5-31-96

Attachment to PP5F4578

Received/Filed under PP 5G4466 on 6/4/1996

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

MAY 31 1996

OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Dietary Exposure Analysis for Glufosinate-ammonium in/on Corn and Soybeans (PP# 5G4466).

FROM: Brian Steinwand BS
Dietary Risk Evaluation Section
Science Analysis Branch/HED (7509C)

Through: Elizabeth Doyle, Section Head E.A. Doyle
Dietary Risk Evaluation Section
SAB/Health Effects Division

TO: Mike Metzger, Chief
RCAB (7509C)

Action Requested

Provide a dietary exposure analysis for the use of glufosinate-ammonium in/on field corn (0.2 ppm), soybeans (2.0 ppm), eggs (0.05 ppm), poultry meat (0.05 ppm), poultry fat (0.05 ppm), and poultry meat-by-products (0.1 ppm).

Discussion

For the purposes of this analysis, the new tolerance on almonds was upgraded to pending status.

There presently exists a published tolerance on meat (cattle, goats, horse, sheep and hogs) at the recommended tolerance levels (See PP# 8F3607).

There is also a pending tolerance (See PP# 8F3607) for poultry at the recommended levels.

Toxicological Endpoint:

The Reference Dose (RfD) used in the analysis is 0.02 mg/kg bwt/day, based on a NOEL of 2.1 mg/kg bwt/day from a two-year rat chronic toxicity study with an uncertainty factor of 100 that demonstrated increased absolute and relative kidney weights in males as an endpoint effect (See memo, G. Ghali, 5/13/92). The RfD has been reviewed by the HED RfD committee (6/24/93).

TABLE 1

CHEMICAL INFORMATION FOR CASWELL NUMBER 580I DATE: 05/23/96 PAGE: 1

CHEMICAL	STUDY TYPE	EFFECTS	REFERENCE DOSES	DATA GAPS/COMMENTS	STATUS
Glufosinate-ammonium Caswell #580I CAS No. 77182-82-2 A.I. CODE: 128850 CFR No. 180.31	2yr feeding- rat NOEL= 2.1000 mg/kg 40.00 ppm LEL= 7.6000 mg/kg 160.00 ppm ONCO: Undetermined.	Increased absolute and relative kidney weights in males. Both carcinogenicity studies did not establish an MTD.	ADI UF -->100 OPP RfD= 0.020000 EPA RfD= 0.000400	Oncogenicity- rat Oncogenicity- mouse (Syn.: Ignite, HOE-38966)	EPA verified 02/18/87 WHO reviewed 1991 RfD/PR reviewed 11/08/91 EPA deferred 03/24/92 RfD/PR reviewed 06/24/93 On IRIS.

FOOD CODE	FOOD NAME	PETITION NUMBER	TOLERANCE (PPM) NEW	PENDING	PUBLISHED
01014AA	GRAPES-FRESH (EXP. 7/99)	8F3607			0.050000
01014DA	GRAPES-RAISINS (EXP. 7/99)	8F3607			0.050000
01014JA	GRAPES-JUICE (EXP. 7/99)	8F3607			0.050000
03001AA	ALMONDS	8F3607		0.100000	
03002AA	BRAZIL NUTS (EXP. 7/99)	8F3607			0.100000
03003AA	CASHEWS (EXP. 7/99)	8F3607			0.100000
03004AA	CHESTNUTS (EXP. 7/99)	8F3607			0.100000
03005AA	FILBERTS, HAZELNUTS (EXP. 7/99)	8F3607			0.100000
03006AA	HICKORY NUTS (EXP. 7/99)	8F3607			0.100000
03007AA	MACADAMIA NUTS (BUSH NUTS) (EXP. 7/99)	8F3607			0.100000
03008AA	PECANS (EXP. 7/99)	8F3607			0.100000
03009AA	WALNUTS (EXP. 7/99)	8F3607			0.100000
03010AA	BUTTER NUTS (EXP. 7/99)	8F3607			0.100000
03013AA	BEECHNUTS (EXP. 7/99)	8F3607			0.100000
04001AA	APPLES-FRESH (EXP. 7/99)	8F3607			0.050000
04001DA	APPLES-DRIED (EXP. 7/99)	8F3607			0.050000
04001JA	APPLES-JUICE (EXP. 7/99)	8F3607			0.050000
06002AA	BANANAS-UNSPECIFIED (EXP. 7/99)	2E4057			0.300000
06002AB	BANANAS-FRESH (EXP. 7/99)	2E4057			0.300000
06002DA	BANANAS-DRIED (EXP. 7/99)	2E4057			0.300000
06016AA	PLANTAINS (EXP. 7/99)	2E4057			0.300000
15029AA	SOYBEANS-SPROUTED SEEDS	5G4466	2.000000		
24002EA	CORN,GRAIN-ENDOSPERM	5G4466	0.200000		
24002HA	CORN,GRAIN-BRAN	5G4466	0.200000		
24002SA	CORN SUGAR	5G4466	0.200000		
27010OA	SOYBEANS-OIL	5G4466	2.000000		
28023AA	SOYBEANS-UNSPECIFIED	5G4466	2.000000		
28023AB	SOYBEANS-MATURE,SEEDS DRY	5G4466	2.000000		
28023MA	SOYBEANS-FLOUR, FULL FAT	5G4466	2.000000		
28023MB	SOYBEANS-FLOUR, LOW FAT	5G4466	2.000000		
28023MC	SOYBEANS-FLOUR,DEFATTED	5G4466	2.000000		
43058AA	WINE AND SHERRY (EXP. 7/99)	8F3607			0.050000
50000DB	MILK-NON-FAT SOLIDS	8F3607			0.020000
50000FA	MILK-FAT SOLIDS	8F3607			0.020000
50000SA	MILK SUGAR (LACTOSE)	8F3607			0.020000
53001BA	BEEF-MEAT BYPRODUCTS	8F3607			0.100000
53001FA	BEEF(BONELESS)-FAT (BEEF TALLOW)	8F3607			0.050000
53001MA	BEEF(BONELESS)-LEAN (W/O REMOVEABLE FAT)	8F3607			0.050000
002BA	GOAT-MEAT BYPRODUCTS	8F3607			0.100000
12FA	GOAT(BONELESS)-FAT	8F3607			0.050000

TABLE 2

TOLERANCE ASSESSMENT SYSTEM ROUTINE CHRONIC ANALYSIS

DATE: 05/23/96 PAGE: 1

CHEMICAL INFORMATION	STUDY TYPE	EFFECTS	REFERENCE DOSES	DATA GAPS/COMMENTS	STATUS
Glufosinate-ammonium Casuell #580I CAS No. 77182-82-2 A.I. CODE: 128850 CFR No. 180.31	2yr feeding- rat NOEL= 2.1000 mg/kg 40.00 ppm LEL= 7.6000 mg/kg 140.00 ppm ONCO: Undetermined.	Increased absolute and relative kidney weights in males. Both carcinogenicity studies did not establish an NTD.	ADI UF -->100 OPP RfD= 0.020000 EPA RfD= 0.000400	Oncogenicity- rat Oncogenicity- mouse (Syn.: Ignite, HOE-38966)	EPA verified 02/18/87 WHO reviewed 1991 RfD/PR reviewed 11/08/91 EPA deferred 03/24/92 RfD/PR reviewed 06/24/93 On IRIS.

POPULATION SUBGROUP	TOTAL THRC (MG/KG BODY WEIGHT/DAY) CURRENT THRC*	NEW THRC**	NEW THRC AS PERCENT OF RFD	DIFFERENCE AS PERCENT OF RFD	EFFECT OF ANTICIPATED RESIDUES ARC	PRC
U.S. POPULATION - 48 STATES	0.000415	0.001212	6.058920	3.982100		
U.S. POPULATION - SPRING SEASON	0.000387	0.001158	5.789680	3.855870		
U.S. POPULATION - SUMMER SEASON	0.000408	0.001203	6.015115	3.976040		
U.S. POPULATION - FALL SEASON	0.000437	0.001256	6.281905	4.099150		
U.S. POPULATION - WINTER SEASON	0.000430	0.001230	6.149825	3.997710		
NORTHEAST REGION	0.000438	0.001150	5.747550	3.558405		
NORTH CENTRAL REGION	0.000416	0.001203	6.014410	3.932580		
SOUTHERN REGION	0.000358	0.001179	5.896915	4.109350		
WESTERN REGION	0.000484	0.001365	6.826725	4.406425		
HISPANICS	0.000538	0.001439	7.194340	4.503830		
NON-HISPANIC WHITES	0.000419	0.001208	6.040375	3.946460		
NON-HISPANIC BLACKS	0.000330	0.001125	5.623230	3.974830		
NON-HISPANIC OTHERS	0.000465	0.001246	6.228140	3.901580		
NURSING INFANTS (< 1 YEAR OLD)	0.000895	0.001777	8.883655	4.409150		
NON-NURSING INFANTS (< 1 YEAR OLD)	0.002124	0.005661	28.303265	17.684980		
FEMALES (13+ YEARS, PREGNANT)	0.000280	0.000813	4.064370	2.664170		
FEMALES 13+ YEARS, NURSING	0.000363	0.001043	5.215935	3.403165		
CHILDREN (1-6 YEARS OLD)	0.001166	0.002720	13.598420	7.768515		
CHILDREN (7-12 YEARS OLD)	0.000654	0.001820	9.098165	5.830325		
MALES (13-19 YEARS OLD)	0.000402	0.001232	6.157905	4.148320		
FEMALES (13-19 YEARS OLD, NOT PREG. OR NURSING)	0.000321	0.001012	5.059015	3.452710		
MALES (20 YEARS AND OLDER)	0.000258	0.000883	4.414490	3.122350		
FEMALES (20 YEARS AND OLDER, NOT PREG. OR NURS)	0.000236	0.000792	3.960935	2.779705		

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

to assess post-application dermal exposures from a non-food use, such as application to turf. The study should be designed to meet the requirements of Subdivision K guidelines 132-1(a) (foliar dislodgeable residue) and 133-3 (dermal passive dosimetry).

RISK CHARACTERIZATION

Dietary Risk- Food: Chronic dietary exposure estimates for glufosinate ammonium assumed tolerance level residues and 100% crop treated for all commodities. Published and proposed glufosinate ammonium tolerances result in a Theoretical Maximum Residue Contribution (TMRC) that is up to 28% of the reference dose. Actual risks using more realistic assumptions may result in risk estimates an order of magnitude or more lower. As there are no acute dietary exposure endpoints of concern for glufosinate ammonium, margin of exposure (MOE) for estimated acute dietary exposure was not calculated.

Non-occupational (Residential) Risks: Glufosinate ammonium is registered for use on non-food sites including golf courses, lawns, ornamental shrubs, and recreational areas. Because there are no data to estimate the potential magnitude of exposures from these uses, the Agency is using a default assumption of 5% of the risk.

Dietary Risk- Water: HED does not have available data to perform a quantitative drinking water risk assessment for glufosinate ammonium at this time. However, since environmental fate data indicate that glufosinate ammonium is moderately persistent and mobile in soil and water, water risks will be assumed to account for 10% of the total allowable chronic and acute risk until further data are provided.

Aggregate Exposure/Risk: Based on the available data and assumptions used for dietary/water/residential exposure and risk estimates, the population group estimated to be the most highly exposed to glufosinate ammonium is non-nursing infants (<1 year old), with a risk estimate from combined sources equalling 43% of the RfD for chronic risk. For short-term risk, the calculated MOE for non-nursing infants (<1 year old) is 292. HED considers the chronic and short-term risks to be acceptable for the purposes of establishing the proposed time-limited tolerances.

Occupational Exposures: Occupational exposure and risk estimates for mixer/loaders and applicators of glufosinate ammonium indicate that MOEs are acceptable for the use of open pouring systems and open cabs during application.

CONCLUSIONS

Hazard Assessment for Glufosinate ammonium

[Note: the following occupational and acute dietary endpoints were selected in an *ad hoc* meeting (K. Baetcke, M. Ioannou, M. Metzger, D. McCall, L. Hansen; 1-7-97).]

1. Occupational Exposure Endpoint Selection for Glufosinate Ammonium:

   a) Short-Term Risk: An interim endpoint for short-term exposure (non-dietary) of 100 mg/kg/day, the NOEL for a 21-day dermal toxicity study in the rat (MRID 40345605), was selected based on neurological clinical signs (hyperactivity, aggressive behavior, piloerection) at the LOEL of 300 mg/kg/day.

   b) Intermediate-term and Chronic Risk: No interim toxicity endpoints were selected because non-dietary intermediate-term or chronic exposures are not anticipated, based on current use patterns.

   c) Cancer Risk: At this time, glufosinate ammonium has not been evaluated by the HED RfD/Cancer Peer Review Committee for carcinogenic potential, due to lack of an acceptable rat carcinogenicity data (MRID nos. 40345607, 41144701; study considered supplementary due to inadequate dosing levels; see RfD memorandum dated 5-12-92). However, no treatment-related increases in tumor incidences were observed in a mouse carcinogenicity study (MRID nos. 40345609, 41144702), nor at the doses tested in the rat chronic toxicity/carcinogenicity study.

   d) Dermal penetration: A dermal penetration value is not needed for this risk assessment since the short-term non-dietary endpoint was based on a dermal toxicity study.

2. Dietary Endpoint Selection for Glufosinate Ammonium

   a) Acute Risk: No toxicity endpoints were identified for an acute dietary risk assessment. Although increased litter and fetal incidence of hydroureter and dilated renal pelvis were noted at 250 mg/kg/day in the rat developmental toxicity study, this effect was only observed at a dose that produced significant maternal toxicity, resulting in sacrifice of 4 and 8 dams at 50 and 250 mg/kg/day, respectively.

   b) Chronic Risk: The RfD is 0.02 mg/kg/day, based on the NOEL of 2.1 from a 2-year rat chronic toxicity study (MRID nos. 40345607, 41147701). Increased absolute and

relative kidney weights were observed in males at the LOEL of 7.6 mg/kg/day. An uncertainty factor (UF) of 100 was used (see RfD memorandum of 5-12-92).

c) Cancer Risk: At this time, glufosinate ammonium has not been evaluated by the HED RfD/Cancer Peer Review Committee for carcinogenic potential, due to lack of an acceptable rat carcinogenicity data (MRID nos. 40345607; 41144701; study considered supplementary due to inadequate dosing levels; see RfD memorandum dated 5-12-92). However, no treatment-related increases in tumor incidences were observed in a mouse carcinogenicity study (MRID nos. 40345609, 41144702), nor at the doses tested in the rat chronic toxicity/carcinogenicity study.

d) Infants and Children

1) Developmental Studies

Rat - By comparative evaluation of 3 rat developmental toxicity studies (MRID nos. 00142445, 00142446, 40345610), it was determined that the maternal (systemic) NOEL is 10 mg/kg/day, based on hyperactivity and vaginal bleeding (leading to sacrifice of 4 dams) at 50 mg/kg/day. The developmental (pup) NOEL is 50 mg/kg/day, based on increased litter and fetal incidence of dilated renal pelvis and/or hydroureter at 250 mg/kg/day.

Rabbit - In the rabbit developmental toxicity study (MRID nos. 40345601, 41144703), the maternal (systemic) NOEL is 6.3 mg/kg/day, based on decreased body weight, increased kidney weight and premature delivery at 20 mg/kg/day. The developmental (pup) NOEL is 20 mg/kg/day (highest dose tested.

2) Reproduction Studies

Rat - In a 2-generation reproduction study in the rat (MRID no. 40345612), the parental NOEL is 4 mg/kg/day (estimated using conversion factor; 40 ppm in diet), based on increased absolute and relative kidney weights in parental males at 12 mg/kg/day (120 ppm). The reproductive NOEL is 12 mg/kg/day (120 ppm), based on decreased numbers of pups at the LOEL of 36 mg/kg/day (360 ppm).

Occupational Exposures

Assumptions used in the exposure calculations are presented in Table 1. Exposure and risk estimates for mixer/loaders and applicators of glufosinate ammonium on corn are presented in Table 2. The data indicate that MOEs are greater than 100 for the use of open pouring systems and open cabs during application. Corn was selected as a representative crop, HED does not expect occupational exposure from use on soybeans to differ significantly.

Table 1. Occupational Exposure Assumptions

PARAMETER	ASSUMPTION
Dermal penetration	Value not needed, since short-term endpoint based on a dermal toxicity study.
Application Method	Groundboom
Minimum Finish Spray	10 gal/acre
Maximum Application Rate	0.365 lb ai/acre
Acres Treated/Day	120 acres (Y. Ng, BEAD)
Average Farm Size (1992 Ag Census)	889 Based on Palm Beach county, FL
Worker Weight	70 Kg
Career Duration	40 years
Lifetime	70 years
Short-term Endpoint	100 mg/Kg/day

Table 2. Occupational Short-Term Exposure and Risk Estimates for Glufosinate Ammonium on Corn.

Exposure Scenario	Unit Exposures, mg/lb ai			ADD[1] (mg/Kg/day)	Short-Term MOE[2]
	Dermal (incl. hands)	Inhalation	Total		
Mixer/Loader, open pour	0.023	0.0012	0.0242	0.015	6700
Applicator, groundboom open cab	0.014	0.0007	0.0147	0.009	11000

Both scenarios reflect a single layer of clothing and chemical resistant gloves.

1. Average Daily Dose
2. MOE = NOEL ÷ exposure

Aggregate Exposure (Dietary- Food, Dietary- Water & Residential)

Dietary Exposure- Food

Based on the available toxicology and dietary exposure data, dietary risk estimates for adults, infants and children for glufosinate ammonium do not exceed HED's level of concern.

The nature of the residue in plants and animals, enforcement methodology and residue chemistry data in support of this petition were all previously evaluated by CBTS (PP#5F4578).

1. The nature of the residues of glufosinate ammonium in/on transgenic corn and soybeans is considered to be understood. HED has concluded that the residues to be regulated are glufosinate ammonium and its metabolites 2-acetamido-4-methylphosphinico-butanoic acid and 3-methylphosphinico-propionic acid expressed as glufosinate free acid equivalents (Memo, M. Rodriguez 3/7/96; D219069 & D211531).

2. The nature of the residues of glufosinate ammonium in/on animals is considered to be understood. HED has concluded that the residues to be regulated are glufosinate ammonium and its metabolites 2-acetamido-4-methylphosphinico-butanoic acid and 3-methylphosphinico-propionic acid expressed as glufosinate free acid equivalents (Memo, M. Rodriguez 3/7/96; D219069 & D211531).

3. AgrEvo Analytical Method AE-24 is adequate for enforcement of the proposed tolerances in glufosinate ammonium resistant field corn and soybean raw and processed commodities. This

method is a modification of the current enforcement Analytical Method HRAV-5A. Method AE-24 includes an additional post-extraction cation exchange procedure to allow for separate detection and measurement of each residue component. In this way, the method accounts for the N-acetylated metabolite found in treated glufosinate-tolerant plants. Final determination is made by gas chromatography with flame photometric detection (GC/FPD) operating in the phosphorus selective mode (P-mode). Residues are expressed as glufosinate ammonium free acid equivalents.

4. Analytical Method BK/03/95 is adequate for enforcement of tolerances for glufosinate ammonium residues in livestock and poultry tissues, milk, and eggs. The method uses extraction, derivatization, clean-up, and gas chromatography. Method BK/03/95 determines the N-acetylated metabolite in addition to the parent and the M-propionic acid metabolite, all derivatized to a common analyte moiety. Residues are expressed as glufosinate free-acid equivalents.

5. As a result of this use, residues of glufosinate ammonium are not expected to exceed:

Field corn grain, 0.2 ppm
Field corn forage, 4.0 ppm
Field corn stover, 6.0 ppm
Soybeans, 2.0 ppm
Soybean hulls, 5.0 ppm
Aspirated grain fractions, 25.0 ppm
Eggs, 0.05 ppm
Poultry, meat, 0.05 ppm
Poultry, fat, 0.05 ppm
Poultry, meat-by-products, 0.10 ppm

6. Secondary residues in animal commodities are expected from this use. However, the established and proposed livestock tolerances are adequate to cover secondary residues which may result from feeding field corn and soybean commodities with residues of glufosinate ammonium to animals.

7. Acute Dietary Risk. There is no acute dietary exposure endpoint of concern for glufosinate ammonium.

8. Chronic Dietary Risk. Chronic dietary exposure estimates (DRES) for glufosinate ammonium are summarized in Attachment II (run dated 5/31/96). The DRES analysis assumed tolerance level residues and 100% crop treated for all commodities. Published and proposed glufosinate ammonium tolerances result in a Theoretical Maximum Residue Contribution (TMRC) that is equivalent to the following percents of the RfD:

U.S Population (48 States)	6%
Hispanics	7%

Non-Hispanic Others	6%
Non-Nursing Infants (<1 year old)	28%
Females (13+ years, pregnant)	4%
Females (13+ years, nursing)	5%
Children (1-6 years old)	14%
Children (7-12 years old)	9%

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

Incremental Dietary Risk. The incremental dietary risk from these new tolerances is 4% of the RfD for the US general population (48 states) and 17% of the RfD for the highest exposed population subgroup, non-nursing infants (<1 year old).

9. Dietary Cancer Risk. At this time, glufosinate ammonium has not been evaluated by the HED RfD/Cancer Peer Review Committee for carcinogenic potential, due to lack of an acceptable rat carcinogenicity data. Therefore, a quantitative dietary cancer risk assessment was not performed.

10. The following Codex Alimentarius Commission (Codex) Maximum Residue Levels (MRLs) for glufosinate ammonium have been established: maize, at 0.1 part per million (ppm), maize forage, at 0.2 ppm and soya bean (dry) at 0.1 ppm. These tolerances are for use-patterns for no-till systems of culture of non-transgenic corn and soybeans. AgrEvo USA Co. states that a petition for the same tolerances as proposed in the November 18, 1996 EPA Notice of Filing is pending with the Joint Meeting of the Food and Agriculture Organization Panel of Experts on Pesticide Residues in Food and the Environment and the World Health Organization Expert Group on Pesticide Residues to establish Codex MRLs for use of glufosinate ammonium in the culture of transgenic corn and soybeans.

The proposed tolerances for corn and soybean commodities are greater than the MRLs established by the Codex Alimentarius Commission because glufosinate ammonium is applied as a post-emergence herbicide in the culture of transgenic corn and soybeans; whereas the Codex MRLs are for preemergence applications of this herbicide in the culture of these crops. Studies showed the level of residues from the post-emergence use was greater.

Dietary Exposure and Risk Estimates- Water

HED does not have available data to perform a quantitative drinking water risk assessment for glufosinate ammonium at this time. No monitoring data are available. However, since environmental fate data indicate that glufosinate ammonium is moderately persistent and mobile in soil and water, **water risks will be assumed to account for 10% of the total allowable chronic and acute risk** until further data are provided (OPP Risk Cup Decision Logic, Food Safety Advisory Committee meeting of 12/5/96). Based on analysis of water monitoring data for a large number of pesticides with varying toxicities, soil mobility characteristics, environmental fate profiles, the assumption of 10% of the total acute and chronic risk allocated to drinking water is considered conservative and protective of the public health.

Non-Occupational Exposure

Glufosinate ammonium is registered for use on non-food sites including golf courses, lawns, ornamental shrubs, and recreational areas. Because there are no data to estimate the potential magnitude of exposures from these uses, **the Agency is using a default assumption of 5% of the risk** (OPP Risk Cup Decision Logic, Food Safety Advisory Committee meeting of 12/5/96). However, in the absence of data to support this assumption, HED is concerned that actual exposures from these residential outdoor uses (especially from post-application dermal contact with treated surfaces, such as turf) may exceed this level. Therefore, in order to proceed with registration for the proposed new use of glufosinate-ammonium, the **petitioner should commit to providing EPA with a study to assess post-application dermal exposures** from a non-food use, such as application to turf. The study should be designed to meet the requirements of Subdivision K guidelines 132-1(a) (foliar dislodgeable residue) and 133-3 (dermal passive dosimetry).

Total Aggregate Exposure (Dietary + Water + Residential)

a) Chronic Risk: Based on the available data and assumptions used for dietary/water/residential exposure and risk estimates, the population group estimated to be the most highly exposed to glufosinate ammonium (and perhaps the most sensitive to adverse effects) is non-nursing infants (<1 year old), with a risk estimate from combined sources equalling 43% of the RfD (dietary = 28% + drinking water = 10% + non-occupational = 5%).

b) Short-Term Risk: Assuming 10% of the risk is reserved

for drinking water and 5% for outdoor residential, the acceptable MOE must be greater than 116. Since the short term NOEL is based on a dermal exposure toxicity, the dietary exposure will be adjusted for a dietary endpoint (from the developmental study). The LEL from the developmental study (50 mg/kg/day) is 6-fold lower than that of the 21-day dermal study (300 mg/kg/day). The adjusted dietary exposure is thus 0.34 mg/kg/day (TMRC of 0.057 mg/kg/day multiplied by 6). As the calculated MOE for non-nursing infants (<1 year old) is 292 (short term NOEL of 100 mg/kg/day divided by adjusted dietary exposure of 0.34 mg/kg/day), HED considers the short-term risk to be acceptable for the purposes of establishing the proposed time-limited tolerances.

Cumulative Effects

Glufosinate ammonium is structurally similar to other members of the phosphate class of herbicides (i.e., glyphosate, glyphosate trimesium and fosamine ammonium). Further, other pesticides may have common toxicity endpoints with glufosinate ammonium.

However, the Agency has not made a determination whether glufosinate ammonium and any other pesticide have a common mode of toxicity and require cumulative risk assessment. For the purposes of these tolerances and registration application, the Agency has considered only risks from glufosinate ammonium. If required, cumulative risks will be assessed as part of Reregistration and tolerance reassessment, and when methodologies for determining common mode of toxicity and for performing cumulative risk assessment are finalized.

Determination of Safety for Infants and Children

The toxicological database for evaluating pre- and postnatal toxicity of glufosinate ammonium is complete. In the rabbit, no developmental toxicity was observed at a dose level that caused maternal toxicity (20 mg/kg/day; highest dose tested). Developmental toxicity in the rat of increased incidence of dilated renal pelvis and hydroureter was observed at a higher dose (250 mg/kg/day, the highest dose tested) than maternal toxicity (50 mg/kg/day). However, this effect was only observed in the presence of significant maternal toxicity that included hyperactivity and vaginal bleeding resulting in sacrifice of several dams (4 at 50 mg/kg/day and 8 at 250 mg/kg/day).

In the rat 2-generation reproduction study, systemic toxicity to parental animals was observed at a lower dose (12 mg/kg/day or

120 ppm in diet) than reproductive toxicity (reduced number of pups per litter at 36 mg/kg/day or 360 ppm in diet), indicating that the pups are not more sensitive than parental animals to the effects of glufosinate ammonium.

Based on the available toxicity data, HED does not have concerns regarding special sensitivities for infants and children exposed to residues of glufosinate ammonium in the diet and concludes that establishment of these time-limited tolerances on field corn and soybeans should not pose an unacceptable risk to infants and children. Thus, the addition of an additional uncertainty factor will not be required.

ATTACHMENTS

I. Magnitude of the Residue - Crop Field Trials

II. DRES analysis for glufosinate ammonium.

cc: PP#5F04578, G. Kramer (HED/CBTS)
RDI: Team (1/13/97), M.S. Metzger (1/16/97)
G.F. Kramer:804V:CM#2:(703)305-5079:7509C:CBTS

Attachment I: Magnitude of the Residue - Crop Field Trials

Magnitude of the Residue - Crop Field Trials

The following summary of residue field trial data are reproduced from previous CBTS reviews as noted below. No new residue data were presented with this revised petition.

CORN (Memo, M. Rodriguez 3/7/96; D219069 & D211531)

MRID # 435156-06: Twelve residue trials with transgenic, glufosinate-tolerant field corn were conducted in the states of CA, IL, IN, IA, MN, MO, NE, ND, SD, and VA. Ignite Herbicide formulated as a soluble liquid was used for all treatments at application rates of 0.32 lb ai/A on 12-inch corn and 0.45 lb ai/A on 12- and 24-inch corn. PHIs were 95-118 days, 60-80 days, and 30 days for grain/fodder, silage, and forage, respectively. In all samples, the principal measurable residue was the N-acetyl-glufosinate metabolite, followed by lower residue levels of parent and the methylphosphinico-propionic acid metabolite. Residue levels in field corn grain were generally below the LOQ, <0.05 ppm, for each residue component and regardless of the application regimen tested. Total residues in corn fodder ranged from 1.5 to 2.3 ppm; in corn silage residues, from 0.15 to 3.44 ppm; and in corn forage, from 0.15 to 3.6 ppm.

MRID #437669-23: Ten residue trials with transgenic, glufosinate-tolerant field corn were conducted in the states of FL, IA, IL, MN, MO, NC, NY, TX, WA, and WI. Two formulations containing glufosinate ammonium were used at all trials in this study. One plot was treated with the 1.25 lb ai/gal formulation and the other with the 1.67 lb ai/gal formulation. Each treated plot received one application of the respective formulation at a nominal rate of 0.35 lb ai/A at the 12-inch corn stage, followed by a second application of the same test substance at a nominal rate of 0.45 lb ai/A at the 24-inch corn stage. All applications were broadcast, over-the-top of the corn plants, by ground spray. Forage was sampled at 29-31 days and at 69-100 days after the last application. Silage (not ensiled) was sampled at 58-60 days after the last application. Fodder and grain were sampled at 69-122 days after the last application, at the mature or hard dent stage. In all matrices, total residues consisted almost exclusively of parent plus the N-acetyl metabolite. For the propionic acid metabolite residues were generally below the LOQ, <0.05 ppm. The maximum total residue in early corn forage samples was 5.23 ppm; in late corn forage, 4.09 ppm; in corn silage, 2.61 ppm; in corn fodder, 5.43 ppm; and in field corn grain, 0.12 ppm.

Since no concentration of residues occurred in the processed field corn commodities, there is no need for tolerances on processed corn commodities. However, total glufosinate ammonium residues

concentrated from the field corn grain into the aspirated grain fractions by a factor of approximately 12.

Soybeans (Memo, M. Rodriguez 3/7/96; D219069 & D211531)

MRID #435156-07: Eight field residue trials with transgenic, glufosinate-tolerant soybeans were conducted in the states of IA, IL, IN, MO, AR, MS, and VA. Ignite Herbicide, formulated as a soluble liquid was used for all treatments. The application rate was 0.45 lb ai/A on six-trifoliate soybeans. PHIs ranged from 85 to 112. In soybean seeds, the N-acetyl glufosinate metabolite was found to be the principal residue component, followed by the parent and the propionic acid metabolite. Total residues ranged from approximately 0.15 to 0.48 ppm.

MRID #437669-24: Ten field residue trials with transgenic, glufosinate-tolerant soybeans were conducted in the states of AR, FL, IA, IL, IN, MO, NC, OH, PA, and VA. Ignite Herbicide, formulated as a soluble liquid was used for all treatments. Two different application regimens were included in the study as follows: both plots received an application of 0.35 lb ai/A at the third node stage of growth, and a second application of 0.45 lb ai/A at the bloom stage of growth. One plot received applications made with a 1.25 lb ai/gal formulation and the other plot with the 1.67 lb ai/gal formulation. All applications were made broadcast, over-the-top of the soybean plants by ground spray. Seeds were collected at 69-102 DAT. The N-acetyl glufosinate metabolite was found to be the principal residue component, followed by the parent and the propionic acid metabolite. The maximum total residue in soybean seeds was 2.02 ppm.

In soybeans, the concentration factor for hulls was 2.66X. Total glufosinate ammonium residues also concentrated from the soybean seed into the aspirated grain fractions by a factor of approximately 9.

RUMINANT (Memo, M. Rodriguez 3/7/96; D219069 & D211531)

Twelve Holstein dairy cows were dosed for 28 days with a ration consisting of approximately 15% glufosinate ammonium (Hoe-039866), the parent compound, and 85% N-acetyl glufosinate (Hoe-099730), the major plant metabolite in transgenic field corn and soybeans. A total daily feed residue equivalent of 9.1 ppm was estimated for the 0.8X dose, 27.3 ppm for the 2.5X dose, and 91.1 ppm for the 8.3X dose of glufosinate free acid.

All milk sample residues corresponding to the 0.8X dosage group were less than the LOQ (<0.02 ppm). The maximum combined residues of Hoe-039866 plus Hoe-099730 were found to be 0.028 ppm in the

2.5X dosage group. Combined residues of Hoe-039866 plus Hoe-099730 ranged from 0.022 to 0.229 ppm in the 8.3X dosage group.

Results of the residue analysis of kidney, muscle, fat, and liver samples were as follows. Residues were less than the LOQ in all cattle commodities from the 0.8X and the 2.5X dosage groups. Residues were less than the LOQ in muscle and fat from the 8.3X dosage group. In kidney from the 8.3X dosage group, maximum residue values ranged from 0.11 to 0.15 ppm for Hoe-039866 plus Hoe-099730 and from less than the LOQ to 0.13 for Hoe-061517. In liver from the 8.3X dosage group, maximum residue values ranged from 0.25 to 0.29 for Hoe-061517. Residues of Hoe-039866 plus Hoe-099730 in that commodity and dosage group were less than LOQ.

Poultry (Memo, M. Rodriguez 3/7/96; D219069 & D211531)

Laying hens were dosed for 28 consecutive days with a ration consisting of approximately 15% glufosinate ammonium (Hoe-039866), the parent compound, and 85% N-acetyl glufosinate (Hoe-099730), the major plant metabolite in transgenic field corn and soybeans. The dosing was performed orally through gelatin capsules. A total daily feed residue equivalent of 0.36 ppm (0.4X), 1.08 ppm (1.2X), and 3.6 ppm (3.9X) of glufosinate free acid was administered daily.

Samples taken from treated animals included skin, liver, muscle, fat, and eggs. No residues above the method LOQ were found in any of the treated samples collected.

Attachment to PPSF4578

Received/Filed under PP 5G4466 on 6/4/1996

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

MAY 31 1996

OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Dietary Exposure Analysis for Glufosinate-ammonium in/on Corn and Soybeans (PP# 5G4466).

FROM: Brian Steinwand BS
Dietary Risk Evaluation Section
Science Analysis Branch/HED (7509C)

Through: Elizabeth Doyle, Section Head E.A. Doyle
Dietary Risk Evaluation Section
SAB/Health Effects Division

TO: Mike Metzger, Chief
RCAB (7509C)

Action Requested

Provide a dietary exposure analysis for the use of glufosinate-ammonium in/on field corn (0.2 ppm), soybeans (2.0 ppm), eggs (0.05 ppm), poultry meat (0.05 ppm), poultry fat (0.05 ppm), and poultry meat-by-products (0.1 ppm).

Discussion

For the purposes of this analysis, the new tolerance on almonds was upgraded to pending status.

There presently exists a published tolerance on meat (cattle, goats, horse, sheep and hogs) at the recommended tolerance levels (See PP# 8F3607).

There is also a pending tolerance (See PP# 8F3607) for poultry at the recommended levels.

Toxicological Endpoint:

The Reference Dose (RfD) used in the analysis is 0.02 mg/kg bwt/day, based on a NOEL of 2.1 mg/kg bwt/day from a two-year rat chronic toxicity study with an uncertainty factor of 100 that demonstrated increased absolute and relative kidney weights in males as an endpoint effect (See memo, G. Ghali, 5/13/92). The RfD has been reviewed by the HED RfD committee (6/24/93).

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TABLE 1

CHEMICAL INFORMATION FOR CASWELL NUMBER 580I

DATE: 05/23/96 PAGE: 1

CHEMICAL	STUDY TYPE	EFFECTS	REFERENCE DOSES	DATA GAPS/COMMENTS	STATUS
Glufosinate-ammonium Caswell #580I CAS No. 77182-82-2 A.I. CODE: 128850 CFR No. 180.31	2yr feeding- rat NOEL= 2.1000 mg/kg 40.00 ppm LEL= 7.6000 mg/kg 160.00 ppm ONCO: Undetermined.	Increased absolute and relative kidney weights in males. Both carcinogenicity studies did not establish an MTD.	ADI UF -->100 OPP RfD= 0.020000 EPA RfD= 0.000400	Oncogenicity- rat Oncogenicity- mouse (Syn.: Ignite, HOE-38966)	EPA verified 02/18/87 WHO reviewed 1991 RfD/PR reviewed 11/08/91 EPA deferred 03/24/92 RfD/PR reviewed 04/24/93 On IRIS.

FOOD CODE	FOOD NAME	PETITION NUMBER	TOLERANCE (PPM) NEW	PENDING	PUBLISHED
01014AA	GRAPES-FRESH (EXP. 7/99)	8F3607			0.050000
01014DA	GRAPES-RAISINS (EXP. 7/99)	8F3607			0.050000
01014JA	GRAPES-JUICE (EXP. 7/99)	8F3607			0.050000
03001AA	ALMONDS	8F3607		0.100000	
03002AA	BRAZIL NUTS (EXP. 7/99)	8F3607			0.100000
03003AA	CASHEWS (EXP. 7/99)	8F3607			0.100000
03004AA	CHESTNUTS (EXP. 7/99)	8F3607			0.100000
03005AA	FILBERTS, HAZELNUTS (EXP. 7/99)	8F3607			0.100000
03006AA	HICKORY NUTS (EXP. 7/99)	8F3607			0.100000
03007AA	MACADAMIA NUTS (BUSH NUTS) (EXP. 7/99)	8F3607			0.100000
03008AA	PECANS (EXP. 7/99)	8F3607			0.100000
03009AA	WALNUTS (EXP. 7/99)	8F3607			0.100000
03010AA	BUTTER NUTS (EXP. 7/99)	8F3607			0.100000
03013AA	BEECHNUTS (EXP. 7/99)	8F3607			0.100000
04001AA	APPLES-FRESH (EXP. 7/99)	8F3607			0.050000
04001DA	APPLES-DRIED (EXP. 7/99)	8F3607			0.050000
04001JA	APPLES-JUICE (EXP. 7/99)	8F3607			0.050000
06002AA	BANANAS-UNSPECIFIED (EXP. 7/99)	2E4057			0.300000
06002AB	BANANAS-FRESH (EXP. 7/99)	2E4057			0.300000
06002DA	BANANAS-DRIED (EXP. 7/99)	2E4057			0.300000
06016AA	PLANTAINS (EXP. 7/99)	2E4057			0.300000
15029AA	SOYBEANS-SPROUTED SEEDS	5G4466	2.000000		
24002EA	CORN,GRAIN-ENDOSPERM	5G4466	0.200000		
24002MA	CORN,GRAIN-BRAN	5G4466	0.200000		
24002SA	CORN SUGAR	5G4466	0.200000		
27010DA	SOYBEANS-OIL	5G4466	2.000000		
28023AA	SOYBEANS-UNSPECIFIED	5G4466	2.000000		
28023AB	SOYBEANS-MATURE,SEEDS DRY	5G4466	2.000000		
28023MA	SOYBEANS-FLOUR, FULL FAT	5G4466	2.000000		
28023MB	SOYBEANS-FLOUR, LOW FAT	5G4466	2.000000		
28023MC	SOYBEANS-FLOUR,DEFATTED	5G4466	2.000000		
43058AA	WINE AND SHERRY (EXP. 7/99)	8F3607			0.050000
50000DB	MILK-NON-FAT SOLIDS	8F3607			0.020000
50000FA	MILK-FAT SOLIDS	8F3607			0.020000
50000SA	MILK SUGAR (LACTOSE)	8F3607			0.020000
53001BA	BEEF-MEAT BYPRODUCTS	8F3607			0.100000
53001FA	BEEF(BONELESS)-FAT (BEEF TALLOW)	8F3607			0.050000
53001MA	BEEF(BONELESS)-LEAN (W/O REMOVEABLE FAT)	8F3607			0.050000
002BA	GOAT-MEAT BYPRODUCTS	8F3607			0.100000
12FA	GOAT(BONELESS)-FAT	8F3607			0.050000

TABLE 2

TOLERANCE ASSESSMENT SYSTEM ROUTINE CHRONIC ANALYSIS

DATE: 05/23/96 PAGE: 1

CHEMICAL INFORMATION	STUDY TYPE	EFFECTS	REFERENCE DOSES	DATA GAPS/COMMENTS	STATUS
Glufosinate-ammonium Casuell #580I CAS No. 77182-82-2 A.I. CODE: 128850 CFR No. 180.31	2yr feeding- rat NOEL= 2.1000 mg/kg 40.00 ppm LEL= 7.6000 mg/kg 140.00 ppm ONCO: Undetermined.	Increased absolute and relative kidney weights in males. Both carcinogenicity studies did not establish an MTD.	ADI UF -->100 OPP RfD= 0.020000 EPA RfD= 0.000400	Oncogenicity- rat Oncogenicity- mouse (Syn.: Ignite, HOE-38966)	EPA verified 02/18/87 WHO reviewed 1991 RfD/PR reviewed 11/08/91 EPA deferred 03/24/92 RfD/PR reviewed 06/24/93 On IRIS.

POPULATION SUBGROUP	TOTAL THRC (MG/KG BODY WEIGHT/DAY) CURRENT THRC*	NEW THRC**	NEW THRC AS PERCENT OF RFD	DIFFERENCE AS PERCENT OF RFD	EFFECT OF ANTICIPATED RESIDUES ARC	PRD
U.S. POPULATION - 48 STATES	0.000415	0.001212	6.058920	3.982100		
U.S. POPULATION - SPRING SEASON	0.000387	0.001158	5.789680	3.855870		
U.S. POPULATION - SUMMER SEASON	0.000408	0.001203	6.015115	3.976040		
U.S. POPULATION - FALL SEASON	0.000437	0.001256	6.281905	4.099150		
U.S. POPULATION - WINTER SEASON	0.000430	0.001230	6.149825	3.997710		
NORTHEAST REGION	0.000438	0.001150	5.747550	3.558405		
NORTH CENTRAL REGION	0.000416	0.001203	6.014410	3.932580		
SOUTHERN REGION	0.000358	0.001179	5.896915	4.109350		
WESTERN REGION	0.000484	0.001365	6.826725	4.406425		
HISPANICS	0.000538	0.001439	7.194340	4.503830		
NON-HISPANIC WHITES	0.000419	0.001208	6.040375	3.946460		
NON-HISPANIC BLACKS	0.000330	0.001125	5.623230	3.974830		
NON-HISPANIC OTHERS	0.000465	0.001246	6.228140	3.901580		
NURSING INFANTS (< 1 YEAR OLD)	0.000895	0.001777	8.883655	4.409150		
NON-NURSING INFANTS (< 1 YEAR OLD)	0.002124	0.005661	28.303265	17.684980		
FEMALES (13+ YEARS, PREGNANT)	0.000280	0.000813	4.064370	2.664170		
FEMALES 13+ YEARS, NURSING	0.000363	0.001043	5.215935	3.403165		
CHILDREN (1-6 YEARS OLD)	0.001166	0.002720	13.598420	7.768515		
CHILDREN (7-12 YEARS OLD)	0.000654	0.001820	9.098165	5.830325		
MALES (13-19 YEARS OLD)	0.000402	0.001232	6.157905	4.148320		
FEMALES (13-19 YEARS OLD, NOT PREG. OR NURSING)	0.000321	0.001012	5.059015	3.452710		
MALES (20 YEARS AND OLDER)	0.000258	0.000883	4.414490	3.122350		
FEMALES (20 YEARS AND OLDER, NOT PREG. OR NURS)	0.000236	0.000792	3.960935	2.779705		

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

concentrated from the field corn grain into the aspirated grain fractions by a factor of approximately 12.

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All milk sample residues corresponding to the 0.8X dosage group were less than the LOQ (<0.02 ppm). The maximum combined residues of Hoe-039866 plus Hoe-099730 were found to be 0.028 ppm in the

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Samples taken from treated animals included skin, liver, muscle, fat, and eggs. No residues above the method LOQ were found in any of the treated samples collected.