is occupied by dietary (food) exposure. The RfD represents the level at or below which daily aggregate dietary exposure over a lifetime will not pose appreciable risks to human health. HED generally has no concern for exposures below 100% of the RfD. The GENECC (0.19 ppb) and SCI-GROW (0.0011 ppb) estimated average water concentrations for glyphosate in surface and ground water are less than the DWLOC_{chronic} for the US population (69,000 ppb) and less than the DWLOC_{chronic} for non-nursing infants <1 year (19,000 ppb). Therefore, taking into account present uses and uses proposed in this action, HED concludes with reasonable certainty that no harm will result from chronic aggregate exposure to glyphosate. An occupational exposure assessment was not required since no endpoints of concern for short- or intermediate-term exposure (the use scenarios expected for glyphosate) were identified. Glyphosate is registered for residential products; however, a residential exposure assessment is not required since there are no endpoints selected for either dermal or inhalation exposure for the different exposure scenarios.

Provided the petitioner submits a revised label which specifies a 30-day plantback interval, HED recommends in favor of establishment of the following tolerances for the combined residues of glyphosate.

commodity	tolerance (ppm)
sugar beet tops	10
sugar beet root	10
dried sugar beet pulp	25

RESIDUE CHEMISTRY

Directions for Use: A proposed supplemental label for Roundup® Ultra Herbicide was submitted with this petition describing the application scenario of glyphosate to glyphosate tolerant sugar beets. A maximum of 4 post-emergent applications at 1 lb ai/acre/application are being proposed (minimum 10 day treatment interval). Therefore the seasonal maximum application of glyphosate is 4 lbs ai/acre. No more than a total of 2 lbs ai/acre can be applied prior to or after the 8 leaf growth stage and no more than a total of 2 lbs ai/acre can be applied after the 8 leaf growth stage. The product is mixed with water. If applied aerially volumes of 3-15 gallons/acre are suggested. If the product is applied with ground spray equipment, volumes of 5-40 gallons/acre are suggested. A minimum preharvest interval (PHI) of 30 days is required. The proposed label has no rotational crop restrictions. The label must be amended to incorporate a 30 day plant back interval (Memo D238398, J. Garbus, 9-Sep-1998).

Residue Analytical Methods: Adequate enforcement methods are available for analysis of residues of glyphosate in or on plant commodities. These methods include GLC (Method I in *Pesticides Analytical Manual (PAM) II*; the limit of detection is 0.05 ppm) and HPLC with fluorometric detection. Use of the GLC method is discouraged due to the lengthiness of the experimental procedure. The HPLC procedure has undergone successful Agency validation and was recommended for inclusion in PAM II (Memo, R. Perfetti, 27-Oct-1992). A GC/MS method for glyphosate in crops has also been validated by EPA's Analytical Chemistry Laboratory (ACL) (Memo, G. Kramer, 21-MAR-1995).

Adequate analytical methods are available for residue data collection and enforcement of the proposed tolerances of glyphosate in/on sugar beet tops, sugar beet root and dried sugar beet pulp (Memo D238398, J. Garbus, 9-Sep-1998).

Crop Field Trials: The petitioner submitted a residue study depicting the magnitude of glyphosate in/on glyphosate tolerant sugar beet RACs (MRID 44331601). Twelve field trials were conducted in the following locations: Clay County Minnesota, Polk County Minnesota, Renville County Minnesota, Saginaw County Michigan, Richland County North Dakota, Scottsbluff County Nebraska, Hockley County Texas, Weld County Colorado, Stanislaus County California (two field trials here), Power County Idaho and Twin Falls County Idaho. A total of 4 lbs ai/acre was applied as follows: 1 lb ai/acre applied at the 2-4 leaf stage, 1 lb ai/acre applied at the 12-14 leaf stage and 2 lbs ai/acre applied after the 12-14 leaf stage. Application volumes ranged from 10-20 gallons/acre. The geographical representation and PHI (22-69 days) were adequate. Glyphosate residues in/on sugar beet tops ranged from 1.753-8.390 ppm and in/on sugar beet root ranged from 3.252-8.637 ppm. The submitted data indicate that residues of glyphosate will not exceed 10 ppm in/on sugar beet root or sugar beet tops given the use patterns defined in this petition (Memo D238398, J. Garbus, 9-Sep-1998).

Processed Food: The petitioner submitted two sugar beet processing studies (MRID 44331602 & 44331603). In each study, sugar beets were treated with glyphosate as follows: 1.1 lbs ai/acre pre-emergence, 1.3 lbs ai/acre at the 2-4 leaf growth stage and 1.3 lbs ai/acre at the 12-14 leaf growth stage (total application rate 3.7 lbs ai/acre). The plants were harvested 116 days (MRID 44331602) and 112 days (MRID 44331603) after the last treatment. Glyphosate concentrations in/on the harvested sugar beet root from both studies were 0.3 ppm. The root was processed and the following fractions collected and analyzed for residue of glyphosate: pulp, press water, raw juice, lime sludge, thin juice, thick juice, raw sugar, molasses and refined sugar. A lab scale processing technology similar to the industrial processing of sugar beets was used. Results from the sugar beet processing study are summarized in Table I (Memo D238398, J. Garbus, 9-Sep-1998).

Table 1: Sugar Beet Processing Studies

processing fraction	glyphosate concentration (ppm)		concentration/reduction factor
	MRID 44331602	MRID 44331603	
sugar beet root	0.3	0.3	--
pulp ¹	0.248 (0.808) ²	0.20 (0.65) ²	2.7, 2.2; average 2.5
molasses	nd ³	nd ³	0.03
raw sugar	nd ²	nd ³	0.03
refined sugar	nd ³	nd ³	0.03

- 1 this pressed pulp contained 27% dry matter; EPA Guidelines OPPTS860.1000 states that dried pulp contains 88% dry matter; to convert from 27% dry matter to 88% dry matter the following equation was used; $[(0.88/0.27) * x]$; where "x" is the concentration in the pulp at 27% dry matter
- 2 the quantity in parentheses represent the concentration in the pulp at 88% dry matter
- 3 LOD = 0.02 ppm; 1/2 LOD used in calculation of concentration reduction factors

Based on the studies outlined above a tolerance of 25 ppm will be established for glyphosate residues in/on dried sugar beet pulp (10 ppm tolerance * 2.5 concentration factor)(Memo D238398, J. Garbus, 9-Sep-1998).

Meat, Milk, Poultry, and Eggs: The proposed glyphosate tolerances in/on sugar beet tops and dried sugar beet pulp (10 ppm and 25 ppm, respectively) will not significantly increase the dietary burden on US animals as compared to the present dietary burden for US animals resulting from registered uses of glyphosate (Memo D238398, J. Garbus, 9-Sep-1998).

Confined Accumulation in Rotational Crops: Currently, there is a requirement for 30-day minimum plant-back interval for crops for which the use of glyphosate is not registered (Memo, G. Kramer, 12-May-1994). The label provided with this petition must be amended to specify a 30 day plant back interval.

International Harmonization of Tolerances: Presently, there are no Canadian, Mexican or Codex MRLs. A US tolerance for glyphosate in/on beets, sugar is established at 0.2 ppm.

FOOD AND WATER EXPOSURE

Water: No monitoring data is available to perform a quantitative drinking water risk assessment for glyphosate. However the Environmental Fate and Effects Division (EFED) provided a Tier 1 drinking water assessment (EFED memo, Kevin Poff and Ibrahim Saheb, 15-May-1998, see Attachment 3). This assessment utilized the GENEEC and SCI-GROW screening models to provide estimates of ground and surface water contamination from glyphosate. Limitations and assumptions for these screening models are documented in the EFED memoranda.

Ground Water: Using available fate parameters and assuming three applications at a rate of 0.75 lbs ai/acre, the estimated ground water concentration from glyphosate using SCI-GROW was 0.0011 ppb. The label application rate allows up to a maximum of 10.6 lbs ai/acre/year.

The drinking water exposure for glyphosate from the ground water screening model, SCI-GROW, yields a peak and chronic Estimated Environmental Concentration (EEC) of 0.0011 ppb in ground water. There may be circumstances under which ground water concentration could exceed the SCI-GROW estimates. However, such exceptions should be rare since the SCI-GROW model is based exclusively on maximum ground water concentrations from studies conducted at sites and under conditions which are most likely to result in ground water contamination. The groundwater concentrations generated by SCI-GROW are based on the largest 90-day average recorded during the sampling period. Since there is relatively little temporal variation in groundwater concentrations compared to surface water, the concentrations can be considered as acute and chronic values (EFED memo, Kevin Poff and Ibrahim Saheb, 15-May-1998).

Surface Water: The GENEEC model was used to estimate surface water concentrations for glyphosate resulting from three applications at 0.75 lbs ai/acre. The label application rate allows up to a maximum of 10.6 lbs ai/acre/year. GENEEC is a single event model (one runoff event), but can account for spray drift from multiple applications. GENEEC represents a 10 hectare field immediately adjacent to a 1 hectare pond that is 2 meters deep with no outlet. The pond receives a spray drift event from each application plus one runoff event. The runoff event moves a maximum of 10% of the applied pesticide into the pond. This amount can be reduced due to degradation on the field and by soil sorption. Spray drift is estimated at 5% of the application rate. The GENEEC values represent upper-bound estimates of the concentrations that might be found in surface water due to glyphosate use. Thus, the GENEEC model predicts that glyphosate surface water concentrations range from a peak of 1.64 ppb to a 56 day average of 0.19 ppb (EFED memo, Kevin Poff and Ibrahim Saheb, 15-May-1998).

Food: *Chronic Exposure and Risk:* The chronic dietary exposure analysis from food sources was conducted using the reference dose (RfD) of 2.0 mg/kg/day (RfD and Population Adjusted Dose are equivalent). The RfD is based on the maternal NOAEL of 175 mg/kg/day from a rabbit developmental study (MRID 00046363) and an uncertainty factor of 100 (applicable to all population subgroups).

The table below summarizes results from the chronic DEEM™ analysis (see Attachment 1). The DEEM™ analysis assumed tolerance level residues in/on all commodities with an existing or proposed glyphosate tolerance. This assumption resulted in a theoretical maximum residue contribution (TMRC) for glyphosate which was used to generate %RfD. HED does not consider exposures below 100% RfD to be of concern.

Table 2: Summary of Results from Chronic DEEM™ Analysis (see Attachment 4):

Subgroups	Exposure, mg/kg bod wt./day	%RfD
U.S. Population (48 states)	0.029960	1.5
Nursing Infants (< 1 year old)	0.026051	1.3
Non-Nursing Infants (< 1 year old)	0.065430	3.3
Children (1-6 years old)	0.064388	3.2
Children (7-12 years old)	0.043017	2.2
Females (13+/nursing)	0.030928	1.5
Non-Hispanic whites	0.030241	1.5
Non-Hispanic blacks	0.030206	1.5
Males (13-19 years)	0.030134	1.5

The subgroups listed above are: (1) the U.S. population (48 states); (2) those for infants and children; and (3) the other subgroups for which the percentage of the RfD occupied is greater than that occupied by the subgroup U.S. population (48 states).

Carcinogenic Exposure and Risk: The carcinogenic potential of glyphosate has been evaluated by the HED Cancer Peer Review Committee (26-Mar-1998). Glyphosate has been classified as a Group E chemical--no evidence of carcinogenicity in two acceptable animal species. Thus, a cancer risk assessment is not required.

Acute Dietary Exposure and Risk: As previously stated, no endpoint was selected by the HIARC Committee (26-Mar-1998) for assessment of acute dietary risk. Thus no acute risk assessment is required.

AGGREGATE RISK

Chronic: GENEEC and SCI-GROW models were run to produce conservative estimates of glyphosate concentrations in surface and ground water, respectively. The model estimates are compared to the drinking water level of comparison (DWLOC_{chronic}). The DWLOC_{chronic} is the theoretical concentration of glyphosate in drinking water so that the aggregate chronic exposure (food + water + residential) will occupy no more than 100% of the RfD. Glyphosate is registered for residential products, however, a residential exposure assessment is not required since there are no endpoints selected for either dermal or inhalation exposure. The Agency's default body weights and consumption values used to calculate DWLOCs are as follows: 70 kg/2L (adult male), 60 kg/2L (adult female), and 10 kg/1L (child).

$$DWLOC_{chronic} = \frac{[\text{chronic water exposure (mg/kg/day)} \times (\text{body weight})]}{[\text{consumption (L)} \times 10^{-3} \text{ mg}/\mu\text{g}]}$$

$$\text{chronic water exposure (mg/kg/day)} = [\text{RfD} - (\text{chronic food} + \text{residential exposure})]$$

Table 3: Comparison of DWLOCs to Screening Model Estimates of Glyphosate in Drinking Water:

Population Subgroup	Chronic Scenario			
	Dietary TMRC ¹ (mg/kg/day)	DWLOC $\mu\text{g/L}$	SCI-GROW Estimate $\mu\text{g/L}$	GENEEC Estimate $\mu\text{g/L}$
U.S. Population (48 states)	0.029960	69,000	0.0011	0.19
Non-Nursing Infants (< 1 year old)	0.065430	19,000	0.0011	0.19
Non-Hispanic whites	0.030241	69,000	0.0011	0.19
Non-Hispanic blacks	0.030206	69,000	0.0011	0.19
Males (13-19 years)	0.030134	69,000	0.0011	0.19

¹ from DEEMTM analysis, RfD 2.0 mg/kg/day, see attachment #4

The estimated average concentrations of glyphosate in surface and ground water are less than HED's DWLOC_{chronic}. Therefore, taking into account present uses and uses proposed in this action, HED concludes with reasonable certainty that no harm will result from chronic aggregate exposure to glyphosate.

For the U.S. population, 1.5% of the RfD is occupied by dietary (food) exposure. For the most highly exposed subgroup, non-nursing infants less than 1 year old, 3.3% of the RfD is occupied by dietary (food) exposure. The RfD represents the level at or below which daily aggregate dietary exposure over a lifetime will not pose appreciable risks to human health. HED generally has no concern for exposures below 100% of the RfD. The estimated average concentrations of glyphosate in surface and ground water are less than HED's level of concern for glyphosate in drinking water as a contribution to chronic aggregate exposure. Therefore, HED concludes with reasonable certainty that residues of glyphosate in drinking water do not contribute significantly to the chronic human health risk, and that no harm will result from aggregate exposure to glyphosate.

The GENEEC and SCI-GROW model estimates were run assuming 3 glyphosate applications at 0.75 lbs ai/acre/application. The maximum application rate for glyphosate is 10.6 lbs ai/acre/year. The modeling estimates should have been generated using the maximum label rate. However, since the DWLOCs calculated were several orders of magnitude greater than the model estimates, the increase in modeling water estimates when assuming the maximum application rate was deemed to be inconsequential.

Acute Aggregate Exposure and Risk: There was no acute dietary endpoint identified, therefore a risk assessment was not conducted.

Short- and Intermediate-term Aggregate Exposure and Risk: Short-term and intermediate-term dermal and inhalation risk assessments for occupational and residential exposures are not required due to the lack of significant toxicological effects observed.

Carcinogenic Aggregate Exposure and Risk: The carcinogenic potential of glyphosate has been evaluated by the HED Cancer Peer Review Committee (26-Mar-1998). Glyphosate has been classified as a Group E chemical--no evidence of carcinogenicity in two acceptable animal species. Thus, a cancer risk assessment is not required.

Attachment 1: Chronic DEEM™ Run: T. Bloem, 22-Feb-1999

cc with attachments: T. Bloem, RAB1 File
RDI: M. Morrow (25-Feb-1999), Chemist Team (25-Feb-1999)



13544

R138278

Chemical: Glyphosate

PC Code:
417300

HED File Code: 11500 Petition Files Chemistry

Memo Date: 2/25/1999

File ID: DPD253421

Accession #: 000-00-0113

HED Records Reference Center
1/25/2007