Executive Summary

Glyphosate is a non-selective herbicide which acts via blocking the activity of the enzyme, 5-enolpyruvylshikimate 3-phosphate synthase (EPSPS). EPSPS is produced only by green plants and is involved in the synthesis of the amino acids tyrosine, tryptophan, and phenylalanine. Glyphosate is registered for use on a variety of fruit, vegetable, and field crops as well as for aquatic and terrestrial uses. Glyphosate is also registered for use on transgenic crop varieties such as canola, corn, cotton, soybeans, sugar beets, and wheat. The most recent human-health risk assessment for glyphosate was completed in 2006 (Memo, J. Tomerlin, 29-Sep-06, D321992). Since that risk assessment, HED has reviewed petitions for application of glyphosate to certain transgenic crops and concluded that revisions to the 29-Sep-2006 risk assessment were unnecessary at the time of review.

Glyphosate is of low acute toxicity following oral, dermal, and inhalation exposure. An acute dose and endpoint have not been selected for any population subgroups because no effects that could be attributed to a single exposure (dose) were observed in oral toxicity studies including the developmental toxicity studies in rats and rabbits. Glyphosate has been classified as a "Group E" chemical (evidence of non-carcinogenicity for humans), based upon lack of convincing evidence of carcinogenicity in adequate studies in two animal species (mice and rats). No significant reproductive or developmental toxic effects were found in toxicity studies in the rat and rabbit. Neurotoxicity has not been observed in any of the acute, subchronic, chronic, developmental, or reproductive studies performed with glyphosate. However, new data requirements which include the requirement of an acute neurotoxicity study and a subchronic neurotoxicity study, as well as an immunotoxicity study, have been established under 40 CFR Part 158 for registration of pesticides for food and non-food uses.

Aminomethylphosphonic acid (AMPA) is a metabolite of glyphosate. In 1992, the HED Metabolism Committee determined that, based on toxicological considerations, AMPA need not be regulated, and in 1994, it was determined that, based on toxicological considerations, AMPA need not be regulated regardless of levels observed in foods or feeds. *N*-acetyl-glyphosate is a metabolite of glyphosate which is formed in certain transgenic crops and is considered to be equally toxic as glyphosate (Memo, T. Bloem, 18-Mar-08, D345923). *N*-acetyl-AMPA was detected as one of the metabolites formed in these crops and was excluded as a residue of concern based on residue and toxicity considerations (Memo, T. Bloem, 18-Mar-08, D345923). The decision that AMPA and *N*-acetyl-AMPA need not be regulated, regardless of levels observed in foods or feeds, may be revisited during the registration review process.

The dietary-exposure database is adequate to support the existing registrations. An acute dietary-exposure assessment was not required because no acute toxicological endpoint has been determined for glyphosate. The 2006 chronic dietary-exposure assessment for glyphosate was conducted using the Dietary Exposure Evaluation Model - Food Consumption Intake Database (DEEM™-FCID, ver. 2.03), and incorporated tolerance-level residues, 100% crop treated data for all commodities, and worst-case scenario drinking water exposure estimates. The residue chemistry database is sufficient to support the current registrations; however, there are some outstanding studies for some of these registrations which, if submitted, would change the registration status from conditional to unconditional.

A new residential exposure risk assessment is required due to the registration of a new residential-use product with an application rate which is higher than the rate previously assessed. A new aggregate risk assessment will need to be conducted once the residential exposure risk assessment has been completed. The increase in the residential application rate is not expected to lead to residential exposures which exceed HED's level of concern (margins of exposure (MOEs)<100) or affect the aggregate risk in such a way that it exceeds HED's level of concern. No occupational handler or occupational post-application assessments were required because no short-term dermal or inhalation toxicity endpoints were identified by HED.

The U.S., Mexico, and Codex residue definitions are harmonized. There are discrepancies between the Canadian residue definition and residue definitions of the U.S., Mexico, and Codex. For some raw agricultural and livestock commodities, the tolerance and Maximum Residue Limits (MRLs) for the U.S., Canada, Mexico, and Codex are harmonized; however there are a variety of tolerances and MRLs for commodities which are not harmonized.

Introduction

HED has evaluated the status of the human-health assessments for glyphosate to determine if sufficient data are available and if any updates are required to support Registration Review. HED has considered the most recent human-health risk assessment for glyphosate (Memo, J. Tomerlin, 29-Sep-06, D321992); the most recent human-health risk assessment for glyphosate applied to transgenic crops (Memo, T. Bloem, 18-Mar-08, D345923); updates to its toxicity, exposure, and usage databases; and the most updated Agency science policy and risk assessment methodologies to determine the scope of work necessary to support Registration Review. In addition, HED conducted an open search to look for new literature relevant to the human-health risk assessment.

Glyphosate is a non-selective herbicide registered for use on a variety of fruit, vegetable, and field crops. Registered uses range from tree nuts, citrus, and grapes to corn, soybeans, cotton, and rice. Glyphosate is also registered for use on transgenic crop varieties such as canola, corn, cotton, soybeans, sugar beets, and wheat. Aquatic and terrestrial registered uses of glyphosate include non-selective control of nuisance aquatic weeds, ornamentals, greenhouses, residential areas, ornamental lawns and turf, fallow land, pastures, and nonagricultural rights-of-way. Glyphosate is formulated in liquid and solid forms, and it is applied using ground and aerial equipment. Application rates of glyphosate to food crops range from <1 pound (lb) of acid equivalent (ae) per acre (A) for a variety of crops to approximately 15 lb ae/A for spray and spot treatments of crops including tree nuts, apples, citrus, and peaches. Residential lawn and turf application rates range from <1 lb ae/A to approximately 10.5 lb ae/A.

The application timing of glyphosate is varied. Glyphosate can be applied early and late in the season, at pre-plant, planting, pre-emergence, pre-bloom, bud stage, pre-transplant, pre-harvest, post-plant, post-transplant, post-bloom, and post-harvest. It can also be applied during dormant stages and to fallow land, established plantings, stubble, and when needed.

Since the glyphosate RED (Reregistration Eligibility Decision) was completed in 1993, the following commodities have been assessed and registered: Aloe vera; Ambarella; Artichoke, globe; Bamboo, shoots; Betelnut; Biriba; Blimbe; Borage, seed; Cacao bean; Cactus, fruit; Cactus, pads; Canola, meal; Canola, seed; Cattle, kidney; Cattle, liver; Chaya; Crambe, seed; Custard apple; Dokudami; Durian; Egg; Epazote; Feijoa; Flax, meal; Flax, seed; Galangal, roots; Ginger, white, flower; Gourd, buffalo, seed; Governor's plum; Gow kee, leaves; Herbs subgroup 19A; Hop, dried cones; Ilama; Imbe; Imbu; Kava roots; Kenaf, forage; Lesquerella, seed; Leucaena, forage; Mangosteen; Meadowfoam, seed; Mioga, flower; Mustard, seed; Noni; Nut, pine; Okra; Oregano, Mexican, leaves; Palm heart; Palm heart, leaves; Papaya, mountain; Pawpaw; Pepper leaf, fresh leaves; Perilla, tops; Pulasan; Quinoa, grain; Rambutan; Rose apple; Safflower; Salal; Sapote, mamey; Sesame, seed; Spanish lime; Spice subgroup 19B; Star apple; Starfruit; Stevia, dried leaves; Strawberry; Surinam cherry; Teff, grain; Ti, leaves; Ti, roots; Ugli fruit; Wasabi, roots; Water spinach, tops; Watercress, upland; Wax jambu; and Yacon, tuber.

The qualitative nature of glyphosate residues in plants and livestock is adequately understood. The terminal residue to be regulated in nontransgenic plants and transgenic corn and canola modified to express the *Agrobacterium sp.* EPSPS and oxireductase genes is glyphosate *per se*. For crops (currently soybeans and corn) which have a transgenic variety that has been engineered to express the microbial glyphosate acetyltransferase gene (*gat*4601), the combined residues to be regulated are glyphosate and *N*-acetyl-glyphosate. The residue chemistry database is sufficient to support the current registrations; however, there are some outstanding studies which, if submitted, would change the registration status from conditional to unconditional.

Data needs and risk assessment updates required under registration review for glyphosate are as follows:

- An immunotoxicity study, acute neurotoxicity study, and a subchronic neurotoxicity are required as specified in the new 40 CFR Part 158 data requirements.
- Two toxicology studies (MRIDs 47311001 and 47311004) have been submitted which are still in the process of being reviewed. Once the reviews are complete, the reviews need to be added to the Integrated Hazard Assessment Database (IHAD).
- Nature of the residue studies in plants and livestock and ruminant and poultry feeding studies which were requested in recent HED Memos (Memo, T. Bloem, 18-Mar-08, D345923; and Memo, T. Bloem, 29-Oct-08, D357880) are still required.
- A new residential exposure risk assessment is required due to the registration of a new residential-use product with an application rate which is higher than the rate previously assessed.
- A new aggregate risk assessment is required once the residential exposure risk assessment has been completed.

Hazard Identification/Toxicology

Glyphosate
Glyphosate is a non-selective herbicide which acts via blocking the activity of EPSPS. EPSPS is produced only by green plants and is involved in the synthesis of the amino acids tyrosine, tryptophan, and phenylalanine.

Glyphosate is of low acute toxicity following oral, dermal, and inhalation exposure, since all studies are in Toxicity Category III or IV. It is a mild eye irritant (Toxicity Category III), slight skin irritant (Toxicity Category IV), and is not a dermal sensitizer in guinea pigs. Inhalation risk assessments (any time period) are not required based on the low toxicity of the formulation products (Toxicity Category III or IV) and the physical characteristics of the technical product (wet cake). An acute dose and endpoint have not been selected for any population subgroups because no effects that could be attributed to a single exposure (dose) were observed in oral toxicity studies including the developmental toxicity studies in rats and rabbits. Therefore, a dose and endpoint were not identified for acute dietary risk assessment.

A chronic feeding/carcinogenicity study in rats found no systemic effects in any of the parameters examined (body weight, food consumption, clinical signs, mortality, clinical pathology, organ weights, and histopathology). In a second chronic feeding/carcinogenicity study in rats tested at higher dietary levels, a lowest-observed-adverse-effect level (LOAEL) was identified at 20,000 parts per million (ppm; approximately 940 mg/kg/day) based on decreased body weight gains in the females and increased incidence of cataracts and lens abnormalities, decreased urinary pH, increased absolute liver weight, and increased relative liver weight/brain weight in males. No evidence of carcinogenicity was found in rats. There was also no evidence of carcinogenicity in mice. In a chronic toxicity study in dogs, no systemic effects were found in all examined parameters.

On 26-Jun-1991, the HED Carcinogenicity Peer Review Committee (CPRC) evaluated the weight of the evidence on glyphosate with particular emphasis on its carcinogenic potential. The Committee concluded that glyphosate should be classified as a "Group E" chemical (evidence of non-carcinogenicity for humans), based upon lack of convincing carcinogenicity evidence in adequate studies in two animal species (mice and rats).

Acceptable developmental toxicity studies in the rat and rabbit are available, as is an acceptable 2-generation reproduction study in the rat. No significant reproductive and developmental toxic effects were found. A focal tubular dilation of the kidneys was observed in a three-generation reproductive study on rats at the 30-mg/kg/day level [highest dose tested (HDT)], however a two-generational reproductive study on rats did not observe the same effect at the 1500-mg/kg/day level (HDT), nor were any adverse reproductive effects observed at any dose level. In 1991, the HED Reference Dose (RfD) Committee concluded that the focal tubular dilation of the kidneys at the 30-mg/kg/day level was a spurious rather than a glyphosate-related effect.

In a prenatal developmental toxicity study in rats, maternal (systemic) effects observed included mortality, increased clinical signs, and reduced body-weight gain at the HDT (3500 mg/kg/day). Developmental (fetal) effects were observed only in the high-dose group and included decreases

in total implantations/dam and nonviable fetuses/dam, increased number of litters and fetuses with unossified sternebrae, and decreased mean fetal body weights. In a prenatal developmental toxicity study in rabbits, maternal (systemic) effects observed included mortality and clinical signs of toxicity at the HDT (350 mg/kg/day). In the rabbits, developmental toxicity was not observed at any dose. On the basis of developmental studies in rats and rabbits and reproductive findings in rats, glyphosate exhibited no evidence of increased susceptibility of offspring.

Neurotoxicity has not been observed in any of the acute, subchronic, chronic, developmental, or reproductive studies performed with glyphosate. New data requirements have been established under the revised 40 CFR Part 158 for registration of pesticides for food and non-food uses which include the requirement of an acute neurotoxicity study and a subchronic neurotoxicity study (Attachment 5). Similarly, 40 CFR Part 158 also requires an immunotoxicity study (Attachment 6).

The endpoints used for risk assessment purposes from the most recent human-health risk assessment (Memo, J. Tomerlin, 29-Sep-2006, D321992) can be found in Attachment 2.

The Food Quality Protection Act (FQPA) Safety Factor Committee (SFC) met on April 6, 1998 and addressed the potential enhanced sensitivity to infants and children as required by the FQPA (Memo, B. Tarplee, 17-Apr-98, TXR012584). The Committee recommended the 10x FQPA SF be reduced to 1x in assessing the risk posed by this chemical because: 1) there is no evidence of quantitative or qualitative increased susceptibility of the young demonstrated in the prenatal developmental studies in rats and rabbits and pre/post natal reproduction study in rats; 2) the toxicology database is adequate for FQPA assessment; 3) a developmental neurotoxicity study is not required and there was no evidence of neurotoxicity in any submitted study; and 4) the dietary (food and drinking water) exposure assessments will not underestimate the potential exposures for infants and children.

AMPA

AMPA is a metabolite of glyphosate. In a 90-day oral toxicity study in rats, a LOAEL was identified for AMPA at 1200 mg/kg/day based on body weight loss and histopathological lesions of the urinary bladder. Previously the HED Metabolism Committee determined that, based on toxicological considerations, AMPA need not be regulated and should be dropped from the tolerance expression (Memo, R.B. Perfetti, 19-Aug-92). Furthermore, in a 17-Mar-94 meeting, the HED Metabolism Committee discussed whether uses that result in significantly higher residues of AMPA in plants and livestock commodities in the future would require that AMPA be reintroduced into the tolerance expression of glyphosate. (1) The Committee determined that, based on toxicological considerations, AMPA need not be regulated regardless of levels observed in foods or feeds (Memo, R.B. Perfetti, 17-Mar-94).

N-Acetyl-Glyphosate

N-acetyl-glyphosate is a metabolite of glyphosate which is formed in certain transgenic crops. The acute oral LD_{50} was greater than 5000 mg/kg in rats. Based on structural similarity with glyphosate, structure-activity relationships [(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 to be equally toxic as glyphosate.

(1) En ce qui concerne l'AMPA HED Metabolism Comité considère qu'en se basant sur des considérations environnementales, l'AMPA n'a pas besoin d'être régulé au niveau des faibles niveaux observés dans les aliments. (1994).

N-Acetyl-AMPA
N-acetyl-AMPA is a minor metabolite of glyphosate which is formed in certain transgenic crops. *N*-acetyl-AMPA is expected to be of low acute toxicity and was negative for mutagenicity. It is not expected to be absorbed quickly from the gastrointestinal (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 in rats with *N*-acetyl-glyphosate indicated that about 99% of the parent compound was isolated in the excreta. Based on this and the minimal plant residue concentrations, *N*-acetyl-AMPA was excluded as a residue of concern.

EPA is required under the Federal Food, Drug, and Cosmetic Act (FFDCA), as amended by FQPA, to develop a screening program to determine whether certain substances (including all pesticide active and other ingredients) "may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." Following the recommendations of its Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC), EPA determined that there were scientific bases for including, as part of the program, androgen and thyroid hormone systems, in addition to the estrogen hormone system. EPA also adopted EDSTAC's recommendation that the Program include evaluations of potential effects in wildlife. When the appropriate screening and/or testing protocols being considered under the Agency's Endocrine Disrupter Screening Program (EDSP) have been developed and vetted, glyphosate may be subjected to additional screening and/or testing to better characterize effects related to endocrine disruption.

Conclusions
As specified in the new 40 CFR Part 158 data requirements, immunotoxicity, acute neurotoxicity, and subchronic neurotoxicity studies should be conducted. The decision that AMPA need not be regulated, regardless of levels observed in foods or feeds, may be revisited during the registration review process.

Residue Chemistry

The qualitative nature of glyphosate residues in plants and livestock is adequately understood. Metabolism studies conducted with nontransgenic corn, cotton, soybeans, and wheat were previously submitted and reviewed. Based on these data, HED concluded that the residue of concern in/on nontransgenic plants is glyphosate *per se* (Memo, R. Perfetti, 19-Aug-1992; Memo, R. Perfetti, 27-Oct-1992, D183202; Memo, R. Perfetti, 17-Mar-1994). Metabolism studies have also been submitted on glyphosate-tolerant canola (Memo, T. Bloem, 30-Nov-1998, D242628) and glyphosate-tolerant corn (Memo, G. Kramer, 14-Mar-1996, D217539). The glyphosate-tolerant canola and corn were genetically modified to express the EPSPS gene derived from *Agrobacterium sp.* (strain CP4) which codes for an EPSPS protein that has reduced affinity for glyphosate as compared to the endogenous EPSPS protein. The glyphosate-tolerant canola and corn were also genetically engineered to express the oxireductase gene which converts glyphosate to the nonherbicidal AMPA. Metabolism in these varieties of transgenic canola and corn was essentially the same as the nontransgenic plants. Therefore, it was concluded that the terminal residue to be regulated in nontransgenic plants and transgenic corn

and canola modified to express the *Agrobacterium sp.* EPSPS and oxireductase genes is glyphosate *per se*.

Subsequent to this decision, DuPont submitted and HED approved a request permitting the commercialization of a new transgenic variety of soybean [Optimum™ GAT™ soybean (DP-356Ø43-5)]. The 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 (results in formation of the nonherbicidal *N*-acetyl-glyphosate). As a result of the introduction of this seed line, HED concluded that the residues of concern in/on plants for tolerance expression and risk assessment should changed from glyphosate *per se* to the combined residues of glyphosate and *N*-acetyl-glyphosate (T. Bloem, 12-Mar-2008, D346713). Following this decision, it was determined that only the tolerance expression for soybeans would change from glyphosate *per se* to the combined residues of glyphosate and *N*-acetyl-glyphosate; the tolerance expression for all other crops would remain as glyphosate *per se*. Studies were then submitted by DuPont and reviewed by HED for Optimum™ GAT™ field corn, a transgenic variety of corn which expresses the microbial glyphosate acetyltransferase gene (*gat*4601). This submission resulted in a change to the tolerance expression for field corn from glyphosate *per se* to the combined residues of glyphosate and *N*-acetyl-glyphosate (Memo, T. Bloem, 29-Oct-08, D357880).

The residue chemistry database is sufficient to support the current registrations; however, there are some outstanding studies regarding the recent Optimum™ GAT™ soybeans and Optimum™ GAT™ field corn submissions which, if submitted, would change the registration status from conditional to unconditional (Memo, T. Bloem, 18-Mar-08, D345923; and Memo, T. Bloem, 29-Oct-08, D357880). The requested studies include nature of the residue studies in plants and livestock, and ruminant and poultry feeding studies. See the data requirements section for more information.

Conclusions

(2) The qualitative nature of glyphosate residues in plants and livestock is adequately understood. The terminal residue to be regulated in nontransgenic plants and transgenic corn and canola modified to express the *Agrobacterium sp.* EPSPS and oxireductase genes is glyphosate *per se*. For crops (currently soybeans and corn) which have a transgenic variety that has been engineered to express the microbial glyphosate acetyltransferase gene (*gat*4601), the combined residues to be regulated are glyphosate and *N*-acetyl-glyphosate. The residue chemistry database is sufficient to support the current registrations; however, there are some outstanding studies which, if submitted, would change the registration status from conditional to unconditional.

Dietary Exposure

The most recent chronic dietary-exposure assessment was performed in conjunction with the September 2006 human-health risk assessment. No toxicological endpoint attributable to a single dose of glyphosate was identified by HED; therefore, an acute dietary-exposure assessment was not conducted. Glyphosate is classified as not likely to be a human carcinogen, so a cancer dietary-exposure analysis is not required. Chronic dietary risk assessments were conducted using DEEM™-FCID, ver. 2.03. DEEM™-FCID incorporates the food consumption

(2) Conclusions : les résidus de G dans la nature (dans les plants) n'est pas très bien compris.

data from the United States Department of Agriculture's (USDA's) Continuing Surveys of Food Intakes by Individuals (CSFII; 1994-1996 and 1998).

The chronic analyses incorporated tolerance-level residues, 100% crop treated data for all commodities, and drinking water exposure estimates. The analysis used drinking water estimates from the direct application of glyphosate to water (230 ppb), which is the most conservative drinking water estimate. EFED has confirmed that the concentration estimate from the direct application of glyphosate to water is still the worst-case scenario estimate for the possible concentration of glyphosate in water.

Based on the 2006 analysis, the chronic exposure estimate of the U.S. population is 2% of the chronic population-adjusted dose (cPAD) and is, therefore, less than HED's level of concern (<100% of the cPAD). Infants <1 year old represent the most highly exposed population subgroup at 7% of the cPAD.

Conclusions

The dietary-exposure database is adequate to support the existing registrations. HED does not require a new chronic dietary risk assessment at this time because the most recent assessment incorporated concentration estimates from the direct application of glyphosate to water, and these estimates still represent the worst-case scenario. If any decisions regarding residues requiring regulation are made during the registration review process, a new dietary-exposure analysis may be required.

Residential Exposure

Glyphosate, a non-selective herbicide, is registered for broadcast and spot treatments on home lawns and gardens. Glyphosate products for homeowner use are packaged as ready-to-mix formulations and ready-to-use sprayers and are common in home and garden stores in the U.S. Glyphosate products are used by lawn care operators (LCOs) for broadcast and spot treatment weed control programs on homeowner lawns. Glyphosate products are also labeled for turf renovation.

Glyphosate is registered for use in recreational areas, including parks and golf courses for control of broadleaf weeds and grasses. Additional registered uses include applications to lakes and ponds, including reservoirs, for non-selective control of nuisance aquatic weeds.

Residential Handlers

Based on the registered residential use patterns, there is a potential for short-term dermal and inhalation exposures to homeowners who mix and apply products containing glyphosate (residential handlers). However, since short- and intermediate-term dermal or inhalation endpoints were not selected, no residential handler assessment is needed.

Residential Post Application

Post-application dermal and inhalation assessments are not needed since short- and intermediate-term dermal or inhalation endpoints were not selected. However, based on the registered use patterns, toddlers may have short-term post-application incidental oral exposures from hand-to-

mouth behavior on treated lawns and swimmers may to have short-term post-application incidental oral exposures from aquatic uses.

The Agency previously assessed post-application incidental oral ingestion exposure for toddlers in the most recent HED human-health risk assessment (Memo, J. Tomerlin, 29-Sep-2006, D321992). The standard operating procedures (SOPs) for Residential Exposure Assessments, Draft, 17-Dec-1997 and Exposure Science Advisory Committee (ExpoSAC) Policy No. 11, 22-Feb-2001: Recommended Revisions to the SOPs for Residential Exposure were used to estimate post-application incidental oral ingestion exposures and risk estimates for toddlers.

Also assessed were incidental oral exposures for adult, children, and toddler swimmers may have short-term post-application incidental ingestion exposures. The exposure assumptions used in the swimmer assessment are based on HED's Standard Operating Procedures for Residential Exposure Assessments, Draft, 17-Dec-1997 and subsequent updates for swimming pools adapted for this assessment, but the Residential SOP assumptions are considered conservative for use in assessing this scenario.

While adult and child golfers may have short-term post-application dermal exposure at golf courses, no dermal assessments were required because HED did not identify short- or intermediate-term dermal endpoints.

In the 2006 risk assessment, the MOEs for post-application toddler oral exposures were calculated using the highest application rate (1.62 lb ae/A) registered at the time of assessment. All of these MOEs were greater than 100 and did not exceed HED's level of concern for residential exposures (MOEs <100). In October of 2008, a new residential use product (Roundup® Weed & Grass Killer Super Concentrate; EPA Reg. No. 71995-25) was registered which has a higher application rate (10.5 lb ae/A). This new application rate is not expected to lead to residential exposures which exceed HED's level of concern (MOEs <100); however, a new residential exposure risk assessment is required.

MOEs for post-application exposure of swimmers to glyphosate after aquatic weed control applications are greater than 100 and do not exceed HED's level of concern for short-term non-occupational (recreational) exposures (MOEs <100). See Attachment 3 for a table which summarizes residential post-application use patterns and corresponding MOEs. Based on the new residential use product (EPA Reg. No. 71995-25) which has a higher rate of application (10.5 lb ae/A), the residential exposures and MOEs for toddlers presented in Attachment 3 will change; however the increased application rate is not expected to lead to exposures which exceed HED's level of concern for residential exposures (MOEs <100). These changes will be reflected in the new residential exposure risk assessment.

Conclusions

There is sufficient information available to assess residential exposure. A new residential exposure risk assessment is required due to the registration of a new residential-use product with an application rate which is higher than the rate previously assessed. The new application rate is not expected to lead to residential exposures which exceed HED's level of concern (MOEs <100).

Attachment 3: Exposure Potential for Adult and Child Short-term Aggregate Risk Estimates

Table 5. Exposure Potential for Adult and Child Short-term Aggregate Risk Estimates[1].					
Exposure Scenario		**Exposure (Dose) mg ai/kg bw/day**	**MOE**	**Combined Exposure (Dose) mg/kg/day[2]**	**Combined MOE[3]**
Toddler – Treated Turf[4]	Incidental oral hand-to-mouth post-application exposure from contacting treated turf	0.0242	7,230	0.03025	5,800
	Incidental oral post-application exposure from ingestion of treated soil	8.13×10^{-5}	$>10^6$		
	Incidental oral post-application exposure from object-to-mouth	0.00605	28,900		
Toddler – Swimmer	Incidental oral post-application exposure from contacting treated water	0.023	7,610	--	--
Adult – Swimmer	Incidental oral post-application exposure from contacting treated water	0.00493	35,500	--	--

[1] Source of information: Memo, J.R. Tomerlin, 29-Sep-06, D321992.

[2] Combined exposure (dose) (mg/kg/day) = $Dose_{Hand\text{-}to\text{-}mouth} + Dose_{soil\ ingestion} + Dose_{Object\text{-}to\text{-}mouth}$.

[3] Combined MOE = NOAEL (175 mg/kg/day) / Combined exposure (dose) (mg/kg/day).

[4] The residential exposures will change based on the new residential use product (EPA Reg. No. 71995-25) which higher rate of application (10.5 lb ae/A); however the increased application rate is not expected to lead to exposures which exceed HED's level of concern for residential exposures (MOEs <100). The new residential exposure risk assessment will reflect the change in rate of application.

Attachment 4: International Residue Limit Status

Table 6. Summary of U.S. Tolerances and International MRLs.				
U.S.		**Canada**	**Mexico[1]**	**Codex**
Residue Definition:				
40CFR180.364 glyphosate *N* -phosphonomethyl)glycine resulting from the application of glyphosate, the isopropylamine salt of glyphosate, the ethanolamine salt of glyphosate, the dimethylamine salt of glyphosate, the ammonium salt of glyphosate, and the potassium salt of glyphosate.		*N*-(phosphonomethyl) glycine, including the metabolite amino methylphosphonic acid (AMPA)	Glyphosate	#158 For compliance with MRLs in plant and animal commodities: Glyphosate.
Commodity Tolerance (ppm) /Maximum Residue Limit (mg/kg)				
Commodity	U.S.	Canada	Mexico	Codex
Acérola	0.2			
Alfalfa, seed	0.5			
Almond, hulls	25			
Aloe vera	0.5			
Ambarella	0.2			