Bensulfuron Methyl
(Londax)

RISK CHARACTERIZATION DOCUMENT

California Department of Food and Agriculture
Division of Pest Management, Environmental
Protection and Worker Health

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Contributors and Acknowledgments

Principal Author:	Keith Pfeifer, Ph.D., DABT Staff Toxicologist Health Assessment Group Medical Toxicology Branch
Exposure Assessment:	Robert Krieger, Ph.D. Chief, Staff Toxicologist Worker Health and Safety Branch
Peer Reviewed By:	James Carlisle, D.V.M., M.S Staff Toxicologist Health Assessment Group Medical Toxicology Branch

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I SUMMARY

Bensulfuron methyl is a sulfonyl urea herbicide selective for pre- or early post-emergence broad leaf weeds and sedges in rice crops. The active ingredient is formulated as a dispersable wettable powder under the trade name of Londax, which contains 10% of the active ingredient. Londax is manufactured by E. I. duPont de Nemours and is the first formulation submitted for Section 3 (full) registration with this new active ingredient. Bensulfuron methyl has been given a conditional registration by the U.S. EPA.

Potential adverse effects were identified in a rat teratology study and an in vitro chromosomal aberration study which determined sister chromatid exchanges in Chinese hamster ovary cells. In the rat teratology study, developmental variations, consisting of extra ossification centers of the lumbar region, and developmental retardations, consisting of decreased ossification of sternebrae, were statistically significant from the concurrent controls only at the highest dose tested, 2000 mg/kg (nominal). The developmental NOEL was 500 mg/kg (nominal), based on the effects occurring at the high dose. When the nominal doses are adjusted to mean analytical dosages, the developmental NOEL is 440 mg/kg.

Exposure estimates for mixer, loader, applicators were based on surrogate information from an insecticide/miticide that is used at very low rates of application, similar to those proposed for Londax. Based on these data, the potential daily absorbed dosage is estimated as 48 ug/kg/day. Other potential sources of exposure are drinking water, fish and rice, all of which have temporary tolerances set by EPA. When all sources of exposure are considered, the total daily exposure for the female mixer, loader, applicator is estimated as approximately 53 ug/kg. The margin of safety for the developmental effects reported in the rat study is greater than 8,000. Margins of safety for the general U.S. population and for various sub-population groups who would drink water and consume fish and rice containing bensulfuron methyl at the tolerance levels are greater than 76,000.

Using surrogate exposure data and conservative assumptions, there are adequate margins of safety for agriculture workers, who perform mixer, loader, applicator activities, and for the non-agricultural population who might be exposed to bensulfuron methyl in drinking water, fish or rice.

Other organ-specific toxicities were reported in the sub-chronic and chronic studies. Liver effects, which occurred at relatively high dietary exposures, were noted in mouse, rat and dog studies. The lowest NOEL for the liver effects was ~20 mg/kg/day and is the value used to assess the risk from chronic intake of bensulfuron methyl. Margins of safety for various sub-population groups who consume water, rice and fish containing bensulfuron methyl at the temporary tolerances are all approximately 5,000.

Bensulfuron methyl has been given Conditional Registration status by CDFA. The following studies are required before full registration will be granted: 1) animal metabolism (in progress) 2) dermal absorption study 3) mixer, loader, applicator study.

II INTRODUCTION

A. BIOLOGICAL ACTIVITY

Bensulfuron methyl [methyl 2[[[[[(4,6-dimethoxy-pyrimidin-2-yl)amino]carbonyl]amino]sulfonyl]methyl]benzoate] is a sulfonyl urea herbicide selective for pre- or early post-emergence broad leaf weeds and sedges in rice crops. Most other crops are highly sensitive to the herbicidal properties of this compound.

B. TECHNICAL/PRODUCT FORMULATIONS

Bensulfuron methyl is formulated as a dispersable wettable powder under the trade name of Londax*, which contains 10% of the active ingredient. Londax* is manufactured by E. I. du Pont de Nemours and Co., Inc. and is the first formulation submitted for Section 3 (full) registration with this new active ingredient.

C. TOLERANCE/RESIDUE CHARACTERISTICS

Bensulfuron methyl is rapidly metabolized by rice. In plant metabolism studies with 14C-labeled bensulfuron methyl, the parent compound was initially metabolized to a pyrimidinyl ring demethylated analog of bensulfuron methyl and other polar compounds (1). The terminal metabolites were sulfonamide [methyl 2-(amino-sulfonylmethyl)benzoate] and homosaccharin [1H-2,3-benzothiazin-4-(3H)-one 2,2-dioxide] hydrolysis products and unextracted "bound" material. With the application of 40 and 200 g/ha the concentration of bensulfuron methyl in mature foliage was <0.001 and 0.001-0.002 ppm, respectively. In "cold" residue studies the concentration of bensulfuron methyl was below the detection limit in grain (0.02 ppm), husks, straw, and bran (0.05 ppm) (2). The proposed residue tolerance in rice is 0.02 ppm (3). EPA set temporary tolerances for bensulfuron methyl in fish and in potable water at 0.3 ppm and 0.1 ppm, respectively (4).

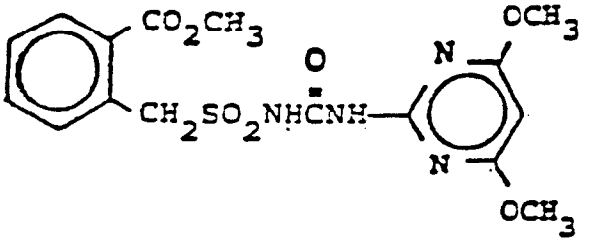
D. PHYSICAL/CHEMICAL PROPERTIES (5)

1. Chemical Name: methyl 2[[[[[(4,6-dimethoxy-pyrimidin-2-yl)amino]carbpnyl]amino]sulfonyl]methyl]benzoate

2. Common Name: bensulfuron methyl

3. CAS Registry Number: 83055-99-6

4. Structural Formula:



D. PHYSICAL/CHEMICAL PROPERTIES (CONTINUED)

5. Empirical Formula: $C_{16}H_{18}N_4O_7S$

6. Molecular Weight: 410.4

7. Physical State: white to pale yellow, solid

8. Melting Point: 181°C

9. pH 6.4 - 6.9

10. Density: 1.41 gm/ml

11. Solubility:

		mg/ml
Water (25°C)		
	pH 4.8	0.0029
	pH 5.8	0.012
	pH 6.8	0.120
	pH 7.8	1.2
Organic Solvents (20°C)		
Hexane		0.00031
Ethyl Acetate		1.66
Methylene Chloride		11.72
Xylene		0.28
Acetonitrile		5.38
Methanol		0.99
Acetone		1.38

12. Vapor Pressure: 2.1×10^{-14} mmHg at 25°C

13. Octanol/Water Partition Coefficient: 282 at pH 1.5
4.1 at pH 7.0

E. STABILITY AND ENVIRONMENTAL FATE

In aqueous solutions, bensulfuron methyl is most stable under slightly alkaline conditions (pH 8) and degrades slowly under acidic conditions (5). Bensulfuron methyl is very stable in organic solvents, except methanol and dimethyl sulfoxide. Samples of the bensulfuron methyl wettable powder/premix moistened with 2.1% water decomposed after 3 months at temperatures above 45°C (6).

Bensulfuron methyl adsorbs weakly to sandy loam soils and strongly to silt loam soils (7,8). Therefore, the mobility classification varied from intermediate to immobile as the percent of organic matter content increased. Bensulfuron methyl is only desorbed slowly.

The half-life of bensulfuron methyl in aerobic soil metabolism studies was 4 - 20 weeks (9). This evidence suggests bensulfuron

E. STABILITY/ENVIRONMENTAL FATE (CONTINUED)

methyl is a moderately residual or persistent pesticide according to the classification system of Harris (10). The major degradation product is CO_2. In sterilized soils the degradation was slower indicating microbes facilitated, but were not essential for, degradation. No carbon dioxide was produced in sterilized soils, but the amounts of the nonvolatile degradation products increased. The two major nonvolatile metabolites were sulfonamide and pyrimidine amine [2-amino-4,6-dimethoxypyrimidine].

In simulated sunlight, bensulfuron methyl is rapidly degraded independent of pH with a half-life of about 4 hours (11). A large number of photodegradation products were formed, but all were present in low concentrations. The most abundant was beta-lactic acid, suggesting a complete breakdown of the phenyl ring.

The hydrolysis of bensulfuron methyl in the dark was dependent on pH with the half-life greater than 30 days at the most stable pH (i.e., at pH 9, 88 - 93% of the parent compound remained) (12). The major hydrolysis products were sulfonamide and pyrimidine amine.

III TOXICOLOGY PROFILE[a]

A. ACUTE TOXICITY--TECHNICAL MATERIAL

Oral LD-50 (rat)	>5000 mg/kg (IV)[b]
Dermal LD-50 (rabbit)	>2000 mg/kg (III)
Inhalation LC-50 (rat,4hr)	>5.0 mg/L (IV)
Eye Irritation (rabbit)	Negative (IV)
Dermal Irritation (rabbit)	Negative (IV)
Dermal Sensitization	Negative

ACUTE TOXICITY--LONDAX (60% AI)

Oral LD-50 (rat)	>5000 mg/kg (IV)
Dermal LD-50(rabbit)	>2000 mg/kg (III)
Inhalation LC-50	Not required[c]
Eye Irritation (rabbit)	Slight to mild (II)
Dermal Irritation (rabbit)	Negative (IV)
Dermal Sensitization	Negative

a CDFA document numbers, record numbers and summaries for all acute and chronic toxicity studies listed in the Toxicology Profile Section can be found in the Summary/Recommendation Sheet (Appendix A), b. Toxicity Category, c. Particle size of formulated material not considered to be inhalable.

B. SUBCHRONIC TOXICITY

Dietary Study-Mouse

Mice (20/sex/dose) were fed bensulfuron methyl (95%) for 13 weeks at levels of 0, 300, 1000, 3000 or 10000 ppm. Minor effects included increased liver weight, cloudy liver color and centrilobular swelling. The NOEL was 300 ppm (39 mg/kg/day) based on liver weight/brain weight ratios in males.

Dietary Study-Rat

Rats (16/sex/dose) were given bensulfuron methyl (96-99%) for 90 days at concentrations of 0, 100, 1500 or 7500 ppm. Minor effects included increased relative liver weights, decreased staining of the centrilobular region, elevated body and organ weights and mild hemolytic anemia. There were no dose-related clinical signs. The NOEL was 1500 ppm (993 and 111 mg/kg/day for males and females, respectively) based on toxicological effects at the next highest dose.

Dietary Study-Dog

Beagle dogs (4/sex/dose) were given bensulfuron methyl (95%) for 90 days at concentrations of 0, 100, 1000 or 10000 ppm. Effects noted only at the high dose included increased serum alkaline phosphatase and alanine aminotransferase, increased liver weights, bile stasis, centrilobular hepatocellular swelling, hepatocyte necrosis and calculi in the gall bladder. The NOEL was 1000 ppm (male = 32 mg/kg/day; female = 36 mg/kg/day) based on the liver effects at 10000 ppm.

C. METABOLISM-RAT

The study submitted by the registrant was considered unacceptable (e.g. only 2 animals/sex/dose used; no rationale given for acetone in dosing vehicles; dosing volumes too large). The registrant has committed to submit a new metabolism study in 1989.

D. CHRONIC TOXICITY-RAT

Rats [Crl:CD (SD)BR strain, 80/sex/dose] were given bensulfuron methyl continuously in their diet for 24 months at levels of 0, 50, 750 or 7500 ppm. Ten rats of each sex and dose group were sacrificed at 12 months. No dose-related gross abnormalities were seen at the one or two year necropsies. Minor histological changes were observed in livers at the one-and two-year necropsy at 7500 ppm, but there were no dose-related proliferative lesions. Decreased food consumption and body weight gain occurred in high dose females, and mild anemia was present in high-dose males at 24 months. The NOEL was 750 ppm (30 and 40 mg/kg/day in males and females, respectively), based on the toxicological effects reported at the next highest dose.

CHRONIC TOXICITY-DOG

Beagle dogs (5/sex/dose) were fed bensulfuron methyl for one year at concentrations of 0, 50, 750 or 7500 ppm. No dose related clinical signs were observed. The NOEL was 750 ppm (male = 21.4 mg/kg/day; female = 19.9 mg/kg/day) based on minor liver effects (e.g. increased weight, serum enzyme increases) which occurred at 7500 ppm.

E. ONCOGENICITY-MOUSE

Mice (CD-1 strain; 92 animals/sex/dose) were given bensulfuron methyl in their diet for 104 weeks at levels of 0, 10, 150, 2500 or 5000 ppm. There were no dose related mortalities nor dose related clinical signs. Centrilobular swelling (males), cortical cysts and pelvic dilation in kidneys (females) and focal hepatocellular necrosis (females) occurred only at the highest dose of 5000 ppm. These effects indicate that a maximum tolerated dose had been achieved and they were not present at the next lower dose. The NOEL for these effects was 2500 ppm (male = 226 mg/kg/day; female = 227 mg/kg/day).

ONCOGENICITY-RAT

See Chronic Toxicity-Rat (above)

F. REPRODUCTION-RAT

Twenty rats/sex/dose were used from the chronic study (above) as a two generation, four litter reproduction study. First generation animals(F_0) were initially mated on days 97-112. These animals were necropsied after one or two years exposure to bensulfuron methyl. There were no dose related mortality or abnormal clinical chemistry in the F_0 generation animals during the reproduction phase and no dose related gross pathology was observed at one or two years. Minor histological changes were noted in the livers of animals in the high dose group only. Decreased food consumption and body weight gain occurred in F_0 females in the high dose group. There were no dose related effects on fertility, fecundity or off-spring viability. No dose related pathology was observed in F_{2b} animals. The NOEL for reproductive effects was 7500 ppm (309 and 405 mg/kg/day in males and females, respectively), the highest dose tested.

G. TERATOLOGY-RAT

Female rats (25/dose group) received 0, 50, 500 or 2000 mg/kg/day of bensulfuron methyl in corn oil by gavage on gestation days 7-16. There were no signs of toxicity or lesions. There were no dose related changes in the incidence of pregnancy, number of corpora lutea, implantation sites, resorptions, live fetuses or fetal weights. No dose-related fetal malformations were observed. Developmental variations, consisting of extra ossification centers of the lumbar region, occurred at 2000 mg/kg; developmental retardations, consisting of decreased ossification of sternebrae, occurred at 2000 mg/kg. The NOEL for maternal toxicity is 2000 mg/kg, the highest dose tested. The NOEL for the conceptus is 500 mg/kg, based on possible adverse effects occurring at 2000 mg/kg. Based on analytical results, the actual dosages ranged from 44 to 94 % of the nominal doses; therefore, when the nominal NOELs are adjusted to the mean analytical dosage, the maternal NOEL = 1374 mg/kg and the fetal (developmental) NOEL = 440 mg/kg. The risk assessment is based on the developmental NOEL of 440 mg/kg/day.

TERATOLOGY-RABBIT

Bensulfuron methyl was given at 0, 30, 300 or 1500 mg/kg/day in 0.5% methyl cellulose by gavage on gestation days 7-19 to 22 female animals (control group) or 20 females (30, 300, 1500 mg/kg dose groups) which had been artificially inseminated on day 0. Maternal toxicity at the high dose consisted of decreased body weight, decreased food consumption, abortion (1/20), complete fetal resorption (2/20), and death (2/20). Maternal NOEL is 300 mg/kg. There was no dose related fetotoxicity or fetal malformations. There was some decrease in fetal weight gain at the high dose (1500 mg/kg), which was probably related to maternal toxicity, and is not considered a developmental effect since this response was not evident at lower dosages.

H. GENOTOXICITY

Gene mutation

In an Ames assay using four strains of Salmonella typhimurium (TA1535, TA1537, TA98, TA100) there were no dose related revertants either without or with microsomal activation at concentrations ranging from 0.01 to 25 ug bensulfuron methyl (95.5%) per plate. No cytotoxicity was observed in this concentration range.

In a hypoxanthine-guanine phosphoribosyl transferase assay using Chinese hamster ovary cells, there was no dose related increase in 6-thioguanine resistance at concentrations of bensulfuron methyl (95.9%) ranging from 0.5 to 4.0 mM per flask.

Chromosomal Aberration

No dose related toxicity or effects on mitotic index or chromosome aberrations were found in an in vivo study in which rats were given 0, 500, 1500 or 5000 mg/kg of bensulfuron methyl (assumed 100%) by single oral gavage.

An in vitro study evaluated the effect of bensulfuron methyl (95.9%) on sister chromatid exchanges in Chinese hamster ovary cells. Concentrations ranged from from 0.135 to 2.7 mM bensulfuron methyl. An increase in sister chromatid exchanges (1.4 x background) without activation was reported at the high dose (2.7mM) and the next lower dose of 1.35 mM bensulfuron methyl indicating a possible adverse effect.

DNA Interactions

In an in vitro assay to assess unscheduled DNA synthesis in primary rat hepatocytes, bensulfuron methyl (95.5%) did not produce any dose related effects at concentrations ranging from 0.001 to 3.5 mM.

IV RISK ASSESSMENT

A. HAZARD IDENTIFICATION

Potential adverse effects were identified in a rat teratology study in which female animals were given 0, 50, 500 or 2000 mg/kg/day (nominal dosage) of bensulfuron methyl. Developmental variations, consisting of extra ossification centers of the lumbar region, and developmental retardations, consisting of decreased ossification of sternebrae, were statistically significant from concurrent control only at the highest dose, 2000 mg/kg. Decreased hyoid ossification also occurred in all dose groups; however, the incidence for all dose groups was within the historical control values (13). The incidence for these developmental effects is presented in Table 1.

Table 1: Developmental effects reported for rat litters after treatment with bensulfuron methyl

Tissue/Effect	Dose (mg/kg) 0	50	500	2000
Ribs/Extra ossification center	2/24 (8%)	3/20 (15%)	7/23 (30%)	8/25* (32%)
Sternebrae/Partially or unossified	20/24 (83%)	19/20 (95%)	20/23 (87%)	23/25 (92%)
Hyoid/Partially or unossified	9/24 (38%)	12/20 (60%)	15/23+ (65%)	17/25+ (68%)

* Significantly different from concurrent controls, $p < 0.05$
\+ Significantly different from concurrent controls, $p < 0.05$, but within the range of historical control values (0-68%) (13)

The developmental NOEL was 500 mg/kg (nominal), based on the effects occurring at 2000 mg/kg. The NOEL for maternal toxicity was 2000 mg/kg, the highest dose tested. When the nominal dosages are adjusted to the mean analytical dosages, the NOELs are 440 mg/kg and 1374 mg/kg for developmental and maternal toxicity, respectively.

The U.S. EPA considered the high dose, 2000 mg/kg (nominal), 1320 mg/kg (their adjusted dose) as the NOEL for maternal toxicity, fetotoxicity, embryotoxicty and teratogenicity (14).

Other organ-specific toxicities were reported in the sub-chronic and chronic studies. Liver effects of limited biological significance occurred at relatively high dietary exposures in mouse, rat and dog studies. The lowest NOEL for the liver effects was ~20 mg/kg/day from the dog chronic study and is the value used by EPA to set the Reference Dose (RfD) for this chemical. The lowest NOEL for sub-chronic exposure was ~32 mg/kg/day from the dog 90 day study and was also based on liver effects at the high dose (340 mg/kg/day).

B. EXPOSURE ASSESSMENT

SHORT TERM-DAILY

Mixer/Loader/Applicator

Exposure data that are specific to mixer/loader/applicators are not currently available for bensulfuron methyl. Exposure estimates to these workers have been based on surrogate information from an insecticide-miticide that is used at very low rates of application, similar to those proposed for Londax. Based on this information, the potential daily absorbed dosage is estimated as 48 ug/kg/day. (See Appendix B for calculations). The following assumptions are used in this calculation: 1) body weight is 54.8 kg (female) 2) exposure is for 8 hour work period per day 3) potential dermal exposure is 0.6 ug/kg/hr 4) 100% dermal absorption 5) based on application rates, potential exposure to Londax is estimated as 10x greater than for surrogate compound 6) protective clothing reduces potential dermal exposure by 90%.

Consumption: Drinking Water

A temporary "tolerance" for bensulfuron methyl in potable water has been recently established at 0.1 ppm (0.1 mg/liter) as part of an experimental use permit by the U.S. EPA (4). Since actual concentrations of bensulfuron methyl in drinking water have not been determined, this value will be used in the risk assessment as a potential "extreme case" scenario. Assuming that an adult female weighs 54.8 kg and consumes 2 liters of water per day, the daily potential exposure from this source is 0.004 mg/kg/day (4 ug/kg/day).

Exposure = 0.1 mg/liter x 2 liters/day x 1/54.8 kg

= 0.004 mg/kg/day
= 4.0 ug/kg/day

Dietary: Fish and Rice

A temporary tolerance for residues of bensulfuron methyl in fish has been recently established at 0.3 ppm (0.3 mg/kg) as part of an experimental use permit by the U.S. EPA (4). The proposed tolerance in rice is 0.02 ppm (3). Since actual residues of bensulfuron methyl in fish and rice have not been determined, the tolerance values are used in the risk assessment as a potential "extreme case" scenario.

Using the TAS Acute Dietary Exposure Model (15), potential dietary intake for various sub-population groups were calculated.

Group	Intake (ug/kg/day)
U.S. Population	0.958
Infants	1.647
Children (1-6 yr)	1.750
Children (7-12 yr)	1.292
Females (13 yr and older)	0.742
Males (13 yr and older)	0.893

Total potential daily exposure for a female agricultural worker (13 years or older), performing mixing, loading and application activities are as follows:

Source	Dosage (ug/kg/day)
Work activities	48.0
Drinking water	4.0
Diet (rice/fish)	0.742
Total	~53

SHORT TERM-SEASONAL

Mixer/Loader Applicator

The daily dosage for the mixer/loader/applicator is adjusted to an average seasonal dosage using the following assumptions: 1) the maximum days per year of Londax use is 49 (~7 weeks). 2) the sub-chronic dog study indicates that liver alterations can occur at least as early as 90 days from continual dietary exposure.

$$\text{Average seasonal dosage} = \text{daily dosage} \times \frac{\text{potential days exposed}}{\text{exposure days for effect}}$$

$$= 53 \text{ ug/kg/day} \times \frac{49 \text{ days}}{90 \text{ days}}$$

$$= 29 \text{ ug/kg/day}$$

Non-Agricultural Exposure

Potential short-term (2 to 90 days) dietary intake for the various sub-population groups would not be greater than the daily dosage. The daily dosage is, therefore, used as a conservative approximation of potential short term exposure. The daily contribution from drinking water would remain at 4 ug/kg/day, based on the consumption of 2 liters per day.

LONG TERM EXPOSURE

Mixer/Loader/Applicator

Long term exposure for the agricultural worker would be similar to the non-agricultural population, since exposure from work activities is short-term and seasonal, and the potential chronic exposure would be primarily from drinking water and dietary sources.

Non-Agricultural Exposure

Using the TAS EXPOSURE 1 (Chronic Dietary Exposure Analysis) (16) and assuming that fish and rice contained bensulfuron methyl at the tolerance levels, potential dietary intake for various sub-population groups were calculated (below). The daily contribution from drinking water would remain at 4 ug/kg/day.

Group	Intake (excluding water) (ug/kg/day)
U.S. Population	0.003
Infants	0.026
Children (1-6 yr)	0.006
Children (7-12 yr)	0.004
Females (20 yr or older)	0.002
Males (20 yrs or older)	0.003

C. RISK CHARACTERIZATION

SHORT TERM-DAILY/ACUTE

Mixer/Loader/Applicator

A margin of safety (MOS) for the potential developmental effects reported in the rat teratology study is calculated as the ratio of the NOEL/Absorbed Daily Dosage. Assuming that a female (13 yrs or older) is exposed to bensulfuron methyl through work-related activities(mixing, loading and applying), through drinking water and through dietary sources, the minimum margin of safety (MOS) would be > 8,000, for combined sources of exposure.

Source of Exposure	Dosage (ug/kg/day)	MOS
Work Activities	48.0	9,200
Drinking Water	4.0	110,000
Diet (rice/fish)	0.742	>593,000
Total	52.742	8,300

Non-Agricultural Exposure

Margins of safety for the various sub-population groups who consume water, rice and fish at the tolerance levels are listed below:

Group	Total Dosage[a] (ug/kg/day)	MOS
U.S. Population	4.958	88,700
Infants	5.647	77,900
Child (1-6 yrs)	5.750	76,500
Child (7-12 yrs)	5.292	83,100
Female (13 yrs and older)	4.742	92,800
Male (13 yrs and older)	4.893	89,900

a Assumes all groups drink 2 liters water per day

SHORT TERM-SEASONAL/SUB-CHRONIC

Mixer/Loader/Applicator

The margin of safety for the agricultural worker potentially exposed to bensulfuron methyl on a seasonal basis (7 weeks) is calculated as the ratio of the NOEL from the sub-chronic dog study/average seasonal dosage.

$$MOS = \frac{32{,}000 \text{ ug/kg/day}}{29 \text{ ug/kg/day}} = 1{,}100$$

Non-Agricultrual Exposure

The lowest margin of safety for non-agricultural exposure is greater than 5,000 for children (1-6 yrs) based on the following assumptions: 1) the child's intake from water, rice and fish occurs at the daily dosage (i.e. 5.750 ug/kg/day) 2) the NOEL is 32 mg/kg/day based on the dog sub-chronic study.

LONG TERM EXPOSURE/CHRONIC

A margin of safety for the potential long term effects reported in the dog chronic study is calculated as the ratio of the NOEL/average annual dosage from dietary sources (water, fish, rice). The NOEL from this study was 20 mg/kg/day.

Margins of safety for the various sub-population groups who consume water, rice and fish at the tolerance levels are all approximately 5,000.

Group	Total Dosage[a] (ug/kg/day)	MOS
U.S. Population	4.003	4,996
Infants	4.026	4,968
Child (1-6 yrs)	4.006	4,993
Child (7-12 yrs)	4.004	4,995
Female (20 yrs or older)	4.002	4,998
Male (20 yrs or older)	4.003	4,996

a Assumes all groups drink 2 liters water per day

V RISK APPRAISAL

Using surrogate exposure data and conservative assumptions, there is an adequate margin of safety for agricultural workers who perform mixer/loader/applicator activities. Before more definitive estimates of worker exposure to bensulfuron methyl can be made, dermal absorption and mixer/loader/applicator studies using current equipment and facilities specific to Londax application methods are required.

Adequate margins of safety exist for the general United States population and for various sub-population groups who might be exposed to bensulfuron methyl in drinking water and consume rice and fish at tolerance levels over short or long periods.

Bensulfuron methyl, as Londax, has been given Conditional Registration status by CDFA pending submission of the following studies by the registrant: 1) animal metabolism (in progress) 2) dermal absorption study 3) worker exposure (mixer, loader, applicator) study.

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VII APPENDICES A-C

APPENDIX A

Toxicology Summary and Recommendation Sheets

Addendum to CDFA Hazard Assessment for Bensulfuran Methyl (Londax)
April 18, 1989

The Worker Health & Safety Branch Data Package Recommendation Sheet for Londax Herbicide stated the following:

1. for the formulated product (60% of the active ingredient) the signal word is `WARNING` based on the eye irritation study indicating Toxicity Category II hazards with the precautionary statements stating "Causes eye irritation" and the recommendations that the users "Wear goggles or face shield when handling"; and,

2. the Dermal Sensitization Study (Haskell Laboratory for Toxicology and Industrial Medicine, Report No. 675-86, Document No. 58670-015) was accepted by the Worker Health & Safety Branch and the product was determined <u>not</u> to be a dermal sensitizer.

Gary T. Patton
Staff Toxicologist
Medical Toxicology Branch

DATA PACKAGE SUMMARY AND RECOMMENDATION SHEET

Active ingredient: Bensulfuron Methyl; Methyl 2-[[[[[(4,6-dimethoxypyrimidin-2-yl)amino]carbonyl]amino]sulfonyl]methyl]benzoate
Formulated product name: Du Pont Londax* Herbicide
Formulation (excluding inerts): 10.5% Bensulfuron Methyl (by weight)
SB 950 #: new active ingredient **ID #:** 113538 (supplemental to 105375, 107500-E)
EPA Reg #: 352-0- -0 **EPA MRID #:**
Document #'s: 50670 - 023, 024
Company name: E. I. du Pont de Nemours & Co., Inc., Wilmington, DE

SUMMARY: ("CDFA One-Liners" from each study worksheet, significant information not mentioned in worksheets, other pertinent information)

ACUTE STUDIES - Technical

	Toxicity Category
Acute Oral Toxicity LD_{50}	IV
Acute Dermal Toxicity LD_{50}	III
Acute Inhalation Toxicity LC_{50}	IV
Primary Eye Irritation	IV
Primary Dermal Irritation	IV

Acute Oral Toxicity

** 50670-003; 38297; "Median Lethal Dose (LD50) OF INF-5384-52 In Rats - EPA Proposed Guidelines" (HLR # 239-84, MR # 4581-146); Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE; 06/04/84; Bensulfuron Methyl, 95.9% pure solid; 300 mg / ml corn oil, 5000 mg/kg to 5 fasted rats/sex by oral gavage; no deaths, no treatment-related abnormalities at 14-day necropsy; LD50 > 5000 mg/kg; toxicity category IV; study acceptable; VdV/KP, 12/30/85; one-liner revised, SRM, 09/28/87.

Acute Dermal Toxicity

** 50670-017; 55518; "EPA Skin Absorption LD50 Test In Rabbits" (Project # 201-620, Report # HLO-225-83, MR # 4581-108); Hazleton Laboratories America, Inc., Vienna, VA; 06/02/83; Bensulfuron Methyl, "about" 94%; 2000 mg/kg applied under occlusive wrap for 24 hours to abraded skin of 5 rabbits / sex, animals observed for 14 days post-exposure; no mortalities, no toxicity observed, no dermal irritation observed; LD50 > 2000 mg/kg (limit test); toxicity category III; study acceptable; GTP, 05/29/87.

Acute Inhalation Toxicity

50670-017; 55519; "Acute Toxicity (End Use Product) 4-Hour Inhalation LC50 Rats (Accession No. 073650) Response To Tox Reviewer's Comments" (HLR-267-84); Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE; 12/16/85; Bensulfuron Methyl; supplemental data requested by EPA to evaluate inhalation study (at doc. # 50670-017, rec. # 55520) which includes individual body weights, location of sampler used to measure concentration and particle size distribution; supplemental data; GTP, 05/29/87.

** 50670-017; 55520; "Inhalation Median Lethal Concentration (LC50) Of INF-5384 By EPA Protocol" (HLR # 332-83, MR # 4581-111); Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE; 09/01/83; Bensulfuron Methyl, "about" 94%; 10 rats / sex / dose exposed to 0, 6.6, or 7.5 mg/l for 4 hours, animals observed for 14 days post-exposure; no mortalities, weight loss on day 1, ocular discharge on days 1-2 and discolored fur on days 2-14 in females (7.5 mg/l), no compound-related pathological findings; LC50(4 hour) > 5.0 mg/l (limit test); toxicity category IV; study acceptable; GTP, 06/01/87.

Primary Eye Irritation

50670-003, 38298; "Eye Irritation Test In Rabbits" (HLR # 687-81, MR # 0581-975, H # 14205); Haskell Laboratory for Toxicological and Industrial Medicine, Newark, DE; 11/04/81; Bensulfuron Methyl, 95% (INF-5384-7); 10 mg solid material placed in conjuctival sac of 1 eye / 2 male rabbits, 1 eye washed after 20 second exposure; slight corneal cloudiness at 1 hour in washed eye with clearing at 4 hours, slight cloudiness in unwashed eye at 1 and 4 hours with clearing at 1 day; study unacceptable (dose too low, treatment groups too small), not upgradeable; VdV/KP, 01/09/86; one-liner revised 10/05/87, SRM.

** 50670-003; 38302; "Primary Eye Irritation Study In Rabbits, Haskell No. 14,793-02, Final Report" (Project # 201-724, HLR # HLO-174-84, MR # 4581-176); Hazleton Laboratories America, Vienna, VA; 03/28/84; Bensulfuron Methyl, 95.9% (INF-5384-52); 29 mg solid placed in conjuctival sac of 1 eye / 9 female rabbits, 3/9 eyes washed 10 seconds after exposure, no ocular irritation seen in any eyes at 24, 48, 72 hours post-exposure; toxicity category not assigned; study unacceptable (no rationale for dose, pages missing); upgradeable; no worksheet; no one-liner; VdV, 12/23/85; rationale for dose accepted (letter, doc. # 50670-014, rec. # 42125; memo 07/02/86); study unacceptable (pages missing); upgradeable; no worksheet; SRM, 09/30/87; missing pages submitted (doc. # 50670-024, rec. # 64875); toxicity category IV; study acceptable; no worksheet; SRM, 01/20/88.

50670-024; 64875. Addendum to 50670-003; 38302. Contains missing pages.

Primary Dermal Irritation

** 50670-013; 41864; "EPA Skin Irritation Study In Rabbits, Haskell No. 14,793-02, Final Report" (Report # 201-725, HLR # HLO-187-84, MR # 4581-176); Hazleton Laboratories America, Inc., Vienna, VA; 04/02/84; Bensulfuron Methyl, 95.9% (INF-5384-52); 0.5 g as aqueous paste applied under occlusive wrapping for 24 hours to 2 abraded and 2 intact skin sites / 6 male rabbits; no dermal irritation observed at 0 and 24 hours post-treatment; toxicity category IV; study acceptable; JSB/JC, 04/04/86; one-liner update, SRM, 10/08/87.

50670-003; 38301; "EPA Skin Irritation Study In Rabbits, Haskell No. 14,793-02, Final Report" (Report # 201-725); Hazleton Laboratories

America, Inc., Vienna, VA; 04/02/84; study unacceptable (pages missing); see complete study doc. # 50670-013, rec. # 41864; VdV/KP 01/09/86.

50670-003; 38299; "Primary Skin Irritation And Sensitization Test On Guinea Pigs" (HLR # 857-81, MR # 0581-975, H # 14,205); Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE; 01/05/82; Primary Dermal Irritation (815); Bensulfuron Methyl, 95% (INF-5384-7); 1, 2.5, 10, 20, or 25 mg in dimethyl phthalate (final vol. 0.05 ml) applied to shaved intact shoulder skin of 3 (1, 10, 20 mg) or 10 (2.5, 25 mg) male albino guinea pigs; no irritation observed at 24 or 48 hours post-treatment; toxicity category not assigned; study unacceptable (no rationale for dose, vehicle, or species); upgradeable; SRM, 10/06/87.

Dermal Sensitization

The need for Dermal Sensitization Studies will be determined by the Worker, Health and Safety Branch.

ACUTE STUDIES - Londax*
[section 3 food use]

	Toxicity Category
Acute Oral Toxicity LD_{50}	IV
Acute Dermal Toxicity LD_{50}	III
Acute Inhalation Toxicity LC_{50}	study exempt (see one-liner)
Primary Eye Irritation	II
Primary Dermal Irritation	IV

Acute Oral Toxicity

** 50670-015; 62105; "Acute Oral Toxicity Study With INF-5384-85 In Rats" (HLR # 680-86, MR # 4581-428, H # 16415); Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE; 12/15/86; Bensulfuron Methyl, 60%; 300 mg / water, 5000 mg/kg (males) or 4900 mg/kg (females) to 5 fasted rats / sex by oral gavage; no deaths, observed 14 days post-exposure, 1-4 % body weight loss in females on day 1, no organ-specific abnormalities at 14-day necropsy; LD50 > 5000 mg/kg; toxicity category IV; JSB/GTP, 02/18/87; study status changed to supplemental; SRM, 09/28/87; study status changed to acceptable; SRM, 12/21/88.

Acute Dermal Toxicity

** 50670-015; 62103; "Acute Dermal Toxicity Study With INF-5384-85 In Rabbits" (HLR # 708-86, MR # 4581-428, H # 16415); Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE; 12/18/86; Bensulfuron Methyl, 60%; aqueous paste, 2000 mg/kg applied to abraded skin under occlusive dressing for 24 hours to 5 rabbits / sex; observed 14 days post-exposure, no deaths, up to 7% weight loss on day 1, mild erythema and edema, all symptoms cleared by day 7, necropsies not performed; LD50 > 2000 mg/kg; toxicity category III; JSB/GTP, 02/10/87; study status changed to supplemental; SRM, 09/28/87; study status changed to acceptable; SRM, 12/21/88.

Acute Inhalation Toxicity

NOTE: The registrant has stated: "An Acute Inhalation toxicity study was not done since the particle size of the product ranges from 250 to 1410 microns and is not inhalable" (letters dated 1/30/87, 11/16/88; CDFA document #'s 50670-015, 50670-029). CDFA finds that an Acute Inhalation Toxicity study is not required because the product does not consist of an inhalable material.

Primary Eye Irritation

** 50670-015; 62107; "Primary Eye Irritation Study With INF-5384-85 In Rabbits" (HLR # 618-86, MR # 4581-428, H # 16415); Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE; 12/10/86; Bensulfuron Methyl, 60%; 0.1 ml undiluted formulation by ocular instillation to 6 female rabbits; slight to mild corneal injury in 6/6 rabbits at 1 hour post-treatment, corneal opacity in 3/6 at 7 days, all symptoms cleared by 14 days; toxicity category II; JSB/GTP, 02/18/87; study status changed to supplemental; SRM, 09/28/87; study status changed to acceptable; SRM, 12/21/88.

Primary Dermal Irritation

** 50670-015; 62104; "Primary Dermal Irritation Study With INF-5384-85 In Rabbits" (HLR # 712-86, MR # 4581-428, H # 16415); Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE; 12/22/86; Bensulfuron Methyl, 60%; 0.5 g in 0.9 ml saline applied to 2 intact and 2 abraded skin sites under occlusive dressing for 24 hours to 6 male rabbits; intact sites had no irritation at 0, 24, 48 hours after patch removal; toxicity category IV; JSB/GTP, 02/10/87; study status changed to supplemental; SRM, 09/28/87; study status changed to acceptable; SRM, 12/21/88.

Dermal Sensitization

The need for Dermal Sensitization Studies will be determined by the Worker, Health and Safety Branch.

ACUTE STUDIES - Supplemental

Acute Oral Toxicity

50670-003; 38304; "Median Lethal Dose (LD50) OF DPX-F5384 10WP In Rats - EPA Proposed Guidelines" (HLR # 249-84, MR # 4581-178); Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE; 06/27/84; Bensulfuron Methyl, 10% (DPX-5384 10WP); 400 mg / ml corn oil, 5000 mg/kg to 5 fasted rats/sex by oral gavage; no deaths, no significant toxicity during 14-day recovery, no treatment-related abnormalities at 14-day necropsy; LD50 > 5000 mg/kg; toxicity category IV; study unacceptable but upgradeable with identification of test material; VdV/KP, 12/30/85; one-liner revised, SRM, 09/28/87; study status changed to supplemental; SRM, 12/20/88.

Acute Dermal Toxicity

50670-003; 38305; "Skin Absorption LD50 Study In Rabbits, Final Report" (Project # 201-728); Hazleton Laboratories America, Inc., Vienna, VA; 04/12/84; Bensulfuron Methyl, 10% (DPX-F5384 10WP); aqueous paste, 2000 mg/kg applied to abraded skin under occlusive dressing for 24 hours to 5 rabbits/ sex; observed 14 days post-exposure, no deaths, no toxic symptoms, no dermal effects, necropsy

not performed; LD50> 2000 mg/kg; toxicity category III; study unacceptable but upgradeable with identification of formulation of test material; VdV/KP, 12/30/85; one-liner revised, SRM, 09/30/87; study status changed to supplemental; SRM, 12/20/88.

Acute Inhalation Toxicity

50670-003; 38306; "Inhalation Median Lethal Concentration (LC50) Of INF-5384-64 By EPA Guidelines" (HLR # 267-84, MR # 4581-178, H # 15,305); Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE; 06/26/84; Bensulfuron Methyl, 10% (DPX-5384 10WP); nose-only exposure of 10 rats / sex to 4.0 or 5.1 mg/l respirable powder for 4 hours; observed 2 weeks, no deaths, "moderate" weight loss on day 1, no significant treatment-related symptoms, necropsies not performed; LC50 > 5 mg/l (4 hours); toxicity category IV; study unacceptable but upgradeable with identification of formulation of test material; VdV/KP, 12/31/85; one-liner revised, SRM, 09/30/87; study status changed to supplemental; SRM, 12/20/88.

Primary Eye Irritation

50670-003; 38309; "Primary Eye Irritation Study in Rabbits, Haskell No. 15,305, Final Report" (Project # 201-729, HLR # HLO-184-84, MR # 4581-178); Hazleton Laboratories America, Vienna, VA; 03/26/84; Bensulfuron Methyl, 10% (DPX-F5384 10WP, INF-5384-64); 33 mg solid placed in conjuctival sac of 1 eye / 9 (male/female?) rabbits, 3/9 eyes washed 10 seconds after exposure, no ocular irritation seen in any eyes at 24, 48, 72 hours post-exposure; toxicity category IV; study unacceptable but upgradeable with identification of formulation of test material; VdV/KP, 12/31/85; one-liner revised, SRM, 10/05/87, 01/20/88; study status changed to supplemental; SRM, 12/21/88.

50670-014; 42125. Addendum to 50670; 38309. Registrant submitted rationale for dose.

50670-024; 64874. Addendum to 50670; 38309. Contains missing pages.

Primary Dermal Irritation

50670-013; 41867; "EPA Skin Irritation Study In Rabbits, Haskell No. 15,305, Final Report" (Project # 201-730, HLR # HLO-177-84, MR # 4581-178); Hazleton Laboratories America, Vienna, VA; 03/26/84; Bensulfuron Methyl, 10% (DPX-F5384 10WP; INF-5384-64); 0.5 g as aqueous paste applied under occlusive wrapping for 24 hours to 2 abraded and 2 intact skin sites / 6 male rabbits; no dermal irritation observed at 0 and 24 hours post-treatment; toxicity category IV; study unacceptable but upgradeable with identification of formulation of test material; JSB/JC, 04/04/86; one-liner update, SRM, 10/13/87; study status changed to supplemental; SRM, 12/21/88.

50670-003; 38307; "EPA Skin Irritation Study In Rabbits, Haskell No. 15,305, Final Report" (Report # 201-730); Hazleton Laboratories America, Inc., Vienna, VA; 03/26/84; study unacceptable (pages missing); see complete study at doc. # 50670-013, rec. # 41867; VdV/KP, 01/09/86.

Dermal Sensitization

Dermal sensitization studies are no longer reviewed by Medical Toxicology. The need and adequacy of these studies will be determined by the Worker, Health and Safety Branch.

50670-003; 38299; "Primary Skin Irritation And Sensitization Test On Guinea Pigs" (HLR # 857-81, MR # 0581-975, H # 14,205); Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE; 01/05/82; Bensulfuron Methyl, 95% (INF-5384-7); study unacceptable; VdV/KP, 01/09/85.

50670-003; 38308; "Primary Skin Irritation And Sensitization Test On Guinea Pigs, Haskell No. 15,305, Revised Final Report" (Project # 201-731, HLR # HLO-296-84, MR # 4581-178); Hazleton Laboratories America, Inc., Vienna, VA; 07/11/84; Bensulfuron Methyl, 10% (DPX-F5384 10WP, INF-5384-64); study unacceptable; VdV/KP, 12/31/85.

50670-014; 42126; "Du Pont Londax® Herbicide CDFA Review of Toxicology"; E. I. du Pont de Nemours & Co., Wilmington, DE; 03/04/86; rebuttal to CDFA's criticisms of dermal sensitization studies (doc. # 50670-003, rec. #'s 38299, 38308); no worksheet; SRM, 10/13/87.

50670-015; 62106; "Dermal Sensitization Study With INF-5384-85 In Guinea Pigs" (HLR # 675-86); Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE; 12/11/86; Bensulfuron Methyl, 60%; study not evaluated for acceptability; no worksheet; SRM, 11/04/87.

Special Studies

50670-013; 41865; "Median Lethal Dose (LD50) OF INF-5384-52 In Rats - Intraperitoneal" (HLR # 252-84, MR # 4581-146); Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE; 06/04/84; Bensulfuron Methyl, purity unspecified; suspension in acetone/saline (15%:85%), 10000 mg/kg to 10 male rats, i.p., animals observed 14 days post-exposure; clinical signs included lethargy, ataxia, no righting reflex, clear and/or red ocular and nasal discharges, wet and/or stained perineum, hunched posture, moderate to severe weight loss for 2 days after dosing, and cyst formation at injection site; no pathology report; LD50 > 10000 mg/kg; supplemental information; no worksheet; SRM, 09/28/87.

> 50670-003; 38303; "Median Lethal Dose (LD50) OF INF-5384-52 In Rats - Intraperitoneal" (HLR # 252-84, MR # 4581-146); Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE; 06/04/84; Bensulfuron Methyl; study unacceptable (missing pages); see complete study at doc. # 50670-013, rec. # 41865; VdV/KP, 12/30/85.

SUBCHRONIC STUDIES

50670-003; 38315; "DPX-F5384: 13-Week Oral Subchronic Toxicity Study In Mice"; The Institute of Environmental Toxicology, Kodaira, Tokyo, Japan; 10/03/84; Bensulfuron Methyl, 95%; 0, 300, 1000, 3000, or 10000 ppm in diet fed to 20 mice / sex for 13 weeks; no treatment-related clinical signs, increased liver weight and cloudy liver color (males 1000, 3000, 10000 ppm, females 10000 ppm); centrilobular swelling (males 3000, 10000 ppm, females 10000 ppm); no adverse effect; NOEL = 300 ppm Z 38.9 mg/kg/day (liver weight / brain weight in males); study unacceptable (not signed, no GLP audit); study upgradeable; DS/AA, 12/30/85; one-liner update, SRM, 10/14/87.

** 50670-005; 38317; "Ninety-day Feeding And One-generation Reproduction Study In Rats With Benzoic Acid, 2-[[[[(4,6-Dimethoxy-2-pyrimidinyl)amino]carbonyl] amino]sulfonylmethyl]-, Methyl Ester*, (INF-5384)" (HLR # 186-83, MR # 4577); Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE; 03/29/84;

Subchronic Oral (821); Bensulfuron Methyl, 95.7 - 98.5%; 0, 100, 1500, 7500 ppm in diet fed to 16 rats / sex for 90 days; 10 rats / sex necropsied; no dose-related clinical signs, increased relative liver weights and decreased staining of centrilobular region in males at 7500 ppm, elevated body and organ weights in females at 100, 1500, 7500 ppm but not dose-related, mild hemolytic anemia in males at 7500 ppm; no adverse effect; NOEL = 1500 ppm (hemolytic anemia in males); study acceptable; VVW/CNA, 12/18/85; one-liner updated, SRM, 10/14/87.

** 50670-007; 38320; "Three-month Feeding Study In Dogs With INF-5384" (HLR # 3-85, MR # 7287-001); Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE; 05/01/85; Bensulfuron Methyl, approx. 95% (INF-5384); 0, 100, 1000, or 10000 ppm in diet fed to 4 beagles / sex for 90 days; no clinical symptoms observed, increased serum alkaline phosphatase and alanine aminotransferase, increased liver weights, bile stasis, centrilobular hepatocellular swelling, hepatocyte necrosis, and calculi in gallbladder at 10000 ppm; no adverse effect; NOEL = 1000 ppm (liver effects); initially reviewed as unacceptable (active ingredient not identified); VVW/FM, 12/20/85; active ingredient identified (at doc. # 50670-003, rec. # 38279); study acceptable; SRM, 10/16/87.

METABOLISM STUDIES

Metabolism, Rat

50670-013; 41866; "Metabolism Of 14C-Labelled DPX-F384 By Male And Female Rats" (HLR # 293-84, MR # 4379-001); Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE; 06/29/84; Bensulfuron Methyl, 98.4%; mixtures of unlabelled and labelled (phenyl-14C, > 99% purity) active ingredient in acetone:corn oil (1:9, low doses, 2 ml; 3:7, high dose, 3 ml + 2 ml corn oil) administered by oral gavage to 2 rats / sex / dose, 1 trial / dose, 14.1 - 20 uCi / rat, either 16 (low dose) or 2000 (high dose, 2 trials) mg/kg alone or 16 mg/kg after 21 days on diet containing 100 ppm unlabelled active ingredient (low dose preconditioned); urine, feces, and expired 14C collected 6-, 24-, 48-, 72- and 96-hours post-dosing; animals sacrificed at 96 hours, LSC analysis of 14C in excreta, body fluids, and tissues; urinary and fecal metabolites isolated and analyzed by solvent extraction, TLC, HPLC, and MS; mean % recoveries of 14C $\pm$ S.D. for all dose groups, total = 91.1 $\pm$ 11.6%, urine + feces = 89.2% $\pm$ 12.2%, expired air = 0%, tissues + carcass = 0.42 $\pm$ 0.52%; unacceptable (5 animals / sex / dose required; no rationale for acetone in dosing vehicles; dosing volumes too large); not upgradeable; JSB/DM, 04/01/86; one-liner update, SRM, 10/29/87, 01/21/88.

> 50670-003; 38314; "Metabolism Of 14C-Labelled DPX-F384 By Male And Female Rats" (HLR # 293-84, MR # 4379-001); Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE; 06/29/84; study unacceptable (pages missing); upgradeable; see complete study at doc. # 50670-013, rec. # 41866; JG, 12/31/85.

NOTE: Registrant has committed to submission of a new metabolism study in 1989 (letter dated 11/16/88, document #50670-029). Conditional registration is recommended pending submission of an acceptable metabolism study in 1989.

SB950-MANDATED HEALTH EFFECTS STUDIES

Chronic Toxicity, Rat

** 50670-019; 55521; "Long-Term Feeding And Two-Generation, Four-Litter Reproduction Study In Rats With INF-5384" (HLR # 662-85, MRP # 4651-001); Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE; 01/17/86; Chronic Toxicity (831); Bensulfuron Methyl, 95 - 95.9%; continuous dietary exposure of 0, 50, 750, or 7500 ppm to 80 rats/sex/dose for 24 months, 20 rats/sex/dose used in reproduction sub-study, 10 rats/sex/dose sacrificed at 12 months; decreased food consumption and body weights in females at 7500 ppm, mild anemia in males at 24 months at 7500 ppm, no dose-related gross pathological abnormalities at 1- or 2-year necropsy, minor histological changes in livers at 1- and 2-year necropsy at 7500 ppm, no dose-related proliferative lesions; no adverse effect; NOEL = 750 ppm (food consumption, body weight, liver effects, anemia); study unacceptable and not upgradeable (no ophthalmological exams); SRM/GTP, 11/12/87; SRM/GTP, 01/26/88; study status changed to acceptable with exemption from ophthalmological data (CDFA memo, 6/14/88) and submission of eye histophathology data (50670-029, 67728); SRM, 12/19/88

50670-006; 38319; "Long-term Feeding And Two-generation, Four-litter Reproduction Study In Rats With Benzoic Acid, 2-[[[[(4,6-Dimethoxy-2-pyrimidinyl)amino]carbonyl]amino]sulfonylmethyl]-, Methyl Ester, INF-5384" (MR # 4651, HLR # 289-84); Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE; 07/30/84 (study conducted 02/08/83 - 02/14/84); Combined Chronic Feeding & Oncogen/Carcin (835); Bensulfuron Methyl, $\geq$ 95%; study unacceptable (interim report); not upgradeable (interim report); see complete report at doc. # 50670-019, rec. # 55521; VVW/CNA, 12/20/85.

50670-023; 64873. Addendum to 50670-019; 55521. Contains complete report.

50670-029; 67728. Addendum to 50670-019; 55521. Contains additional eye histopathology data and statements of adequacy of eye examinations.

Chronic Toxicity, Dog

** 50670-018; 55522; "A One-Year Feeding Study In Dogs With H14793" (Project # 84-2835); Bio/dynamics, Inc., East Millstone, NJ; 01/16/86; Bensulfuron Methyl, 95.9%; 0, 50, 750, or 7500 ppm in the diet of 5 beagles / sex / dose for 1 year; no dose-related clinical signs observed, increased alanine aminotransferase, alkaline phosphatase, and liver weights and brown pigmented material in bile canaliculi at 7500 ppm; no adverse effect; NOEL = 750 ppm (liver effects, male - 21.4 mg/kg/day, female - 19.9 mg/kg/day); study unacceptable and not upgradeable (no ophthalmological data); SRM, 11/05/87; study status changed to acceptable with exemption from ophthalmological data (CDFA memo, 6/14/88) and submission of eye histophathology data (50670-029, 67729); SRM, 12/19/88

50670-029; 67729. Addendum to 50670-018; 55522. Contains additional eye histopathology data and statements of adequacy of eye examinations.

Oncogenicity, Rat

** 50670-019; 55521; "Long-Term Feeding And Two-Generation, Four-Litter Reproduction Study In Rats With INF-5384" (HLR # 662-85, MR # 4651-001); Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE; 01/17/86; Oncogenicity/Carcinogenicity Study (832); Bensulfuron Methyl, 95 - 95.9%; continuous dietary exposure of 0, 50, 750, or 7500 ppm to 80 rats/sex/dose for 24 months, 20 rats/sex/dose used in reproduction sub-study, 10 rats/sex/dose sacrificed at 12 months; decreased food consumption and body weights in females at 7500 ppm, mild anemia in males at 24 months at 7500 ppm, no dose-related gross pathological abnormalities at 1- or 2-year necropsy, minor histological changes in livers at 1- and 2-year necropsy at 7500 ppm, no dose-related proliferative lesions; no adverse effect; NOEL = 750 ppm (food consumption, body weight, liver effects, anemia); study acceptable as Oncogenicity/Carcinogenicity Study; SRM/GTP, 11/12/87, 01/26/88; one-liner update, SRM, 12/22/88.

50670-023; 64873. Addendum to 50670-019; 55521. Contains complete report.

Oncogenicity, Mouse

** 50670-020; 55530; "DPX-F5384: 24-Month Oral Chronic Toxicity And Oncogenicity Study In Mice" (Report # TX5384-1-86); The Institute of Environmental Toxicology, Tokyo, Japan; 04/07/86; Bensulfuron Methyl, 95.9%; continuous dietary exposure of 0, 10, 150, 2500, or 5000 ppm to 92 mice/sex/dose for 104 weeks; 10 mice/sex/dose sacrificed at 52 and 78 weeks; no dose-related mortalities; no dose-related clinical signs; centrilobular hepatocellular swelling (males), cortical cysts and pelvic dilation in kidneys (females), focal hepatocellular necrosis (females) at 5000 ppm; no adverse effects; NOEL = 2500 ppm (male - 226 mg/kg/day, female - 227 mg/kg/day, liver and kidney effects); study acceptable as an oncogenicity study only; 11/13/87, SRM; one-liner update, SRM, 01/06/88.

Reproduction, Rat

** 50670-019; 55521; "Long-Term Feeding And Two-Generation, Four-Litter Reproduction Study In Rats With INF-5384" (HLR # 662-85, MR # 4651-001); Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE; 01/17/86; Reproductive & Fertility Effects (834); Bensulfuron Methyl, 95 - 95.9%; continuous dietary exposure to 0, 50, 750, or 7500 ppm, 20 F0 rats/sex/dose mated on days 97 - 112, F1a pups sacrificed 21 days postpartum, 10 days later F0's mated again, F1b pups weaned 21 days postpartum, 90 days later 20 F1b rats/sex/dose mated, F2a pups sacrificed 21 days postpartum, 10 days later F1b's mated again, 10 F2b pups/sex/dose necropsied 21 days postpartum, F0's necropsied after 1 or 2 years exposure; decreased food consumptions and body weights in female F0's at 7500 ppm, no dose-related mortality or abnormal clinical chemistry observed in F0's during reproduction study, no dose-related gross pathological abnormalities in F0's at 1- or 2-year necropsy, minor histological changes in F0 livers at 1- and 2-year necropsy at 7500 ppm; no dose-related effects on fertility, fecundity, or offspring viability; no dose-related pathology observed in F2b's; no adverse effect; NOEL = 7500 ppm (highest dose tested); doses justified by 90-day pilot study (at doc. # 50670-005, rec.# 38317); study acceptable as a reproduction study; SRM, 11/10/87; one-liner update, SRM, 01/06/88, 12/22/88.

Teratology, Rat

**** 50670-004; 38316**; "Developmental Toxicity Study of INF-5384-38 By Gavage In The Rat" (MR # 4648-001, HLR # 1-84); Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE; 04/17/84; Bensulfuron Methyl; 0, 50, 500, or 2000 mg/kg in corn oil by gavage on gestation days 7-16 to 25 females mated on day 1, sacrificed on day 21; **analytical doses = 44 - 94% nominal doses**; no maternal clinical signs observed, no maternal pathology observed; no dose-related changes in incidence of pregnancy, number of corpora lutea, implantation sites, resorptions, live fetuses, fetal weights; no dose-related fetal malformations; developmental variations - extra ossification centers of lumbar region (2000 mg/kg); developmental retardations - decreased ossification of sternebrea (2000 mg/kg); NOEL(maternal) = 2000 mg/kg (limit test, no toxicity at $\geq$ 1000 mg/kg), NOEL(conceptus) = 500 mg/kg (skeletal developmental variations and retardations); **possible adverse effect - skeletal variations and retardations, NOEL(conceptus, 440 mg/kg) < NOEL(maternal, 1374 mg/kg), nominal doses adjusted to mean analytical doses;** study unacceptable (revised pages not supplied, no rationale for dose levels, no fetal eye measurement data, no historical data for delayed developmental effects, insufficient explanation for variance in analysis of dose); NLH/JAP, 12/17/85; request for revised pages withdrawn (see CDFA memo. 07/31/86); rationale for dose levels, fetal eye measurement data, and historical control data adequately addressed (at doc. # 50670-014, rec. # 42128; see CDFA memo., 03/14/86); registrant's explanation for variance in dose (at doc. # 50670-014, rec. # 42127) unacceptable (see CDFA memo., 03/14/86); study acceptable (**nominal doses to be adjusted to mean analytical doses for NOEL's and exposure assessment**, see CDFA memo., 03/14/86); SRM, 10/20/87.

> 50670-014; 42127; "F-5384 Du Pont Londax* Herbicide: Response To EPA Concerns"; Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE; 12/17/85; Bensulfuron Methyl; supplemental data addressing deficiencies in dosing analysis of rat teratology study (at doc. # 50670-004, rec. # 38316); registrant's explanation for variance in dose unacceptable, nominal doses to be adjusted to mean analytical doses for NOEL's and exposure assessment (see CDFA memo., 03/14/86); SRM, 10/20/87.
>
> 50670-014; 42128; "Response To Questions On Haskell Laboratory Report 1-84 (Developmental Toxicity Study INF-5384-38 By Gavage In The Rat)"; Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE; 03/04/86; Bensulfuron Methyl; supplemental data addressing deficiencies in rationale for dose levels, fetal eye measurement data, and historical control data of rat teratology study (at doc. # 50670-004, rec. # 38316); registrant's explanations acceptable (see CDFA memo., 03/14/86); SRM, 10/20/87.

Teratology, Rabbit

** 50670-021; 55524; "INF-5384. Developmental Toxicity Study In Rabbits Dosed By Gavage On Days 7-19 Of Gestation" (HLR # 704-85, MR # 7364-001); 11/15/85; Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE; Bensulfuron Methyl, 99%; 0, 30, 300, or 1500 mg/kg in 0.5% methyl cellulose by gavage on gestation days 7-19 to 22 (0 mg/kg) or 20 (30 - 1500 mg/kg) females artificially inseminated on day 0, sacrificed on day 30; maternal toxicity at 1500 mg/kg - decreased body weight and food consumption, 1/20 aborted, 2/20 complete fetal resorption, 2/20 deaths; no dose-related fetal toxicity or malformations, decreased fetal weight at 1500 mg/kg; NOEL(maternal) = 300 mg/kg (body weight, food consumption, abortion, complete resorption, death),

NOEL(conceptus) = 300 mg/kg (decreased fetal weight); no adverse effect, NOEL(conceptus) = NOEL(maternal); study acceptable; SRM, 11/09/87.

Mutagenicity, Gene Mutation

** 50670-003; 38310; "Mutagenicity Evaluation In Salmonella typhimurium" (HLR # 609-1, MR # 0581-975); Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE; 10/15/81; Bensulfuron Methyl, 95% (INF-5384-7); 0, 0.01, 0.05, 0.1, 0.5, 1, 5, 10, or 25 ug / 108 bacteria / 2.2 ml 4.5% DMSO / plate, ± activator (1.6 mg S-9 protein from Aroclor-induced rat livers, final 2.7 ml 3.7 % DMSO), 2 plates / trial, 2 trials / tester strain (TA1535, TA1537, TA98, TA100), incubated 37 :C for 48 hours, adequate positive controls; no cytotoxicity observed, decreased spontaneous revertants at 25 ug / plate; no dose-related increases in revertants / plate; no adverse effects; study acceptable; DS/JG, 12/19/85; one-liner update, SRM, 10/23/87, 12/22/88.

** 50670-013; 41868; "CHO/HGPRT Assay For Gene Mutation" (HLR # 212-84, MR # 4581-146); Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE; 05/09/84; Bensulfuron Methyl, 95.9% (INF-5384-52); 3 ml of 0, 0.5, 1.0, 2.0, 3.0, or 4.0 mM Bensulfuron Methyl, 1% DMSO, / 5 X 105 CHO-K1/BH4 cells / flask, 2 flasks / trial, 2 trials / dose, ± activation (S-9 protein from Aroclor-induced rat livers, 1 mg/ml), treated 18-19 (without activation) or 5 hours (with activation), post-incubated 0 (w/o activation) or 21-25 hours (w activation), 200 cells plated for viability test (7 day incubation), rest of cells maintained in log phase for 7 days by subculturing 1 X 106 cells 3 times, 2 X 105 cells plated to measure resistance to 1 X 10^{-5} M 6-thioguanine (7 day incubation), adequate positive controls; decreased viability at 4 mM (test material precipitated), no dose-related increase in 6-thioguanine resistance; no adverse effects; study acceptable; JSB/JG, 12/19/86; one-liner update, SRM, 10/26/87, 12/22/88.

> 50670-003; 38312; "CHO/HGPRT Assay For Gene Mutation" (HLR # 212-84, MR # 4581-146); Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE; 05/09/84; study unacceptable (pages missing); see complete study at doc. # 50670-013, rec. # 41868; DS/JG, 12/31/87.

Mutagenicity, Chromosome

** 50670-003; 38313; "In Vivo Bone Marrow Chromosome Study In Rats, H# 14,793, Final Report" (HLA Project # 201-694, HLO-210-84, MR-4581-156); Hazleton Laboratories America, Inc., Vienna, VA; 04/19/84; Bensulfuron Methyl, "assumed 100%" (INF-5384-52); 0, 500, 1500, or 5000 mg/kg by single oral gavage to 5 rats / sex / group, single ip. injection of colchicine (2 mg/kg) 2 hours before sacrifice (sacrifice at 6, 22, or 48 hours), femur bone marrow cells scored for chromosome aberrations, adequate positive controls; no dose-related toxicity observed, no dose-related effect on mitotic index or chromosome aberrations, limit test; no adverse effects; study acceptable; DS/JG, 12/19/85; one-liner update, SRM, 10/27/87.

**** 50670-021; 55523;** "In Vitro Evaluation Of INF-5384-52 For Sister Chromatid Exchange In Chinese Hamster Ovary (CHO) Cells" (HLR # 683-86, MR # 4581-424); Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE; 10/31/86; Bensulfuron Methyl, 95.9%; 106 CHO/K1/BH4 cells plated / flask, 24 hours later treated for 2 hours with 10 ml of 0, 0.135, 0.27, 0.8, 1.35, or 2.7 mM Bensulfuron Methyl (1% DMSO) / flask, 2 flasks / trial, 2 trials / dose, ± activation (1 mg S-9 protein from Aroclor-induced rat livers), followed by treatment for 24 - 26 hours with 3 ug BUdR / ml, incubated last 3 hours with 0.1 ug Colcemid®/ ml, harvested by mitotic shake-off, adequate positive controls;

mitotic delay seen at 2.7 mM + activation; **possible adverse effect - SCE at 1.35 and 2.7 mM without activation (1.4 X background)**; study acceptable; SRM/BD, 12/04/87.

Mutagenicity, DNA

** 50670-003; 38311; "Unscheduled DNA Synthesis/Rat Hepatocytes In Vitro" (HLR # 278-84, MR # 4581-146); Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE; 06/25/84; Bensulfuron Methyl, 95.9% (INF-5384-52); 2 ml of 0, 0.001, 0.01, 0.033, 0.1, 0.33, 1, 2, 3, or 3.5 mM in 1% DMSO were applied to primary rat hepatocytes (attached to glass during 2-hour post-isolation incubation) along with 10 uCi thymidine [methyl-3H], incubated 18 hours at 37 :C, cells swollen with 1% sodium citrate and fixed with ethanol-glacial acetic acid (3:1), incorporation of 3H measured radioautographically, 6 (0 mM) or 2 (0.001 - 3.5 mM) replicates / trial, 2 trials / dose, adequate positive controls; dose-related release of lactate dehydrogenase; no dose-related difference in 3H incorporation; no adverse effect; study acceptable; DS/JG, 12/19/85; one-liner update, SRM, 10/27/87.

SUPPLEMENTAL STUDIES

50670-003; 38300; "Ten-dose Oral Subacute Test In Rats" (HLR # 381-82, MR # 0581-975); Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE; 06/17/82; Special Toxicological Testing (857); Bensulfuron Methyl, 95%; 2200 mg in corn oil/kg/day, po, 5 times / week for 2 weeks to 6 young adult rats, 3 rats necropsied 4 hours after last dose, 3 rats recovered for 14-days then necropsied; slight decrease in body weight during first week of treatment; study found acceptable to support registration as a Subchronic Oral Study (821); VdV, 12/23/85; rereview determined that this was a pilot study; study status changed to supplemental information; SRM, 10/13/87.

50670-011; 38353; "Mutagenicity Evaluation In Salmonella Typhimurium" (HLR # 589-84, MR # 4581-241); Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE; 01/11/85; Benzoic acid, 2-[[[[(5-chloro-4,6-dimethoxy-2-pyrimidinyl)amino]carbonyl]amino]sulfonylmethyl]-, methyl ester; study acceptable, DS/JG, 12/19/85; rereview determined study assessed the mutagenicity of a chlorinated degradation product of Bensulfuron Methyl that could be found in drinking water; study status changed to supplemental information; SRM, 10/23/87.

CONCLUSIONS: Do data support registration?

YES Data support registration in the toxicity category ascribed.

RECOMMENDATIONS: In case of ongoing registration, register or do not register? What other specific studies or data are requested?

CONDITIONAL REGISTRATION pending submission of an acceptable metabolism study in 1989.

Registrant submitted a new APPLICATION FOR REGISTRATION OF ECONOMIC POISON (PESTICIDE) and new label for a new formulation for DU PONT LONDAX® HERBICIDE (63% active ingredient). The compound listed as the active ingredient and the statements of formulation on the present APPLICATION FOR REGISTRATION OF ECONOMIC POISON (PESTICIDE) and label are essentially in agreement and essentially correct.

The acute oral, acute dermal, acute inhalation, primary eye irritation, and primary dermal irritation studies on the technical active ingredient are acceptable.

Acute oral, acute dermal, primary eye irritation, and primary dermal irritation studies conducted with 60% ingredient are acceptable for registration of the formulated product.

An acute inhalation toxicity study is not required for the formulated product because it does not consist of an inhalable material.

The subchronic, reproduction, teratology, oncogenicity and mutagenicity studies are acceptable.

The rat metabolism study is unacceptable and not upgradeable. Registrant has committed to submission of a new metabolism study in 1989.

Registrant submitted additional histopathological examination data for the rat and dog chronic toxicity studies. In the course of evaluating other Chronic Toxicity Studies submitted by Du Pont, CDFA has stated that: "The ophthalmoscopic exam deficiency has been noted in data submitted to support registration of other products of Du Pont. The submission of the results of multiple sections of eyes for microscopic examination from studies on these other products may upgrade those studies" (CDFA memo dated 6/14/88). CDFA finds the rat and dog chronic toxicity studies acceptable.

_____ _____
Stanton Morris Date
Pesticide Evaluation Toxicologist

_____ _____
Gary Patterson Date
Staff Toxicologist

_____ _____
Joyce Gee Date
Staff Toxicologist

ONGOING REGISTRATION
SUPPLEMENTAL INFORMATION OR REVIEW WORKSHEET

I. STUDY IDENTIFICATION

Active Ingredient: Methyl 2-[[[[[(4,6-dimethoxypyrimidin-2-yl)amino]carbonyl] amino]sulfonyl]methyl]benzoate; Bensulfuron Methyl
Formulated Product Name: Du Pont Londax® Herbicide
SB 950 #: new active ingredient **Document #:** 50670-004 **Record #:** 38316
Addendum to Document #: **Addendum to Record #:**
Study Type: Teratogenicity (833) **CAS #:**
Full Study Title: "Developmental Toxicity Study of INF-5384-38 By Gavage In The Rat" (MR # 4648-001; HLR # 1-84)
EPA Reg #: **ID #:** 105375
Company Sponsor: E. I. du Pont de Nemours and Co., Inc., Wilmington, DE
Conducting Laboratory: Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE
Final Report Date: 02/17/84

II. STUDY STATUS

A. **Does this supplemental information or review lead to new conclusions regarding the study's acceptability or changes in the status of possible adverse health effects, compared to the most recent review?** no

B. **Is record** # 38316 **now complete?** yes
Is record # 38316 **now acceptable?** yes

Could study be upgraded with additional information (see VI)?

C. **New "one liner". One or two sentence summary of the study, its status, and the conclusions, taking into account any supplemental information.**

50670-004; 38316; "Developmental Toxicity Study of INF-5384-38 By Gavage In The Rat" (MR # 4648-001, HLR # 1-84); Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE; 04/17/84; Bensulfuron Methyl; 0, 50, 500, or 2000 mg/kg in corn oil by gavage on gestation days 7-16 to 25 females mated on day 1, sacrificed on day 21; **analytical doses = 44 - 94% nominal doses**; no maternal clinical signs observed, no maternal pathology observed; no dose-related changes in incidence of pregnancy, number of corpora lutea, implantation sites, resorptions, live fetuses, fetal weights; no dose-related fetal malformations; developmental variations - extra ossification centers of lumbar region (2000 mg/kg); developmental

(one-liner continued on next page)

D. **Are data adequate to support registration (if applicable)?** yes

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_____ _____
Stanton Morris Date
Pesticide Evaluation Toxicologist

_____ _____
Gary Patterson Date
Staff Toxicologist

(one-liner continued from previous page)
retardations - decreased ossification of sternebrea (2000 mg/kg); NOEL(maternal) = 2000 mg/kg (limit test, no toxicity at ≥ 1000 mg/kg), NOEL(conceptus) = 500 mg/kg (skeletal developmental variations and retardations); **possible adverse effect - skeletal variations and retardations, NOEL(conceptus, 440 mg/kg) < NOEL(maternal, 1374 mg/kg), nominal doses adjusted to mean analytical doses;** study unacceptable (revised pages not supplied, no rationale for dose levels, no fetal eye measurement data, no historical data for delayed developmental effects, insufficient explanation for variance in analysis of dose); NLH/JAP, 12/17/85; request for revised pages withdrawn (see CDFA memo. 07/31/86); rationale for dose levels, fetal eye measurement data, and historical control data adequately addressed (at doc. # 50670-014, rec. # 42128; see CDFA memo., 03/14/86); registrant's explanation for variance in dose (at doc. # 50670-014, rec. # 42127) unacceptable (see CDFA memo., 03/14/86); study acceptable (**nominal doses to be adjusted to mean analytical doses for NOEL's and exposure assessment**, see CDFA memo., 03/14/86); SRM, 10/20/87.

III. NATURE OF SUPPLEMENTAL INFORMATION

IV. DISCUSSION

No new data were reviewed. A summary of the data on significant developmental effects was prepared for hazard assesment.

Summary of Significant Developmental Effects
(affected fetuses / total no. fetuses examined,
[affected litters / total no. litters examined])

Dose (mg/kg)	0	50	500	2000
Total Fetuses	304	274	313	333
Tissue / Effect — Total Litters	24	20	23	25
ribs				
extra ossification				
center	6/304 [2/24]	5/274 [3/20]	10/313 [7/23]	16/333[1] [8/25]
sternebrea				
partially or unossified	88/304 [20/24]	121/274 [19/20]	145/313 [20/23]	156/333[1] [23/25]
hyoid				
partially or unossified	14/151 [9/24]	23/131 [12/20]	35/1492 [15/23]	31/156[2] [17/25]

[1] Significantly different from 0 ppm ($p \leq 0.05$).
[2] Significantly different from 0 ppm ($p \leq 0.05$) but within range of historical controls.

CALIFORNIA DEPARTMENT OF FOOD AND AGRICULTURE
MEDICAL TOXICOLOGY BRANCH

SUPPLEMENTAL INFORMATION OR REVIEW WORKSHEET

I. STUDY IDENTIFICATION

Active ingredient: Bensulfuron Methyl; Methyl 2-[[[[[(4,6-dimethoxypyrimidin-2-yl)amino]carbonyl]amino]sulfonyl]methyl]benzoate
Formulated product name: Du Pont Londax® Herbicide
SB 950 #: new active ingredient **Document #:** 50670-023 **Record #:** 064873
Addendum to Document #: 50670-019 **Addendum to Record #:** 55521
Study Type: Oncogenicity/Carcinogenicity (832) **CAS #:**
Full Study Title: "Long-Term Feeding And Two-Generation, Four-Litter Reproduction Study In Rats With INF-5384" (HLR # 662-85, MR # 4651-001)
EPA Reg #: **ID #:** NA
Company Sponsor: E. I. du Pont de Nemours & Co., Inc., Wilmington, DE
Conducting Laboratory: Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE
Final Report Date: 01/17/86
Study Period: 02/08/83 - 02/15/85

II. STUDY STATUS

A. **Does this supplemental information or review lead to new conclusions regarding the study's acceptability or changes in the status of possible adverse health effects, compared to the most recent review?** no

B. **Is record** # 55521 **now complete?** yes, as an Oncogenicity Study only
Is record # 55521 **now acceptable?** yes, as an Oncogenicity Study only

C. **New "one liner". One or two sentence summary of the study, its status, and the conclusions, taking into account any supplemental information.**

50670-019; 55521; "Long-Term Feeding And Two-Generation, Four-Litter Reproduction Study In Rats With INF-5384" (HLR # 662-85, MR # 4651-001); Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE; 01/17/86; Oncogenicity/Carcinogenicity Study (832); Bensulfuron Methyl, 95 - 95.9%; continuous dietary exposure of 0, 50, 750, or 7500 ppm to 80 rats/sex/dose for 24 months, 20 rats/sex/dose used in reproduction sub-study, 10 rats/sex/dose sacrificed at 12 months; decreased food

(one-liner continued on next page)

D. **Are data adequate to support registration (if applicable)?**
yes, as an Oncogenicity Study only

Stanton Morris
Pesticide Evaluation Toxicologist

Date

Gary Patterson
Staff Toxicologist

Date

(one-liner continued from previous page)
consumption and body weights in females at 7500 ppm, mild anemia in males at 24 months at 7500 ppm, no dose-related gross pathological abnormalities at 1- or 2-year necropsy, minor histological changes in livers at 1- and 2-year necropsy at 7500 ppm, no dose-related proliferative lesions; no adverse effect; NOEL = 750 ppm (food consumption, body weight, liver effects, anemia); study acceptable as Oncogenicity/Carcinogenicity Study only; SRM/GTP, 11/12/87; SRM/GTP, 01/26/88.

III. NATURE OF SUPPLEMENTAL INFORMATION

IV. DISCUSSION

No new data were reviewed. A summary of the data on neoplastic lesions was prepared for hazard assesment.

Summary of Neoplastic Lesions for
Interim One-year Sacrifice, Males
(tumors / no. organs examined)

Dose (ppm)	0	50	750	7500
Tissue / Tumor | No. in Group	10	10	10	10
pituitary				
adenoma, pars distalis	0/10	2/9	1/10	0/10
Total	0	2	1	0

Summary of Neoplastic Lesions for
Interim One-year Sacrifice, Females
(tumors / no. organs examined)

Dose (ppm)	0	50	750	7500
Tissue / Tumor | No. in Group	10	10	10	10
pituitary				
adenoma, pars distalis	0/10	0/10	1/10	0/10
Total	0	0	1	0

Summary of Neoplastic Lesions for
Final Two-year Sacrifice, Males
(tumors / no. organs examined)

Tissue / Tumor	Dose (ppm) / No. in Group	0 25	50 34	750 31	7500 23
liver					
adenoma, hepatocellular		1/25	1/34	0/31	1/23
* carcinoma, hepatocellular		0/25	2/34	1/31	0/23
kidney					
hemangioma		1/25	0/34	0/31	0/23
kidney					
papilloma, transitional cell		0/25	1/34	0/31	0/23
* carcinoma, tubular		0/25	0/34	1/31	1/23
* hemangiosarcoma		0/25	0/34	1/31	0/23
skeletal muscle					
* histiocytic sarcoma, multicentric		0/25	0/34	0/31	1/23
sleen					
hemangioma		0/25	0/34	0/31	1/23
* hemangiosarcoma		0/25	0/34	0/31	1/23
* histocytic sarcoma, multicentric		0/25	1/34	0/31	0/23
brain					
* astrocytoma		0/25	0/34	0/31	1/23
* ependymoma		0/25	0/34	1/31	0/23
* granular cell tumor		0/25	0/34	1/31	0/23
mesenteric lymph node					
hemangioma		0/25	0/34	1/31	0/23
pancreas					
adenoma, islet cell		4/25	7/34	4/31	2/23
adrenals					
adenoma, cortex		0/25	0/34	1/31	0/23
pheochromocytoma		3/25	3/34	0/31	1/23
* pheochromocytoma		1/25	2/34	2/31	0/23
pituitary					
adenoma, pars distalis		13/25	19/32	11/31	13/22
adenoma, pars intermedia		1/25	0/32	0/31	0/22
sciatic nerve					
neurofibroma		1/25	0/34	0/31	0/23
* histocytic sarcoma, multicentric		0/25	0/34	0/31	1/23
thyroid					
adenoma, C-cell		0/25	1/34	3/30	0/23
adenoma, follicular cell		1/25	2/34	1/30	0/23
* cacinoma, C-cell		2/25	2/34	2/30	0/23

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Summary of Neoplastic Lesions for
Final Two-year Sacrifice, Males
(tumors / no. organs examined)
(continued from previous page)

Tissue / Tumor	Dose (ppm) / No. in Group	0 25	50 34	750 31	7500 23
thymus					
hemangioma		0/21	1/34	0/27	0/21
mammary gland					
adenoma		0/18	1/25	0/26	0/21
femur					
* osteosarcoma		0/25	1/34	0/31	0/23
nose					
* carcinoma, squamous cell, hard palate		0/25	0/34	1/31	0/23
* osteosarcoma		1/25	0/34	0/31	0/23
testes					
adenoma, interstitial cell		2/25	3/34	2/31	2/23
* carcinoma, seminal vesicle, metastatic		0/25	0/34	1/31	0/23
adipose tissue					
hemangioma, mesenteric lipogranuloma		0/25	0/34	0/31	1/23
lipoma, ventrum		2/25	0/34	0/31	0/23
miscellaneous					
fibroma, subcutis, dorsum		0/13	1/15	0/21	0/14
fibroma, subcutis, ventrum		0/13	2/15	0/21	0/14
hemangioma, skin, scrotum		0/13	0/15	0/21	1/14
leiomyoma, subcutis, ventrum		0/13	1/15	0/21	1/14
neurofibroma, tail		1/13	0/15	0/21	0/14
papilloma, pinna, ear		1/13	0/15	0/21	1/14
papilloma, skin, head		0/13	1/15	0/21	0/14
* carcinoma, basal cell, ventrum		0/13	1/15	0/21	0/14
* carcinoma, squamous cell, dorsum		1/13	0/15	0/21	0/14
* carcinoma, squamous cell, zymbal gland		0/13	0/15	1/21	0/14
* hemangiosarcoma, renal, metastatic, mesentery		0/13	0/15	1/21	0/14
* histiocytic sarcoma, mesentery, multicentric		0/13	0/15	0/21	1/14
* histiocytic sarcoma, multicentric		0/13	0/15	0/21	1/14
* histiocytic sarcoma, subcutis, multicentric		0/13	0/15	0/21	1/14
Number of Primary Tumors		36	52	36	28
Number of Malignant Primary Tumors		5	8	12	4

* malignant tumors

Summary of Neoplastic Lesions for
Final Two-year Sacrifice, Females
(tumors / no. organs examined)

Tissue / Tumor	Dose (ppm) / No. in Group	0 33	50 29	750 36	7500 35
liver					
adenoma, hepatocellular		1/33	0/29	0/36	0/35
* carcinoma, hepatocellular		0/33	0/29	1/36	0/35
kidney					
lipoma		0/33	1/29	0/36	0/35
* carcinoma, tubular, osseous metaplasia		1/33	0/29	0/36	0/35
lung					
* sarcoma, uterine, metastatic		0/33	0/29	0/36	1/35
colon					
* adenocarcinoma		0/33	0/29	1/36	0/35
pancreas					
adenoma, islet cell		0/33	2/29	4/36	0/35
adrenals					
adenoma, cortex		0/33	1/29	0/36	0/35
pheochromocytoma		2/33	0/29	0/36	0/35
pituitary					
adenoma, pars distalis		23/31	19/29	19/36	22/35
thyroid					
adenoma, C-cell		0/33	0/29	0/36	1/35
* carcinoma, C-cell		0/33	0/29	1/36	1/35
thymus					
thymoma		1/30	0/21	0/34	1/30
mammary gland					
adenoma		1/33	0/29	0/36	2/34
fibroadenoma (A)		12/33	10/29	11/36	11/34
fibroadenoma (B)		5/33	4/29	2/36	2/34
fibroadenoma (C)		0/33	0/29	1/36	1/34
fibroma (C)		0/33	0/29	0/36	1/34
* adenocarcinoma (A)		2/33	3/29	3/36	1/34
* adenocarcinoma (B)		0/33	0/29	1/36	1/34
* fibrosarcoma		1/33	0/29	0/36	0/34
* sarcoma, uterine, metastatic		0/33	0/29	0/36	1/34
nose					
fibroma		1/32	0/29	1/36	0/35
* carcinoma, squamous cell		0/32	1/29	0/36	1/35
ovaries					
granulosa cell tumor		0/33	1/29	0/36	0/35

(continued on next page)

Summary of Neoplastic Lesions for
Final Two-year Sacrifice, Females
(tumors / no. organs examined)
(continued from previous page)

Dose (ppm)	0	50	750	7500
Tissue / Tumor	No. in Group	33	29	36	35
uterus					
* sarcoma		0/33	0/29	0/36	1/35
adipose tissue					
lipoma, mediastinum		1/32	0/29	0/36	0/35
miscellaneous					
adenoma, clitoral gland		0/9	1/14	0/11	0/11
fibroma, ventrum		0/9	0/14	1/11	0/11
papilloma, ear, pinna		0/9	0/14	0/11	1/11
* carcinoma, basal cell, ventrum		0/9	0/14	0/11	1/11
* carcinoma, squamous cell, dorsum		1/13	0/15	0/21	0/14
Number of Primary Tumors		51	43	46	48
Number of Malignant Primary Tumors		4	4	7	6

* malignant tumors

CALIFORNIA DEPARTMENT OF FOOD AND AGRICULTURE
MEDICAL TOXICOLOGY BRANCH

SUPPLEMENTAL INFORMATION OR PEER REVIEW WORKSHEET

I. STUDY IDENTIFICATION

Active Ingredient: Bensulfuron Methyl; Methyl 2-[[[[[(4,6-dimethoxypyrimidin-2-yl)amino]carbonyl]amino] sulfonyl]methyl]benzoate
Formulated Product Name: Du Pont Londax® Herbicide
SB 950 #: new active ingredient **Document #:** 50670-020 **Record #:** 55530
Study Type: Oncogenicity/Carcinogenicity (832) **CAS #:**
Full Study Title: "DPX-F5384: 24-Month Oral Chronic Toxicity And Oncogenicity Study In Mice" (Report # TX5384-1-86)
EPA Reg #: **ID #:** 105375
Company Sponsor: E. I. du Pont de Nemours and Company, Inc., Wilmington, DE
Conducting Laboratory: The Institute of Environmental Toxicology, Tokyo, Japan
Final Report Date: 04/07/86

II. SUMMARY OF WORKSHEET

A. **STUDY STATUS: Is report complete?** - yes
Is study acceptable? - yes

yes - **Meets EPA guidelines**
- **Minor variances from guidelines**
- **Major variances from guidelines**
- **Could be upgraded with additional information (see VI-A)**

yes - **Has useful data**
- **Insufficient data**
- **Non EPA validated study**
- Other_____

B. **CONCLUSIONS: Does this study as reported demonstrate a possible adverse health effect?:** no
If so, in what area?

C. **ONE LINER-One or two sentence summary of the study:**

50670-020; 55530; "DPX-F5384: 24-Month Oral Chronic Toxicity And Oncogenicity Study In Mice" (Report # TX5384-1-86); The Institute of Environmental Toxicology, Tokyo, Japan; 04/07/86; Bensulfuron Methyl, 95.9%; continuous dietary exposure of 0, 10, 150, 2500, or 5000 ppm to 92 mice/sex/dose for 104 weeks; 10 mice/sex/dose sacrificed at 52 and 78 weeks; no dose-related mortalities; no dose-related clinical signs; centrilobular hepatocellular swelling (males), cortical cysts and pelvic

(one-liner continued on next page)

D. **ARE DATA ADEQUATE TO SUPPORT REGISTRATION (if applicable)?** yes

---

_____ _____
Stanton Morris Date
Pesticide Evaluation Toxicologist

_____ _____
Gary Patterson Date
Staff Toxicologist

(one-liner continued from previous page)
dilation in kidneys (females), focal hepatocellular necrosis (females) at 5000 ppm; no treatment-related increase in tumors; no adverse effects; NOEL = 2500 ppm (male - 226 mg/kg/day, female - 227 mg/kg/day, liver and kidney effects); study acceptable; 03/27/89, SRM.

III. NATURE OF SUPPLEMENTAL INFORMATION

IV. DISCUSSION

No new data were reviewed. A summary of the data on neoplastic lesions was prepared for hazard assesment.

Summary of Neoplastic Lesions for
All Animals Examined, Males
(number of tumors)

Tissue / Tumor	Dose (ppm)	0	10	150	2500	5000
	No. Examined	92	92	92	92	92
hematopoietic & lymphatic system						
diagnosis:						
* myeloid leukemia		1	0	0	0	1
* malignant lymphoma		9	14	9	9	14
lymph nodes (others):						
* hemangiosarcoma		0	0	1	0	0
spleen:						
* hemangiosarcoma		1	1	3	0	1
respiratory system						
nasal cavity:						
* adenocarcinoma		0	1	0	1	0
lung:						
adenoma		16	14	10	13	16
* adenocarcinoma		24	26	22	16	15
<nodule/mass not in section>		0	0	1	3	1
digestive system						
stomach (non-glandular):						
papilloma		0	0	0	1	0
stomach (glandular):						
adenoma		1	0	1	0	1
* osteosarcoma		0	0	0	0	1
small intestine:						
* adenocarcinoma		0	1	0	0	0
anus:						
* squamous cell carcinoma		1	0	0	0	0
liver:						
hepatocellular adenoma		36	42	37	27	40
cystic cholangioma		0	0	0	0	1
hemangioma		1	1	0	0	2
* hepatocellular carcinoma		5	2	8	5	9
* fibrosarcoma		0	0	1	0	0

(continued on next page)

Summary of Neoplastic Lesions for
All Animals Examined, Males
(number of tumors)
(continued from previous page)

Tissue / Tumor	Dose (ppm)	0	10	150	2500	5000
	No. Examined	92	92	92	92	92
liver (continuation)						
* hemangiosarcoma		1	2	0	0	0
<nodule/mass not in section>		0	0	0	0	1
pancreas:						
acinar cell adenoma		0	2	0	0	0
islet cell adenoma		0	2	0	0	0
urinary system						
kidney:						
adenoma		1	0	1	0	1
<nodule/mass not in section>		2	0	0	0	0
urinary bladder:						
* transitional cell carcinoma		0	0	1	0	0
genital system						
testis:						
adenoma		0	2	1	2	2
interstitial cell tumor		1	2	1	4	2
epididymis:						
adenoma		0	0	0	1	0
vas deference:						
<nodule/mass not in section>		0	0	0	1	0
seminal vesicle:						
adenoma		0	1	0	0	0
* leiomyosarcoma		0	0	0	1	0
preputial gland:						
adenoma		1	0	0	0	0
endocrine system						
pituitary:						
* anterior adenocarcinoma		0	1	0	0	0
thyroid:						
follicular adenoma		0	0	1	0	1
parathyroid:						
adenoma		0	0	0	0	1
adrenal:						
cortical adenoma		1	1	0	1	3
pheochromocytoma		1	0	0	0	0
sense organs						
harderian gland:						
adenoma		12	11	10	13	12
* adenocarcinoma		0	1	0	0	0
integumentary system						
skin:						
papilloma		1	0	1	0	1
fibroma		0	0	1	0	0
* sebaceous adenocarcinoma		0	0	0	1	0

(continued on next page)

Summary of Neoplastic Lesions for
All Animals Examined, Males
(number of tumors)
(continued from previous page)

Dose (ppm)	0	10	150	2500	5000
Tissue / Tumor	No. Examined	92	92	92	92	92
skin (continuation)						
* fibrosarcoma		0	2	0	2	2
* hemangiosarcoma		1	1	2	0	0
* osteosarcoma		1	0	0	1	0
<nodule/mass not in section>		0	1	1	0	1
Number of Tumors		118	131	113	102	129
Number of Malignant Tumors		46	53	49	40	46

* malignant tumors

Summary of Neoplastic Lesions for
All Animals Examined, Females
(number of tumors)

Dose (ppm)	0	10	150	2500	5000
Tissue / Tumor	No. Examined	92	92	92	92	92
hematopoietic & lymphatic system						
diagnosis:						
* myeloid leukemia		0	0	1	0	0
* malignant lymphoma		25	25	26	32	33
lymph nodes (others):						
* hemangiosarcoma		1	0	0	0	0
spleen:						
hemangioma		2	0	1	0	0
* hemangiosarcoma		1	2	0	3	1
respiratory system						
lung:						
adenoma		11	6	16	8	17
* adenocarcinoma		14	17	8	11	11
<nodule/mass not in section>		2	2	0	1	2
digestive system						
esophagus:						
papilloma		0	0	1	0	0
stomach (glandular):						
* leiomyosarcoma		0	1	0	0	0
small intestine:						
* adenocarcinoma		0	0	0	1	0
* hemangiosarcoma		0	0	1	0	0
anus:						
papilloma		0	1	0	0	0
* squamous cell carcinoma		0	0	0	0	1
liver:						
hepatocellular adenoma		3	2	5	4	6
cystic cholangioma		0	0	0	0	1

(continued on next page)

Summary of Neoplastic Lesions for
All Animals Examined, Females
(number of tumors)
(continued from previous page)

Tissue / Tumor	Dose (ppm)	0	10	150	2500	5000
	No. Examined	92	92	92	92	92
liver (continuation):						
hemangioma		1	0	1	0	0
* hemangiosarcoma		0	0	0	0	1
<nodule/mass not in section>		0	0	0	0	1
pancreas:						
islet cell adenoma		0	2	0	1	0
genital system						
ovary:						
granulosa cell tumor		0	1	0	0	0
theca cell tumor		0	0	1	1	0
luteoma		1	0	1	1	0
adenoma		1	0	1	0	2
hemangioma		0	0	0	2	0
* adenocarcinoma		0	0	0	0	1
* fibrosarcoma		0	0	0	1	0
* hemangiosarcoma		2	1	0	0	0
* leiomyosarcoma		0	0	1	0	1
<nodule/mass not in section>		0	0	0	1	0
uterus:						
endometrial stromal polyp		4	5	1	2	2
adenoma		0	0	2	3	0
hemangioma		0	0	0	1	2
leiomyoma		2	1	2	4	1
* adenocarcinoma		0	0	0	1	0
* hemangiosarcoma		0	1	0	0	0
* endometrial stromal sarcoma		0	0	0	1	1
* leiomyosarcoma		1	3	5	1	4
vagina:						
leiomyoma		0	0	0	0	1
endocrine system						
pituitary:						
anterior adenoma		3	4	5	3	2
* anterior adenocarcinoma		0	0	0	0	1
thyroid:						
follicular adenoma		0	0	1	0	0
adrenal:						
cortical adenoma		2	0	1	1	0
pheochromocytoma		1	0	0	0	1
nervous system:						
cerebrum:						
* malignant meningioma		0	0	0	0	1
musculo-skeletal system						
bone (femur):						
osteoma		0	0	0	0	1
* hemangiosarcoma		0	1	0	0	0

(continued on next page)

Summary of Neoplastic Lesions for
All Animals Examined, Females
(number of tumors)
(continued from previous page)

Tissue / Tumor	Dose (ppm)	0	10	150	2500	5000
	No. Examined	92	92	92	92	92
bone (others):						
osteoma		0	0	0	0	1
sense organs						
harderian gland:						
adenoma		7	9	7	8	8
* adenocarcinoma		1	0	0	0	1
auricle:						
* fibrosarcoma		1	0	0	0	0
integumentary system						
skin:						
papilloma		0	1	0	0	0
fibroma		2	0	0	0	1
* squamous cell carcinoma		0	0	0	0	1
* fibrosarcoma		2	3	0	2	3
* liposarcoma		0	1	0	0	0
* hemangiosarcoma		2	1	0	3	0
* leiomyosarcoma		0	0	0	1	0
* rhabdomyosarcoma		0	1	3	1	0
<nodule/mass not diagnosed due to autolysis>		0	0	1	0	0
mammary gland:						
adenoma		1	2	1	2	1
* adenocarcinoma		4	3	3	6	4
body cavities						
abdominal cavity:						
* liposarcoma		1	0	0	0	0
* hemangiosarcoma		0	1	0	0	1
* malignant fibrous histocytoma		0	0	0	0	1
Number of Tumors		98	97	95	107	117
Number of Malignant Tumors		57	63	48	66	70

* malignant tumors

CALIFORNIA DEPARTMENT OF FOOD AND AGRICULTURE
MEDICAL TOXICOLOGY BRANCH

SUPPLEMENTAL INFORMATION OR PEER REVIEW WORKSHEET

I. STUDY IDENTIFICATION

Active Ingredient: Bensulfuron methyl
Formulated Product Name: Du Pont Londax Herbicide
EPA Reg #: **ID #:**
Document #: 50670-018 **Record #:** 055522
SB 950 #: New Active ingredient, none assigned
Addendum to Document #: Same **Addendum to Record #:** Same
Study Type: 831 - dog - chronic
Full Study Title: A one-year Feeding Study in Dogs with H14793
Company Sponsor: Du Pont
Conducting Laboratory: Bio/dynamics, NJ,, Project 84-2835
Final Report Date: 1/16/86

II. STUDY STATUS

A. **Does this supplemental information or peer review lead to new conclusions regarding the study's acceptability or changes in the status of possible adverse health effects, compared to the most recent review?** NO

B. **STUDY STATUS: Is report complete?** - Yes (as before)
Is study acceptable? - Yes (as before)

Yes
- **Meets EPA guidelines**
- **Minor variances from guidelines**
- **Major variances from guidelines**
- **Could be upgraded with additional information (see Discussion)**

Yes
- **Has useful data**
- **Insufficient data**
- **Non EPA validated study**
- **Other**_____

C. **CONCLUSIONS: Does this study as reported demonstrate a possible adverse health effect?:** No (as before but see Discussion Section)
If so, in what area?

D. **New "one liner". Summary of the study, its status, and the conclusions, taking into account any supplemental information or peer review changes.**

No new 1-liner - see review of 12/88, W067729.831.

50670-018; 55522; "A One-Year Feeding Study In Dogs With H14793" (Project # 84-2835); Bio/dynamics, Inc., East Millstone, NJ; 01/16/86; Bensulfuron Methyl, 95.9%; 0, 50, 750, or 7500 ppm in the diet of 5 beagles / sex / dose for 1 year; no dose-related clinical signs observed, increased alanine aminotransferase, alkaline phosphatase, and liver weights and brown pigmented material in bile canaliculi at 7500 ppm; no adverse effect; NOEL = 750 ppm (liver effects, male - 21.4 mg/kg/day, female - 19.9 mg/kg/day); study unacceptable and not upgradeable (no ophthalmological data); SRM, 11/05/87; study status changed to acceptable with exemption from ophthalmological data (CDFA memo, 6/14/88) and submission of eye histophathology data (50670-029, 67729); SRM, 12/19/88

_____ _____
Staff Toxicologist Date

III. NATURE OF SUPPLEMENTAL INFORMATION

No new data.

IV. DISCUSSION

In the course of preparing the risk assessment document for Londax, it was noted that the review of the one-year dog study indicated a NOEL of 750 ppm, the mid-dose, rather than 7500 ppm, the high dose, based upon liver changes and elevated enzyme levels at 7500 ppm. At the time of the initial review and the supplementary review, these changes were not identified as "possible adverse effects". The reason for this decision was based on a judgment that they were not of toxicological concern but, being conservative, the NOEL was considered to be 750 ppm. The incidences of the findings reported are given below:

	0	50	750	7500 ppm
Brown pigment in bile canaliculi				
Males	1/5	0/5	0/5	5/5[a]
Females	0/5	0/5	0/5	5/5*

[a] This incidence was not indicated as statistically significant in the report but has a p = 0.024 by Fisher's exact test without correction. The incidence in females was noted with and "*" as $p < 0.05$ when actually p = 0.004 by Fisher's exact without correction.

In addition, alkaline phosphatase and alanine aminotransferase levels in blood were elevated at 7500 ppm in males and females as early as month 1 of the study. At termination, they were as follows:

Alk Phosphatase (IU/L)				
Males	34	33	39	164
Females	52	35	53	160
Alanine aminotransferase (SGPT) (IU/L)				
Males	21	23	27	60
Females	21	23	24	43

The only control range of values for these enzymes in the dog (type not stated) is from an unknown source from the literature. The range for SGPT is 5 - 40 units/100 ml and for alkaline phosphatase as 1 - 4 units/100 ml without the "units" being defined.

CALIFORNIA DEPARTMENT OF FOOD AND AGRICULTURE
MEDICAL TOXICOLOGY BRANCH

SUPPLEMENTAL INFORMATION OR PEER REVIEW WORKSHEET

I. STUDY IDENTIFICATION

Active Ingredient: Bensulfuron methyl (Londax)
Formulated Product Name:
EPA Reg #: **ID #:**
Document #: 50670-020 **Record #:** 055530
SB 950 #: None assigned, new active ingredient
Addendum to Document #: Same **Addendum to Record #:** Same
Study Type: 832 - oncogenicity - mouse
Full Study Title: DPX-F5384: 24-Month Oral Chronic Toxicity and Oncogenicity Study in Mice
Company Sponsor: du Pont
Conducting Laboratory: The Institute of Environmental Toxicology, Japan
Final Report Date: 4/7/86

II. STUDY STATUS

A. **Does this supplemental information or peer review lead to new conclusions regarding the study's acceptability or changes in the status of possible adverse health effects, compared to the most recent review?** NO

B. **STUDY STATUS: Is report complete?** - Yes (as before)
Is study acceptable? - Yes (as before)

Yes - **Meets EPA guidelines**
- **Minor variances from guidelines**
- **Major variances from guidelines**
- **Could be upgraded with additional information (see Discussion)**

Yes - **Has useful data**
- **Insufficient data**
- **Non EPA validated study**
- **Other**_____

C. **CONCLUSIONS: Does this study as reported demonstrate a possible adverse health effect?:** No (as before) See Discussion section below.
If so, in what area?

D. **New "one liner". Summary of the study, its status, and the conclusions, taking into account any supplemental information or peer review changes.**
No new one-liner - see previous worksheets.

_____ _____
Staff Toxicologist Date

III. NATURE OF SUPPLEMENTAL INFORMATION

None.

IV. DISCUSSION

In the course of preparing the risk assessment document for Londax, the issue of potential effects in the liver arose as liver effects were noted in several

studies. Although the neoplastic findings have been addressed in detail (see W055530.S02), the non-neoplastic incidences were not compiled in the review document. These are now listed below:

	0	10	150	2500	5000 ppm
Liver					
Hepatocellular swelling					
Males	0/92	0/92	0/92	1/92	7/92**
Females	Not listed in the table				
Focal necrosis					
Males	4/92	3/92	5/92	2/92	3/92
Females	5/92	2/92	8/92	5/92	12/92ns
Kidney					
Cysts					
Males	15/92	14/92	14/92	10/92	10/92
Females	7/92	13/92	8/92	7/92	13/92ns
Pelvic dilation					
Males	24/92	29/92	25/92	16/92	15/92
Females	2/92	8/92*	9/92*	9/92*	6/92ns

ns: not significant by Fisher's exact test.
* $p < 0.05$, ** $p < 0.01$ by the same test.

The study was considered negative for tumorigenicity and the inconsistency of the other findings above between sexes make toxicological significance doubtful, especially at reasonably high doses. A NOEL of 2500 ppm was established for these effects.

APPENDIX B

Exposure Assessment

APPENDIX B

California Department of Food and Agriculture
Worker Health and Safety Branch

Human Exposure Assessment

LONDAX

April 10, 1989

Londax Herbicide is to be used in rice at very low rates of application, i.e., 1 oz a.i. per acre. It is a dry flowable formulation and contains 60 percent bensulfuron methyl. Mixing and loading for typical application in Sutter, Yolo and Colusa counties were considered.

Limited data are available for very dilute mixtures [mixer/loader exposure (6 ug/kg/hr) for an insecticide-miticide used at low rates (0.1 - 0.3 oz a.i. per acre in citrus (Document No. 50406-005)], such as the proposed Londax mixture. A 0.15 EC containing two percent active ingredient is used as a surrogate for Londax Herbicide. Potential Dermal Exposure was 6 ug/kg/hr. Based on the use rates the potential mixer/loader exposure is low.

The respective rates of application are 0.1 - 0.3 oz a.i. per acre for the surrogate and 1.0 oz a.i. per acre for Londax Herbicide. Therefore, we have included a correction factor of 1.0/0.1 in the estimate of Potential Daily Absorbed Dosage. Assuming an eight (8) hour work day, the potential daily absorbed dosage for Londax Herbicide, corrected for clothing penetration (10 percent) and assuming 100 percent dermal absorption in 24 hours, would be estimated as follows:

Potential Daily Absorbed Dosage

$$= (1.0/0.1)(6 \text{ ug/kg/hr})(8 \text{ hr})(0.10) = 48 \text{ ug/kg}$$

These exposure estimates are based upon conservative assumptions. Before final estimates can be made, Dermal Absorption and Mixer-Loader-Applicator Studies using current equipment and facilities are required.

Characteristics of bensulfuron methyl (Londax®) applications on rice

Method: air

Formulation: dry flowable

Application rate: 1.67 ounces of product (1 ounce active ingredient) per acre or 117.2 g/ha (70.2 g ai/ha)

Carrier: Water, minimum of five gallons per acre (46.75 l/ha)

Tank mixes: antidrift agents (polyvinyl alcohol and polyacrylamide based materials) are recommended, may be mixed with methyl parathion

Application season: April 25 through June 10, with great majority of applications occurring over a three-week period in May, corresponding with the one to three leaf stage of rice seedlings

Mixer/loader activities: During the bensulfuron methyl application season, mixer/loaders also prepare airplanes to apply molinate and thiobencarb and, to a lesser degree, to seed newly flooded rice fields and to apply carbofuran and MCPA. During peak application periods, mixer/loaders have the potential to be exposed to bensulfuron methyl for six to eight hours per day.

JML: 4/18/89

APPENDIX C

TAS Printout

MENU SCREEN ANALYSIS FOR LONDAX DATE OF ANALYSIS: 04-06-1989
RESIDUE FILE NAME: LONDAX
DATE RESIDUE FILE CREATED OR LAST UPDATED: 04-06-1989/07:17:49
RELEVANT DOSE VALUE = 440.0000 MG/KG BODY WT/DAY
CHEMICAL IS ASSUMED TO BE UNIFORMLY DISTRIBUTED
COMMENT:

ACUTE EXPOSURE FOR CHILDREN 7-12 YEARS

	MENU SCREEN CATEGORY	EXPOSURE MG/KG BODY WT/DAY	EXPOSURE PERCENT OF RDV
1	MEATS	0.001220	0.00%
2	DRY BEANS/PEANUTS	0.000000	0.00%
3	EGGS	0.000000	0.00%
4	MILK: NON-FAT SOLID	0.000000	0.00%
5	MILK: FAT SOLIDS	0.000000	0.00%
6	GRAINS (EXCL. RICE)/SOYBEANS/VE	0.000071	0.00%
7	STARCHY VEG. INCL. RICE/ SWEETP	0.000000	0.00%
8	TOMATOES	0.000000	0.00%
9	OTHER VEGETABLES INCL. BRASSICA	0.000000	0.00%
10	FRUITS	0.000000	0.00%
11	NUTS AND SEEDS	0.000000	0.00%
12	SUGARS	0.000000	0.00%
13	MISCELLANEOUS FOODS	0.000000	0.00%
14	WATER: FOOD BASED	0.000000	0.00%
27	WATER: NON-FOOD BASED	0.000000	0.00%
	TOTAL ACUTE EXPOSURE:	0.001292	0.00%

MARGIN OF SAFETY: %340607.84

FOODS USED IN MENU SCREEN ANALYSIS:

	FOOD/FOODFORM	RESIDUE (PPM)	ADJUSTMT FACTOR
1	FISH-UNSPECIFIED	0.300000	1.00
6	RICE-ROUGH	0.020000	1.00

ENU SCREEN ANALYSIS FOR LONDAX DATE OF ANALYSIS: 04-06-1989
ESIDUE FILE NAME: LONDAX
ATE RESIDUE FILE CREATED OR LAST UPDATED: 04-06-1989/07:17:49
ELEVANT DOSE VALUE = 440.0000 MG/KG BODY WT/DAY
HEMICAL IS ASSUMED TO BE UNIFORMLY DISTRIBUTED
OMMENT:

ACUTE EXPOSURE FOR OVERALL 48-STATE POPULATION

MENU SCREEN CATEGORY	EXPOSURE MG/KG BODY WT/DAY	EXPOSURE PERCENT OF RDV
1 MEATS	0.000912	0.00%
2 DRY BEANS/PEANUTS	0.000000	0.00%
3 EGGS	0.000000	0.00%
4 MILK: NON-FAT SOLID	0.000000	0.00%
5 MILK: FAT SOLIDS	0.000000	0.00%
6 GRAINS (EXCL. RICE)/SOYBEANS/VE	0.000046	0.00%
7 STARCHY VEG. INCL. RICE/ SWEETP	0.000000	0.00%
8 TOMATOES	0.000000	0.00%
9 OTHER VEGETABLES INCL. BRASSICA	0.000000	0.00%
10 FRUITS	0.000000	0.00%
11 NUTS AND SEEDS	0.000000	0.00%
12 SUGARS	0.000000	0.00%
13 MISCELLANEOUS FOODS	0.000000	0.00%
14 WATER: FOOD BASED	0.000000	0.00%
27 WATER: NON-FOOD BASED	0.000000	0.00%
TOTAL ACUTE EXPOSURE:	0.000958	0.00%

MARGIN OF SAFETY: %459407.19

ODS USED IN MENU SCREEN ANALYSIS:

FOOD/FOODFORM	RESIDUE (PPM)	ADJUSTMT FACTOR
FISH-UNSPECIFIED	0.300000	1.00
RICE-ROUGH	0.020000	1.00

MENU SCREEN ANALYSIS FOR LONDAX DATE OF ANALYSIS: 04-06-1989
RESIDUE FILE NAME: LONDAX
DATE RESIDUE FILE CREATED OR LAST UPDATED: 04-06-1989/07:17:49
RELEVANT DOSE VALUE = 440.0000 MG/KG BODY WT/DAY
CHEMICAL IS ASSUMED TO BE UNIFORMLY DISTRIBUTED
COMMENT:

ACUTE EXPOSURE FOR INFANTS

	MENU SCREEN CATEGORY	EXPOSURE MG/KG BODY WT/DAY	EXPOSURE PERCENT OF RDV
1	MEATS	0.001538	0.00%
2	DRY BEANS/PEANUTS	0.000000	0.00%
3	EGGS	0.000000	0.00%
4	MILK: NON-FAT SOLID	0.000000	0.00%
5	MILK: FAT SOLIDS	0.000000	0.00%
8	TOMATOES	0.000000	0.00%
10	FRUITS	0.000000	0.00%
11	NUTS AND SEEDS	0.000000	0.00%
12	SUGARS	0.000000	0.00%
13	MISCELLANEOUS FOODS	0.000000	0.00%
14	WATER: FOOD BASED	0.000000	0.00%
21	BRASSICA VEGETABLES	0.000000	0.00%
22	OTHER VEGETABLES EXCL. BRASSICA	0.000000	0.00%
23	SOYBEANS	0.000000	0.00%
25	GRAINS AND STARCHY VEGETABLES	0.000109	0.00%
27	WATER: NON-FOOD BASED	0.000000	0.00%
	TOTAL ACUTE EXPOSURE:	0.001647	0.00%

MARGIN OF SAFETY: %267217.38

FOODS USED IN MENU SCREEN ANALYSIS:

	FOOD/FOODFORM	RESIDUE (PPM)	ADJUSTMT FACTOR
1	FISH-UNSPECIFIED	0.300000	1.00
25	RICE-ROUGH	0.020000	1.00

ENU SCREEN ANALYSIS FOR LONDAX DATE OF ANALYSIS: 04-06-1989
ESIDUE FILE NAME: LONDAX
ATE RESIDUE FILE CREATED OR LAST UPDATED: 04-06-1989/07:17:49
ELEVANT DOSE VALUE = 440.0000 MG/KG BODY WT/DAY
HEMICAL IS ASSUMED TO BE UNIFORMLY DISTRIBUTED
OMMENT:

ACUTE EXPOSURE FOR CHILDREN 1-6 YEARS

	MENU SCREEN CATEGORY	EXPOSURE MG/KG BODY WT/DAY	EXPOSURE PERCENT OF RDV
1	MEATS	0.001650	0.00%
2	DRY BEANS/PEANUTS	0.000000	0.00%
3	EGGS	0.000000	0.00%
4	MILK: NON-FAT SOLID	0.000000	0.00%
5	MILK: FAT SOLIDS	0.000000	0.00%
6	GRAINS (EXCL. RICE)/SOYBEANS/VE	0.000100	0.00%
7	STARCHY VEG. INCL. RICE/ SWEETP	0.000000	0.00%
8	TOMATOES	0.000000	0.00%
10	FRUITS	0.000000	0.00%
11	NUTS AND SEEDS	0.000000	0.00%
12	SUGARS	0.000000	0.00%
13	MISCELLANEOUS FOODS	0.000000	0.00%
14	WATER: FOOD BASED	0.000000	0.00%
21	BRASSICA VEGETABLES	0.000000	0.00%
22	OTHER VEGETABLES EXCL. BRASSICA	0.000000	0.00%
27	WATER: NON-FOOD BASED	0.000000	0.00%
	TOTAL ACUTE EXPOSURE:	0.001750	0.00%

MARGIN OF SAFETY: %251445.84

OODS USED IN MENU SCREEN ANALYSIS:

	FOOD/FOODFORM	RESIDUE (PPM)	ADJUSTMT FACTOR
1	FISH-UNSPECIFIED	0.300000	1.00
6	RICE-ROUGH	0.020000	1.00

MENU SCREEN ANALYSIS FOR LONDAX DATE OF ANALYSIS: 04-06-1989
RESIDUE FILE NAME: LONDAX
DATE RESIDUE FILE CREATED OR LAST UPDATED: 04-06-1989/07:17:49
RELEVANT DOSE VALUE = 440.0000 MG/KG BODY WT/DAY
CHEMICAL IS ASSUMED TO BE UNIFORMLY DISTRIBUTED
COMMENT:

ACUTE EXPOSURE FOR FEMALES 13 YEARS OR OLDER

MENU SCREEN CATEGORY	EXPOSURE MG/KG BODY WT/DAY	EXPOSURE PERCENT OF RDV
1 MEATS	0.000710	0.00%
2 DRY BEANS/PEANUTS	0.000000	0.00%
3 EGGS	0.000000	0.00%
4 MILK: NON-FAT SOLID	0.000000	0.00%
5 MILK: FAT SOLIDS	0.000000	0.00%
6 GRAINS (EXCL. RICE)/SOYBEANS/VE	0.000031	0.00%
7 STARCHY VEG. INCL. RICE/ SWEETP	0.000000	0.00%
8 TOMATOES	0.000000	0.00%
9 OTHER VEGETABLES INCL. BRASSICA	0.000000	0.00%
10 FRUITS	0.000000	0.00%
11 NUTS AND SEEDS	0.000000	0.00%
12 SUGARS	0.000000	0.00%
13 MISCELLANEOUS FOODS	0.000000	0.00%
14 WATER: FOOD BASED	0.000000	0.00%
27 WATER: NON-FOOD BASED	0.000000	0.00%
TOTAL ACUTE EXPOSURE:	0.000742	0.00%

MARGIN OF SAFETY: %593187.44

'OODS USED IN MENU SCREEN ANALYSIS:

FOOD/FOODFORM	RESIDUE (PPM)	ADJUSTMT FACTOR
1 FISH-UNSPECIFIED	0.300000	1.00
6 RICE-ROUGH	0.020000	1.00

MENU SCREEN ANALYSIS FOR LONDAX DATE OF ANALYSIS:
RESIDUE FILE NAME: LONDAX
DATE RESIDUE FILE CREATED OR LAST UPDATED: 04-06-1989/07:17:49
RELEVANT DOSE VALUE = 440.0000 MG/KG BODY WT/DAY
CHEMICAL IS ASSUMED TO BE UNIFORMLY DISTRIBUTED
COMMENT:

ACUTE EXPOSURE FOR MALES 13 YEARS OR OLDER

	MENU SCREEN CATEGORY	EXPOSURE MG/KG BODY WT/DAY	EXPOSURE PERCENT OF RDV
1	MEATS	0.000853	0.00%
2	DRY BEANS/PEANUTS	0.000000	0.00%
3	EGGS	0.000000	0.00%
4	MILK: NON-FAT SOLID	0.000000	0.00%
5	MILK: FAT SOLIDS	0.000000	0.00%
6	GRAINS (EXCL. RICE)/SOYBEANS/VE	0.000040	0.00%
7	STARCHY VEG. INCL. RICE/ SWEETP	0.000000	0.00%
8	TOMATOES	0.000000	0.00%
9	OTHER VEGETABLES INCL. BRASSICA	0.000000	0.00%
10	FRUITS	0.000000	0.00%
11	NUTS AND SEEDS	0.000000	0.00%
12	SUGARS	0.000000	0.00%
13	MISCELLANEOUS FOODS	0.000000	0.00%
14	WATER: FOOD BASED	0.000000	0.00%
27	WATER: NON-FOOD BASED	0.000000	0.00%
	TOTAL ACUTE EXPOSURE:	0.000893	0.00%

MARGIN OF SAFETY: %492889.3

FOODS USED IN MENU SCREEN ANALYSIS:

	FOOD/FOODFORM	RESIDUE (PPM)	AI F
1	FISH-UNSPECIFIED	0.300000	
6	RICE-ROUGH	0.020000	

EXPOSURE ANALYSIS FOR LONDAX — DATE OF ANALYSIS: 04-11-1989
RESIDUE FILE NAME: LONDAX
DATE RESIDUE FILE CREATED OR LAST UPDATED: 04-11-1989/12:25:08
ACCEPTABLE DAILY EXPOSURE = .0900000 MG/KG BODY WT/DAY
COMMENT: ~~fish, rice~~

TOTAL EXPOSURE BY POPULATION SUBGROUP

POPULATION SUBGROUP	TOTAL EXPOSURE MG/KG BODY WT/DAY	TOTAL EXPOSURE % OF ACCEPTABLE DAILY EXPOSURE
U.S. POP - 48 STATES - ALL SEASONS	0.000003	0.00%
U.S. POPULATION - SPRING SEASON	0.000003	0.00%
U.S. POPULATION - SUMMER SEASON	0.000004	0.00%
U.S. POPULATION - AUTUMN SEASON	0.000003	0.00%
U.S. POPULATION - WINTER SEASON	0.000003	0.00%
NORTHEAST REGION	0.000004	0.00%
NORTH CENTRAL REGION	0.000002	0.00%
SOUTHERN REGION	0.000003	0.00%
WESTERN REGION	0.000003	0.00%
HISPANICS	0.000009	0.00%
NON-HISPANIC WHITES	0.000002	0.00%
NON-HISPANIC BLACKS	0.000005	0.00%
NON-HISPANIC OTHER THAN BLACK OR WHITE	0.000016	0.00%
NURSING INFANTS (<1 YEAR OLD)	0.000012	0.00%
NON-NURSING INFANTS (<1 YEAR OLD)	0.000026	0.00%
FEMALES (13+/PREGNANT/NOT NURSING)	0.000002	0.00%
FEMALES (13+/NURSING)	0.000003	0.00%
CHILDREN (1-6 YEARS)	0.000006	0.00%
CHILDREN (7-12 YEARS)	0.000004	0.00%
MALES (13-19 YEARS)	0.000003	0.00%
FEMALES (13-19 YRS/NOT PREG. OR NURSING)	0.000002	0.00%
MALES (20+ YEARS)	0.000003	0.00%
FEMALES (20+ YEARS/NOT PREG. OR NURSING)	0.000002	0.00%

EXPOSURE ANALYSIS FOR LONDAX DATE OF ANALYSIS: 04-11-1989
RESIDUE FILE NAME: LONDAX
DATE RESIDUE FILE CREATED OR LAST UPDATED: 04-11-1989/12:25:08
ACCEPTABLE DAILY EXPOSURE = 19.900000 MG/KG BODY WT/DAY
COMMENT: fish, rice

COMPLETE COMMODITY CONTRIBUTION ANALYSIS FOR
FEMALES (13+/PREGNANT/NOT NURSING)

CROP GROUP = (O) CEREAL GRAINS

FOOD NAME	RESIDUE (PPM)	ADJ. FACTOR	EXPOSURE ANALYSIS MG/KG BODY WT/DAY	EXPOSURE ANALYSIS % OF ACCEPT. DAILY EXPOSURE
RICE-ROUGH	0.020000	1.00	0.0000001	0.00%
RICE-MILLED	0.020000	1.00	0.0000022	0.00%
CROP GROUP SUBTOTAL			0.0000023	0.00%

CROP GROUP = (W) FISH

FOOD NAME	RESIDUE (PPM)	ADJ. FACTOR	EXPOSURE ANALYSIS MG/KG BODY WT/DAY	EXPOSURE ANALYSIS % OF ACCEPT. DAILY EXPOSURE
FISH-UNSPECIFIED	0.300000	1.00	0.0000000	0.00%
CROP GROUP SUBTOTAL			0.0000000	0.00%
POPULATION SUBGROUP TOTAL			0.0000023	0.00%

EXPOSURE ANALYSIS FOR LONDAX DATE OF ANALYSIS: 04-11-1989
RESIDUE FILE NAME: LONDAX
DATE RESIDUE FILE CREATED OR LAST UPDATED: 04-11-1989/12:25:08
ACCEPTABLE DAILY EXPOSURE = 19.900000 MG/KG BODY WT/DAY
COMMENT: fish, rice

COMPLETE COMMODITY CONTRIBUTION ANALYSIS FOR
FEMALES (13-19 YRS/NOT PREG. OR NURSING)

CROP GROUP = (O) CEREAL GRAINS

FOOD NAME	RESIDUE (PPM)	ADJ. FACTOR	EXPOSURE ANALYSIS MG/KG BODY WT/DAY	EXPOSURE ANALYSIS % OF ACCEPT. DAILY EXPOSURE
RICE-ROUGH	0.020000	1.00	0.0000000	0.00%
RICE-MILLED	0.020000	1.00	0.0000023	0.00%
CROP GROUP SUBTOTAL			0.0000023	0.00%

CROP GROUP = (W) FISH

FOOD NAME	RESIDUE (PPM)	ADJ. FACTOR	EXPOSURE ANALYSIS MG/KG BODY WT/DAY	EXPOSURE ANALYSIS % OF ACCEPT. DAILY EXPOSURE
FISH-UNSPECIFIED	0.300000	1.00	0.0000001	0.00%
CROP GROUP SUBTOTAL			0.0000001	0.00%
POPULATION SUBGROUP TOTAL			0.0000024	0.00%

EXPOSURE ANALYSIS FOR LONDAX DATE OF ANALYSIS: 04-11-1989
RESIDUE FILE NAME: LONDAX
DATE RESIDUE FILE CREATED OR LAST UPDATED: 04-11-1989/12:25:08
ACCEPTABLE DAILY EXPOSURE = 19.900000 MG/KG BODY WT/DAY
COMMENT: fish, rice

COMPLETE COMMODITY CONTRIBUTION ANALYSIS FOR
FEMALES (13-19 YRS/NOT PREG. OR NURSING)

CROP GROUP = (O) CEREAL GRAINS

FOOD NAME	RESIDUE (PPM)	ADJ. FACTOR	EXPOSURE ANALYSIS MG/KG BODY WT/DAY	EXPOSURE ANALYSIS % OF ACCEPT. DAILY EXPOSURE
RICE-ROUGH	0.020000	1.00	0.0000000	0.00%
RICE-MILLED	0.020000	1.00	0.0000023	0.00%
CROP GROUP SUBTOTAL			0.0000023	0.00%

CROP GROUP = (W) FISH

FOOD NAME	RESIDUE (PPM)	ADJ. FACTOR	EXPOSURE ANALYSIS MG/KG BODY WT/DAY	EXPOSURE ANALYSIS % OF ACCEPT. DAILY EXPOSURE
FISH-UNSPECIFIED	0.300000	1.00	0.0000001	0.00%
CROP GROUP SUBTOTAL			0.0000001	0.00%
POPULATION SUBGROUP TOTAL			0.0000024	0.00%

EXPOSURE ANALYSIS FOR LONDAX DATE OF ANALYSIS: 04-11-1989
RESIDUE FILE NAME: LONDAX
DATE RESIDUE FILE CREATED OR LAST UPDATED: 04-11-1989/12:25:08
ACCEPTABLE DAILY EXPOSURE = 19.900000 MG/KG BODY WT/DAY
COMMENT: fish, rice

COMPLETE COMMODITY CONTRIBUTION ANALYSIS FOR
FEMALES (20+ YEARS/NOT PREG. OR NURSING)

CROP GROUP = (O) CEREAL GRAINS

FOOD NAME	RESIDUE (PPM)	ADJ. FACTOR	EXPOSURE ANALYSIS MG/KG BODY WT/DAY	EXPOSURE ANALYSIS % OF ACCEPT. DAILY EXPOSURE
RICE-ROUGH	0.020000	1.00	0.0000001	0.00%
RICE-MILLED	0.020000	1.00	0.0000018	0.00%
CROP GROUP SUBTOTAL			0.0000019	0.00%

CROP GROUP = (W) FISH

FOOD NAME	RESIDUE (PPM)	ADJ. FACTOR	EXPOSURE ANALYSIS MG/KG BODY WT/DAY	EXPOSURE ANALYSIS % OF ACCEPT. DAILY EXPOSURE
FISH-UNSPECIFIED	0.300000	1.00	0.0000002	0.00%
CROP GROUP SUBTOTAL			0.0000002	0.00%
POPULATION SUBGROUP TOTAL			0.0000020	0.00%