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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

February 28, 2002

MEMORANDUM

SUBJECT: Asulam. HED Human Health Assessment for the Tolerance Reassessment Eligibility Decision (TRED). Chemical No. 106901/02. No MRID #. DP Barcode No. D276505.

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This memorandum and attachments are the Health Effects Division's Tolerance Reassessment Eligibility Decision Document (TRED) for asulam, taking into consideration requirements of the 1996 Food Quality Protection Act (FQPA). This assessment only discusses the human health risk assessment required for reassessment of tolerances and does not include an occupational risk assessment required for reregistration of products. Cumulative risk assessment considering risks from other pesticides which may have a common mechanism of toxicity is also not addressed in this document.

Attachments:
Hazard Identification Review Committee (HIARC) report (J. Liccione, 12/6/01)
FQPA Committee Report (C. Christensen, 2/5/02)
Toxicology Chapter (J. Liccione, 12/12/01)
Chemistry Chapter (J. Morales, 12/6/01)
Dietary Exposure Analysis (J. Morales, 12/18/01)
Drinking Water Assessment to Support the TRED for Asulam (N. Birchfield, 1/8/02)

ASULAM

HED's HUMAN HEALTH RISK ASSESSMENT

1.0 Executive Summary

The Health Effects Division (HED) has conducted a human health risk assessment for **asulam** for the purpose of making a Tolerance Reassessment Eligibility Decision. HED evaluated the toxicology, residue chemistry, and residential databases for asulam and determined that the data are adequate to support a Tolerance Reassessment Eligibility Decision (TRED).

Use Profile

Asulam (methyl sulfanilylcarbamate) is a selective, postemergent systemic, carbamate herbicide whose chemical structure and biological properties differ considerably from those of carbamate insecticides. It is structurally related to chlorpropham and phenmedipham. It has no registered residential uses. Therefore, potential residential exposures are not anticipated as a result of applications of asulam. Use sites include sugarcane (the only registered food use), Christmas tree plantings, turf (for sod only), ornamentals (junipers & yews only), and non-crop land (e.g., rights-of-way, fence rows, etc.). Sugarcane represents 95 percent of asulam utilization; therefore, the remaining five percent is utilized on the other use sites.

Hazard Profile

The toxicity database for asulam included asulam technical (98 - 100% ai) and the sodium salt of asulam (88% ai). 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.

Subchronic and chronic toxicity studies demonstrate that the thyroid gland is a target organ for asulam in the rat and dog. Thyroid findings, consisting of hyperplastic changes in thyroid follicular cells in male rats reported in a two-year combined chronic/oncogenicity feeding study were observed at the lowest-observed-adverse-effect-level (LOAEL) of 180 mg/kg/day; the no-observed-adverse-effect-level (NOAEL) was 36 mg/kg/day. The chronic RfD for asulam is derived from the NOAEL of 36 mg/kg/day, based on thyroid follicular hyperplasia at 180 and 953 mg/kg/day. An uncertainty factor of 100 was applied to the NOAEL for interspecies extrapolation and intraspecies variability. Thyroid weights were not monitored in the study.

Other toxicological effects included adrenal medullary hyperplastic alterations in male rats, and decreased body weight gains in male and female rats. In a six-month dog study, increased thyroid weights (elevated absolute weights in females at 300 mg/kg/day and elevated absolute and relative weights in males and females at 1500 mg/kg/day) were reported. Similar findings were noted in a three-month gavage study in the dog.

Asulam is classified as Group C, possible human carcinogen, based on thyroid and adrenal tumors in the rat study. The Cancer Peer Review Committee determined that a low dose linear extrapolation risk model was not appropriate for asulam (memorandum dated 2/17/88). The 12/06/01 HIARC document, has concluded that the submission and review of a new mouse study did not impact the current classification of asulam as a Group C, possible human carcinogen or the CARC conclusion that a cancer risk assessment is not required.

A two-generation reproduction study in the rat study provided evidence for a quantitative increased susceptibility of the rat fetus to asulam exposure relative to adults. Additionally, the HIARC determined that a comparative thyroid rat assay in adults and offspring be conducted. In the rat reproductive toxiciity study, significantly fewer mean live births per litter were observed at 250 mg/kg/day and 1250 mg/kg/day in the first generation. A dose-response relationship was evident. The LOAEL for offspring effects was 250 mg/kg/day. No effects on mean live births per litter were observed at 50 mg/kg/day, the NOAEL for offspring toxicity. The LOAEL for parental systemic toxicity is 1250 mg/kg/day and was based on decreased body weights (F_0 males, F_1 females) and organ weight effects (increased absolute and relative thyroid weights in F_1 males and F_2 males and females; increased absolute and relative liver weights in F_1 females; and increased ovarian weights in F_1 females at 31 days old, but not at terminal necropsy). The NOAEL for parental systemic toxicity is 250 mg/kg/day.

Asulam has been evaluated for potential developmental effects in the rat and the rabbit. There was no indication of treatment-related effects on developmental parameters (at dose levels up to 750 mg/kg/day) in a developmental toxicity study in the rabbit. In the developmental study in the rat, a slight-to-moderate increase in preimplantation loss was observed at the high dose level (1,500 mg/kg/day). Decreased maternal body weight gain was noted at 1,500 mg/kg/day, but not at 1,000 mg/kg/day. In a developmental toxicity study in the rabbit, decreased maternal body weight gain was observed at a LOAEL of 750 mg/kg/day; the NOAEL is 300 mg/kg/day.

Asulam was tested in several genetic toxicology studies, which included assessments of gene mutation, chromosomal aberrations, and cell transformation. All assays were negative.

FQPA Safety Factor

Based upon the developmental studies reviewed, there does not appear to be any quantitative or qualitative evidence of increased susceptibility of rat or rabbit fetuses following *in utero* exposure to asulam. However, there was evidence of quantitative susceptibility for offspring (significantly fewer mean live births) in a two-generation reproduction study in the rat. Although neurotoxicity studies were not performed, there was no indication of neurotoxicity in the submitted studies or in the published literature. A developmental neurotoxicity study was not required by HIARC, however a comparative thyroid rat assay in adults and offspring is being required. The FQPA Safety Factor Committee (12/10/01) determined that for asulam, the 10-fold safety factor for the protection of infants and children should be retained because:

1) There was evidence of quantitative susceptibility in a two-generation reproduction study in the rat; and,

2) HIARC recommended the requirement for a comparative thyroid rat assay in adults and offspring and this is considered a data gap for asulam.

Toxic Endpoints Selected for Risk Assessment

The HED Hazard Identification Assessment Review Committee (HIARC) met on 11/13/01 to select endpoints for human health risk assessments and to reevaluate increased susceptibility of offspring and fetuses to asulam exposures. The quality of the toxicity studies for asulam provided reasonable confidence in the toxicity endpoints and doses selected for risk assessment. All doses for risk assessment purposes were assessed along with the uncertainty factors of 10X for interspecies extrapolation and 10X for intraspecies variability.

No acute dietary toxicity endpoint was identified because no adverse effect attributable to a single dose of asulam was observed. 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. A chronic dietary risk assessment was conducted to estimate risks from average exposures to asulam in foods.

Short-, intermediate-, and long-term dermal and inhalation endpoints were selected because there are occupational exposures. Although dermal and inhalation toxicity studies were available, these studies did not include an examination of the thyroid gland, the target organ for asulam. Therefore, oral endpoints were selected for dermal and inhalation endpoints. Because the risk assessments conducted for this document are intended to support a TRED, no occupational exposure and risk assessments were conducted.

No endpoints for short-, or intermediate-term incidental ingestion were selected. Although dermal and inhalation endpoints were selected, dermal and inhalation risk assessments for residential exposures were not conducted because there are no registered residential uses of asulam. Although asulam is classified as a C carcinogen, it has not been quantified as per the CARC (memo dated 2/17/88). Therefore, a quantitative exposure and risk assessment for cancer has not been conducted.

Chronic Dietary Risk Assessment

The risk estimates for chronic dietary exposures to asulam analyses reflect a refined exposure assessment. Anticipated residues (ARs) and percent crop treated information were incorporated in the analysis. ARs were calculated using field trial data. There are no monitoring data (USDA PDP) available for asulam.

Chronic dietary risk is estimated by using average consumption and residue values. A risk estimate that is less than 100% of the chronic Population Adjusted Dose (cPAD) does not exceed HED's level of concern. The cPAD (0.036 mg/kg/day) is the RfD (0.36 mg/kg/day) divided by the FQPA safety factor (10x for asulam).

Chronic dietary risks estimated using a cPAD of 0.036 mg/kg/day are below the Agency's level of concern (< 100% cPAD) for all population subgroups. The chronic dietary risk estimate for children 1-6 years (the highest exposed population subgroup) is 1% of the cPAD. All other population subgroups have chronic dietary risk estimates that are < 1% of the cPAD.

Drinking Water Risk Assessment

The Environmental Fate and Effects Division (EFED) provided a drinking water assessment using simulation models to estimate the potential concentration of asulam and its degradates, sulfanilamide and sulfanilic acid, in surface water. Sulfanilamide is a major soil and water degradate of asulam (Reregsitration Eligibility Decision (RED) September 1995). EFED used the FIRST reservoir model to calculate estimated environmental concentrations (EECs) in surface water. A prospective groundwater study was used to estimate the groundwater EEC for residues of asulam and the sulfanilamide degradate. Since no data are available on degradates, FIRST modeling assumed immediate conversion upon application to very persistent and mobile degradates.

With respect to the exposure in surface water, conservative Tier I (FIRST) modeling indicated that EECs in surface water are not likely to exceed an average concentration of 6.6 ppb for asulam, and an average concentration of 272 ppb for asulam plus the degradates (sulfanilamide and sulfanilic acid) for use in chronic exposure assessments. Residues of asulam and sulfanilamide in ground water are not likely to exceed a maximum of 154 ppb, and an average of 43 ppb. These EECs represent upper bound concentrations for asulam residues in surface water and groundwater as can be seen by a comparison with monitoring data provided in the synopsis below.

In a separate water monitoring study, asulam was detected in public drinking water sources from ground and surface water. At the request of EPA, Rhone-Poulenc conducted a drinking water monitoring study in areas of high asulam use in Florida and Louisiana. The surface water study was designed to sample raw surface water in up to 15 community water systems in Florida and 4 systems in Louisiana. Samples were collected monthly for one year and analyzed for asulam and the metabolite sulfanilamide at a detection limit of 1 ppb. In addition to surface water collection, the study collected samples from potable wells in Florida and Louisiana that were located within 1,000 feet of an asulam treated area.

Seven of the ten surface water community systems sampled contained traces (< 1 ppb) of asulam residues during May through June. Four of the community systems were located in Louisiana and three were in Florida.

A total of 28 drinking water wells were sampled in Florida. Because of poor water quality in this area of Florida, many of the wells reportedly use some type of treatment system prior to use. Three wells contained quantifiable asulam residues up to 1.92 ppb. Ten other wells contained detectable traces (<1 ppb). Reportedly, the depth of the well and distance to treated area did not have any statistically significant effects on the concentrations observed. No residues were detected in 12 wells sampled in the "sandier" areas of Hendry County. Rhone-Poulenc reported that there was less intensive use of asulam in this area. No residues were detected in ground water samples in Louisiana.

Occupational Risk Assessment

Because this assessment is a TRED, occupational handler and post application scenarios will not be assessed.

Residential Risk Assessment

Potential residential exposures are not anticipated as a result of applications of asulam. All end use product labels contain the following statements: "FOR AGRICULTURAL OR COMMERCIAL USE ONLY" and "NOT FOR USE BY HOMEOWNERS". Use sites include sugarcane, Christmas tree plantings, turf (for sod only), ornamentals (junipers & yews only), and non-cropland (e.g. rights-of-way, fence rows, etc.). Sugarcane represents 95 percent of asulam utilization; so therefore, the remaining five percent is utilized on the other use sites. Based on the registrants total estimate of 235,000-245,000 gallons of asulam sold and used annually in the US, the amount used annual 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. In summation, residential exposures are considered unlikely.

Aggregate Risk Assessment

In examining aggregate exposure, HED 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). Risk assessments for aggregate exposure consider both short-, intermediate- and long-term (chronic) exposure scenarios considering the toxic effects which would likely be associated with each exposure duration. There are no residential uses of asulam. Therefore, the considerations for aggregate exposure are those from food and water. Since modeling was done to estimate concentrations in drinking water, Drinking Water Levels of Comparison (DWLOCs) were calculated. A DWLOC is a theoretical upper concentration limit for a pesticide in drinking water based on how much of the PAD remains once exposures in food and in the home have been estimated and subtracted. For asulam, only chronic DWLOCs were calculated since an acute endpoint was not selected. HED compares DWLOCs to surface water and groundwater EECs. If the EECs for residues of asulam in surface water and groundwater are less than the DWLOCs for residues of asulam, HED has no concern for aggregate exposures to asulam residues in food and drinking water.

Upon comparison of the chronic DWLOCs (1,254 ppb for males; 1,075 ppb for females; 355 ppb for children) with the EECs for residues of asulam in surface and groundwater, all EECs are less than the chronic DWLOCs for all populations. Consequently, HED has no concerns for chronic exposures to combined residues of asulam in food and drinking water, regardless of the drinking water source (surface water or groundwater).

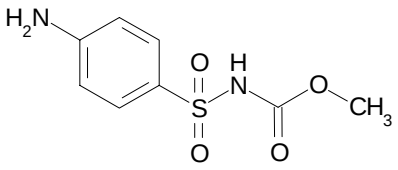
Table 1. Chronic DWLOCs Compared to Surface Water and Groundwater EECs

Population Subgroups	DWLOCs (ppb)	Surface Water EEC (ppb) (average concentration)	Groundwater EEC (ppb) (maximum/average concentration)
Adult males	1254	6.6 (asulam)/ 272 (asulam + degradates)	154 (maximum)/43 (average)
Adult females	1075	6.6 (asulam)/ 272 (asulam + degradates)	154 (maximum)/43 (average)

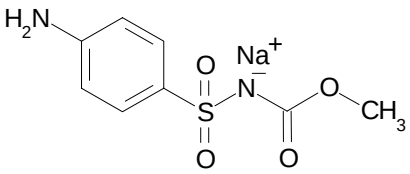
Children (1 to 6 years old)	335	6.6 (asulam)/ 272 (asulam + degradates)	154 (maximum)/43 (average)

2.0 Physical/Chemical Properties Characterization

Asulam (methyl sulfanilylcarbamate) is an herbicide used for weed control on sugarcane. Asulam is formulated into and applied as the asulam sodium salt.



Asulam



Asulam, sodium salt

Empirical Formula:	$C_8H_{10}N_2O_4S$ (asulam)
	$C_8H_9N_2NaO_4S$ (asulam sodium salt)
Molecular Weight:	230.2 (asulam)
	252.2 (asulam sodium salt)
CAS Registry No.:	3337-71-1 (asulam)
	2302-17-2 (asulam sodium salt)
Shaughnessy No.:	106901 (asulam)
	106902 (asulam sodium salt)

Asulam is a colorless crystalline solid with a melting point of 143-145 °C. Asulam sodium salt is a buff-colored powder with a melting point of 212-215 °C. Asulam is soluble at approximately 0.5% in water, and moderately soluble in chlorinated hydrocarbons, petroleum oils, and hydroxylic solvents. Asulam sodium salt is soluble at >100 g/100 mL in water at pHs 5, 6.5, and 9.

3.0 Hazard Characterization

3.1 Hazard Profile

Toxicology data are used by HED to assess the potential hazards to humans. The data are derived from a variety of acute, subchronic, and chronic toxicity tests; developmental/reproductive tests; and tests to assess mutagenicity and pesticide metabolism. The database for asulam is adequate to support this TRED

Acute toxicity values and toxicity categories for asulam are summarized in Table 2. The data indicate that asulam has low acute oral (category IV), dermal (category III), and inhalation (category IV) toxicity. Asulam is category III with respect to ocular irritation. It is not a dermal sensitizer. A primary dermal irritation study shows that asulam is category III.

Table 2. Acute Toxicity of Asulam

Study Type	MRID No.:	Result
81-1. Acute Oral Toxicity - rat. Rhone-Poulenc Ag Co., Study No.: 51-260, November 7, 1988	409605-01	LD_{50} > 5000 mg/kg. Toxicity Category IV Classification: Guideline
81-2. Acute Dermal Toxicity - rabbit. Rhone-Poulenc Ag Co., Study No.: 51-260, November 8, 1988	409605-01	LD_{50} >4000 mg/kg. Toxicity Category III Classification: Guideline
81-3. Acute Inhalation Toxicity - rat. Rhone-Poulenc Ag Co., Study No.:51-583, November 7, 1988	409605-02 413616-01	LC_{50} > 5 mg/L Toxicity Category IV Classification: Minmum
81-4. Primary Ocular Irritation - rabbit. Rhone-Poulenc Ag Co., Study No.: R. Tox. 57, June 1981	00098534	Some chemosis, redness, and irritation were noted, but eyes were clear by day 7. Toxicity Category III Classification: Minimum
81-5. Primary Dermal Irritation - rabbit. Rhone-Poulenc Ag Co., Study No.: RES 2853, March 1977	00098535	No dermal irritation was observed. Toxicity Category III Classification: Minimum
81-6. Dermal Sensitization - guinea pig. Rhone-Poulenc Ag Co., Study No.: RES 2853, March 1977	00098535	No evidence of sensitization in the Guinea Pig. Classification: Minimum.

No subchronic oral toxicity studies in the rodent per se were identified in the data base for asulam. However, the chronic oral studies in the rodent provided frequent monitoring of clinical signs and interim measurements of body weights, food consumption, hematology, clinical chemistry and urinalysis, and the results provided insight into potential subchronic effects.

In a subchronic oral (90-day) study, dogs displayed increased thyroid weights. Although the study was classified as "unacceptable guideline", it was supported by the findings of the 6-month oral dog study. The results of the two studies were similar (i.e., the LOAEL and NOAEL based on increased thyroid weights).

A one-month inhalation toxicity study and 21-day dermal toxicity study were available; however, neither study included assessment of thyroid weights and pathology. The data base for

subchronic toxicity is considered complete for oral and dermal studies. A 28-day subchronic inhalation study is required, one that includes examination of thyroid weights and thyroid pathology.

The 21/28-day dermal toxicity study in the rat showed that no apparent treatment-related systemic effects were observed when body weight, food consumption, clinical pathology, organ weights, ophthalmology, urinalysis, and histopathology were examined. Also, local skin irritation, which was slight and transient, was observed in a small number of treated females.

There are no 90-day inhalation toxicity studies available on asulam. However, a one-month inhalation toxicity study (MRID # 00098537) in the rat was available. This study is limited because of the lack of thyroid weight measurements and pathological examination of the thyroid.

Developmental studies in rats and rabbits, designed to identify possible adverse effects on the developing organism which may result from the in-utero exposure to the pesticide were also conducted. The data base for prenatal developmental toxicity is considered complete. The prenatal developmental toxicity study in the rat showed that there were no treatment-related effects on other maternal parameters including mortality, clinical signs, and food consumption. A slight to moderate increase (not statistically significant) in preimplantation loss was observed in the mid- and high-dose groups (compared to controls). The slight increase in postimplantation loss at the high dose (1500 mg/kg/day) was not statistically significantly different from control values, and was not of any apparent biological significance.

In the prenatal developmental toxicity study in rabbits, the high dose selected was 1,500 mg/kg/day. However, severe maternal toxicity (greater than 20% weight loss, mortality, and signs of starvation) occurred after administration of the 1,500 mg/kg/day dose level. All animals in this group died or were sacrificed for humane reasons. A new group was added to the study using a lower dose of 750 mg/kg/day. Mean maternal body weight gain was markedly reduced (35% but not statistically significant) in the 750 mg/kg/day group than in controls during the dosing period. In addition, mean maternal body weight gains were markedly reduced during days 5-9, 5-13, and 5-17. During the postdosing period, mean body weights of rabbits treated with 750 mg/kg/day were comparable to those of controls, and rabbits displayed some improvement in body weight gain. Rabbits given 750 mg/kg/day exhibited a non-statistically significant decrease in food consumption at several intervals during dosing. There were no apparent treatment-related effects on mortality or clinical signs.

The data base for reproductive toxicity is considered complete. No additional studies are required at this time. Systemic effects observed at the high dose (25,000 ppm) included decreased body weights in F_0 males and F_1 females, increased absolute and/or relative thyroid weights in F_1 males and F_2 males and females, increased absolute and relative liver weights in F_1 females, and increased ovarian weights in F_1 females (at age 31 but not at terminal necropsy). The LOAEL for systemic toxicity is 25,000 ppm (1250 mg/kg/day) based on decreased body weights (F_0 males, F_1 females) and organ weight effects (increased absolute and relative thyroid weights F_1 males and F_2 males and females, increased absolute and relative liver weights in F_1 females, and increased ovarian weights in F_1 females at 31 days old but not at terminal necropsy).

The data base for chronic toxicity is considered complete. No additional studies are required at this time. In the six-month chronic toxicity study in the dog, there was no apparent relationship between test material administration and mortality. Treatment-related findings included reductions in body weight gains and food consumption in the high-dose males and females; increased frequency of emesis and diarrhea in the high-dose males and females; increased absolute thyroid weights in the mid- and high-dose females and in the high-dose males; increased relative (to body weight) thyroid weights in the high-dose males and females; decreased absolute testes and lung weights in the high-dose males; decreased relative testes weights in the high-dose males; and increased relative kidney weights in the high-dose males. No histopathological effects of toxicological significance were observed. There were no apparent effects on prothrombin time, kaolin partial thromboplastin time or platelet counts in males. Platelet counts were slightly decreased in treated females; however, the decreases were not dose-related at most intervals and control values appeared to be slightly elevated. Platelet count in the high-dose females was significantly lower at the 26-week interval only. Plasma and brain cholinesterase activities were not affected by treatment in either sex.

The carcinogenicity data base for asulam is considered complete. There is one acceptable combined chronic toxicity/oncogenicity dietary study in the rat, and one acceptable oncogenicity dietary study in the mouse. In a two-year combined chronic feeding/carcinogenicity study in the rat, there was a statistically significant increase in thyroid gland C-cell carcinomas in both the low- and mid-dose males. There was also a statistically-significant increase in adrenal medullary pheochromocytomas at the high dose in males. With the exception of a non-dose-related enlargement of the pituitary gland in female rats, no unusual toxicological findings occurred in the animals sacrificed at 78 weeks.

In the two-year carcinogenicity toxicity study in the mouse, increased mortality was observed in the high-dose females; however, the number of high-dose females was adequate to assess the carcinogenic potential of asulam. There was no treatment-related effect on food consumption. Hematologic findings in the high-dose males and females consisted of increased leukocyte counts, decreased erythrocyte counts, and decreased hematocrit levels. Organ weight changes included decreased brain weight in the high-dose females, and increased spleen weight in the high-dose males. There was an increased incidence of brown granular pigment deposits in the livers of males of all treatment groups and high-dose females. Increased incidences of brown granular pigment deposits were also noted in the spleens of the high-dose rats of both sexes. The brown granular pigment deposit was not identified, and is therefore of uncertain toxicological significance. There was no increase in the incidence of any tumors.

With the exception of the dominant lethal mutation assay in mice, all other mutagenicity assays were found to be acceptable. These studies satistfy the pre-1991 guideline requirements for mutagenicity studies; no further testing is required at this time. The data indicate that there is no mutagenicity/genetic toxicity concern.

No acute, subchronic, or developmental neurotoxicity studies have been conducted. However, there is no evidence of neurotoxicity in the available acute, subchronic, chronic, and oncogenicity studies. In the March 31, 1998 HIARC meeting, the HIARC concluded: " *The data and information provided by the Registrant demonstrate that Asulam, being a carbamate herbicide*

rather than a carbamate insecticide, has chemical structure and biological properties considerably different from those of the insecticides. Several studies were cited to illustrate the lack of cholinesterase inhibition and the absence of clinical signs suggestive of neurotoxicity. Based on these factors, the Agency waived the requirements for acute, subchronic, and developmental neurotoxicity studies (memorandum, L. Taylor to C. Peterson, dated January 29, 1992."

The data base for metabolism is considered to be complete. No additional studies are required at this time. The urinary route is the predominant route of elimination in the rat.

Table 3. Toxicology Profile for Asulam

Guideline No./ Study Type	MRID No. (year)/ Classification /Doses	Results
870.3100 90-Day oral toxicity in rodents	See combined chronic feeding and carcinogenicity study.	See combined chronic feeding and carcinogenicity study.
870.3150 90-Day oral toxicity in nonrodents	00056414 (1968)/ Unacceptable/Guideline/0, 5, 50 or 500 mg/kg/day.	LOAEL = 500 mg/kg/day, based on increased absolute and relative thyroid weights in male and female dogs. NOAEL = 50 mg/kg/day
870.3200 21-Day dermal toxicity in rabbits	41076901 (1989) Acceptable/Guideline/0 or 1000 mg/kg/day.	NOAEL = 1000 mg/kg/day
870.3250 90-Day dermal toxicity	No study.	No study.
870.3465 90-Day inhalation toxicity	No study.	No study
870.3700a Prenatal developmental in rodents	00098538/(1981)/Accept-able/guideline/0, 500, 1,000, or 1,500 mg/kg/day	**Maternal** l LOAEL = 1,500 mg/kg/day based on body weight gain decrement. The maternal **Maternal** NOAEL = 1,000 mg/kg/day. **Developmental** LOAEL = 1,500 mg/kg/day based on slight to moderate increase in preimplantation loss. **Developmental** NOAEL = 1,000 mg/kg/day.
870.3700b Prenatal developmental in rabbits	00098539/ 1981/ Acceptable/Guideline/0, 60, 300, or 750 mg/kg/day	**Maternal** LOAEL = 750 mg/kg/day based on decreased body weight during the dosing period. **Maternal** NOAEL = 300 mg/kg/day. **Developmental** NOAEL = 750 mg/kg/day.

Guideline No./ Study Type	MRID No. (year)/ Classification /Doses	Results
870.3800 Reproduction and fertility effects	00098540/1981/ Acceptable/0, 50, 250 or 1250 mg/kg/day.	**Parental/Systemic** LOAEL = 1250 mg/kg/day (HDT) based on decreased body weights (F0 males, F1 females) and organ weight effects (increased absolute and relative thyroid weights in F1 males and F2 males and females, increased absolute and relative liver weights in F1 females, and increased ovarian weights in F1 females at 31 days old but not at terminal necropsy). **Parental/Systemic** NOAEL = 250 mg/kg/day. **Reproductive/Offspring** LOAEL = 250 mg/kg/day based on decreased mean live births per litter. **Reproductive/Offspring** NOAEL = 50 mg/kg/day.
870.4100a Chronic toxicity rodents	See combined chronic feeding and carcinogenicity study.	See combined chronic feeding and carcinogenicity study.
870.4100b Chronic toxicity dogs	00098536/1979/ Acceptable/Nonguideline/ 0, 60, 300, or 1,500 mg/kg/day.	LOAEL = 300 mg/kg/day, based on significant ($p < 0.05$) increases in absolute thyroid weights in females. Absolute and relative thyroid weights were elevated at the high-dose (1500 mg/kg/day) in both males and females. The increased absolute thyroid weights in the mid- and high-dose females appeared dose related. NOAEL = 60 mg/kg/day.
870.4200 Combined Chronic Feeding and Carcinogenicity rats	00098543/1981/Acceptable-Guideline/0, 36, 180 and 953 mg/kg/day in males and 0, 47, 243 and 1,280 mg/kg/day in females.	LOAEL =180 mg/kg/day, based on hyperplastic changes in the adrenal medulla and in thyroid follicular cells of males. NOAEL = 36 mg/kg/day. **Under the conditions of this study, there was evidence of an increase in tumor incidence in males when compared to controls. Therefore, asulam is a potential oncogen in this study.**

Guideline No./ Study Type	MRID No. (year)/ Classification /Doses	Results
870.4300 Carcinogenicity mice	42338201/1982/ Acceptable/Guideline/0, 74, 730 and 8,040 mg/kg/day in males and 0, 95, 938 and 10,353 mg/kg/day in females	LOAEL = 8,040 mg/kg/day in males, and 10,353 mg/kg/day in females, based on increased spleen weight and decreased body weight gain in males, and decreased brain weight and survival in females. NOAEL = 730 mg/kg/day in males and 938 mg/kg/day in females. **Under the conditions of this study, there was no evidence of carcinogenicity of asulam.**
870.4300 Carcinogenicity mice	00081183/1978/ Unacceptable/Guideline/0, 225, and 750 mg/kg/day.	LOAEL = 225 mg/kg/day, based on enlargement of the spleen in females, decreased absolute and relative thyroid weights in females, intestinal calcification in males and females, and a dose-related increase in the incidence of mild skin/subcutis hyperkeratosis in males. NOAEL was not achieved. **Under the conditions of this study, there was no definitive evidence of carcinogenicity of asulam.**
One-Month Inhalation study in the rat	00098537/1977/Acceptable Nonguideline/ nose-only exposure at concentrations of 0, 1.6, 3.9, or 15.3 mg/L for 4 hours per day, 5 days per week, for 4 weeks.	NOAEL = 15.3 mg/L (HDT).
Oral Range-Finding in mice	42110002/1989/Acceptable Nonguideline/0, 512, 1,673, 5,103, and 9,022 mg/kg/day for males, and 0, 675, 2,263, 6,835, and 10,828 mg/kg/day for females	LOAEL = 9,022 mg/kg/day based on decreased body weight and body weight gain in males. NOAEL is 5,103 mg/kg/day.
Gene Mutation 870.	A table presenting the mutagenicity data base is already included under section 4.7.	
870.6200a Acute neurotoxicity screening battery	No study.	No study

Guideline No./ Study Type	MRID No. (year)/ Classification /Doses	Results
870.6200b Subchronic neurotoxicity screening battery	No study.	No study.
870.6300 Developmental neurotoxicity	Not required.	
870.7485 Metabolism and pharmaco-kinetics	41345601 (1989)	Metabolism studies in the rat demonstrate that asulam was rapidly eliminated, primarily in the urine, following administration of a single oral or intravenous dose, or after repeated intravenous doses for 14 days. No unusual localization of asulam occurred in tissues. Unchanged parent compound was identified as the major excretory product, with acetylasulam and acetylsulphanilamide as minor metabolites.
870.7600 Dermal absorpt-ion	No Study.	No Study.

Table 4. Mutagenicity/Genotoxicity Studies for Asulam

Study	Results
Bacterial mutagenicity (Ames test) - *Salmonella typhimurium*. Litton Bionetics, Inc., Study No.: E-9177, 1983. MRID No.: 40415302	Not mutagenic with and without metabolic activation at doses up to 2000 μg/plate. Classification: Acceptable-Guideline
Dominant lethal - Mouse - Hess & Clark (Div. of Rhodia), Study No.: SEH-75, 1975 MRID No.: 00082250	No evidence of induction of dominant lethal effect at dietary concentrations of 1500 or 5000 ppm. Classification: Unacceptable because purity information on the test material was not provided.
In vitro cell transformation assay in C3H/10T1/2 cells. Mason Research Institute. Study No.: 596-249-8, October 1979. MRID No.: 00098542	No evidence of induction of morphological transformation at dose levels of 256, 512, 1024, or 2048 μg/mL for 18 hours exposure. Cytotoxicity was apparent at 2048 μg/mL. Classification: Acceptable (Nonguideline).
In vitro cytogenetics in human lymphocytes. Litton Bionetics, Inc. Study No.: 20990, March 1984. MRID No.: 40415301 Cabinet d'Etudes et de Recherches en Tox. Study No.: 658, May 10, 1982. MRID No.: 00144051	No evidence of induction of a clastogenic response at doses of 125-2500 μg/mL (absence of metabolic activation) or 250-2500 μg/mL. Classification: Acceptable.

3.2 FQPA Considerations

The FQPA Safety Factor Committee evaluated the available hazard and exposure data for asulam on December 10th, 2001 and made the recommendation for the FQPA safety factor to be used in human health risk assessments (as required by Food Quality Protection Act of August 3, 1996). The committee concluded that the FQPA safety factor be retained (10x) in assessing the risk posed by this chemical.

The Committee recommended that the FQPA safety factor be **retained (10x)** for the following reasons:

- There was evidence of quantitative susceptibility in a two-generation reproduction study in the rat; and,
- HIARC recommended the requirement for a comparative thyroid rat assay in adults and offspring and this is considered a data gap for asulam.

The safety factor is required for all population subgroups when assessing chronic dietary exposure since the evidence for increase susceptibility was seen in the two-generation study, and the results from the comparative thyroid study, may provide an endpoint for chronic risk assessment.

3.3 Dose Response Assessment

On November 13, 2001, the Health Effects Division (HED) Hazard Identification Assessment Review Committee (HIARC) reviewed the recommendations of the toxicology reviewer for asulam with regard to the acute and chronic Reference Doses (RfDs) and the toxicological endpoint selection for use as appropriate in occupational/residential exposure risks assessments. This is the first re-evaluation after a 1995 RED.

Acute RfD: No appropriate toxicological endpoint clearly attributable to a single exposure was identified including the oral developmental toxicity studies in rats and rabbits.

Chronic RfD: NOAEL of 36 mg/kg/day based on hyperplastic changes in the adrenal medulla and in thyroid follicular cells observed in male rats at 180 mg/kg/day. An uncertainty factor of 100 was applied to this endpoint. This endpoint is of the appropriate route and duration of exposure and applies to the population of concern (general population, including infants and children).

Classification of Carcinogenic Potential: On November 12, 1987, the Carcinogenicity Peer Review Committee met to discuss and evaluate the weight-of-the evidence on asulam with particular reference to its carcinogenic potential (Peer Review of Asulam - memo date 2/17/88). The Committee concluded that the available data for asulam provided limited evidence for the carcinogenicity of the chemical in rats, and asulam was classified as a Category C Carcinogen. The Committee recommended that the 18-month carcinogenicity mouse study (MRID 00081183; unacceptable-guideline) be repeated and agreed to reevaluate the classification when a new mouse study on asulam was submitted and reviewed.

A new mouse study (MRID # 423382-01; discussed previously) was submitted by the registrant and reviewed. The committee considered the new mouse study to be acceptable. The dose levels tested in the mouse study were considered to be adequate for carcinogenicity testing. The high dose tested was higher than the limit dose level as specified under Subpart F of the Pesticide Assessment Guideline for carcinogenicity testing in mice. The treatment did not alter the spontaneous tumor profile for this strain of mouse. The Committee concluded that the new mouse study did not impact the current classification of asulam as a “Group C,” possible human carcinogen, not requiring a quantitative risk assessment.

Short-Term (1 Day - 1 Month) Incidental Oral Exposure: Since there are no residential uses, toxic endpoints were not selected.

Intermediate-Term (1-6 Months) Incidental Oral Exposure: Since there are no residential uses, toxic endpoints were not selected.

Dermal Absorption Factor: 100%. There are no dermal absorption studies with asulam. Comparison of the developmental oral rabbit study to the dermal rabbit study is not appropriate. The dermal rabbit study did not include examination of the thyroid, the target organ.

Short-Term Dermal (1 Day - 1 Month) Exposure: For this exposure scenario, the two-generation reproduction study in the rat (MRID# 00098540) is selected for risk assessment because the decreased mean live births per litter occurred during days 0 - 30, which is the appropriate duration of exposure for this risk assessment. It is also protective of offspring/reproductive effects, and possibly protective of thyroid effects. A dermal absorption study was not available. A dermal absorption factor of 100% will be used for route-to-route extrapolation.

Intermediate-Term Dermal (1-6 Months) Exposure: For this exposure scenario, the two-generation reproduction study in the rat (MRID# 00098540) is selected for risk assessment because the decreased mean live births per litter occurred during days 0 - 30, which is the appropriate duration of exposure for this risk assessment. It is also protective of offspring/reproductive effects, and possibly protective of thyroid effects. A dermal absorption study was not available. A dermal absorption factor of 100% will be used for route-to-route extrapolation.

Long-Term Dermal (Longer than 6 Months) Exposure: A long-term dermal toxicity study was not available. In addition, there was no dermal absorption study. The combined chronic toxicity/carcinogenicity oral study in the rat is of the appropriate duration of exposure. An inhalation absorption factor of 100% will be used for route-to-route extrapolation.

Short-term Inhalation (1 Day - 1 Month) Exposure: For this exposure scenario, the two-generation reproduction study in the rat (MRID# 00098540) is selected for risk assessment because the decreased mean live births per litter occurred during days 0 - 30, which is the appropriate duration of exposure for this risk assessment. It is also protective of offspring/reproductive effects, and possibly protective of thyroid effects. An inhalation absorption study was not available. An inhalation absorption factor of 100% will be used for route-to-route extrapolation.

Intermediate-term Inhalation (1-6 Months) Exposure: For this exposure scenario, the two-generation reproduction study in the rat (MRID# 00098540) is selected for risk assessment because the decreased mean live births per litter occurred during days 0 - 30, which is the appropriate duration of exposure for this risk assessment. It is also protective of offspring/reproductive effects, and possibly protective of thyroid effects. An inhalation absorption study was not available. An inhalation absorption factor of 100% will be used for route-to-route extrapolation.

Long-term Inhalation (Longer than 6 Months) Exposure: A long-term inhalation toxicity study was not available. In addition, there was no inhalation absorption study. The combined chronic toxicity/carcinogenicity oral study in the rat is of the appropriate duration of exposure. An inhalation absorption factor of 100% will be used for route-to-route extrapolation.

Margins of Exposure for Occupational/Residential Risk Assessments: A margin of exposure (MOE) of 100 is adequate for dermal/inhalation occupational exposure risk assessment. The acceptable MOEs for non-occupational and dietary exposures will be determined by the FQPA SF Committee.

Recommendation for Aggregate Exposure Risk Assessments: There are no residential uses for asulam. The chronic aggregate risk assessment is therefore limited to food and water.

The specific doses and endpoints are summarized as follows:

Table 5. 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 = 36 mg/kg/day UF = 100 FQPA Safety Factor = 10	The LOAEL 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**	
Incidental Oral, Short-Term	A toxicity endpoint was not selected because there are no residential uses.		
Incidental Oral, Intermediate-Term	A toxicity endpoint was not selected because there are no residential uses.		
Dermal, Short-Term	Oral NOAEL[a] = 50 mg/kg/day	The LOAEL was 250 mg/kg/day based on significant decreases in mean live births per litter.	Two Generation Reproduction Study in the rat
Dermal, Intermediate-Term	Oral NOAEL[a] = 50 mg/kg/day	The LOAEL was 250 mg/kg/day based on significant decreases in mean live births per litter.	Two Generation Reproduction Study in the rat
Dermal, Long-Term	Oral NOAEL[a] = 36 mg/kg/day	The LOAEL 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
Inhalation, Short-Term	Oral NOAEL[b] = 50 mg/kg/day	The LOAEL was 250 mg/kg/day based on significant decreases in mean live births per litter.	Two Generation Reproduction Study in the rat
Inhalation, Intermediate-Term	Oral NOAEL[b] = 50 mg/kg/day	The LOAEL was 250 mg/kg/day based on significant decreases in mean live births per litter.	Two Generation Reproduction Study in the rat
Inhalation, Long-Term	Oral NOAEL[b] = 36 mg/kg/day	The LOAEL 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

[a]Apply 100% dermal absorption factor for route-to-route extrapolation.
[b]Assume 100% inhalation absorption factor for route-to-route extrapolation.

3.4 Endocrine Disruption

EPA is required 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 was scientific bases for including, as part of the program, the 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. For pesticide chemicals, EPA will use FIFRA and, to the extent that effects in wildlife may help determine whether a substance may have an effect in humans, FFDCA authority to require the wildlife evaluations. As the science develops and resources allow, screening of additional hormone systems may be added to the Endocrine Disruptor Screening Program (EDSP).

When the appropriate screening and/or testing protocols being considered under the Agency's EDSP have been developed, asulam may be subjected to additional screening and/or testing to better characterize effects related to endocrine disruption.

4.0 Exposure Assessment and Characterization

4.1 Summary of Registered Uses

Asulam (methyl-4-sulfanilylcarbamate) is a postemergent systemic carbamate herbicide marketed under the trade name ASULOX® Herbicide by Aventis CropScience. ASULOX® contains the sodium salt of asulam and is registered for use on sugarcane as a 3.34 lb/gal soluble concentrate/liquid (SC/L) formulation. This formulation may be applied postemergence as a band or broadcast application using ground or aerial equipment or as a spot treatment. Apart from its food use on sugarcane, asulam is used on christmas tree plantations, ornamentals, turf (sod farms only) and non-cropland uses.

Asulam is primarily used in agriculture with key markets in Florida and Louisiana. Sugarcane is the major use site for asulam (95% of the market). The asulam use rate, for sugarcane, ranges from 2.5 to 3.34 lbs a.i./A and can applied up to two times per year. For all other uses, it can be applied only once. The average rate of 2.5 lbs ai/acre is the typical labeled use rate for Sugarcane.

Apart from its use on sugarcane, asulam is used on Christmas tree plantations, ornamentals, turf (Sod Farms Only) and non-cropland uses (boundary fences, fencerows, hedgerows, lumberyards, storage areas and industrial plant sites, and warehouse lots). For Christmas trees and ornamentals, the label use rate is 3.34 lbs a.i./A and can be applied once per year as a postemergent treatment. For turf, the label use rate is about 2 lbs. a.i./A and can be applied once per year. For non-cropland uses, the label use rate ranges between 2.9 lbs a.i./A to 3.34 lbs a.i./A and can be applied once per year.

4.2 Dietary Exposure/Risk Pathway

4.2.1 Residue Profile

A tolerance is established for negligible residues of asulam *per se* in/on sugarcane at 0.1 ppm *[40 CFR §180.360]*. HED has recommended that the tolerance expression be revised to include all metabolites containing the sulfanilamide moiety. An adequate enforcement method is available for the determination of combined residues of asulam and all metabolites containing the sulfanilamide moiety in/on sugarcane.

The qualitative nature of the residue in plants is adequately understood based on sugarcane metabolism studies. The terminal residues of concern are free and conjugated asulam, sulfanilamide, N_4-acetylasulam, and N_4-acetylsulfanilamide determined as a common moiety.

The qualitative nature of the residue in animals is adequately understood based on acceptable poultry and ruminant metabolism studies. The terminal residues of concern are free and conjugated asulam, sulfanilamide, N_4-acetylasulam, and N_4-acetylsulfanilamide determined as a common moiety.

4.2.2 Acute Dietary

An acute dietary risk assessment was not performed since there was no acute endpoint identified by HIARC.

4.2.3 Chronic Dietary

The asulam chronic dietary exposure assessment was conducted using the Dietary Exposure Evaluation Model (DEEM™) software Version 7.73, which incorporates consumption data from USDA's Continuing Surveys of Food Intake by Individuals (CSFII), 1989-1992. The 1989-92 data are based on the reported consumption of more than 10,000 individuals over three consecutive days, and therefore represent more than 30,000 unique "person days" of data. Foods "as consumed" (e.g., apple pie) are linked to raw agricultural commodities and their food forms (e.g., apples-cooked/canned or wheat-flour) by recipe translation files internal to the DEEM software. Consumption data are averaged for the entire US population and within population subgroups for chronic exposure assessment, but are retained as individual consumption events for acute exposure assessment.

Anticipated residues were calculated using field trial data. No monitoring data exist for asulam. In addition, estimates of percent crop treated (%CT) generated by BEAD were used to refine the assessment. This refined Tier 2/3 chronic dietary risk assessment was conducted for all supported (i.e., currently registered and proposed) asulam food uses.

For chronic exposure and risk assessment, an estimate of the residue level in each food or food-form (e.g., orange or orange-juice) on the commodity residue list is multiplied by the average daily consumption estimate for that food/food form. The resulting residue consumption estimate for each food/food form is summed with the residue consumption estimates for all other food/food forms on the commodity residue list to arrive at the total estimated exposure. Exposure estimates

are expressed in mg/kg body weight/day and as a percent of the cPAD. This procedure is performed for each population subgroup.

HED notes that there is a degree of uncertainty in extrapolating exposures for certain population subgroups from the general U.S. population which may not be sufficiently represented in the consumption surveys, (e.g., nursing and non-nursing infants or Hispanic females). Therefore, risks estimated for these population subgroups were included in representative populations having sufficient numbers of survey respondents (e.g., all infants or females, 13-50 years).

Exposures >100% of the cPAD exceed HED's level of concern. That is, estimated exposures above this level are of concern, while estimated exposures at or below this level are not of concern. The DEEM analyses estimate the dietary exposure of the U.S. population and 26 population subgroups. The results reported in Table 6 are for the U.S. Population (total), all infants (<1 year old), children 1-6, children 7-12, females 13-50, males 13-19, males 20+, and seniors 55+ years of age. The results for the other population subgroups are not reported in Table 6. This is because the numbers of respondents in the other subgroups were not sufficient, and thus the exposure estimates for these subgroups contained higher levels of uncertainty. However, the respondents in these subgroups were also part of larger subgroups which are listed in Table 6. For example, nursing and non-nursing infants are included in all infants. The subgroups which are broken down by region, season, and ethnicity are also not included. This assessment concludes that for all commodities, the chronic risk estimates are below the Agency's level of concern (<100% cPAD) for the general U.S. population (<1% of the cPAD) and all population subgroups. The chronic dietary exposure estimate for children 1-6 years [highest exposed population subgroup] is 1% of the cPAD.

Table 6. 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%

4.2.4 Cancer Dietary

A cancer dietary risk assessment is not required for asulam.

4.3 Water Exposure/Risk Pathway

The Environmental Fate and Effects Division (EFED) provided a drinking water assessment using simulation models to estimate the potential concentration of asulam and its degradates, sulfanilamide and sulfanilic acid, in surface water. Sulfanilamide is a major soil and water degradate of asulam (Reregsitration Eligibility Decision (RED) September 1995). EFED used the FIRST reservoir model to calculate estimated environmental concentrations (EECs) in surface water. A prospective groundwater study was used to estimate the groundwater EEC for residues of asulam and the sulfanilamide degradate. Since no data are available on degradates, FIRST modeling assumed immediate conversion upon application to very persistent and mobile degradates.

With respect to the exposure in surface water, conservative Tier I (FIRST) modeling indicated that EECs in surface water are not likely to exceed an average concentration of 6.6 ppb for asulam, and an average concentration of 272 ppb for asulam plus the degradates (sulfanilamide and sulfanilic acid) for use in chronic exposure assessments. Residues of asulam and sulfanilamide in ground water are not likely to exceed a maximum of 154 ppb, and an average of 43 ppb. These EECs represent upper bound concentrations for asulam residues in surface water and groundwater as can be seen by a comparison with monitoring data provided in the synopsis below.

In a separate water monitoring study, asulam was detected in public drinking water sources from ground and surface water. At the request of EPA, Rhone-Poulenc conducted a drinking water monitoring study in areas of high asulam use in Florida and Louisiana. The surface water study was designed to sample raw surface water in up to 15 community water systems in Florida and 4 systems in Louisiana. Samples were collected monthly for one year and analyzed for asulam and the metabolite sulfanilamide at a detection limit of 1 ppb. In addition to surface water collection, the study collected samples from potable wells in Florida and Louisiana that were located within 1,000 feet of an asulam treated area.

Seven of the ten surface water community systems sampled contained traces (< 1 ppb) of asulam residues during May through June. Four of the community systems were located in Louisiana and three were in Florida.

A total of 28 drinking water wells were sampled in Florida. Because of poor water quality in this area of Florida, many of the wells reportedly use some type of treatment system prior to use. Three wells contained quantifiable asulam residues up to 1.92 ppb. Ten other wells contained detectable traces (<1 ppb). Reportedly, the depth of the well and distance to treated area did not have any statistically significant effects on the concentrations observed. No residues were detected in 12 wells sampled in the "sandier" areas of Hendry County. Rhone-Poulenc reported that there was less intensive use of asulam in this area. No residues were detected in ground water samples in Louisiana.

4.4 Residential and Occupational Exposure/Risk Pathway

Because this assessment is for a TRED, occupational handler and post application scenarios will not be assessed.

Potential residential exposures are not anticipated as a result of applications of asulam. All end use product labels contain the following statements: "FOR AGRICULTURAL OR COMMERCIAL USE ONLY" and "NOT FOR USE BY HOMEOWNERS". Use sites include sugarcane, Christmas tree plantings, turf (for sod only), ornamentals (junipers & yews only), and non-cropland (e.g. rights-of-way, fence rows, etc.). Sugarcane represents 95 percent of asulam utilization; so therefore, the remaining five percent is utilized on the other use sites. Based on the registrants total estimate of 235-245,000 gallons of asulam sold and used annually in the US, the amount used annual 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. In summation, residential exposures are considered unlikely.

Spray drift is always a potential source of exposure to the public or near spraying operations. This is particularly the case with aerial application, but, to a lesser extent, could also be a potential source of exposure from groundboom application methods. The Agency has been working with the Spray Drift Task Force, EPA Regional Offices and State Lead Agencies for pesticide regulation and other parties to develop the best spray drift management practices. The Agency is now requiring interim mitigation measures for aerial applications that must be placed on product labels/labeling. The Agency has completed its evaluation of the new data base submitted by the Spray Drift Task Force, a membership of U.S. pesticide registrants, and is developing a policy on how to appropriately apply the data and the AgDRIFT computer model to its risk assessments for pesticides applied by air, orchard airblast and ground hydraulic methods. After the policy is in place, the Agency may impose further refinements in spray drift management practices to reduce off-target and risks associated with aerial as well as other application types where appropriate.

5.0 Aggregate Risk Assessments and Risk Characterizations

Because an acute toxicity endpoint was not identified by HIARC, an acute aggregate risk assessment is not required.

In examining aggregate exposure, HED 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). Risk assessments for aggregate exposure consider both short-, intermediate- and long-term (chronic) exposure scenarios considering the toxic effects which would likely be associated with each exposure duration. There are no residential uses of asulam. Therefore, the considerations for aggregate exposure are those from food and water. Since conservative modeling was done to estimate concentrations in drinking water, Drinking Water Levels of Comparison (DWLOCs) were calculated. A DWLOC is a theoretical upper concentration limit for a pesticide in drinking water based on how much of the PAD remains once exposures in food and in the home have been estimated and subtracted. For asulam, only chronic DWLOCs were calculated since an acute endpoint was not selected. HED compares DWLOCs to surface water and groundwater EECs.

If the EECs for residues of asulam in surface water and groundwater are less than the DWLOCs for residues of asulam, HED has no concern for aggregate exposures to asulam residues in food and drinking water.

Upon comparison of the chronic DWLOCs (1,254 ppb for males; 1,075 ppb for females; 355 ppb for children) with the EECs for residues of asulam in surface and groundwater, all EECs are less than the chronic DWLOCs for all populations. Consequently, HED has no concerns for chronic exposures to combined residues of asulam in food and drinking water, regardless of the drinking water source (surface water or groundwater).

Table 7. Chronic DWLOCs Compared to Surface Water and Groundwater EECs

Population Subgroups	DWLOCs (ppb)	Surface Water EEC (ppb) (average concentration)	Groundwater EEC (ppb) (maximum/average concentration)
Adult males	1254	6.6 (asulam)/ 272 (asulam + degradates)	154 (maximum)/43 (average)
Adult females	1075	6.6 (asulam)/ 272 (asulam + degradates)	154 (maximum)/43 (average)
Children (1 to 6 years old)	335	6.6 (asulam)/ 272 (asulam + degradates)	154 (maximum)/43 (average)

6.0 Cumulative

The Food Quality Protection Act (1996) stipulates that when determining the safety of a pesticide chemical, EPA shall base its assessment of the risk posed by the chemical on, among other things, available information concerning the cumulative effects to human health that may result from dietary, residential, or other non-occupational exposure to other substances that have a common mechanism of toxicity. The reason for consideration of other substances is due to the possibility that low-level exposures to multiple chemical substances that cause a common toxic effect by a common mechanism could lead to the same adverse health effect as would a higher level of exposure to any of the other substances individually. A person exposed to a pesticide at a level that is considered safe may in fact experience harm if that person is also exposed to other substances that cause a common toxic effect by a mechanism common with that of the subject pesticide, even if the individual exposure levels to the other substances are also considered safe.

Although asulam had been included in the list of potential carbamates for cumulative risk assessment of carbamates as a group, it will not be included in the carbamate cumulative assessment. The available data indicate that asulam is a carbamate herbicide that has chemical structure and biological properties that are considerably different from those of the carbamate insecticides. For instance, several studies on asulam (e.g., chronic oral dog, combined chronic toxicity/oncogenicity dietary rat) demonstrate the lack of cholinesterase inhibition and absence of clinical signs suggestive

of neurotoxicity. Acute studies reveal a low toxicity for asulam (e.g., no deaths and clinical signs of nonspecific origin). There are no specific mechanism of toxicity studies on asulam.

Before undertaking any cumulative risk assessment, HED will follow procedures for identifying chemicals that have a common mechanism of toxicity as set forth in the "*Guidance for Identifying Pesticide Chemicals and Other Substances that Have a Common Mechanism of Toxicity*" (64 FR 5795-5796, February 5, 1999).

7.0 Tolerance Reassessment Recommendations

7.1 Tolerance Reassessment Recommendation

Table 8 summarizes the tolerance reassessment for asulam.

Table 8. Tolerance Reassessment Summary

Commodity	Current Tolerance (ppm)	Tolerance Reassessment (ppm)	Comment
Tolerance 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	

8.0 Data Needs/Label Requirements

8.1Toxicology

- Comparative thyroid rat assay in adult and offspring.
- 21-day Dermal Study in Rats with examination of thyroid weight and pathology.
- 28-day Inhalation Study in Rats with examination of thyroid weight and pathology.

8.2 Product and Residue Chemistry

- Because hydroquinone/quinone remains a chemical of toxicological concern, if the registrant proposes new uses for this chemical, new plant metabolism studies must be performed (relevant to the proposed new uses), aimed specifically at determining the presence and concentration of radiolabeled hydroquinone/quinone. The registrant should also determine the naturally occurring background levels of hydroquinone/quinone and arbutin in sugarcane. The Metabolism Committee will reconsider its position if new metabolism studies show that quinone/hydroquinone/arbutin comprises a significant portion of the radiolabeled residue.

- HED has recommended that the registrant request label amendments specifying a maximum of two asulam applications per year to sugarcane at a maximum single application rate of 3.34 lbs. a.i./A, a PHI of 100 days for Louisiana, a PHI of 140 days for the remainder of the US mainland, and a PHI of 400 days for Hawaii. If the regsitrant requests the recommended label changes, no further sugarcane field trial data are required for asulam at this time. If the registrant does not propose the recommended label changes, existing labels must be supported by new field trials.

- The following product chemistry data guidelines remain unfulfilled for the technical asulam sodium salt: GLN 830.6317 (Storage Stability) and 830.6320 (Corrosion Characteristics).

- Tolerance Reassessment

1. The existing tolerance of 0.1 ppm for asulam residues on sugar cane established in 40 CFR § 180.360 has been reassessed. HED recommends the tolerance be raised to 1.0 ppm;

2. HED recommends a tolerance of 30 ppm for asulam residues in molasses from sugar cane be established in 40 CFR § 180.360;

3. HED recommends a tolerance of 0.05 ppm for asulam residues in milk, and meat and fat from cattle, goats, hogs, horses, and sheep be established in 40 CFR § 180.360;

4. HED 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;

5. Because there are no poultry feed items associated with asulam's use, tolerances on poultry tissues and eggs are not warranted.