UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

MEMORANDUM

Date: 18-March-2008

Subject: Petition: 6F7146. Glyphosate-Isopropylammonium and Pyrithiobac Sodium. Human-Health Risk Assessment for Application to Glyphosate-Tolerant Soybean.

Petition:	6F7146	DP #s:	345923 and 348895
Registration:	352-606 - DuPont Staple Plus Herbicide	Decision #s:	372859 and 388020
40 CFR 180.	364 (glyphosate) 487 (pyrithiobac sodium)	PC Code:	103601 - glyphosate isopropylammonium salt 417300 - glyphosate; free acid 078905 - pyrithiobac sodium

From: Tom Bloem, Chemist
Registration Action Branch 1 (RAB1)/Health Effects Division (HED) (7509P)

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Through: Dana Vogel, Branch Chief
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RAB1/HED (7509P)

To: James Tompkins RM 25
Registration Division (RD; 7505P)

The HED of the Office of Pesticide Programs (OPP) is charged with estimating the risk to human health from exposure to pesticides. The RD of OPP requested that HED evaluate hazard and exposure data and conduct dietary, occupational, residential, and aggregate exposure assessments, as needed, to estimate the risk to human health that will result from all registered/proposed glyphosate and pyrithiobac sodium uses.

A summary of the findings and an assessment of human risk resulting from the registered/ proposed uses are provided in this document. Tom Bloem (RAB1) provided the risk assessment and residue chemistry review and PV Shah (RD) provided the hazard characterization.

Received in RRB 3/20/2008 EW

SUMMARY

DuPont requested a Section 3 registration for the preplant application of the herbicides glyphosate and pyrithiobac sodium to glyphosate-tolerant soybean. The petitioner is also working to commercialize a genetically modified soybean designated as Optimum™ GAT™ soybean (DP-356Ø43-5). The petitioner indicated that Optimum™ GAT™ soybean was engineered to express the microbial glyphosate acetyltransferase gene (*gat*4601), which confers tolerance to glyphosate via acetylation of the secondary amine group of glyphosate, and the *gm-hra* gene, which confers tolerance to acetolactate synthase (ALS) inhibiting herbicides via encoding for an ALS protein which is not sensitive to the ALS-inhibiting herbicides. As a result of the introduction of this genetically modified soybean, the petitioner is requesting that the glyphosate tolerance expression (40 CFR 180.364(a)) be altered from glyphosate *per se* to the combined residues of glyphosate and *N*-acetyl-glyphosate. The petitioner did not request a change in the numerical values of the currently-established glyphosate tolerances. The petitioner also did not request a change in the pyrithiobac sodium tolerance expression or tolerances.

HED notes that based on the proposed application scenario and with the introduction of Optimum™ GAT™ soybean, a discussion concerning the risk assessment for glyphosate (dietary, aggregate, and occupational), pyrithiobac sodium (dietary, aggregate, and occupational), and ALS herbicides which are currently registered for application to soybean (dietary and aggregate) is required. A discussion of the risk assessment for ALS inhibiting herbicides which are registered for application to soybean is required as these compounds may also be applied to Optimum™ GAT™ soybean.

Proposed Use: The petitioner submitted proposed supplemental labeling for the preplant application of DuPont Staple® Plus herbicide (EPA Reg. No. 352-606; 40.2% glyphosate; 1.7% pyrithiobac sodium; water-soluble packet/water soluble liquid) to glyphosate-tolerant soybeans (10-month plant-back interval (PBI)). Table 1 is a summary of the proposed application scenario. The label indicates a restricted-entry interval (REI) of 24 hours. HED concludes that the proposed application instructions are adequate. HED notes that glyphosate and ALS-inhibiting herbicide formulated products that are currently registered for application to soybean may also be applied to Optimum™ GAT™ soybean.

Table 1: Summary of Proposed Glyphosate-Tolerant Soybean Application Scenario.

App. Timing, Type, and Equip.	Formulation (EPA Reg. No.)	App. Rate (lb ai/acre)	Max. No. App. per Season	Use Directions and Limitations
preplant burndown, broadcast sprays using ground (5-20 GPA) or aerial equipment (≥3GPA)	water-soluble packet/water soluble liquid (352-606)	pyrithiobac sodium - 0.032 glyphosate - 0.75	1	-Allow at least 10 months between app. and planting of glyphosate-tolerant soybean. -App. through irrigation equipment is prohibited.

[1] GPA = gallons per acre

Pyrithiobac Sodium - Dietary and Aggregate Risk Assessment: The petitioner is proposing preplant application to glyphosate-tolerant soybean (10-month PBI). Based on the proposed application scenario and since pyrithiobac sodium is not currently registered for application to soybean, HED concludes that the nature of the residue in primary crops is not relevant to the current petition. Furthermore, since residues in/on soybean are expected to be insignificant as a result of the proposed use (see next paragraph), the nature of the residue in livestock is also not relevant to the current petition (D346713, T. Bloem, 12-Mar-2008).

The HED Metabolism Assessment Review Committee (MARC) reviewed a confined rotational crop study and determined that the residue of concern in rotational crops is pyrithiobac sodium *per se* (D216002, G. Kramer, meeting of 1-Jun-1995). The confined rotational crop study employed a single bare soil application at 0.125 lb ai/acre (3.9x the proposed rate) with soybean, carrot, lettuce, and wheat planted 30, 120, and 240/263 days after application. For those crops/extracts which required analysis, residues of pyrithiobac-sodium were ≤0.003 ppm (D195332, G. Kramer, 13-Jun-1994). Based on these data and since the label indicates that glyphosate-tolerant soybean may not be planted for 10 months following application, HED concludes that residues in soybean as a result of the proposed use will be insignificant. Therefore, tolerance on soybean commodities and revised dietary and aggregate risk assessments are unnecessary.

ALS-Inhibiting Herbicides (other than pyrithiobac sodium) - Dietary and Aggregate Risk Assessment: As indicated above, ALS-inhibiting herbicide formulated products that are currently registered for application to soybean may also be applied to Optimum™ GAT™ soybean. The petitioner has not submitted information concerning the nature/magnitude of these residues in/on Optimum™ GAT™ soybean. The petitioner indicated that the *gm-hra* gene, which confers tolerance to ALS-inhibiting herbicides, is a modified version of the endogenous soybean ALS gene; this modified ALS gene codes for an ALS protein that is not sensitive to ALS-inhibiting herbicides (ALS herbicides can not bind with the modified ALS protein). The petitioner indicated that the modified protein is >99% identical to the endogenous soybean ALS protein with two amino acid changes known to confer herbicide tolerance. The petitioner submitted a rationale (letter dated 21-Feb-2008, Jacob Vukich, DuPont Crop Protection) concerning the need for data pertaining to the nature/magnitude of ALS-inhibiting herbicides in/on Optimum™ GAT™ soybean (reviewed by the Chemistry Science Advisory Committee (ChemSAC)).

Since ALS tolerance is conferred via modification of the endogenous ALS soybean gene such that the plant is no longer sensitive (*i.e.*, tolerance is not conveyed via metabolism of the herbicide), HED concludes that the nature/magnitude of the residue data submitted in support of the registration for application of ALS-inhibiting herbicides to nontransgenic soybean are applicable to the application to Optimum™ GAT™ soybean (additional nature/magnitude of the residue are unnecessary; ChemSAC minutes of 27-Feb-2008 meeting; D346713, T. Bloem, 12-Mar-2008). Therefore, revised risk assessments for ALS-inhibiting herbicides that are currently registered for application to soybean are unnecessary.

Glyphosate - Dietary and Aggregate Risk Assessment: The petitioner is proposing preplant application of glyphosate to glyphosate-tolerant soybean (10-month PBI). Based on previously-reviewed confined rotational crop studies (3.71 lb ai/acre; MRIDs 41543201 and 41543202, A. Abramovitch, 14-Oct-1992), HED concluded that a 30-day PBI was appropriate for all nonlabeled crops (D200041, G. Kramer, 12-May-1994). Since the rate conducted in the confined rotational crop study was 4.9x the proposed rate and since the label indicates the soybean may not be planted

for 10 months following application, HED concludes that residues in soybean, as a result of the proposed use, will be insignificant. However and as indicated above, glyphosate formulated products that are currently registered for application to soybean may also be applied to Optimum™ GAT™ soybean (foliar including harvest aid application is registered for application to glyphosate-tolerant soybean). The petitioner has submitted information concerning the nature and magnitude of glyphosate residues in/on Optimum™ GAT™ soybean following foliar application. The petitioner has also submitted information concerning the nature of *N*-acetyl-glyphosate, a metabolite found in Optimum™ GAT™ soybean following application of glyphosate, in livestock. Based on these data, HED concluded that the glyphosate tolerance expression should change from glyphosate *per se* to the combined residues of glyphosate and *N*-acetyl-glyphosate (expressed as glyphosate); along with the change in the tolerance expression, HED concluded that the soybean hull and aspirated grain fractions (AGF) tolerances should be increased to 120 ppm and 310 ppm, respectively (a revised Section F is requested; D346713, T. Bloem, 12-Mar-2008).

The existing toxicity database for glyphosate is complete and without data gaps. There is high confidence in the quality of the existing studies and the reliability of the toxicity endpoints identified for use in risk assessment. A complete discussion of the glyphosate toxicological data can be found in the most recent glyphosate risk assessment (D321992, J. Tomerlin, 29-Sep-2006). HED concludes that revised glyphosate dietary and aggregate risk assessment are unnecessary for the following reasons: **(1)** HED has determined that *N*-acetyl-glyphosate is toxicologically equivalent to glyphosate (see attachments 2 and 3); **(2)** the numerical value of all food tolerances will remain the same; and **(3)** the most recent dietary analysis assumed tolerance level residues, 100% crop treated, and drinking water estimates derived from a direct application to water at 3.75 lb ae/acre (D321992, J. Tomerlin, 29-Sep-2006).

Occupational Exposure: Based on the proposed use, there may be both intermediate-term dermal and inhalation exposure to pesticide handlers and workers. The following text is a summary of the occupational exposure assessment for glyphosate and pyrithiobac-sodium. The proposed 24-hour REI is appropriate for both glyphosate and pyrithiobac sodium.

For glyphosate, there are no short-, intermediate-, or long-term dermal or inhalation endpoints and glyphosate has been classified as a Group E chemical (no evidence of carcinogenicity); therefore a glyphosate occupational exposure assessment is unnecessary.

For pyrithiobac sodium, there are no short- or intermediate-term dermal or inhalation endpoints; however, pyrithiobac sodium has been classified as a Group C - possible human carcinogen (Q_1^* = 0.00105 $(mg/kg/day)^{-1}$). HED has not performed a cancer risk assessment for the proposed application to glyphosate-tolerant soybean; however, a cancer assessment was conducted as part of a cotton petition (1x 0.125 lb ai/acre (PHI = 45 days); 3.9x the proposed rate) which resulted in cancer risks which are not of concern to HED ($\leq 4.52 \times 10^{-8}$; D235143, G. Kramer, 15-Jul-1997). Since the cotton use rate is 3.9x the proposed soybean application rate and since the assumptions made when conducting an occupational cancer assessment when cotton is the target crop are conservative when compared to the assumptions made when soybean is the target crop, HED concludes that a revised occupational cancer assessment is unnecessary.

Recommendation: Provided the petitioner submits a revised Section F (see below) and the Analytical Chemistry Laboratory (ACL) is able to successfully validate the plant/livestock enforcement methods, HED concludes that the toxicological, residue chemistry, and occupational/residential databases support a conditional registration for the preplant application of glyphosate and pyrithiobac sodium to glyphosate-tolerant soybean. In addition, HED concludes that the tolerance expression for 40 CFR 180.364(a) may be altered from glyphosate *per se* to the combined residues of glyphosate and *N*-acetyl-glyphosate. A revised Section F specifying the tolerances listed in Table 2 for the combined residues of glyphosate and *N*-acetyl-glyphosate (expressed as glyphosate) resulting from the application of glyphosate, the ethanolamine salt of glyphosate, the ammonium salt of glyphosate, and the potassium salt of glyphosate, is requested.

Table 2: Tolerance Summary.

Commodity	Proposed Tolerance (ppm)	HED-Recommended Tolerance (ppm)	Comments
soybean, hulls	100	120	increase tolerances; change tolerance expression (see underlined above)
grain, aspirated fractions	100	310	

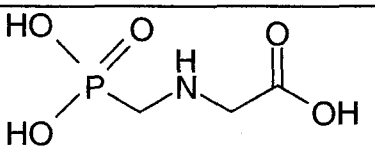
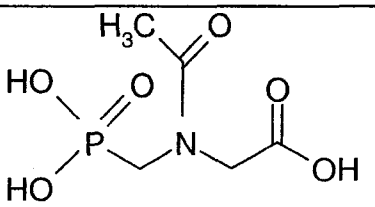
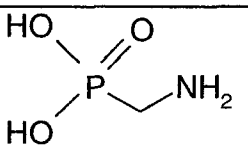
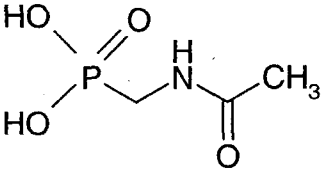
An unconditional registration may be acceptable upon submission of data that adequately addresses the following issues:

- Nature of the Residue - Plants: The petitioner is requested to submit the full Optimum™ GAT™ soybean metabolism study as specified in 860.1300.
- Nature of the Residue - Livestock: The petitioner is requested to submit the ruminant and poultry metabolism studies referenced in the livestock method validation study (MRID 47311011; dosed with ^{14}C-*N*-acetyl-glyphosate).
- Plant/Livestock Enforcement Methods: The petitioner is requested to submit radiovalidation data for *N*-acetyl-glyphosate (plant method) and revise the plant method as specified in the ILV (water bath temperature used to precipitate proteins (80-85 °C)); in addition, the petitioner will be required to make all requested revisions to the plant and/or livestock methods, if any, requested in the forthcoming PMV. Also, upon review of the poultry metabolism data, the adequacy of the already submitted radiovalidation data for the livestock enforcement method will be evaluated.
- Meat, Milk, Poultry, and Eggs: The petitioner is requested to submit the ruminant and poultry feeding studies referenced in the livestock validation study (MRID 47311011; dosed with *N*-acetyl-glyphosate).

RDI: RAB1 (5-Mar-2008)
T. Bloem:S10945:Potomac Yard 1:703-605-0217:7509P:RAB1

Attachment 1 - Chemical Structures
Attachment 2 - Toxicological Summary for *N*-Acetyl-Glyphosate and *N*-Acetyl-AMPA
Attachment 3 - Toxicological Profile for Glyphosate

Attachment 1 - Chemical Structures

compound	structure
Glyphosate *N*-(phosphonomethyl)glycine	
N-acetyl-glyphosate *N*-acetyl-*N*-(phosphonomethyl)glycine	
AMPA (aminomethyl)phosphonic acid	
N-acetyl-AMPA [(acetylamino)methyl]phosphonic acid	

***N*-Acetyl-Glyphosate**	
Guideline No./ Study Type	Results
870.1100 Acute Oral Toxicity- Rat	LD_{50} = greater than 5000 mg/kg in male and female rats
870.3150 90-Day Oral (feeding) Toxicity-Rat	NOAEL = 1157/1461 mg/kg/day (m/f), highest dose tested LOAEL = was not established
Bacterial Gene Mutation 870.5100	Non-mutagenic when tested up to 5000 ug/plate, in presence and absence of activation in S. *typhimurium* strains TA100, TA1535 and TA1537 and in Escheria coli strain WP2urvA.
Gene Mutation 870.5300	Non-mutagenic at the HGPRT locus in Chinese hamster ovary cells tested up to 2091 µl/ml, in presence and absence of metabolic activation.
In Vivo Cytogenetics - Bone Marrow 870.5395	No chromosomal aberrations were detected in male and mice at doses up to 2000mg/kg.
870.5375 Mammalian Cytogenic Assay	No evidence of chromosomal aberration in Chinese Hamster Ovary cells when tested at doses up to 2800 µg/mL with or without metabolic activations
870.7485 Metabolism and pharmacokinetics (Rat)	Absorption was estimated to be approximately 66% of the administered dose as estimated based on urinary excretion. The mean maximum concentrations in blood and plasma were 2.93 and 5.31 µg equiv/g at 1 and 2 hours postdose, respectively. The half-life was 20.1 h in blood and 15.6 h in plasma. After 168 h postdose, only 0.2% of the dose remained in the carcass, and 2.8% of the dose was isolated in the cage wash and wipe. A total of 97.25% of the dose was identified, and 97.18% of the dose was identified as parent. The remaining 0.07% of the identified dose was glyphosate, isolated in the feces. In the plasma, 100% of the sample radioactivity was identified as the parent. Similarly, 99.3-100% of the radiolabeled compounds from each sample was identified as parent in the urine and feces.

Glyphosate Subchronic, Chronic, and Other Toxicity Profile	
Guideline No./ Study Type	Results
870.3800 Reproduction and fertility effects, 2-generation (Rat)	**Parental/Systemic** NOAEL = 500 mg/kg/day in males and females LOAEL = 1500 mg/kg/day in males and females based on soft stools, decreased body weight gain and food consumption. Focal dilation of the kidney observed at 30 mg/kg/day in the 3-generation study was not observed at any dose level in this study. **Reproductive** NOAEL ≥ 1500 mg/kg/day (HDT) in males and females **Offspring** NOAEL = 500 mg/kg/day in males and females LOAEL = 1500 mg/kg/day in males and females based on decreased body weight gain during lactation.
870.4100b Chronic toxicity (dog)	NOAEL = 500 mg/kg/day in males and females (HDT) LOAEL = not established.
870.4300 Carcinogenicity (Mice)	NOAEL = 750 mg/kg/day in males and females LOAEL = 4500 mg/kg/day in males and females based on significant decreased body weight gain in both sexes, hepatocyte necrosis and interstitial nephritis in males, and increased incidence of proximal tubule epithelial basophilia and hypertrophy in the kidney of females. **No evidence of carcinogenicity**
870.4300 Chronic/Carcino-genicity (Rat)	NOAEL = 362 mg/kg/day in males, 447 mg/kg/day in females LOAEL = 940 mg/kg/day in males, 1183 mg/kg/day in females based on decreased body weight gain in females, decreased urinary pH in males, increased incidence of cataracts and lens abnormalities in males, and increased absolute and relative (to brain) liver weight in males. **No evidence of carcinogenicity**
Gene Mutation 870.5265	Non-mutagenic when tested up to 1000 ug/plate, in presence and absence of activation in S. *typhimurium* strains TA98, TA100, TA1535 and TA1537.
Gene Mutation 870.5300	Non-mutagenic at the HGPRT locus in Chinese hamster ovary cells tested up to cytotoxic concentrations or limit of solubility, in presence and absence of activation.
In Vivo Cytogenetics - Bone Marrow 870.5385	Non-mutagenic in rat bone marrow chromosome assay up to 1000 mg/kg in both sexes of Sprague Dawley rats.
870.5550 Rec - Assay and Gene Mutation Assay	There was no evidence of recombination in the rec-assay up to 2,000 ug/disk with *B. subtilis* H17 (rec+) and M45 (rec-). Negative for reverse gene mutation, both with and without S-9, up to 5,000 ug/plate (or cytotoxicity) with *E.coli* SP2hcrA and *S. typhimuarium* TA98, TA100, TA1535, TA1537, and TA1538.
870.7485 Metabolism and pharmacokinetics (Rat)	Absorption was 30-36% in males and females. Glyphosate was excreted unchanged in the feces and urine (97.5% minimum). The only metabolite present in the excreta was AMPA. Less than 1% of the absorbed dose remained in the carcass, primarily bone. Repeat dosing did not alter metabolism, distribution, and excretion.

Attachment 3 - Toxicological Profile for Glyphosate

Glyphosate Acute Toxicity Profile				
Guideline No.	Study Type	MRID(s)	Results	Toxicity Category
870.1100	Acute oral	41400601	LD_{50} > 5,000 mg/kg	IV
870.1200	Acute dermal	41400602	LD_{50} > 5,000 mg/kg	IV
870.1300	Acute inhalation	None	The requirement for an acute inhalation LC_{50} study was waived	None
870.2400	Acute eye irritation	41400603	Corneal opacity or irritation clearing in 7 days or less	III
870.2500	Acute dermal irritation	41400604	Mild or slight irritant	IV
870.2600	Skin sensitization	41642307	Not a sensitizer	None

Glyphosate Subchronic, Chronic, and Other Toxicity Profile	
Guideline No./ Study Type	Results
870.3100 90-Day oral toxicity (Mouse)	NOAEL = 1500 mg/kg/day in males and females LOAEL = 4500 mg/kg/day in males and females based on decreased body weight.
870.3100 90-Day oral toxicity (Range finding)	NOAEL = not established LOAEL = 50 mg/kg/day in males and females based on possible increased phosphorus and potassium values.
870.3150 90-Day oral toxicity (Rat) - Aminomethyl phosphoric acid - glyphosate plant metabolite	NOAEL = 400 mg/kg/day in males and females LOAEL = 1200 mg/kg/day in males and females based on body weight loss and histopathological lesions of the urinary bladder.
870.3200 21/28-Day dermal toxicity (Rabbit)	NOAEL = 1000 mg/kg/day in males and females LOAEL = 5000 mg/kg/day based on slight erythema and edema on intact and abraded skin of both sexes, and decreased food consumption in females.
870.3485 28-Day inhalation toxicity (rat)	NOAEL = 0.36 mg/L (HDT); LOAEL not established based on 6 hours/day, 5 days/week for 4 weeks
870.3700a Prenatal developmental in rodents (Rat)	**Maternal** NOAEL = 1000 mg/kg/day LOAEL = 3500 mg/kg/day based on inactivity, mortality, stomach hemorrhages and reduced body weight gain. **Developmental** NOAEL = 1000 mg/kg/day LOAEL = 3500 mg/kg/day based on increased incidence in the number of fetuses and litters with unossified sternebrae and decreased fetal body weight.
870.3700b Prenatal developmental in (Rabbit)	**Maternal** NOAEL = 175 mg/kg/day LOAEL = 350 mg/kg/day based on mortality, diarrhea, soft stools, and nasal discharge. **Developmental** NOAEL = 350 mg/kg/day (HDT) LOAEL = not established.
870.3800 Reproduction and fertility effects, 3-generation (Rat)	**Parental/Systemic** NOAEL = 30 mg/kg/day (HDT) **Reproductive** NOAEL = 30 mg/kg/day (HDT) **Offspring** NOAEL = 10 mg/kg/day LOAEL = 30 mg/kg/day based on focal dilation of the kidney in male F_{3b} pups.

Attachment 2 - Toxicological Summary for *N*-Acetyl-Glyphosate (IN-MCX20) and *N*-Acetyl-AMPA (IN-EY252)

N-Acetyl-Glyphosate (IN-MCX20)

1. Acute Oral LD_{50} was greater than 5000 mg/kg in rats (MRID 47007301)
2. In a 90-subchronic oral (feeding) toxicity, no systemic toxicity was observed in male and female rats at doses up to 18,000 ppm (equal to 1157/1461 mg/kg/day in males/females, respectively). This dose is considered well above the limit dose (1000 mg/kg/day), (MRID 47119201).
3. It was negative for mutagenicity in the following mutagenic battery:
    - Bacterial revesrse gene mutation assay (MRID 47007905)
    - Mouse micronucleus assay (MRID 47007904)
    - *In vitro* Chromosomal Aberration Assay in Chinese Hamster Ovary (CHO) cells (MRID 47007903)
    - *In vitro* Mammalian Cell Gene Mutation Assay in Chinese Hamster Ovary (CHO) cells (MRID 47007902)

N-Acetyl-AMPA (IN-EY252)

1. It is expected to be of low acute toxicity based on oral LD_{50} of 8300 mg/kg for aminomethylphosphonic acid (AMPA)
2. *N*-acetyl-AMPA was negative for mutagenicity in the following mutagenic battery:
    - *In vitro* bacterial mutagenicity (Ames) assay
    - *In vitro* chromosome aberration assay using human lymphocytes
    - *In vitro* mammalian cell mutagenicity (CHO/HGPRT) assay
    - *In vivo* mouse bone marrow assay
3. In-EY252 was detected as one of the metabolite formed following oral administration of *N*-acetyl-glyphosate.(IN-MCX20). It is not expected to be absorbed quickly from the GI tract since it is a charged molecule at the physiological pH. Therefore, it is expected to be less toxic than *N*-acetyl-glyphosate. The metabolism study with *N*-acetyl-glyphosate indicate that about 99% of the parent compound was isolated in the excreta. Less than 1% of glyphosate was isolated in feces (MRID 47007906).

Glyphosate has extensive toxicological database. It is not acutely toxic. In a subchronic toxicity study in mice, decreased body weight was observed at 4500 mg/kg/day with a NOAEL of 1500 mg/kg/day. No toxicity was observed in a 1 year toxicity study in dogs at doses up to 500 mg/kg/day. It is not a carcinogenic in rats and mice. It is negative for mutagenicity in a battery of mutagenic assays. It is not a developmental or reproductive toxicant. Based on structural similarity with glyphosate, SAR (lack of structural alerts for carcinogenicity, mutagenicity and endocrine effects), low acute toxicity, low subchronic toxicity and lack of mutagenicity, *N*-acetyl-glyphosate is considered as equally toxic to glyphosate. The toxicity of *N*-acetyl-AMPA is considered low and of limited concern based on the available data described above, lack of any structural alerts, and a metabolite of *N*-acetyl-glyphosate which is a charged molecule at the physiological pH.

13544

R158247

Chemical:	**Pyrithiobac** **Glyphosate-isopropylammonium** **Glyphosate**
	PC Code: **078905** **103601** ***417300***
HED File Code:	
Memo Date:	**3/18/2008**
File ID:	**DPD345923** **DPD348895** **DPD346713** ***DPD195332*** **DPD200041** **DPD321992** **DPD235143**
Accession #:	**000-00-0124**

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3/31/2008