OVERVIEW OF ASULAM RISK ASSESSMENT

August 2, 2002

Introduction

The Agency has completed its review and announces the tolerance reassessment decision for asulam. This decision also releases to the public the human health assessment, as presented fully in the document entitled "Asulam: HED Human Health Assessment for the Tolerance Reassessment Eligibility Decision (TRED)" dated February 28, 2002, and related documents supporting this decision. The purpose of this overview is to assist the reader by identifying the key features and findings of this risk reassessment in order to better understand the conclusions reached in the tolerance reassessment. This overview was developed in response to comments and requests from the public, which indicated that the risk assessments (and other like documents) were difficult to understand, that they were too lengthy, and that it was not easy to compare the assessments for different chemicals due to the use of different formats.

FFDCA requires the Agency to review all the tolerances for registered chemicals in effect on or before the date of the enactment of FQPA. In reviewing these tolerances, the Agency must consider, among other things, aggregate risks from non-occupational sources of pesticide exposure, whether there is increased susceptibility to infants and children, and the cumulative effects of pesticides with a common mechanism of toxicity. The tolerances are considered reassessed once the safety finding has been made or a tolerance revocation occurs. A reregistration eligibility decision (RED) for asulam was completed in September 1995, prior to FQPA enactment; therefore it needed to be updated to consider the provisions of the Act.

FQPA requires that the Agency, when considering whether to establish, modify, or revoke a tolerance, consider "available information" concerning the cumulative effects of the particular pesticide's residues and "other substances that have a common mechanism of toxicity." The Agency does not, at this time, have sufficient reliable information available to determine whether asulam has a common mechanism of toxicity with other substances. Therefore, for the purposes of this risk assessment, the Agency has not assumed that asulam has a common mechanism of toxicity with other substances. If EPA identifies other substances that share a common mechanism of toxicity with asulam, a cumulative risk assessment for those substances will be performed.

The risk assessment and documents pertaining to the Agency's report on FQPA tolerance reassessment progress and decision for asulam are available on the Internet at http://www.epa.gov/pesticides/reregistration/status.htm and in the public docket. Because the risks posed by the use of asulam are low and not of concern to the Agency, the normal process of meeting stakeholders (i.e., growers, extension offices, environmental and commodity groups, and other government offices) to discuss risks of concern and solicit input on risk mitigation strategies was not necessary for this chemical. Rather, the Agency's report on FQPA tolerance

reassessment progress and interim risk management decision for asulam will be announced in the Federal Register. Since there are no risk concerns for asulam alone, no further actions are warranted at this time pending a determination of whether a cumulative risk assessment for asulam may be needed and is completed.

Risks summarized in this document are those that result only from the use of asulam. The Food Quality Protection Act (FQPA) requires that the Agency consider "available information" concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity." Since it is possible that this chemical and other substances could share a common mechanism of toxicological action, adverse health effects and cumulative low-level exposures, this review needs to consider this potential interaction.. The Agency did not perform a cumulative risk assessment as part of this tolerance reassessment of asulam because the Agency has not yet initiated a review to determine if there are any other chemical substances that have a mechanism of toxicity common with that of asulam. If the Agency identifies other substances that share a common mechanism of toxicity with asulam, then a cumulative risk assessment will be conducted that includes asulam once the final framework the Agency will use for conducting cumulative risk assessments is available. Asulam's potential contribution to cumulative risk be reevaluated at that time and additional studies may be required.

Use Profile

Herbicide: Asulam (methyl sulfanilylcarbamate) is a selective postemergent systemic carbamate herbicide registered for sugarcane, Christmas tree plantations, ornamentals, turf (use for sod farms only) and non-cropland uses (boundary fences, fencerows, hedgerows, lumberyards, storage areas and industrial facilities, and warehouse lots). There are no residential uses for asulam products.

Targeted Weeds: western brackenfern, marestail, horseweed, alexandergrass, barnyardgrass, broadleaf panicum, bullgrass, crabgrass, foxtail, goosegrass, itchgrass, johnsongrass, paragrass, and sandbur.

Formulations: The only end-use formulation of asulam is the sodium salt of asulam (sodium salt of methyl sulfanilylcarbamate) which is formulated as soluble concentrate/liquid (36.2% a.i.).

Methods of Application: Apply to sugarcane as broadcast, band, or spot treatment with ground equipment or broadcast by air at 3.34 pounds active ingredient/acre (lb ai/A). Apply to Christmas trees as a delayed dormant spray with air or ground equipment at 3.34 lb ai/A. Apply to ornamental and/or shade trees or ornamental woody shrubs and vines as a postemergence ground broadcast at 3.34 lb ai/A. Apply to ornamental lawns and turf as a postemergence spray with ground equipment at 2.088 lb ai/A. Apply to industrial areas (outdoor), nonagricultural rights-of-way/fencerows, or nonagricultural uncultivated areas when needed as spray with ground equipment at 3.34 lb ai/A.

Use Summary: Based on pesticide usage information mainly for 1992 through 2000 for agriculture and 1994 through 1999 for non-agriculture, total annual domestic usage of sodium asulam is approximately 1.3 million pounds active ingredient allocated by site mainly to sugarcane (95%), lawn care operators and sod farms (2% each) and institutional turf (1%). The average percent crop treated for sugarcane, the only registered agricultural crop, is about 42%, while its average use rate per acre is 2.5 pounds a.i. per application and 3.0 pounds a.i. per year. Generally, asulam is applied once per season with a follow-up spot application to clean up field ends. States with the most usage are Florida, Louisiana, and Texas.

Registrant: Aventis CropScience

Classification: General Use

Table 1. Asulam Usage

Crop	Acres Grown (000)	Acres Treated (000)		% Crop Treated		Lbs A.I. Applied (000)		States of Most Usage (% of lbs a.i. Used)
		Avg	Max	Avg	Max	Avg	Max	
Sugarcane	939	398	498	42%	53%	1,211	1,513	FL LA TX (100%)
Lawn Care Operators[1]	-	-	-	-	-	26	40	FL 100%
Sod Farms	-	-	-	-	-	21	32	FL (most)
Institutional Turf[2]	-	-	-	-	-	17	25	-
Ornamentals	-	-	-	-	-	3	4	FL TX
Golf Courses	-	-	-	-	-	2	3	FL GA
TOTALS	-	-	-	-	-	1,280	1,600	FL LA (97%)

COLUMN HEADINGS
Avg = Weighted average in which the most recent years and more reliable data are weighted more heavily.
Max = Estimated maximum, which is estimated from available data.
[1] Lawn Care operators make applications to commercial, not residential, turf
[2] Institutional turf consists of maintained turf of educational facilities, cemeteries, and parks.

Human Health Risk Assessment

Hazard

The acute toxicity of asulam is low. The acute oral LD_{50} for asulam in rats exceeded 5000 mg/kg. The acute inhalation LC_{50} was greater than 5 mg/L in rats. The acute dermal LD_{50} for asulam in rabbits exceeded 4000 mg/kg. Application of technical asulam to rabbit eyes produced mild chemosis, irritation, and redness which cleared by day seven post-treatment. Asulam was not an irritant in a primary skin irritation study in rabbits. It did not cause dermal sensitization in guinea pigs.

Acute Dietary (Food) Risk

Acute dietary risk is estimated based on may be eaten in one day. Acute dietary exposure that is less than 100% of the acute Population Adjusted Dose (aPAD) does not exceed the Agency's level of concern. The aPAD is the reference dose (RfD)adjusted for the FQPA Safety Factor. The acute RfD is the dose at which an individual could be exposed in a single day with no adverse health effects expected.

An acute dietary risk assessment was not conducted for asulam because no appropriate toxicological endpoint clearly attributable to a single exposure was identified. Therefore, an acute reference dose (aRfD) was not established.

Chronic Dietary (Food) Risk

Chronic dietary risk is calculated by using the average consumption values for food and average residue values on those foods over a lifetime or the duration of exposure assessed (i.e., 1 year for infants, 6 years for children ages 1-6 years and 37 years for females of childbearing age 13-50 years old.). Chronic dietary exposure that is less than 100% of the chronic Population Adjusted Dose (cPAD) does not exceed the Agency's level of concern. The cPAD is the chronic reference dose (cRfD) adjusted for the FQPA Safety Factor. The chronic RfD is the dose at which an individual could be exposed over the course of a lifetime with no adverse health effects expected.

The chronic dietary assessment for asulam and its degradate sulfanilamide was conducted using a Tier II analysis which assumes anticipated residues from field trial data and includes percent crop treated estimates. No monitoring data exist for asulam. The chronic dietary exposure analysis is conducted using the Dietary Exposure Evaluation Model (DEEM™). A three-day average of consumption for each subpopulation is combined with tolerance residues in commodities to determine average exposures in mg/kg/day.

- The toxicity endpoint for the chronic dietary was based on hyperplastic changes in the adrenal medulla and thyroid follicular cells on males in a rat study (NOAEL=36 mg/kg/day). The effects were observed at 180 mg/kg/day (LOAEL).

- The uncertainty factor is 1000x; 10x for individual variability and 10x for intraspecies extrapolation. An additional 10x was added due to increased susceptibility in offspring/fetuses based on evidence of mean live births per litter. The FQPA Safety Factor was retained because (i) there was evidence of quantitative susceptibility in a two-generation reproduction study in the rat; and, (ii) the Agency does not have data that includes an examination of the thyroid gland; therefore, the Agency recommended the requirement for a comparative thyroid rat assay in adults and offspring to examine thyroid weight and pathology.

- A chronic Reference Dose (cRfD) of 0.36 mg/kg/day was established based on the NOAEL of 36 mg/kg/day, and a 100X uncertainty factor for interspecies extrapolation,

and intraspecies variability. An additional safety factor of 10X was applied to the cRfD to account for quantitative increased susceptibility in offspring/fetuses resulting in a chronic Population Adjusted Dose (cPAD) of 0.036 mg/kg/day.

- Chronic dietary (food) risks for asulam and its degradate are below the Agency's level of concern for the general U.S. population and all population subgroups (<1% of the cPAD).

Table 2. Summary of Toxicity Endpoints and Doses for Risk Assessment

EXPOSURE SCENARIO	DOSE (mg/kg/day)	ENDPOINT	STUDY
Acute Dietary	An appropriate endpoint attributable to a single dose was not identified.		
	Acute RfD = not established		
Chronic Dietary	NOAEL[1] = 36 mg/kg/day UF = 100 FQPA Safety Factor = 10	The LOAEL[2] was 180 mg/kg/day based on hyperplastic changes in the adrenal medulla and in thyroid follicular cells of males.	Combined Chronic Toxicity/Oncogenicity in the rat
		Chronic RfD = 0.36 mg/kg/day **Chronic PAD = 0.036 mg/kg/day**	

NOAEL[1] = no observed adverse effect level.
LOAEL[2] = lowest observed adverse effect level.

Table 3. Results of Chronic Dietary Exposure Analysis

Population Subgroup	cPAD (mg/kg/day)	Exposure (mg/kg/day)	% cPAD
U.S. Population (total)	0.036	0.000157	<1%
All Infants (< 1 year)	0.036	0.000300	<1%
Children 1-6 years	0.036	0.000449	1%
Children 7-12 years	0.036	0.000275	<1%
Females 13-50 years	0.036	0.000107	<1%
Males 13-19 years	0.036	0.000185	<1%
Males 20+ years	0.036	0.000105	<1%
Seniors 55+ years	0.036	0.000087	<1%

Cancer Dietary (Food) Risk

EPA previously classified Asulam as a Group C, possible human carcinogen, based on available studies in rats and mice. Based on the weight-of-evidence of all available data, a quantitative estimation of cancer risk to humans was not performed. A recent re-evaluation of the data (including a second mouse study) reaffirmed the Agency's previous conclusion that a quantitative estimation of cancer risk to humans is not appropriate.

Drinking Water Dietary Risk

Drinking water exposure to pesticides can occur through surface and/or ground water contamination. EPA considers acute (one day) and chronic (lifetime) drinking water risks and uses either modeling or actual monitoring data, if available, to estimate those risks. Modeling is carried out in tiers of further refinement, and is designed to provide a high-end estimate of exposure. To determine the maximum allowable contribution from water allowed in the diet, EPA first looks at how much of the overall allowable risk is contributed by food and then determines a "Drinking Water Level of Comparison" (DWLOC) to ascertain whether modeled or monitored Estimated Environmental Concentrations (EECs) exceed this level. EECs that are above the corresponding DWLOC are of concern to the Agency.

Based on environmental fate data, asulam is very mobile and has a strong potential to leach into ground water or move offsite into surface water. Sulfanilamide is a major soil and water degradate of asulam. Since there are no residential uses associated with asulam, only dietary exposure from food is considered for purposes of calculating the DWLOC.

A drinking water assessment for asulam involved analysis of FIRST (Tier I-surface water) computer modeling to estimate surface water concentrations. Estimated drinking water concentrations for ground water are based on a groundwater study that sampled potable wells in Florida and Louisiana that were located within 1,000 feet of an asulam treated area. The monitoring study was compared to SCI-GROW (Tier I-ground water) modeling which had lower detectable traces of asulam residues. This assessment includes concentrations of parent asulam and the degradate sulfanilamide.

- For chronic risk, potential exposure to asulam (combined with sulfanilamide) from drinking water derived from surface water results in a chronic EEC of 272 ppb, and for groundwater the chronic EEC is 154 ppb. Upon comparison of the chronic DWLOCs (1,254 ppb for males; 1,075 ppb for females; and 355 ppb for children) with the EECs for residues in surface and groundwater, all EECs are less than the chronic DWLOCs for all populations. Therefore, the Agency is not concerned with potential chronic exposure to asulam through surface and groundwater.

Table 4. Drinking Water DWLOC and EEC Comparisons

Population Subgroup		EECs (ppb)	
	Chronic	Ground Water	Surface Water
Adult males	1254	154	272
Adult Females	1075		
Children (1-6 years)	335		

Residential Risk

Potential residential exposures are not anticipated as a result of applications of asulam. Use sites include Christmas tree plantings, turf (for sod only), ornamentals (junipers & yews only), and non-cropland (e.g. rights-of-way, fence rows, etc.). The amount of asulam used annually on use sites other than sugarcane is approximately 12,000 gallons. Of these use sites, no residential exposures would be anticipated from the Christmas tree plantings and non-cropland sites. The use on turf is restricted to sod farms, and the application to the sod is made four to five months prior to the sod being pulled up and subsequently sold. Therefore, no residential exposures would be anticipated from the turf/sod use. The registrant stated that use of asulam on ornamentals is very limited, since its cost is high. Use of asulam on ornamentals in a residential setting would not be expected.

Aggregate Risk

In examining aggregate exposure, EPA takes into account the available and reliable information concerning exposures from pesticide residues in food and other exposures including drinking water and non-occupational exposures, e.g., exposure to pesticides used in and around the home (residential). The aggregate risk assessment for asulam considered only chronic exposures since acute dietary and water exposures are not expected to be toxicologically significant. There are no residential uses of asulam. Therefore, the considerations for aggregate exposure are those from food and water.

- Combining both the chronic dietary (food) risk estimates with the surface and ground water estimated concentrations (drinking water) for asulam, the chronic aggregate (food + drinking water) are below EPA levels of concern. Chronic dietary risks estimates for all populations are less than 100% of the cPAD. Upon comparison of the chronic DWLOCs with the EECs for residues of asulam in surface and groundwater, all EECs are less than the chronic DWLOCs for all populations.

Occupational and Ecological Risk

Because asulam is under review for tolerance reassessment only, no occupational or ecological risk assessment was conducted for this TRED. Occupational and ecological risk management decisions were made as part of the 1995 Asulam RED and have been implemented.

Tolerance Reassessment Summary

Sufficient data are now available to reassess all tolerances associated with asulam use listed in 40 CFR § 180.360. The Agency recommends that the tolerance expression be revised to include all metabolites containing the sulfanilamide moiety. Some product chemistry deficiencies remain outstanding, but they do not impact the tolerance reassessment eligibility decision. However, the registrant needs to resolve all outstanding deficiencies as listed below.

- The existing tolerance of 0.1 ppm for asulam residues on sugar cane established in 40 CFR§ 180.360 has been reassessed. The Agency recommends the tolerance be raised to

1.0 ppm.

- EPA recommends a tolerance of 30 ppm for asulam residues in molasses from sugarcane be established in 40 CFR§ 180.360.

- Based on diets containing 10% molasses in feed, EPA recommends a tolerance of 0.05 ppm for asulam residues in milk, meat, and fat from cattle, goats, hogs, horses, and sheep be established in 40 CFR§ 180.360.

- Based on diets containing 10% molasses in feed, EPA recommends a tolerance of 0.2 ppm for asulam residues in meat byproducts from cattle, goats, hogs, horses, and sheep be established in 40 CFR§ 180.360.

Table 5. Tolerance Reassessment Summary

Commodity	Current Tolerance (ppm)	Tolerance Reassessment (ppm)	Comment
Tolerances listed under 40 CFR §180.360			
Sugarcane, cane	0.1	1.0	
Tolerances to be Established Under 40 CFR §180.360			
Sugarcane, molasses	-	30	
Milk	-	0.05	
Cattle, meat Cattle, fat Goat, meat Goat, fat Hog, meat Hog, fat Horse, meat Horse, fat Sheep, meat Sheep, fat	-	0.05	
Cattle, meat byproducts Goat, meat byproducts Hog, meat byproducts Horse, meat byproducts Sheep, meat byproducts	-	0.2	

Summary of Pending Data

The following deficiencies were noted and remain outstanding:

- GLN 860.1200: Directions for Use
- GLN 830.6317: Storage Stability
- GLN 830.6320: Corrosion Characteristics
- GLN 870.3200: 21-day Dermal Study in Rats with examination of thyroid weight and pathology
- No GLN: 28 - day Inhalation Study in Rats with examination of thyroid weight and pathology. The guidelines for this study are under development.
- No GLN: Comparative thyroid rat assay in adult and offspring. The adult study should include interim measures (e.g.,7,14, and 28 days). The thyroid parameters selected for the comparative study should be based on Agency guidelines (under current development) for thyroid testing.