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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

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MEMORANDUM

SUBJECT: Benfluralin: Human Health Risk Assessment (Revised)

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The following human health risk assessment for benfluralin has been prepared by the Health Effects Division for Phase One of the reregistration process. Revision is based on comments (MRID 46082401) received from the registrant (Dow Agro Sciences) dated 9/26/03. Risk assessment for benfluralin is based on the following memoranda:

Benfluralin: Third Report of the Hazard Identification Assessment Review Committee (D. Anderson memo, 4/8/03)

Toxicology Chapter for the RED for Benfluralin (Phase 1 corrected) (D. Anderson memo, 10/28/03)

Benfluralin: Report of the Cancer Assessment Review Committee (S. Diwan memo, 12/27/01)

Benfluralin: Residue Chemistry Chapter for the Reregistration Eligibility Decision (R. Griffin memo, 5/28/03)

Benfluralin: Health Effects Division (HED) Metabolism Assessment Review Committee (MARC) Decision Document (R. Griffin/D. Anderson memo, 4/29/03)

Quantitative Usage Analysis for Benfluralin (J. Alsadek memo, 5/14/02)

Drinking Water Estimates for Benfluralin (W. Eckel memo, 1/31/03)

Addendum to Drinking Water Estimates for Benfluralin (W. Eckel memo, 3/5/03)

Second Addendum to Drinking Water Estimates for Benfluralin (W. Eckel memo, 4/25/03)

Review of Benfluralin Incident Reports (J. Blondell/M. Spann memo, 4/30/03)

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1.0 SUMMARY

Benfluralin [also known as benefin; N-butyl-N-ethyl-2,6-dinitro–4-(trifluoromethyl) benzenamine] is an herbicide registered for use on a single food crop (pre-plant on lettuce), feed crops (pre-plant on alfalfa, clover, trefoil), non-bearing fruit and nut trees, non-bearing berries, non-bearing vineyards, turf, and ornamentals. A tolerance for use on peanuts will be revoked by the Agency. The reregistration of benfluralin is being supported by Dow AgroSciences LLC (formerly DowElanco). Benfluralin products are sold under the trade name Balan™ and are formulated as a dry flowable (DF) for food/feed crops and as a granular (G) for non-bearing fruit and nut trees, non-bearing berries, non-bearing vineyards, turf, and ornamentals. In plants, benfluralin, like other dinitroaniline herbicides is absorbed through the roots, but poorly translocated into the plant. It is believed to inhibit several hormone-induced enzymes and uncouple oxidative-phosphorylation.

The toxicity data base is sufficient for reregistration. The studies submitted to support guideline requirements are supplemented by relevant open literature publications. Benfluralin has low acute toxicity by the oral, dermal, and inhalation routes (Toxicity Category IV). Benfluralin is placed in Toxicity Category III for primary skin and eye irritations and the technical grade is a skin sensitizer. Formulations of benfluralin were not skin sensitizers, however, in the 21-day rabbit dermal study, skin reactions (slight to moderate edema, hyperplasia and/or inflammation) were noted at all dose levels starting on day 3 of dosing and severe skin reactions (including necrosis and pustules) were noted at the two top dose levels. In order to protect potentially sensitive users, the Agency is recommending that products containing benfluralin be labeled as skin sensitizers unless adequate data shows otherwise.

In long term studies, benfluralin is toxic to the kidneys and liver, and at high dose levels to the thyroid. Rats show a LOAEL based on kidney toxicity. Dogs show a LOAEL based on liver toxicity and mice show a LOAEL based on liver and kidney toxicity. Other dinitroaniline pesticides show a mixture of kidney, liver, hematological and thyroid toxicity at their respective LOAELs. There are no absorption studies with benfluralin, but good analogs are poorly absorbed through the skin at 3% of the applied dose. Metabolism studies with benfluralin show that the pattern of excretion in the urine is 13-17% of dose, and 73-75% of dose in feces (the urine and feces each contained approximately 100 components).

In the 21-day rabbit study, no *systemic* toxicity was observed at the highest dose tested (1,000 mg/kg/day). Based on the results of this study, the Agency is not concerned that dermal exposure to benfluralin will lead to the toxic effects observed in other studies. However, technical grade benfluralin caused typical delayed hypersensitivity in guinea pigs. Repeated dermal applications to rabbits resulted in skin lesions that progressed in severity and therefore may have the potential for adverse

effects (other dermal sensitizing studies on benfluralin *formulations* show no sensitization). However, the Agency is concerned that dermal exposure to benfluralin may cause adverse skin sensitization; and, since this risk cannot be adequately quantified, the HIARC recommends that products containing benfluralin should be labeled as "SENSITIZER" and contact should be avoided to the extent possible.

The HED Hazard Identification Assessment Review Committee (HIARC) has reviewed the benfluralin toxicity data and selected the appropriate studies, endpoints, and dose levels for human health risk assessment (D. Anderson memo, 04/03/2003). No appropriate endpoint attributed to a single dose was identified. An acute Population Adjusted Dose (aPAD) was not established. A chronic Population Adjusted Dose (cPAD) of 0.005 mg/kg/day was established based on the NOAEL (0.5 mg/kg/day) of a chronic toxicity/carcinogenicity study in rats. The endpoint of concern is increased histopathologic lesions in the kidney and the uncertainty factor is 100, based on 10x for inter-species extrapolation, 10x intra-species variability, and 1x for FQPA considerations. Risk assessment for short-term "incidental" oral and for short-term inhalation exposure is based on the NOAEL (100 mg/kg/day) of the rabbit developmental study. Risk assessment for intermediate-term inhalation exposure is based on the NOAEL (7.2 mg/kg/day) of the rat reproduction study. The Agency considers a Margin of Exposure (MOE) of 100 to be adequately protective for each assessment.

The toxicity data base is adequate for FQPA consideration. Acceptable rabbit and rat developmental toxicity studies are available in addition to an acceptable 2-generation study on reproduction in the rat. No developmental effects were seen at the highest doses tested in rats or rabbits. Similar effects (weight decrement, liver and kidney toxicity) were seen in pups, adult offspring and parents at the two highest doses tested. No effects were seen at the lowest dose tested either in pups or parents. No obvious endocrine related effects were noted on the organs of reproduction. The HIARC concluded that the FQPA Safety factor should be removed because there is no evidence (quantitative or qualitative) of increased susceptibility in rats or rabbits following pre- and/or postnatal studies, and no residual uncertainty.

The HIARC also concluded that the acute and subchronic neurotoxicity studies are not required (in spite of the neurotoxicity/neuropathy) because the effects of concern (sciatic nerve degeneration and brain weight decrement) will not likely occur at the doses that are required by the testing guidelines. Suggestive evidence of neuropathy occurring only in the chronic study in rats and only at study termination was evaluated by the HIARC. This neuropathy was considered to be due to normal age related neuropathy in aging rats exacerbated by excessive dose levels. The HIARC concluded that acute and subchronic neurotoxicity studies are not required because the neuropathy would not likely occur at the doses that would be tested in these studies.

The HED Cancer Assessment Review Committee (CARC) classified benfluralin into the category "suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential" based on the occurrence of liver tumors in female mice. The Committee further recommended that the quantification of human cancer risk would not be required. Mutagenicity studies for reverse mutations, mouse lymphoma mutations, chromosomal aberrations and DNA repair were all negative.

The HED Metabolism Assessment Review Committee (MARC) reviewed benfluralin toxicology and metabolism data (3/19/03) and concluded that tolerances for enforcement (and dietary risk assessment) should be based on benfluralin *per se.* In fate studies, nine of the 26 identified degradates are estimated to exceed 10% of the applied parent concentration. Of those, 6 degradates were identified in "aerobic" aqueous photolysis and soil photolysis studies. The MARC also concluded that risk estimates for drinking water should be based on benfluralin *per se,* the 6 degradates identified in fate studies, and a degradate identified as B12 which may be found in ground water.

An upper-bound (tier 1) chronic dietary risk assessment was conducted by comparing dietary exposure to the chronic Population Adjusted Dose (cPAD). Human dietary exposure was determined by considering the level of benfluralin residue in/on food commodities and the estimated consumption by various population subgroups. The residue estimate for lettuce, the only direct food use for benfluralin, is based on the level set for tolerance (0.05 ppm). Usage on lettuce is assumed to be 100%. Food consumption data are from USDA's Continuing Surveys of Food Intakes by Individuals (CSFII),1994-1996/1998, combined to form the Food Commodity Intake Database (FCID). Estimated chronic dietary risk estimates for all population subgroups are less than 1% of the benfluralin cPAD (0.005 mg/kg/day) and do not indicate a concern for this route of exposure.

Benfluralin products are marketed for homeowner use on residential lawns and for homeowner use on landscape ornamentals. Benfluralin containing products are also marketed for use by professional applicators on residential turf, on golf courses, other turf such as recreational/commercial areas, and on ornamental plantings. Based on these uses, benfluralin is assessed for the residential applicator (or "handler") and for post-application exposure that may occur from children's turf contact. For residential handlers, all estimated inhalation MOEs are above the target MOE of 100. Since a dermal toxicological endpoint was not selected for benfluralin, only post-application non-dietary ingestion (i.e., soil ingestion, granule ingestion, and hand-/object-to-mouth) exposures to children were calculated. Estimated MOEs for soil, granule, and hand-/object-to-mouth exposures are above the target MOE of 100. However, although the risk cannot be adequately quantified, the Agency remains concerned about *dermal sensitization* reactions to adults and children who are exposed to benfluralin in residential settings.

Aggregate risk assessment uses the food exposure estimates and the residential exposure estimates (combined) to evaluate the estimates of drinking water contamination modeled for both surface and ground water by the Environmental Fate and Effects Division (EFED). These modeled EEC estimates were compared to "Drinking Water Levels of Comparison" or DWLOCs that represent the upper-bound of "allowable" exposure from a water source with consideration for food and residential exposure. The estimated maximum groundwater EEC (0.07 ug/L) is below the short-term/chronic DWLOC for all population subgroups and the estimated maximum surface water EEC (3.5 ug/L) is below the short-term/chronic DWLOC for all population subgroups and a conclusion can be drawn that no adverse toxicological effect will occur due to aggregate benfluralin exposure.

HED did not complete a cumulative risk assessment as part of this reregistration review for benfluralin because HED has not yet initiated a review to determine if there are any other chemical substances that have a common mechanism of toxicity.

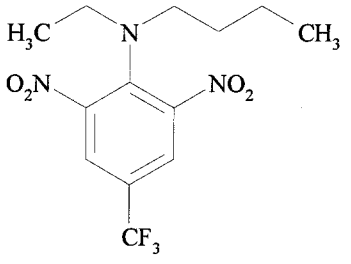
Worker exposure to benfluralin can occur in a variety of patterns for a single day or up to weeks at a time for commercial applicators who are completing a number of applications for a number of different clients. HED identified 13 occupational exposure scenarios based on the use sites, formulations, and the various equipment that may be used for benfluralin applications. Scenarios assessed are for mixer/loaders using the dry flowable or granular formulation, for applicators using the dry flowable or granular formulation, and for mixer/loader/applicators using the dry flowable or granular formulation. Occupational exposure estimates are based, in part, on proprietary data. Margin of Exposure estimates, based on both a short- and intermediate-term exposure duration (inhalation exposure only), are well above the target MOE of 100. However, the Agency remains concerned about dermal sensitization reactions in persons occupationally exposed to benfluralin. At present, HED has no method for determining a quantitative endpoint for benfluralin skin sensitization and, therefore, has no means of quantitatively assessing the risk resulting from benfluralin's sensitization potential. As a risk mitigation measure, EPA will require a sensitization warning statement on all benfluralin end-use product labels and a recommendation that contact with the skin be avoided (the HIARC recommends that the products containing benfluralin should be labeled as SENSITIZER and contact should be avoided). In addition, EPA has determined that long-sleeved shirts, long pants, shoes, socks, and chemical-resistant gloves will be required on all occupational end-use products containing benfluralin.

Relatively few incidents of illness in workers have been reported due to benfluralin. There is evidence of dermal effects (flushing, skin irritation or pain, and itching) sufficient to require medical attention. These effects appear to be due to not wearing required personal protective equipment. Poison Control Center data (1993-1998) show 46 non-occupational exposures, 31 of which were children under six years of age. For adults and older children, there were five cases involving minor symptoms,

mostly dermal in nature among the eight cases receiving follow-up.

2.0 PHYSICAL / CHEMICAL PROPERTIES CHARACTERIZATION

Chemical Structure:



Empirical Formula:	$C_{13}H_{16}F_3N_3O_4$
Molecular Weight:	335.3
CAS Registry No.:	1861-40-1
Physical State:	yellowish-orange crystalline solid
Melting Point:	65-68 C
Density:	78 lb/cu ft (packed)
Octanol/Water Partition Coefficient (log P_{ow}):	5.29
Vapor Pressure:	6.57 x 10^{-5} mm/Hg at 25 C
Water Solubility:	(0.1 ppm at pH 7 and 25 C)
Organic Solvents:	
Acetone:	> 500 mg/mL
Chloroform:	> 500 mg/mL
Xylene:	> 450 mg/mL
Methanol:	40 mg/mL

3.0 HAZARD CHARACTERIZATION

3.1 Hazard Profile

Table 1. Acute Toxicity Data

Guideline No./ Study Type	MRID No.	Results	Toxicity Category
870.1100 Acute oral toxicity	00024255 (1965)	LD50 >10 g/kg (adults) 0/10 died at 5 and 10 g/kg	IV
870.1200 Acute dermal toxicity	41751701 (1990)	LD50 > 5 g/kg	IV
870.1300 Acute inhalation toxicity	41613807 (1989) 0024275 (1964)	LC50 >2.3 mg/L LC50 >1.3 mg/L/hr 5% benfluralin in dimethylformamide	IV III
870.2400 Acute eye irritation	00024265 (1976)	Slightly irritating, reversible within 7 days	III
870.2500 Acute dermal irritation	41751702 (1990)	Moderate erythema and edema at day 7, which cleared by day 11. The study indicates a skin irritation category of III.	III
870.2600 Skin sensitization	00144283 (1990)	7/12 guinea pig tested positive in the Buehler test	Skin sensitizer

Table 2. Toxicity Profile

Guideline No./ Study Type	MRID No. (year)/ Classification /Doses	Results
SUBCHRONIC TOXICITY STUDIES		
870.3100 90-Day oral toxicity rodents	44050001 (1996) 15 males and 15 females/grp Doses: R33989- 0, 0.025%, 0.11%, 0.5% (M:0, 17, 74, 341 mg/kg/day; F: 0, 20, 94, 395 mg/kg/day) Doses: R44089-0, 0, 0.75% (M: 0, 522: F: 0, 605) Doses: R29990 - 0, 0.005%, 0.05%, 0.5% (M: 0, 3, 32, 322 mg/kg/day) Acceptable	NOAEL = 0.005% (3.23 mg/kg/day) LOAEL For males 0.025% (17 mg/kg/day) based on dose related chronic nephrosis in males and at 0.025% (20 mg/kg/day) in females, cortical tubular epithelial pigment deposition, absolute and relative liver and kidney weight increase and at 0.05% (32 mg/kg/day) cortical tubular epithelial regeneration, urinary AST increase and liver hypertrophy in males, and hyaline droplet formation in males kidneys. [a] [a] The HIARC (TXR# 0051761) revised the NOAEL/LOAEL to 3.2/17 mg/kg/day from the values in TXR# 02260 of NOAEL/LOAEL of 3.23/None mg/kg/day. The HIARC (TXR# 0051761) concluded that hyaline droplet formation alone is not appropriate for endpoint selection since this a normal occurrence in males rats. Guidance for this determination was obtained from the Risk Assessment Forum Document titled "Alpha2μ-Globulin: Association with Chemically Induced Renal Toxicity and Neoplasia in the Male Rat." (Purple Book) which states that " Hyaline droplets in proximal tubules of normal male rats contain alpha2μ-globulin, and their occurrence appears to parallel the variable synthesis of this protein. Thus, hyaline droplets become apparent in male rats at the time of puberty, but decline progressively with increasing age after 18 months. In female rats, protein droplets in the proximal tubules are either absent or considerably less frequent than in males, and they do not contain alpha2μ-globulin.
870.3150 90-Day oral toxicity in nonrodents	43072301 (1993) Doses: 0, 5, 25, 125 mg/kg/day Acceptable	NOAEL = 5 mg/kg/day LOAEL = Male/Female - 25 mkd based on splenic pigment. At 125 mkd male abs & rel liver wt incr. (Probably due to p450 enzyme induction.) Colored emesis was seen in females at all dose levels and in males at the 2 top doses.

Guideline No./ Study Type	MRID No. (year)/ Classification /Doses	Results
870.3200 21/28-Day dermal toxicity	43020201 (1993) Doses: 0, 100, 500, 1000 mg/kg/day Acceptable	NOAEL = None LOAEL = Male/Female - 100 mg/kg/day (HDT) based on skin lesions (edema, hyperkeratosis) and dose related severity. Skin lesions at >100 mg/kg/day were severe (necrosis, ulcers). The study showed no systemic toxicity. Since it is a skin sensitizer, the severity may have been partly due to delayed hypersensitivity.
870.3250 90-Day dermal toxicity	Not Required	-
870.3465 90-Day inhalation toxicity	Required (see text)	-
DEVELOPMENTAL AND REPRODUCTIVE TOXICITY STUDIES		
870.3700a Prenatal developmental in rodents	000147535 (1985) Dose levels: 0, 50, 475, 1000 mg/kg/day Acceptable	**Maternal** NOAEL = 225 mg/kg/day LOAEL = 475 based body wt decrement GD 11 & 16 & Bwt gain dec GD 6-11. **Developmental** NOAEL= 1000 (HDT) mg/kg/day LOAEL = None
870.3700b Prenatal developmental in nonrodents	42039101 (1991) Dose levels: 0, 25, 50, 100, 225 mg/kg/day Acceptable	**Maternal** NOAEL = 100 mg/kg/day LOAEL = 225 mkd based on decreased body weight gain and decreased food consumption, GD 6-19. mg/kg/day. **Developmental** NOAEL = 225 mg/kg/day LOAEL = None

Guideline No./ Study Type	MRID No. (year)/ Classification /Doses	Results
870.3800 Reproduction and fertility effects	43628701 (1995) Dose levels: Males=0, 7.2, 68.1, 342 mg/kg/day; Females=0, 8.8, 80.0, 437 mg/kg/day Acceptable	**Parental/Systemic** NOAEL = M/F=7.2/8.8 mg/kg/day LOAEL = M/F=68.1/74.4 based on absolute and relative liver wts and hyaline droplets (graded minimal) in males and chronic progressive nephropathy in males and females (graded moderate). **Reproductive**: No effects on fertility or organs of reproduction. **Offspring** NOAEL = 80 mg/kg/day LOAEL = 437 mg/kg/day based on pup wt decrement and at 437 mg/kg/day decrease live litters at day 0 and day 4.
CHRONIC TOXICITY AND CARCINOGENICITY STUDIES		
870.4100a Chronic toxicity rodents	See 870.4300 below	-
870.4100b Chronic toxicity dogs	43628702 (1995) Dose levels: 0, 5, 25, 125 mg/kg/day Acceptable	NOAEL Females = 5 mg/kg/day; Males = 25 mg/kg/day LOAEL Females = 25 mg/kg/day based on elevated ALT and sinusoidal cell pigment in livers; and LOAEL Males = 125 based on elevated ALT and sinusoidal cell pigment in livers.

Guideline No./ Study Type	MRID No. (year)/ Classification /Doses	Results
870.4300 Combined Chronic/Carcin o-genicity rats	44050002 (1996) & 44545501(1998) Doses: 0, 10, 100, 2500, 5000 ppm (equivalent to 0, 0.5, 5.4, 136.3 or 274.8 mg/kg/day in males and 0, 0.7, 6.8, 167.9 or 331.3 mg/kg/day in females) Acceptable	NOAEL = 0.5 mg/kg/day LOAEL = M/F=5.4/6.8 based on kidney lesions **Cancer**- liver adenomas/carcinomas at 2 top dose levels and thyroid follicular adenomas/carcinomas at 2 top dose levels. Excess toxicity at the 2 top doses.
870.4300 Carcinogenicity mice	41021501 (1988) Dose levels; 0, 0.005, 0.03, or 0.15% M=0, 6.0, 36.4, 184.7; F=0, 6.9, 41.8, 223.5 mg/kg/day. Acceptable	NOAEL: Females = 6.9; Males =36.4 mg/kg/day LOAEL: Females = 41.8 mg/kg/day based on liver nodules & at 223.5 mkd, liver enzyme increase, alanine aminotransferase & alkaline phosphatase and multifocal hyperplasia in females (223.5 mkd); Males = 185 mg/kg/day based on death by mouse urologic syndrome and mouse urologic syndrome (all severities) . Evidence of carcinogenicity in females at HDT (Combined liver adenomas/carcinomas)
MUTAGENICITY STUDIES		
Gene Mutation 870.5100	00160863 Ames/*Salmonella typhimurium,* reverse mutation Acceptable	Assay shows no dose related reverse mutations with any of the 5 strains at insoluble doses (≥ 300 µg/plate +S9 and 750 µg/plate -S9). No cytotoxicity was shown up to 5000 µg/plate.

Guideline No./ Study Type	MRID No. (year)/ Classification /Doses	Results
Gene Mutation 870.5300	L5178Y TK+/- Mouse Lymphoma cell forward mutation Acceptable	Assay shows no dose related increase in mutation frequency up to severely cytotoxic doses (<10% cell survival)(≥30 µg/mL -S9; ≥20 µg/mL +S9). Doses in DMSO solvent & up to 25 µg/mL
Cytogenetics 870.5375	00160866 *In vitro* chromosomal aberrations in Chinese Hamster ovary (CHO) cells Acceptable	Assay shows no dose related increase in clastogenic activity (evidence of mutagenic potential) up to at precipitating doses were tested. Doses in DMSO solvent & up to 40 µg/mL, -S9, and 125 µg/mL, +S9, were tested. Mitotic index was reduced 40% to 60% at top dose.
Other Effects 870.5550	Not required	-
870.6200a Acute neurotoxicity screening battery	Not required	-
870.6200b Subchronic neurotoxicity screening battery	Not required	-
870.6300 Developmental neurotoxicity	Not required	-
870.7485 Metabolism and pharmacokinetics	40693201-40693207 (1988) Acceptable	Excreted in urine - 13-17% of dose, excreted in feces - 73-75% of dose (each with approx. 100 metabolites), 6-13% in bile. Parent - 33% in feces. Only parent, mono- and dinitro- reduced benfluralin identified in feces. Plasma ½ life was 54-63 days in both sexes.

Guideline No./ Study Type	MRID No. (year)/ Classification /Doses	Results
870.7600 Dermal penetration	Not required	-
Special studies	Not required	-

3.1.1 Hazard Characterization

Benfluralin has low acute toxicity by the oral (Toxicity Category IV), dermal (Toxicity Category IV) and inhalation (Toxicity Category IV) routes. Benfluralin was placed in Toxicity Category III for primary skin and eye irritations. The technical grade is a skin sensitizer where 7/12 Guinea Pigs were positive in the Buehler test. In the 21-day rabbit dermal study, skin reactions (slight to moderate edema, hyperplasia and/or inflammation) were noted at all dose levels and severe skin reactions (including necrosis and pustules) at the two top dose levels. These lesions started three days after benfluralin administration. However, other dermal sensitizing studies on benfluralin formulations show no sensitization. This suggests that benfluralin is not a skin sensitizer at formulated concentrations or that formulated benfluralin interferes with the test.

In long-term studies, benfluralin is toxic to the kidneys and liver, and is toxic to the thyroid at high dose levels. Rats show a LOAEL based on kidney toxicity. Dogs show a LOAEL based on liver toxicity and mice show a LOAEL based on liver and kidney toxicity. Other dinitroaniline pesticides show a mixture of kidney, liver, hematological, and thyroid toxicity at their respective LOAELs.

In accord with the Agency's Draft Guidelines for Cancer Risk Assessment (July, 1999), the HED Cancer Assessment Review Committee (CARC) classified benfluralin into the category "suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential.

Suggestive evidence of neuropathy occurring only in rats and only at study termination was evaluated by the HED Hazard Identification Review Committee (HIARC). This neuropathy was considered to be due to normal age related neuropathy in aging rats exacerbated by excessive dose levels. The HIARC concluded that acute and subchronic neurotoxicity studies are not required because the neuropathy effects would not likely occur at the doses that would be tested in these studies.

Benfluralin shows no developmental toxicity in two adequately conducted studies in the rat and rabbit at maternally toxic doses. The 2-generation reproduction study showed pup weight decrement at parentally toxic dose levels and decreased live pups at the highest dose level tested. Thus, there was no evidence for quantitative or qualitative increased susceptibility of fetuses or offspring.

No obvious endocrine related effects were noted on the organs of reproduction. Thyroid toxicity in rats was seen at the highest dose, but whether or not these thyroid effects were directly related to endocrine modulation by benfluralin can not be determined based on the data submitted.

Good analogs of benfluralin are poorly absorbed through the skin at 3% of the applied dose, but there are no absorption studies with benfluralin.

Metabolism studies with benfluralin show that the pattern of excretion in the urine is 13 -17% of dose, and 73 -75% of dose in feces (the urine and feces each contained approximately 100 components). In the feces, parent and small amounts of benfluralin reduced at one of the nitro groups were identified. The remaining components were believed to be composed of reduced, dealkylated and conjugated benfluralin metabolites. No parent was found in the urine, but reduced, dealkylated and conjugated metabolite were believed to be present among the 100 or so unidentified urinary metabolites. The only metabolite identified in the urine was 2,6-dinitro-4-trifluro-methyl-aniline (0.2% of dose).

3.2 FQPA Considerations

3.2.1 Database Summary Relative to FQPA

The toxicity data base is adequate for FQPA consideration. Acceptable rabbit and rat developmental toxicity studies are available in addition to an acceptable 2-generation study on reproduction in the rat. The HIARC concluded that the acute and subchronic neurotoxicity studies are not required (in spite of the observed neurotoxicity/ neuropathy) because the effects of concern (sciatic nerve degeneration and brain weight decrement) will not likely occur at the doses that would be tested in these studies.

3.2.2 Evidence of Quantitative / Qualitative Susceptibility

The HIARC concluded that there is not a concern for pre- and/or postnatal toxicity resulting from exposure to benfluralin as there is no evidence (quantitative or qualitative) of increased susceptibility following pre- and/or postnatal exposure. No developmental effects were seen at the highest doses tested in rats or rabbits. Similar effects (weight decrement, liver and kidney toxicity) were seen in pups, adult offspring

and parents at the two highest doses tested. No effects were seen at the lowest dose tested either in pups or parents. There are no concerns nor residual uncertainties for pre- and/or postnatal toxicity since there was no evidence of increased susceptibility in rats or rabbits. In the reproduction study, dead and missing pups at the mid dose were neither dose related nor statistically significant.

The HIARC concluded that there is not a concern for developmental neurotoxicity resulting from exposure to benfluralin. The HIARC believed that the neuropathy seen in the rat chronic study was the indirect effect of normal age related neuropathy exacerbated by excessive doses in the chronic rat study. Additionally, it is noted that no neuropathy was shown at the interim sacrifice in the chronic rat study or the chronic studies with dogs and mice.

3.2.3. Special FQPA Safety Factor(s):

The HIARC concluded that the FQPA Safety factor should be removed (equivalent to1X) based on a conclusion of no increased susceptibility and no residual uncertainty. The Special FQPA Safety Factor recommendation by the HIARC assumes that the exposure databases (food, drinking water, and residential) are complete, the risk assessment for each potential exposure scenario includes all metabolites and/or degradates of concern, and does not underestimate the potential risk for infants and children. This criteria has been met in the benfluralin risk assessment. The food (dietary) assessment for benfluralin is a Tier 1, or screening type assessment, because it is based on tolerance level residues and assumes 100% of considered crops are treated with benfluralin. The drinking water (dietary) assessment is based on an adequate environmental fate database for parent benfluralin and, in the absence of complete fate data for all degradates of concern, upper-bound estimates were made using data on the parent compound such that the EECs are not underestimated. The benfluralin residential risk assessment is also considered an upper-bound assessment since it is based on maximum use rates, the Agency's Residential SOPs (which tend to the high end) and more recent (and reliable) data from the Outdoor Residential Exposure Task Force (ORETF).

3.3 Dose Response Assessment

Table 3. Summary of Toxicology Endpoint Selection

Exposure Scenario	Dose used in Risk Assessment, UF (mg/kg/day)	Special FQPA SF* and Level of Concern for Risk Assessment	Study and Toxicological Effects
Acute Dietary	An appropriate endpoint attributable to single dose was not identified. An acute RfD / aPAD was not established.		
Chronic Dietary (All populations)	NOAEL = 0.5 mg/kg/day UF = 100 Chronic RfD = 0.005 mg/kg/day	FQPA SF = x1 cPAD = 0.005/1 = 0.005 mg/kg/day	Chronic /carcinogenicity-Rat LOAEL = 5.4 based on increased histopathologic lesions of the kidneys seen in males (5.4 mg/kg/day for males and 6.8 mg/kg/day for females).
Incidental Oral, Short-Term (1-30 days)	NOAEL= 100 mg/kg/day	Residential LOC for MOE = 100 (includes the FQPA SF)	Developmental Toxicity - Rabbits LOAEL = 225 mg/kg/day based on decreases in maternal body weight gain over a 13 day dosing period.
Incidental Oral, Intermediate-Term (1-6 months)	NOAEL= 7.2 mg/kg/day	Residential LOC for MOE = 100 (includes the FQPA SF)	Reproduction and fertility effects-Rats LOAEL = 68.1 mg/kg/day based on Hyaline droplet formation in the kidneys of adult males and progressive chronic nephropathy in adult males and females and pup weight decrement.
Dermal, Short, Intermediate and Long-Term	None	There was no systemic toxicity in the 21-day dermal study and dermal toxicity showed no NOAEL. Benfluralin has been shown to be a sensitizer, but risk following dermal exposure can not be quantified. The label should indicate that this compound is a skin sensitizer.	

Exposure Scenario	Dose used in Risk Assessment, UF (mg/kg/day)	Special FQPA SF* and Level of Concern for Risk Assessment	Study and Toxicological Effects
Inhalation, Short-Term (1-30 days)	Oral study NOAEL= 100 absorption rate = 100%	Residential LOC for MOE = 100 (includes FQPA SF) Occupational LOC for MOE = 100	Developmental toxicity - Rabbits LOAEL = 225 mg/kg/day based on decreases in maternal body weight gain over a 13 day dosing period.
Inhalation, Intermediate-Term (1-6 months)	NOAEL= 7.2 mg/kg/day absorption rate = 100%	Residential LOC for MOE = 100 (includes the FQPA SF)	Reproduction and fertility effects-Rats LOAEL = 68.1 mg/kg/day based on Hyaline droplet formation in the kidneys of adult males and progressive chronic nephropathy in adult males and females and pup weight decrement.
Inhalation, Long-Term (>6 months)	Oral study NOAEL= 0.5 mg/kg/day MOE = 100	Residential LOC for MOE = 100 (includes FQPA SF) Occupational LOC for MOE = 100	Chronic/carcinogenicity-Rat LOAEL = 5.4 mg/kg/day based on increased histopathologic lesions of the kidneys were seen in males (5.4 mg/kg/day for males and 6.8 mg/kg/day for females).
Cancer (oral)	"Suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential" "The Committee further recommended that the quantification of human cancer risk is not required."		

UF = uncertainty factor, FQPA SF = Special FQPA safety factor, NOAEL = no observed adverse effect level, LOAEL = lowest observed adverse effect level, PAD = population adjusted dose (a = acute, c = chronic) RfD = reference dose, MOE = margin of exposure, LOC = level of concern, NA = Not Applicable

3.3.1 Endpoint Selection Discussion

Acute Dietary Exposure: An endpoint attributable to a single dose was not available from the developmental studies in rabbits or rats or any other appropriate study.

Chronic Dietary Exposure: In a chronic toxicity/oncogenicity study, benfluralin was administered to Fischer 344 rats (60/sex/dose) in the diet at dose levels of 10, 100, 2500 or 5000 ppm for up to 2 years (equivalent to 0.5/0.7, 5.4/6.8, 136/167 or 275/331 mg/kg/day for males/females). In this study, the following treatment-related effects were observed: 1) body weights were significantly lower in males and females at 2500 and 5000 ppm; 2) survival was significantly reduced in males at study termination at 100, 2500 and 5000 ppm; 3) significant decreases in erythrocyte count, hemoglobin, and hematocrit in males and females at 2500 and 5000 ppm; 4) platelets increased significantly in males and females at various time points at 2500 and 5000 ppm; 5) increases in urea nitrogen, creatinine, total protein, total albumin, and total globulin at 2500 and 5000 ppm; 6) significant increases in absolute and relative liver weights in both sexes at 2500 and 5000 ppm; 7) significant increases in hepatocellular hypertrophy, and hepatocellular pigment in males and females at 2500 and 5000 ppm and 8) increased kidney tubule karymegally, transition cell hyperplasia, renal calculi and hyalin droplets at 100, 2500 and 5000 ppm inmales and hyalin droplets in females at 100, 2500 and 5000 ppm.

The NOAEL for chronic toxicity was 0.5 mg/kg/day for males and 0.7 mg/kg/day for females, based on an increased incidence of histologic lesions of the kidney at the LOAEL. The LOAEL was 5.4 mg/kg/day for males and 6.8 mg/kg/day for females based on increased incidence of histologic lesions of the kidney, such as kidney tubule cell karyomegally, transition cell hyperplasia, pelvic calculi and hyalin droplets in males and kidney hyalin droplets in females. Similar histological effects were seen (and peripheral nerve degeneration) at 136 and 275 mg/kg/day in males and at 168 and 331 mg/kg/day in females. These effects were in addition to liver histopathology and oncogenicity at the two highest dose levels.

The Reference Dose (RfD) for benfluralin is based on the study NOAEL for males (0.5 mg/kg/day) and a standard uncertainty factor (UF) of 100 (10x for interspecies extrapolation and 10x for intraspecies variability). No additional factor is used for FQPA considerations, making the chronic Population Adjusted Dose (cPAD) 0.005 mg/kg/day (the dose level for estimating dietary risk).

Short-Term Incidental Oral Exposure: This endpoint is determined to assess oral exposure, of a duration up to 30 days. In a rabbit developmental study, benfluralin (Technical) was administered to rabbits at 0, 25, 50, 100 or 225 mg/kg/day (by gavage) from gestational day (GD) 6 through 18. Body weights were determined on days 0, 6, 9, 12, 15, 19, 24, and 29 (sacrifice). Food consumption was also measured. The maternal NOAEL was determined to be 100 mg/kg/day and the LOAEL 225 mg/kg/day, based on dose related nominal body weight gain decrement, few feces, and reduced food consumption.

Risk estimates, expressed as a Margin of Exposure (MOE), are based on the

NOAEL dose of 100 mg/kg/day and a MOE of 100 (based on 10x for interspecies extrapolation and 10x for intraspecies variability) is considered adequately protective. Intermediate-term incidental oral exposure is not expected based on current use patterns and labeling.

Dermal Exposure: There are no dermal absorption studies for benfluralin. However, the HIARC estimated a 3% dermal absorption factor for benfluralin based on the results of the dermal absorption study for ethalfluralin, a structurally related compound. In a 21-day dermal toxicity study, rabbits received 15 repeated dermal applications of technical benfluralin (95.8%) in distilled water at dose levels of 0, 100, 500 or 1,000 mg/kg/day for 6 hours/day, 5 days/week. Dose-related dermal toxicity included epidermal hyperplasia, hyperkeratosis, parakeratosis, chronic-active inflammation, edema and hyperplasia of the sebaceous glands, *but no systemic toxicity was shown at any dose*. Erythema and edema were progressively worse in both sexes up to 21 days. Other induced dermal lesions began as slight skin erythema and edema starting at day 3 of dosing, progressing to slight to moderate erythema, edema, necrosis, and sebaceous gland hyperplasia by day 21. For dermal toxicity, the LOAEL was 100 mg/kg/day, the lowest dose tested; a NOAEL was not established. *No systemic toxicity was seen at any dose level.*

In a modified Buehler topical patch test in 12 Guinea pigs, 7 responded with a typical delayed hypersensitivity reaction to a challenge with technical benfluralin at 5% in 95% ethanol. At 48 hours, 9/12 pigs exhibited slight to moderate erythema and 8/12 pigs exhibited very slight to slight edema. *Formulated* products showed no evidence of sensitization in Beuhler's assays when tested concentrations ranged from 19% to 60% benfluralin. The lack of sensitization potential for the formulated products possibly occurred because; 1) benfluralin in the formulated product was not of sufficient concentration; 2) benfluralin did not penetrate the skin; or 3) the material in formulation interfered with the test. Therefore, since the technical causes skin sensitization, the potential skin sensitization of products containing benfluralin is not eliminated.

Dermal Hazard Summary: In the 21-day rabbit study, no *systemic* toxicity was observed at the highest dose tested (1,000 mg/kg/day). Based on the results of this study, the Agency is not concerned that dermal exposure to benfluralin will lead to the toxic effects observed in other studies. However, technical grade benfluralin caused typical delayed hypersensitivity in guinea pigs. Repeated dermal applications to rabbits resulted in skin lesions that progressed in severity and therefore may have the potential for adverse effects. The Agency is concerned that dermal exposure to benfluralin may cause adverse skin sensitization; however, since this risk cannot be adequately quantified, the HIARC recommends that products containing benfluralin should be labeled as "SENSITIZER" and contact should be avoided to the extent possible.

Short-Term Inhalation Exposure: Except for an acute inhalation study, which

placed benfluralin in Toxicity Category IV, no other studies are available for this route of exposure. Risk assessment for inhalation exposure to benfluralin is based instead on an oral study. The HIARC selected the developmental study in rabbits (described above) to be the basis for short-term inhalation risk assessment. Also, an assumption is made that 100% of the estimated inhalation dose will be absorbed. Risk estimates, expressed as a Margin of Exposure, are based on the NOAEL dose of 100 mg/kg/day and a MOE of 100 (10x for interspecies extrapolation and 10x for intraspecies variability) is considered adequately protective.

Intermediate-Term Inhalation Exposure: The dose and endpoint selected for this exposure scenario is based on the NOAEL of 7.2 mg/kg/day observed in the 2-generation rat reproduction study, where liver and kidney toxicity was observed at the LOAEL of 68 mg/kg/day. As in short-term inhalation risk assessment, an assumption is made that 100% of the estimated inhalation dose will be absorbed. Risk estimates, expressed as a Margin of Exposure, are based on the NOAEL dose of 7.2 mg/kg/day and a MOE of 100 (10x for interspecies extrapolation and 10x for intraspecies variability) is considered adequately protective.

3.4 Carcinogenic Potential

On September 26, 2001, the HED Cancer Assessment Review Committee (CARC) met and evaluated the carcinogenic potential of benfluralin. In accord with the Agency's Draft Guidelines for Cancer Risk Assessment (July, 1999), the CARC classified benfluralin into the category "suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential" by the oral route based on the following weight of the evidence considerations:

1. In male and female rats, there was an increase in tumors of the liver and thyroid at the two highest doses. However since these doses were considered excessive by the CARC and no tumors were seen at lower doses which were adequate for cancer testing, this study contributes little to the overall weight of evidence for a positive finding for benfluralin.

2. Female mice had a borderline statistically significant increase in liver tumors by both trend and pairwise tests at doses that were adequate. No tumors were seen in the male mice but after an additional meeting with new data, the CARC determined that the doses tested in the males was not high enough and this part of the mouse cancer testing should be repeated.

3. Contributing factors to the CARC decision were; (1) the lack of carcinogenic potential in rats; (2) a lack of mutagenic potential in a battery of tests; and (3) structurally related pesticides such as trifluralin, ethalfluralin, oryzalin, flumetralin and pendimethalin were classified as "C" carcinogens with their respective mutagenicity

studies showing no uniform pattern of mutagenicity.

Consistent with this weak evidence of carcinogenic effects, the CARC indicated that a dose-response assessment for cancer (either linear low dose extrapolation or Margin of Exposure calculation was not needed.

3.5 Endocrine Disruption

No obvious endocrine related effects were noted on the organs of reproduction. Thyroid toxicity in rats was seen at the highest dose, but whether or not these thyroid effects were directly related to endocrine modulation by benfluralin can not be determined based on the data submitted. However, the EPA is required under the FFDCA, as amended by FQPA, to develop a screening program to determine whether certain substances (including all pesticide active and other ingredients) *"may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or other such endocrine effects as the Administrator may designate."* Following the recommendations of its Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC), EPA determined that there was scientific bases for including, as part of the program, the androgen and thyroid hormone systems, in addition to the estrogen hormone system. EPA also adopted EDSTAC's recommendation that the Program include evaluations of potential effects in wildlife. For pesticide chemicals, EPA will use FIFRA and, to the extent that effects in wildlife may help determine whether a substance may have an effect in humans, FFDCA authority to require the wildlife evaluations. As the science develops and resources allow, screening of additional hormone systems may be added to the Endocrine Disruptor Screening Program (EDSP). When the appropriate screening and/or testing protocols being considered under the Agency's EDSP have been developed, benfluralin may be subjected to additional screening and/or testing to better characterize effects related to endocrine disruption.

4.0 EXPOSURE ASSESSMENT

4.1 Usage Summary

Benfluralin [also known as benefin; N-butyl-N-ethyl-2,6-dinitro–4-(trifluoromethyl) benzenamine] is an herbicide registered for use (preplant) on alfalfa, birdsfoot trefoil, clover, and lettuce. Benfluralin formulations are also registered for use on ornamental plants, forest trees, established turf, non-bearing fruit and nut trees, non-bearing vineyards, and non-bearing berries.

4.1.1 Product Summary

The reregistration of benfluralin is being supported by Dow AgroSciences LLC

(formerly DowElanco) and the Platte Chemical Company. Benfluralin products are sold under the trade name Balan™ and may be applied as preplant soil incorporated treatments to alfalfa, birdsfoot trefoil, clover, and lettuce using ground equipment. Benfluralin end-use products with registered food/feed applications are formulated as a dry flowable (DF). Benfluralin end-use products with registered non-food applications are formulated as a granular (G). Risk assessment is based on the following registrations:

Table 4. Product Summary

Product Name (EPA Reg Number)	Registrant	% A.I. or lb/gal	Formulation Type	Crop Type/ Use Site	Application Equipment	Maximum Application Rate
Balan Dry Flowable (34704-746)	Platte Chemical Company	60% (0.6 lbs ai/lb)	DF	Lettuce	groundboom	1.5 lbs ai/A
Balan Dry Flowable (34704-746)	Platte Chemical Company	60% (0.6 lbs ai/lb)	DF	Alfalfa, Birdsfoot Trefoil, Clover	groundboom	1.5 lbs ai/A
Balan Dry Flowable (62719-127)	DOW AgroSciences	60% (0.6 lbs ai/lb)	DF	Turf: golf course	low-pressure handwand, backpack, handgun, groundboom	3 lbs ai/A
XL 2G (62719-136)	DOW AgroSciences	1.0% (0.5 lbs ai/50 lb bag)	G	Christmas Trees	push-type spreader, bellygrinder, shaker can, backpack granular spreader, tractor-drawn spreader	4 lbs ai/A
XL 2G (62719-136)	DOW AgroSciences	1.0% (0.5 lbs ai/50 lb bag)	G	Container and Field Grown Ornamentals	push-type spreader, bellygrinder, shaker can, backpack granular spreader	3 lbs ai/A
T&O Fertilizer contains Balan 0.575% and Surflan 0.575% (62719-149)	DOW AgroSciences	0.575% (0.288 lb ai/50 lb bag)	G	Landscape Ornamentals	push-type spreader, bellygrinder, shaker can, backpack granular spreader	3 lbs ai/A

Product Name (EPA Reg Number)	Registrant	% A.I. or lb/gal	Formulation Type	Crop Type/ Use Site	Application Equipment	Maximum Application Rate
XL 2G (62719-136)	DOW AgroSciences	1.0% (0.5 lbs ai/50 lb bag)	G	Non-cropland Areas & Right-of-Way	push-type spreader, bellygrinder, tractor-drawn spreader	6 lbs ai/A
XL 2G (62719-136)	DOW AgroSciences	1.0% (0.5 lbs ai/50 lb bag)	G	Ornamental Bulbs	push-type spreader, bellygrinder, shaker can, backpack granular spreader	1.5 lbs ai/A
Turf Fertilizer Contains Balan 0.92% (62719-146)	DOW AgroSciences	0.92 % (0.46 lbs ai/50 lb bag)	G	Turf: golf course, commercial	push-type spreader, bellygrinder, tractor-drawn spreader	3 lbs ai/A
Turf Fertilizer Contains Balan 0.92% (62719-146)	DOW AgroSciences	0.92 % (0.46 lbs ai/50 lb bag)	G	Turf: residential	push-type spreader, bellygrinder	3 lbs ai/A
Super Team 1.25% (62719-327)	DOW AgroSciences	0.82% (0.328 lb ai/40 lb bag)	G	Turf: residential	push-type spreader, bellygrinder	0.0451 lbs ai/1000 sq ft (2 lb ai/A)
Super Team 1.15% (62719-331)	DOW AgroSciences	0.76% (0.304 lb ai/40 lb bag)	G	Turf: residential	push-type spreader, bellygrinder	0.0456 lbs ai/1000 sq ft (2 lb ai/A)
Super Team 0.92% (62719-332)	DOW AgroSciences	0.61% (0.244 lb ai/40 lb bag)	G	Turf: residential	push-type spreader, bellygrinder	0.0458 lb ai/1000 sq ft (2 lb ai/A)

4.1.2 Agency Usage Estimates

Based on EPA, USDA/NASS, CAL EPA, and National Center for Food and Agricultural Policy (NCFAP) data, a profile of past and current benfluralin usage has been developed by the OPP Biological and Economic Analysis Division (J. Alsadek memo, 5/14/02). For the years of 1991 through 2000, an annual estimate of benfluralin's total domestic usage averaged approximately 831,000 pounds active

ingredient (a.i.) for 172,000 acres treated. Most of the acreage is treated with one pound a.i. (or less) per application and almost two pounds a.i. (or less) per year. Benfluralin is a broad spectrum herbicide with its largest markets, in terms of total pounds active ingredient allocated, being lawn care operators (52%), landscape (10%), turf (7%), alfalfa and peanuts (6% each), and golf (5%). The remaining usage is primarily on lettuce with a maximum of 8 - 9% of total U.S. acres planted to lettuce each year. Most usage is in Michigan, California, Arizona, Maryland, North Carolina, Georgia, Alabama, Washington, and Idaho.

4.2 Dietary Exposure

4.2.1 Tolerance Summary

Benfluralin tolerances are established under 40 CFR §180.208 and are currently expressed in terms of benfluralin *per se* in/on the raw agricultural commodities (RACs) of alfalfa, birdsfoot trefoil, clover, lettuce, and peanuts at 0.05 ppm (a level termed "negligible"). No registrants have committed to support benfluralin use on peanuts. Peanuts will be deleted from all benfluralin end-use product labels, and the established tolerance for peanuts will be revoked. Tolerances are not required for processed food/feed commodities, nor required for livestock commodities. Feeding studies in ruminants and poultry demonstrated that, based on the expected residue levels in treated feed items (alfalfa, birdsfoot trefoil, clover), there would in turn be no expectation of finite residue in the livestock commodities of milk, meat, and eggs [this type of tolerance exemption is defined under Category 3, 40 CFR §180.6(a)]. Adequate methods are available for the purpose of tolerance enforcement. The Pesticide Analytical Manual (PAM, Vol. II, Section 180.208) lists two methods (designated as Methods I and A) as available for determination of benfluralin *per se* in/on plant commodities.

The HED Metabolism Assessment Review Committee (MARC) met on March 19, 2003 to discuss benfluralin residues in plants, livestock, and drinking water. The MARC reaffirmed that benfluralin *per se* is the residue of concern for tolerance expression and for dietary risk assessment. Agency reviewed metabolism studies on alfalfa, lettuce and peanut indicate that benfluralin *per se* was found at very low levels. Up to half of the radioactivity was incorporated into natural components (lignin, cellulose, and proteins), while the remaining aqueous- and ethyl acetate-extractable residues contained many components of varying polarities. No single component constituted a significant percentage (>10%) of the total radioactive residue (TRR). The MARC concludes that, based on the structures of the metabolites observed in the rat metabolism study, it is unlikely that any of the identified metabolites in plants will be significantly more toxic than the parent. The MARC also concurred with the Agency's previous decision on no "reasonable" expectation of finite benfluralin residue (or benfluralin metabolites) in meat, milk, poultry, or eggs.

4.2.2 Metabolism in Plants and Animals

The purpose for conducting metabolism studies is to determine the qualitative metabolic fate of the active ingredient. Many pesticides undergo change during or after application to the soil, water, crop, or livestock. In a metabolism study, the pesticide is labeled with a radioactive atom and followed to see if and where it breaks down within a plant or livestock.

Plants: The qualitative nature of benfluralin residues in plants is adequately understood based on acceptable studies conducted on alfalfa, lettuce, and peanuts. In alfalfa approximately half of the radioactivity was incorporated into the natural components of lignin, cellulose, and proteins. The remaining aqueous- and ethyl acetate-extractable residues contained many components of varying polarities; no single component constituted a significant (10% or more) percentage of the Total Radioactive Residue (TRR) expressed as benfluralin equivalents. Little benfluralin was found in lettuce (1.3% TRR). According to the registrant, 17.7% of the TRR in lettuce was associated with isolated lignin. Additional work demonstrated the radiolabel was incorporated into monosaccharides used in the synthesis of cell wall polysaccharides.

Livestock: The qualitative nature of benfluralin residues in livestock is adequately understood based on acceptable dairy cattle metabolism and poultry metabolism studies. The Agency has determined there is no expectation of finite residues of benfluralin in meat, milk, poultry, and eggs [Category 3, 40 CFR §180.6(a)] from the use of benfluralin under the currently registered use pattern (this determination was confirmed by the HED Metabolism Assessment Review Committee on 3/19/03). Based on this determination, guideline data requirements for meat, milk, poultry, and egg tolerances; for livestock commodity analytical method(s); and for data depicting "magnitude of the residue" in meat, milk, poultry, and eggs have been waived by the Agency.

Ruminants: A dairy cow study was conducted at 100x the maximum theoretical dietary exposure to ruminants (see GLN 860.1480 for calculation of the livestock dietary exposure). The TRR (expressed as benfluralin equivalents) were 0.006 ppm in milk (Day 3), 0.320 ppm in liver, 0.073 ppm in kidney, 0.004 ppm in muscle, and 0.006 ppm in fat. Milk and tissue analysis indicated that the radioactive (labeled) residue consisted of multiple components, none of which accounted for more than 5% of the sample TRR. Benfluralin, the parent compound, was not detected in milk or tissue samples.

Poultry: A hen study was conducted at 0.2 ppm (40x) and 15 ppm (3,000x) the maximum theoretical dietary exposure for poultry. The maximum TRR (expressed as benfluralin equivalents) from the 0.2-ppm dose group was 0.003 ppm in eggs (Day 7 - 28); 0.010 ppm in liver; nondetectable in muscle; and 0.004 ppm in skin/fat. The TRR (expressed as benfluralin equivalents) from the 15-ppm dose group was 0.219 ppm

(Day 10) in eggs; 1.072 ppm in liver; 0.092 ppm in muscle; and 0.266 ppm in skin/fat. The parent compound, benfluralin, was detected in eggs (4% TRR) and in skin/fat (34% TRR). All other metabolites were <10% of TRR.

4.2.3 Residue Analytical Methods

The reregistration requirements for residue analytical methods are fulfilled. Adequate methods are available for data collection and for the enforcement of tolerances for residues of benfluralin *per se* in/on plant commodities. Since no tolerances exist, or required, for milk, eggs, and edible livestock tissues, enforcement methods for the determination of benfluralin residues in livestock commodities are not needed.

Enforcement methods: The Pesticide Analytical Manual (PAM, Vol. II, Section 180.208) lists two methods, designated as Methods I and A, for determination of benfluralin *per se* in/on plant commodities. Method I lists the PAM, Vol. I multiresidue methods for organochlorine compounds. Method A is a GC/ECD method with detection limits of 0.005-0.01 ppm.

Data-collection methods: Samples of alfalfa and lettuce from more recent study submissions were analyzed using the Dow AgroSciences GC/ECD Method Am-AA-CA-R027-AA-755 in a study titled *"Determination of Benefin in Agricultural Crops and Soil."* The reported Limit of Quantitation (LOQ) was 0.01 ppm. This method is similar to Method A in PAM Vol. II.

Multiresidue Methods: The 10/99 FDA PESTDATA database (PAM Volume I, Appendix I) indicates that benfluralin is completely recovered (>80%) by Multiresidue Method Sections 302 (Luke Method; Protocol D), 303 (Mills, Onley, Gaither Method; Protocol E, nonfatty foods), and 304 (Mills Method; Protocol E, fatty foods).

4.2.4 Field Trial Data (Magnitude of the Residue)

Field trials determine the amount of residue in plant commodities at the time of harvest. Field trial data are used to set tolerance levels and are often used as the basis for dietary exposure estimates. Overall, adequate field trial data for benfluralin food/feed uses, based on the maximum registered use patterns, have been submitted and reviewed by the Agency. The reregistration requirements for "magnitude of the residue" in/on alfalfa forage, alfalfa hay, and lettuce have been fulfilled and the data available for alfalfa can be used to satisfy, via translation, the requirements for birdsfoot trefoil and clover.

Residues of benfluralin were < 0.01 ppm (nondetectable) and <0.01-0.014 ppm, respectively, in/on alfalfa forage and hay harvested 57-219 days following a single

preplant or pre-emergence soil incorporated application of the 60% DF formulation at ~1.5 lb ai/A (~1x the maximum seasonal application rate). These data support the established tolerance of 0.05 ppm for residues of benfluralin *per se* in/on "alfalfa". Residues of benfluralin ranged from <0.01 (nondetectable) to 0.02 ppm in/on head and leaf lettuce harvested 44-122 days following a single preplant or pre-emergence soil incorporated application of the 60% DF formulation at ~1.5 lb ai/A (~1x the maximum seasonal application rate). These data indicate that residues of benfluralin are not expected to exceed the established tolerance of 0.05 ppm.

Meat, Milk, Poultry, Eggs: The data requirements for the magnitude of benfluralin residue in meat, milk, poultry, and eggs have been waived based on low levels of radioactive residues observed in ruminant and poultry metabolism studies. The Agency has determined that there is no reasonable expectation of finite residues in meat, milk, poultry, and eggs from the use of benfluralin under the *current* registered use pattern. If additional feed items are registered in the future this conclusion may need to be reassessed.

4.2.5 Residue Estimates for Risk Assessment

Dietary risk assessment for benfluralin is based on lettuce *only*. Although benfluralin is used on livestock feed items (alfalfa, birdsfoot trefoil, clover) there is no expectation of finite residues in meat products, milk, or eggs (see above discussion). Dietary risk assessment estimates for lettuce are based on the residue level of 0.05 ppm, the same level used for tolerances and the enforcement method LOQ. The low residue level observed with benfluralin is consistent with data observed in other pre-plant herbicides.

4.2.6 Dietary Risk Estimates

Acute Dietary Exposure / Risk: Acute dietary risk is *not* assessed for benfluralin based on the conclusion of the HIARC Committee that no appropriate endpoint, attributed to a single dose can be identified.

Carcinogenic Risk: Benfluralin has been classified into the category defined as "*suggestive evidence of carcinogenic potential by all routes of exposure, but not sufficient to assess human carcinogenic potential*". A quantified carcinogenic risk estimate is not appropriate for benfluralin.

Chronic Dietary Exposure / Risk: Based on the conclusions of the HED HIARC committee, dietary risk for benfluralin is assessed by comparing chronic dietary exposure estimates (in mg/kg/day) to the benfluralin cPAD. Dietary risk is expressed as a percent of the cPAD. The cPAD is the chronic Population Adjusted Dose, which is the chronic Reference Dose (0.005 mg/kg/day) modified by the FQPA safety factor.

The benfluralin cPAD is 0.005 mg/kg/day based on a RfD of 0.005 mg/kg/day (see Section 3.3.1, Endpoint Selection Discussion), and incorporating the FQPA safety factor of 1x (no special factor) for the overall U.S. population or any population subgroups.

The cPAD method of risk assessment is applicable to the oral exposure route and is used to assess both food and drinking water exposure. Exposure estimates that are less than 100% of the cPAD indicate a determination of safety can be concluded. The following summarizes the Agency's current method for determining exposure due to use on food commodities. Chronic dietary risk is estimated for the general U.S. population and population subgroups defined by sex, age, region, and ethnicity. Durations of chronic exposure vary from one-year as represented by "all infants", to lifetime exposure as represented by the general U.S. population which combines all population subgroups to form a mean exposure value. It should be noted that all parameters of chronic dietary exposure estimates are averaged values (i.e. average food consumption, average residue, etc.). Dietary exposure estimates may also be factored by the estimated weighted average usage, or "percent crop treated" data (although not used in this case).

Consumption Data/DEEM Software: The benfluralin chronic dietary exposure assessment was conducted using the Dietary Exposure Evaluation Model software with the Food Commodity Intake Database (DEEM-FCID™, Version 1.3) which incorporates consumption data from the USDA Continuing Surveys of Food Intakes by Individuals (CSFII), 1994-1996 and 1998. The 1994-96, 98 data are based on the reported consumption of more than 20,000 individuals over two non-consecutive survey days. Foods "as consumed" (e.g., rhubarb pie) are linked to EPA-defined food commodities using publicly available recipe translation files developed jointly by USDA/ARS and EPA. Consumption data are averaged for the entire U.S. population and within population subgroups for chronic exposure assessment, but are retained as individual consumption "events" for acute exposure assessment. Based on analysis of the 1994-96, 98 CSFII consumption data which took into account dietary patterns and survey respondents, HED concluded that it is appropriate to report risk for the following population subgroups: the general U.S. population, all infants (<1 year old), children 1-2, children 3-5, children 6-12, youth 13-19, adults 20-49, females 13-49, and adults 50+ years old. Exposure estimates (Table 5) are expressed in mg/kg body weight/day and as a percent of the cPAD.

An upper-bound (tier 1) chronic dietary risk assessment was conducted for benfluralin. The residue estimate for lettuce, the only direct food use for benfluralin, is based on the level set for tolerance (0.05 ppm). Also, an assumption is made that 100% of the U.S. lettuce crop is treated with benfluralin. Estimated chronic dietary risk estimates for all population subgroups are less than 1% of the benfluralin cPAD (0.005 mg/kg/day) and do not indicate a concern for this route of exposure.

Table 5. Dietary Risk Estimates

Population	Exposure mg/kg/day	% Chronic PAD
U.S. Population	0.000012	<1
All Infants (<1 year)	<0.000001	<1
Children 1-2 years	0.000007	<1
Children 3 - 5 years	0.000010	<1
Children 6 -12 years	0.000011	<1
Youth 13 -19 years	0.000011	<1
Females 13 - 49	0.000014	<1
Adults 20 - 49 years	0.000014	<1
Adults 50+ years	0.000012	<1

4.3 Drinking Water Exposure

4.3.1 Residue Profile

Environmental Persistence: Data indicate that the fastest fate process for benfluralin is aqueous photolysis, with a half-life of 9.9 hours. Benfluralin is stable to hydrolysis and is metabolized relatively slowly in soil. No studies of metabolism in aerobic soil-water systems were submitted. The upper 90th percentile on the mean half-life from 6 studies was 65 days, and the range of half-lives was 20 to 86 days, with a mean of 49 days. One study of metabolism in anaerobic soil gave a half-life of 12 days, at a slightly elevated temperature of 29°C.

Mobility/Volatility: Parent benfluralin is immobile in soil (average Koc is 10,750). Several studies show that it does not leach into ground water. Benfluralin is a semi-volatile compound with a vapor pressure of 0.000066 mmHg (at 25°C). Volatilization may be a major fate process for non-soil-incorporated uses, such as turf, but may also occur in incorporated uses, to a lesser extent.

Degradates: Benfluralin has (at least) 26 identified degradates. In fate studies, nine of the degradates are estimated to exceed 10% of the applied parent concentration. Of those, 6 degradates were identified in "aerobic" aqueous photolysis and soil photolysis studies. The 6 degradates are:

LY-48800 (B35)	or	2,6-dinitro-N-ethyl-4-trifluoromethyl-benzeneamine
LY-67255	or	2-methyl-6-trifluoromethyl-4-nitro-1H-benzimidazole
LY-50030	or	5-trifluoromethyl-3-nitro-1,2-benzenediamine
LY-274766	or	4-nitro-2-propyl-6-trifluoromethyl-1H-benzimidazole
LY-65138	or	1-hydroxy-2-methyl-4-nitro-6-trifluoromethyl-1H-benzimidazole
LY-51783 (B34)	or	N-(N-butyl)-2,6-dinitro-4-trifluoromethyl-benzeneamine

Further metabolism of LY-51783 and LY-48800 is expected in aerobic and anaerobic soil and LY-51783 is further metabolized in fish. Based on structure-activity analysis, the degradates are all expected to be more mobile in soil (lower Kow), more soluble in water, and equally/or less volatile than the parent. Thus, they have a greater tendency to remain in water than the parent. Note: the trifluoromethyl moiety ($-CF_3$) is not metabolized in any of the major or principal minor degradates. This is consistent with the observation of trifluoroacetic acid (CF_3COOH) as the major degradate in the confined rotational crop study. *Trifluoroacetic acid is expected to be very stable in the environment, and to accumulate in lakes and reservoirs.* In the short term, the six degradates (identified above) are the most likely water contaminants, since the rate of aqueous photolysis is so much greater than other fate processes. No fate data has been submitted for these degradates, beyond the fate studies for the parent in which they were identified. In the long term, trifluoroacetic acid is expected to be the ultimate water contaminant.

Degradate B12 (2,6-dinitro-4-trifluoromethyl-phenol) was found at a high level of 0.133 ppm in an aerobic soil study, and fate data indicate that B12 is more mobile than parent benfluralin, and has a higher potential to leach to ground water than parent. On this basis, degradate B12 is also considered in drinking water assessment.

Treatment / Action Level(s): The Agency has no information on the effect of water treatment on parent benfluralin, or degradates. Benfluralin was proposed for inclusion on the TRI list of reportable compounds (59 FR 1788, Jan. 12, 1994). Benfluralin was identified as a "Potential Hazardous Polluting Substance" in Appendix 2 of the "Agreement between Canada and the United States of America on Great Lakes Water Quality, 1978."

4.3.2 Surface Water

Monitoring Data: At the present time, the Agency has limited monitoring data on the concentrations of benfluralin and/or degradates in surface water. The U.S. Geological Survey (USGS) has performed monitoring for parent benfluralin under the NAWQA program (http://ca.water.usgs.gov/pnsp/allsum/index.html#t1). In 5,196 samples from 1,058 surface water sites, benfluralin was detected in 92 samples at a

maximum concentration of 0.097 ppb. In 1,000 samples taken from 40 agriculture-impacted streams, benfluralin was detected in 5 samples at a maximum concentration of 0.007 ppb. In 327 samples from 11 urban streams, benfluralin was detected in 11 samples at a maximum concentration of 0.011 ppb. In 245 samples from 14 "integrator" sites, benfluralin was detected in 4 samples at a maximum of 0.009 ppb.

Modeling: For risk assessment, the Agency has used Estimated Environmental Concentrations (EECs) for drinking water provided to HED by the Environmental Fate and Effects Division (EFED). Estimates for benfluralin in surface water are based on the PRZM-EXAMS model and estimates for benfluralin in ground water are based on the SCIGROW model. Benfluralin water concentrations have been estimated for use on alfalfa, turf, Christmas tree farms, rights-of-way, non-bearing vineyards, fruit trees, nut trees, and berries. EECs have been calculated for three types of dietary risk assessment and are termed; 1) acute or peak concentration; 2) non-cancer chronic concentration; and 3) cancer chronic concentration. Based on the conclusions of the HIARC committee the EECs of interest for benfluralin are the chronic (non-cancer) concentrations, which are defined as the highest (90^{th} percentile) in a ten-year span.

Surface Water Chronic EECs

Alfalfa	0.17 ppb
Christmas Trees	0.17 ppb
Turf (Florida)	0.64 ppb
Peaches (Georgia)	1.40 ppb
Citrus (Florida)	2.00 ppb
Apples (North Carolina)	3.50 ppb

Note that the EECs (modeled for parent benfluralin) are considered upper-end estimates based on the following: 1) the use maximum application rates, maximum number of applications, at minimum re-application intervals; 2) the use of default percent cropped area (0.87), which is probably higher than actual cropped area for the various crops; 3) the use of a 65-day soil half-life (slow) and stable in water/sediment (upper-bound); 4) no consideration for volatilization and atmospheric oxidation, which would have reduced DF numbers to less than one-half of what they are for granulars; 5) no major degradates (>10% of parent mass) are formed in soil metabolism studies; 6) soil incorporation of spray (lettuce, alfalfa) and use of granules reduces photolysis, which is the source of most degradates; and 7) the effect of watertreatment plant processes (coagulation, chlorination, etc) not considered.

4.3.3 Ground Water

The SCI-GROW model was used to estimate potential ground water concentrations. SCI-Grow is a screening, or tier 1 model for ground water. It is based on a regression approach which relates the concentrations found in ground water in Prospective Ground Water studies to aerobic soil metabolism rate and soil-water partitioning properties of the chemical.

Ground Water EECs

Alfalfa	0.009 ppb
Turf	0.020 ppb
Rights-of-Way	0.070 ppb

4.4 Residential Exposure

Residential risk assessment considers all potential pesticide exposure, other than exposure due to residues in foods or in drinking water. Exposure may occur during and after application at homes; or after applications at golf courses, parks, schools, etc. Each route of exposure (oral, dermal, inhalation) is assessed, where appropriate, and risk is expressed as a Margin of Exposure (MOE), which is the ratio of estimated exposure to an appropriate No-Observed-Adverse-Effect-Level (NOAEL) dose. Benfluralin products are marketed for homeowner use on residential lawns and for homeowner use on landscape ornamentals. Benfluralin containing products are also marketed for use by professional applicators (Pest Control Operators, or PCOs) on residential turf, on golf courses, other turf such as recreational/commercial areas, and on ornamental plantings. Based on these uses, benfluralin is assessed for the residential applicator (or "handler") and for children's post-application exposure that may occur from turf contact.

4.4.1 Residential Applicator (Handler)

Homeowners (or other) may be exposed to benfluralin while treating their lawns. The product is in granular form with the active ingredient (ai) comprising up to 1.25% of total formulation. Benfluralin is applied by typical push-type spreaders or bellygrinders before seasonal weed emergence, at a rate up to 2 lbs. ai/acre. A number of assumptions, or estimates, such as adult body weight and area treated per application, are made by the Agency for residential risk assessment. Also, note that residential handlers are addressed somewhat differently than occupational handlers in that homeowners are assumed to complete all elements of an application (mix/load/apply) without use of protective equipment (assessments are based on an assumption that individuals will be wearing shorts and short-sleeved shirts).

HED has developed residential exposure scenarios based on the use sites, formulations, and the various equipment that may be used for benfluralin applications. The quantitative exposure/risk assessment developed for residential handlers is based on these scenarios:

Granular formulation:	loading/applying with bellygrinder spreader
Granular formulation:	loading/applying with push-type spreader
Granular formulation:	loading/applying with shaker can

Benfluralin-specific data to assess the above exposure scenarios were not submitted to the Agency in support of reregistration. Instead, exposure estimates for these scenarios are taken from the Pesticide Handlers Exposure Database (PHED, Version 1.1 August 1998) which is used to assess handler exposures for regulatory actions when chemical-specific monitoring data are not available. In addition to PHED data, this risk assessment relies on data from the Outdoor Residential Exposure Task Force (ORETF) and proprietary studies. (See appendix)

Exposure Factors / Other Estimates: Average body weight of an adult handler is 70 kg and represents the general adult population (effects identified in the selected toxicity studies were not sex specific). Other factors used for the benfluralin assessment are taken from the Health Effects Division Science Advisory Committee *Policy 12: Recommended Revisions To The Standard Operating Procedures For Residential Exposure Assessment* (February 22, 2001) and include the area treated estimates of: 1) 0.5 acres for lawn and ornamental treatments using granular formulations with a bellygrinder spreader or push-type spreader; and 2) 1,000 square feet for ornamental treatments using a shaker can. (Note that the estimate of 0.5 acres for a bellygrinder is considered an upper-bound estimate). All scenarios were assessed at the maximum rate of application.

Based on the conclusions of the HIARC, benfluralin is not assessed for systemic dermal toxicity, but *is* assessed for systemic inhalation toxicity. Since the seasonal duration of benfluralin exposure to homeowner applicators is thought to be less than 30 days (sometimes described as "episodic") the risk assessment is based on the *short-term* dose level of 100 mg/kg/day. A Margin of Exposure of 100 (or more) is considered adequately protective for this assessment.

The following table summarizes residential applicator (handler) exposure and risk estimates.

Table 6. Residential Handler Exposure / Risk Estimates

Exposure Scenario (Data Source)	Crop or Target	Application Rate[a]	Area Treated Daily[b]	Baseline Inhalation Unit Exposure (ug/lb ai)[c]	Baseline Inhalation MOE[d]
Mixer/Loader/Applicator					
Loading/Applying Granulars with a Belly Grinder	residential turf	3 lb ai/acre	0.5 acres	62	75,000
	ornamentals: outdoor	3 lb ai/acre	0.5 acres	62	75,000
	ornamental bulbs	1.5 lb ai/acre	0.5 acres	62	150,000
Loading/Applying Granulars with a Push Type Spreader (ORETF)	residential turf	3 lb ai/acre	0.5 acres	0.88	5,300,000
	ornamentals: outdoor	3 lb ai/acre	0.5 acres	0.88	5,300,000
	ornamental bulbs	1.5 lb ai/acre	0.5 acres	0.88	11,000,000
Loading/Applying Granulars with a Bucket and Spoon (MRID 452507-01)	ornamentals: outdoor	0.689 lb ai/1000 sq ft	1000 sq ft	45	230,000
	ornamental bulbs	0.0344 lb ai/1000 sq ft	1000 sq ft	45	4,500,000
Loading/Applying Granulars with a Shaker Can (PHED)	ornamentals: outdoor	0.689 lb ai/1000 sq ft	1000 sq ft	467	22,000
	ornamental bulbs	0.0344 lb ai/1000 sq ft	1000 sq ft	467	440,000

Footnotes

a Application rates are the maximum application rates determined from EPA registered labels for benfluralin.

b Amount handled per day values are EPA estimates of acreage treated or gallons applied based on Exposure SAC Policy #9 "Standard Values for Daily Acres Treated in Agriculture".

c Baseline inhalation unit exposure values from PHED Surrogate Exposure Guide (or other) and represent no respiratory protection.

d Baseline inhalation MOE = short-term NOAEL (100 mg/kg/day) / baseline inhalation dose (mg/kg/day), where baseline inhalation dose = baseline inhalation unit exposure (µg/lb ai) x application rate x amount handled per day x 1mg / 1000µg) / body weight (70 kg).

Residential Handler Risk Summary: For residential handlers, all estimated MOEs for inhalation-based *systemic* toxicity are above the target level of 100.

4.4.2 Residential Post-Application

Benfluralin uses in the residential setting include applications to ornamentals and to lawns. Although the type of site that benfluralin may be used on varies from golf courses to ornamental gardens, the scenario chosen for risk assessment (residential turf use) represents what the Agency considers the likely upper-end of possible exposure. For this assessment, children are the population group of concern. Since *systemic* toxicity was not observed in a dermal toxicity study, up to a dose level of 1,000 mg/kg/day, the only risk addressed in this assessment is the possible oral exposure of small children from treated turf, or from treated soil (i.e., soil ingestion, granule ingestion, and hand-/object-to-mouth). A Margin of Exposure of 100 (or more) is considered adequately protective for this assessment.

Dose from hand-to-mouth activity from treated turf: Postapplication dose among children from the "incidental" ingestion of pesticide residues on treated turf from hand-to-mouth transfer (i.e., those residues that end up in the mouth from a child touching turf and then putting their hands in their mouth);

Dose from object-to-mouth activity from treated turf: Postapplication dose among children from incidental ingestion of pesticide residues on treated turf from object-to-mouth transfer (i.e., those residues that end up in the mouth from a child mouthing a handful of treated turf);

Dose from soil ingestion activity: Postapplication dose among children from incidental ingestion of soil in a treated area;

Dose from ingestion of benfluralin granules from treated turf: Postapplication dose among children from the "episodic" ingestion of pesticide granules picked up from treated turf. This assessment is not needed for benfluralin since an endpoint and dose for acute oral risk assessment was not identified by the HIARC.

The term "episodic" is used to denote an event (granule ingestion) that is infrequent to very infrequent. The term "incidental" is used to denote the more likely oral ingestion that may occur following typical lawn treatments. Both terms are used to distinguish the inadvertent oral exposure associated with lawn use from the expected and perhaps more regular exposure associated with treated foods, or from residue in drinking water. The exposure estimates of the oral ingestion scenarios (except granule ingestion) are combined to establish the *possible* (if not likely) upper-end of oral exposure from lawn (or similar) use.

Exposure Factors / Other Estimates: 1) 5% of the application rate has been used to calculate the 0-day residue level for hand-to-mouth behavior estimates; 2) 20% of the application rate has been used to calculate the 0-day residue level for object-to-mouth behavior estimates (a higher percent transfer has been used for object-to-mouth behaviors because it involves a teething action believed analogous to DFR/leaf wash sample collection where 20 percent is also used); 3) 3 year old children are expected to weigh an average 15 kg; 4) hand-to-mouth exposures are based on a frequency of 20 events/hour and a surface area per event of 20 cm^2 representing the palmar surfaces of three fingers; 5) saliva extraction efficiency is 50% (meaning that every time the hand goes in the mouth approximately ½ of the residues on the hand are removed); 6) object-to-mouth exposures are based on a 25 cm^2 surface area; 7) exposure durations are expected to be 2 hours based on information in the Agency's *Exposure Factors Handbook*; and 7) soil residues are contained in the top centimeter.

Table 7. Post-Application Oral Exposure (Child)

Exposure Scenario	Route of Exposure	Application Rate[a]	Exposure mg/kg/day	MOE[b]
Outdoors				
Hand to Mouth Activity on Turf[c]	Oral	3.0 lb ai/acre	0.448552	2200
Object to Mouth Activity on Turf[d]	Oral	3.0 lb ai/acre	0.011214	8,900
Soil Ingestion[e]	Oral	3.0 lb ai/acre	0.000150	670,000
Ingestion of Pellets[f]	Oral	3.0 lb ai/acre	0.100000	N/A

Footnotes:

[a] Application rates represent maximum label rates from current EPA registered labels.

[b] MOEs calculated using residues which would be found on day of treatment Oral MOE = Oral NOAEL 100 mg/kg/day/Oral Dose (mg/kg/day). Target MOE is 100.

[c] Hand-to-mouth Dose Calculation: oral dose to child (1-6 year old) on the day of treatment (mg/kg/day) = [application rate (lb ai/acre) x fraction of residue dislodgeable from potentially wet hands (5%) x 11.2 (conversion factor to convert lb ai/acre to µg/cm^2)] x median surface area for 1-3 fingers (20 cm^2/event) x hand-to-mouth rate (20 events/hour) x exp. time (2 hr/day) x 50% saliva extraction factor x 0.001 mg/µg] / bw (15 kg child).

[D] Object to Mouth Dose Calculation: oral dose to child (1-6 year old) on the day of treatment = [TTR (µg/cm^2) x ingestion rate of grass (25 cm^2/day) x 0.001 mg/µg] / bw (15 kg child).

[e] Soil Ingestion Dose Calculation: oral dose to child (1-6 year old) on the day of treatment (mg/kg/day) = [(application rate (lb ai/acre) x fraction of residue retained on uppermost 1 cm of soil (100% or 1.0/cm) x 4.54E+08 µg/lb conversion factor x 2.47E-08 acre/cm^2 conversion factor x 0.67 cm^3/g soil conversion factor) x 100 mg/day ingestion rate x 1.0E-06 g/µg conversion factor] / bw (15 kg).

[f] Pellet Ingestion Dose Calculation: oral dose to child (1-6 year old) on the day of treatment (mg/kg/day) = [(application rate (lb ai/acre) x percent active ingredient x 300 mg/day ingestion rate/ bw (15 kg) (Assessment not applicable)

Note: Assumptions used in dose calculations (e.g., transfer coefficients) are from Residential SOPs (revised 2/01).

Table 8. Oral Ingestion / Combined Exposure

Exposure Scenario				Margins of Exposure (MOEs) (UF=100)			
				Dermal	Inhalation	Oral MOE	Total Oral MOE
Child	Turf: (3.0 lb ai/acre)	Postapp	Hand to Mouth	N/A	N/A	2,200	1,800
			Object to Mouth	N/A	N/A	8,900	
			Soil Ingestion	N/A	N/A	670,000	

Dermal Sensitization: The Agency is concerned about dermal sensitization reactions in adults and children due to benfluralin exposure in residential settings. At present, HED has no method for determining a quantitative endpoint for skin sensitization and, therefore, has no means of quantitatively assessing the risk resulting from benfluralin's sensitization potential. Also, data on the sensitization potential of benfluralin *end-use* products is inadequate for the Agency to determine the likelihood that sensitization reactions will occur from exposures to the formulated product.

However, the Agency's current policy is that it is not feasible to require personal protective equipment for homeowner pesticide users due to concerns about noncompliance. Therefore, HED recommends that the current labeling requirements for long-sleeved shirts, long pants, shoes, and socks be removed from benfluralin homeowner labels. For the benfluralin granular products, EPA will require a sensitization warning statement on the labels and a recommendation that contact with the skin be avoided.

4.4.3 Spray drift:

Spray drift is always a potential source of exposure to residents nearby to spraying operations. This is particularly the case with aerial application, but, to a lesser extent, groundboom use as with benfluralin can also be a source of exposure. The Agency has been working with the Spray Drift Task Force, EPA Regional Offices and State Lead Agencies for pesticide regulation and other parties to develop the best spray drift management practices. The Agency is now requiring interim mitigation measures for aerial applications that must be placed on product labels/labeling. The Agency has completed its evaluation of the new data base submitted by the Spray Drift Task Force, a membership of U.S. pesticide registrants, and is developing a policy on how to appropriately apply the data and the AgDRIFT computer model to its risk assessments

for pesticides applied by air, orchard airblast and ground hydraulic methods. After the policy is in place, the Agency may impose further refinements in spray drift management practices to reduce off-target drift and risks associated with aerial as well as other application types where appropriate.

5.0 AGGREGATE EXPOSURE ASSESSMENT

As part of the reregistration eligibility decision, the Agency is required by the Food Quality Protection Act to ensure *"that there is reasonable certainty that no harm will result from aggregate exposure to pesticide chemical residue, including all anticipated dietary exposures and other exposures for which there is reliable information."*

The following aggregate risk assessment uses the dietary exposure estimates completed for benfluralin food uses and the residential exposure estimates to evaluate the estimates of drinking water contamination modeled by the Environmental Fate and Effects Division. For benfluralin aggregate assessment, the intervals of exposure to be assessed are chronic (one year or more) and short-term (up to 30 days). The routes of exposure to be assessed are oral (food + water + incidental) and inhalation (residential handlers). Intermediate and chronic residential exposures to benfluralin are not expected and, therefore, not included in this aggregate assessment. Aggregate risk, and related drinking water levels of comparison (DWLOC) estimates have been made in accord with the HED interim guidance (*Updated "Interim Guidance for Incorporating Drinking Water Exposure into Aggregate Risk Assessments,"* 8/1/99).

HED uses "drinking water levels of comparison" (DWLOC) values as surrogate measures of exposure. As part of aggregate risk assessment, HED compares the calculated DWLOC to the EEC(s) estimated for surface water and groundwater. If the DWLOC is greater than the estimated surface and groundwater concentration (i.e., if the DWLOC > EEC) a determination of safety can be made by the Agency for aggregate exposure to a particular pesticide. If the DWLOC values are not greater than the EEC values the Agency may require additional data concerning water contamination. (Note that the theoretical limit for a benfluralin DWLOC estimate is 100 ppb, based on benfluralin solubility in water).

5.1 Aggregate Short-Term Risk Assessment / DWLOC Calculations

The following equation was used to calculate the short-term DWLOC value required for benfluralin aggregate risk assessment:

$$DWLOC_{short\text{-}term}\ (\mu g/L) = \frac{[\text{allowable chronic water exposure (mg/kg/day) x (kg body weight)}]}{[\text{consumption (L/day) x } 10^{-3}\ \text{mg/}\mu g]}$$

where "allowable" water exposure (mg/kg/day) = NOAEL (100 mg/kg/day) minus estimated chronic food exposure (mg/kg/day) and estimated short-term exposure. DWLOCs are calculated for adult male or female "handlers" and for children who may be orally exposed following application to residential turf. Estimates are based on default water consumption estimates of two liters per day for adults and one liter per day for children.

Table 9. Short-Term Drinking Water Levels of Comparison

Short-Term DWLOC Calculations						
Population Subgroup	**NOAEL (mg/kg/day)**	**Exposure Food and Residence (mg/kg/day)**	**Maximum Chronic Water Exposure (mg/kg/day)**	**Groundwater EEC (µg/L)**	**Surface Water EEC (µg/L)**	**DWLOC (µg/L)**
Children	100	0.4599	0.5400	Range of 0.009 - 0.07	Range of 0.17 - 3.5	>100
Females	100	0.0046	0.9950	Range of 0.009 - 0.07	Range of 0.17 - 3.5	>100
Males	100	0.0046	0.9950	Range of 0.009 - 0.07	Range of 0.17 - 3.5	>100

The EEC estimates for benfluralin and degradates are less than the estimated DWLOC; and a conclusion can be drawn (based on the MOE approach) that no adverse toxicological effect will occur due to aggregate short-term exposure.

5.2 Aggregate Chronic Risk Assessment / DWLOC Calculations

The following equation was used to calculate the chronic DWLOC value required for benfluralin aggregate risk assessment:

$$DWLOC_{chronic}\ (\mu g/L) = \frac{[\text{allowable chronic water exposure (mg/kg/day) x (kg body weight)}]}{[\text{consumption (L/day) x } 10^{-3}\ \text{mg/µg}]}$$

where allowable chronic water exposure (mg/kg/day) = cPAD (0.005 mg/kg/day) minus estimated chronic food exposure (mg/kg/day). DWLOCs are calculated for adults (70 kg) and children (10 kg) based on default water consumption estimates of two liters per day for adults and one liter per day for children.

Table 10. Chronic Drinking Water Levels of Comparison

Chronic DWLOC Calculations						
Population Subgroup	**cPAD (mg/kg/day)**	**Chronic Food Exposure (mg/kg/day)**	**Maximum Chronic Water Exposure (mg/kg/day)**	**Groundwater EEC (µg/L)**	**Surface Water EEC (µg/L)**	**DWLOC chronic (µg/L)**
Children	0.005	0.000011	0.00499	Range of 0.009 - 0.07	Range of 0.17 - 3.5	50
Females	0.005	0.000014	0.00499	Range of 0.009 - 0.07	Range of 0.17 - 3.5	>100
Males	0.005	0.000012	0.00499	Range of 0.009 - 0.07	Range of 0.17 - 3.5	>100

The EEC estimates for benfluralin and degradates are less than the estimated DWLOC, and a conclusion can be drawn (based on the MOE approach) that no adverse toxicological effect will occur due to aggregate chronic exposure.

6.0 CUMULATIVE EXPOSURE ASSESSMENT

Section 408(b)(2)(D)(v) of the FFDCA requires that, when considering whether to establish, modify, or revoke a tolerance, the Agency consider "available information" concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity."

EPA does not have, at this time, available data to determine whether benfluralin has a common mechanism of toxicity with other substances. Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding as to benfluralin and any other substances. For the purposes of this tolerance action, therefore, EPA has not assumed that benfluralin has a common mechanism of toxicity with other substances. For information regarding EPA's efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see the policy statements released by EPA's Office of Pesticide Programs concerning common mechanism determinations and procedures for cumulating effects from substances found to have a common mechanism on EPA's website at http://www.epa.gov/pesticides/cumulative/.

7.0 OCCUPATIONAL EXPOSURE ASSESSMENT

Occupational risk is assessed for exposure at the time of application (termed "handler" exposure) and assessed for exposure following application, or post-application exposure. Application parameters are generally defined by the physical nature of the formulation (e.g., formula and packaging), by the equipment required to deliver the chemical to the use site, and by the application rate required to achieve an efficacious dose. Post-application risk is assessed for activities such as scouting, irrigating, pruning, and harvesting and is based primarily on dermal exposure estimates. Note that occupational risk estimates are intended to represent professional pesticide workers, and on this basis assumptions are made concerning acres treated per day and the seasonal duration of exposure.

Endpoint / Dose Selection for Occupational Risk Assessment: Occupational risk estimates are expressed as Margins of Exposure, or MOEs, which are the ratio of estimated exposure to an established dose level (NOAEL/LOAEL). Benfluralin MOEs are determined by a comparison of specific exposure scenario estimates to the dose level (NOAEL) of 100 mg/kg/day for short-term assessment or 7.2 mg/kg/day for intermediate-term assessment. For benfluralin users the Agency has established a "target" MOE of 100 (for both short- and intermediate-term exposure) based on the standard uncertainty factors of 10x for interspecies extrapolation and 10x for intraspecies variability. Long-term worker exposure is not expected for benfluralin.

7.1 Use Sites

Professional pesticide workers are exposed to benfluralin while making applications to the following use sites:

Food Crop:	lettuce
Food/Feed Crops:	alfalfa, birdsfoot trefoil, clover
Other:	agricultural rights-of-way, fencerows/hedgerows, Christmas tree plantations, recreational areas, commercial/industrial lawns, container and field grown ornamentals, landscape ornamentals, ornamental bulbs

7.2 Occupational Handler

The Agency uses the term "handlers" to describe those individuals who are involved in the pesticide application process. For occupational risk assessment , the Agency identifies the distinct job functions, or tasks, related to application methods and estimates exposures depending on the specifics of each task. Job requirements such

as amount of chemical to be used in an application, the kinds of equipment used, the target being treated, and the circumstances of the user (e.g., the level of protection used by an applicator) can cause exposure levels to differ in a manner specific to each application event. The Agency always completes risk assessments using maximum application rates for each scenario for screening purposes. The Agency has developed a series of general descriptions for tasks that are associated with pesticide applications:

Occupational Mixers and/or Loaders: these individuals perform tasks in preparation for an application. For example, prior to application, they would prepare dilute spray solutions and load those dilute spray solutions into application equipment such as a groundboom tractor or they would load/transfer solid materials (granulars) into tractor-drawn spreader equipment.

Occupational Applicators: these individuals operate application equipment such as groundboom sprayers for liquids or tractor-drawn spreaders for granular materials.

Occupational Mixer/Loader/Applicators: these individuals are involved in the entire pesticide application process (i.e., they do all job functions related to a pesticide application event). These individuals prepare dilute spray solutions and also apply the solution. The Agency always considers some exposures to be mixer/loader/applicator exposures because of the equipment used and the logistics associated with such applications. For example, if one uses a small handheld device, such as a low-pressure handwand sprayer, it is anticipated that one individual will mix the spray solution and then apply it, because of labor and logistical considerations.

It is likely that benfluralin exposures can occur in a variety of patterns. Occupational benfluralin exposures can occur for a single day, or up to weeks at a time for custom (commercial) applicators who are completing a number of applications for a number of different clients. Intermittent exposures over several weeks are also anticipated for some workers.

Occupational handler exposure assessments are completed by the Agency using different levels of personal protection. The Agency typically evaluates all exposures with a tiered approach. The lowest tier is represented by the baseline exposure scenario (i.e., long-sleeve shirt, long pants, shoes, and socks) followed by increasing the levels of personal protective equipment or PPE (e.g., gloves, double-layer body protection, and respirators) and engineering controls (e.g., closed cabs and closed mixing/loading systems). This approach is always used by the Agency in order to define label language using a risk-based approach. In addition, the minimal level of adequate protection for a chemical is generally considered by the Agency to be the most practical option for risk reduction because over-burdensome risk mitigation measures are not considered a practical alternative.

7.2.1 Exposure Scenario Summary

HED identified 13 occupational exposure scenarios based on the use sites, formulations, and the various equipment that may be used for benfluralin applications.

Mixer/Loader:

Dry Flowable Formulation: mixing/loading to support ground applications
Granular Formulation: loading to support ground applications

Applicator:

Dry Flowable Formulation: applying sprays with groundboom equipment
Granular Formulation: applying granules with a tractor / ATV-drawn spreader

Mixer/Loader/Applicator:

Dry Flowable Formulation: low pressure handwand sprayer
Dry Flowable Formulation: backpack sprayer
Dry Flowable Formulation: low pressure/high volume turf/handgun sprayer
Granular Formulation: pump-feed backpack spreader
Granular Formulation: gravity-feed backpack spreader
Granular Formulation: bellygrinder spreader
Granular Formulation: push-type spreader
Granular Formulation: bucket and spoon
Granular Formulation: shaker can

7.2.2 Exposure Factors / Other Estimates

Body Weight: Average body weight of an adult handler is 70 kg and represents the general adult population (effects identified in the selected toxicity studies were not sex specific (i.e., NOAELs selected by HIARC were the same for males and females). The average occupational workday is assumed to be 8 hours.

Exposure Data: Chemical-specific data to assess the above exposure scenarios were not submitted to the Agency in support of the reregistration of benfluralin. Analyses were completed using acceptable surrogate exposure data for the scenario assessed. Several handler assessments were completed using data from the Pesticide Handler Exposure Database (ver 1.1). No data were available to assess mixing/loading/applying *dry flowable* formulations with a low-pressure handwand sprayer, therefore PHED data for mixing/loading/applying *liquid* formulations with a low-pressure handwand sprayer was used as a reasonable surrogate. Some handler assessments (i.e., handheld handgun equipment, push-type spreader) were completed

using data from the Outdoor Residential Exposure Task Force (ORETF).

Application Rates / Area Treated: The daily areas to be treated were defined for each handler scenario (in appropriate units) by best scientific judgement. When possible, the assumptions for daily areas treated are taken from the Health Effects Division Science Advisory Committee on Exposure *Policy 9: Standard Values for Daily Acres Treated in Agriculture* (July 5, 2000).

Rate:

Noncrop land and rights-of-way treatments are assessed at 6.0 pounds active ingredient per acre;

Christmas trees are assessed at 4.0 pounds active ingredient per acre;

Landscape ornamentals, field/container grown ornamentals, residential and golf course turfgrass (dry flowable formulations) are assessed at 3.0 pounds active ingredient per acre;

Residential and golf course turfgrass (granular formulations) are assessed at 2.0 pounds active ingredient per acre;

Alfalfa, birdsfoot trefoil, clover, lettuce, and ornamental bulbs are assessed at 1.5 pounds active ingredient per acre;

Area:

For alfalfa, birdsfoot trefoil, and clover, the area treated daily was assumed to be 200 acres for ground applications;

For lettuce, noncrop lands, and rights-of-way, the area treated daily was assumed to be 80 acres for ground applications;

For Christmas tree and ornamental (other than bulb) applications, the area treated daily was assumed to be 40 acres for tractor- or ATV-drawn spreaders; 10 acres for backpack spreaders; 5 acres for push-type spreaders, 1 acre for bellygrinder spreaders, and 5,000 square feet for shaker cans;

For turf applications, the area treated daily was assumed to be 40 acres for ground applications (golf courses); 5 acres for ground applications (commercial areas), 5 acres for low-pressure handwand sprayers, handgun sprayers, and push-type spreaders; and 1 acre for bellygrinders;

For ornamental bulb applications, the area treated daily was assumed to be 5 acres for tractor- or ATV-drawn spreaders; 10 acres for backpack spreaders; 5 acres for push-type spreaders, 1 acre for bellygrinder spreaders, and 5,000 square feet for shaker cans.

Duration of Exposure: This assessment presents handler risk estimates for both short- and intermediate-term exposure durations. For most benfluralin handlers, exposure likely does not extend to 30 or more days since it is used pre-plant, or timed specifically for the seasonal emergence of weeds. However, since the duration of exposure is uncertain, intermediate-term risk estimates are provided as an upper-bound assessment.

Unit Exposure: The Agency uses a method known as *unit exposure* to assess handler exposures to pesticides which are presented as mg active ingredient exposure *per* pound of active ingredient handled. The Agency has developed a series of unit exposures that are unique for each exposure scenario and level of protection. The *unit exposure* concept has been established in the scientific literature and also through various exposure monitoring guidelines published by the U.S. EPA and international organizations such as Health Canada and OECD (Organization For Economic Cooperation and Development).

7.2.3 Occupational Handler Risk Estimates

The occupational handler exposure and risk calculations are presented in this section as Margins of Exposure (MOE) estimates for short- and intermediate-term durations. Inhalation exposure was calculated by normalizing the daily inhalation exposure value by body weight and accounting for inhalation absorption (no specific inhalation absorption factor is available for benfluralin so a factor of 100 percent has been used. Daily dose was calculated using the following formula:

Daily Exposure (mg ai/day) =

Unit Exposure (mg ai/lb ai) x Application Rate (lb ai/area) x Daily Area Treated (area/day)

where:

Daily Exposure	Amount active ingredient inhaled, also referred to as potential dose (mg ai/day);
Unit Exposure	Normalized exposure value derived from August 1998 PHED Surrogate Exposure Table and various referenced exposure studies noted above (mg ai/lb ai);

Application Rate	Normalized application rate based on a logical unit treatment, such as acres, square feet, gallons, or cubic feet. Maximum values are generally used (lb ai/A, lb ai/sq ft, lb ai/gal, lb ai/cu ft); and
Daily Area Treated	Normalized application area based on a unit treatment such as acres (A/day), square feet (sq ft/day), gallons per day (gal/day), or cubic feet (cu ft/day).

Daily dose (inhalation) was calculated by normalizing the daily inhalation exposure value by body weight (70kg) and accounting for inhalation absorption (100%).

$$Average\ Daily\ Dose\left(\frac{mg\ ai}{kg/day}\right) = Daily\ Exposure\left(\frac{mg\ ai}{day}\right) x \left(\frac{AbsorptionFactor(\%/100)}{Body\ Weight\ (kg)}\right)$$

where:

Average Daily Dose	=	The amount as absorbed dose received from exposure to a pesticide in a given scenario (mg pesticide active ingredient/kg body weight/day, also referred to as ADD);
Daily Exposure	=	Amount inhaled, also referred to as potential dose (mg ai/day);
Absorption Factor	=	A measure of the flux or amount of chemical that crosses a biological boundary such as the lungs (% of the total available absorbed);
Body Weight	=	Body weight determined to represent the population of interest in a risk assessment (kg).

Finally, the calculations of daily inhalation dose received by handlers were then compared to the appropriate endpoint (i.e., NOAEL). Inhalation MOEs for all short-term durations were calculated using an NOAEL of 100 mg/kg/day and for all intermediate-term durations were calculated using an NOAEL of 7.2 mg/kg/day. All MOE values were calculated using the formula below:

$$MOE = \frac{NOAEL\left(\frac{mg\ ai}{kg/day}\right)}{Average\ Daily\ Dose\left(\frac{mg\ ai}{kg/day}\right)}$$

Table 11. Occupational Handler Risk Summary / Short-Term

Exposure Scenario	Crop or Target	Application Rate[a]	Area Treated Daily[b]	Baseline Inhalation Unit Exposure (ug/lb ai)[c]	Baseline Inhalation MOE[d]
Mixer/Loader					
Mixing/Loading Dry Flowables for Groundboom Application (1)	alfalfa, birdsfoot trefoil, clover	1.5 lb ai/acre	200 acres	0.77	30,000
	lettuce	1.5 lb ai/acre	80 acres	0.77	76,000
	turf: golf courses	3 lb ai/acre	40 acres	0.77	76,000
	turf: residential and commercial areas	3 lb ai/acre	5 acres	0.77	610,000
Loading Granulars for Drop Type Tractor (or ATV) Drawn Spreader Application (2)	turf: commercial areas and golf courses; and ornamentals: container grown, field grown and landscape	3 lb ai/acre	40 acres	1.7	34,000
	Christmas trees	4 lb ai/acre	40 acres	1.7	26,000
	non-crop land, rights-of-way	6 lb ai/acre	80 acres	1.7	8,600
	ornamental bulbs	1.5 lb ai/acre	5 acres	1.7	550,000
Applicator					
Applying Sprays with Groundboom Application (3)	alfalfa, birdsfoot trefoil, clover	1.5 lb ai/acre	200 acres	0.74	32,000
	lettuce	1.5 lb ai/acre	80 acres	0.74	79,000
	turf: golf courses	3 lb ai/acre	40 acres	0.74	79,000
	turf: residential and commercial areas	3 lb ai/acre	5 acres	0.74	630,000
Applying Granulars with Drop Type Tractor (or ATV) Drawn Spreader (4)	turf: commercial areas and golf courses; and ornamentals: container grown, field grown and landscape	3 lb ai/acre	40 acres	1.2	49,000
	Christmas trees	4 lb ai/acre	40 acres	1.2	36,000
	non-crop land, rights-of-way	6 lb ai/acre	80 acres	1.2	12,000
	ornamental bulbs	1.5 lb ai/acre	5 acres	1.2	780,000
Mixer/Loader/Applicator					
Mixing/Loading/Applying Dry Flowables with a Low Pressure Handwand (5)	turf	3 lb ai/acre	5 acres	30	16,000
Mixing/Loading/Applying Dry Flowables with a Backpack Sprayer (6)	turf	3 lb ai/acre	5 acres	30	16,000
Mixing/Loading/Applying Dry Flowables with a Handheld Handgun (ORETF) (7)	turf	3 lb ai/acre	5 acres	2.2	210,000

Exposure Scenario	Crop or Target	Application Rate[a]	Area Treated Daily[b]	Baseline Inhalation Unit Exposure (ug/lb ai)[c]	Baseline Inhalation MOE[d]
Loading/Applying Granulars with a Pump Feed Backpack Granular Spreader (MRID 451672-01) (8)	Christmas trees	4 lb ai/acre	10 acres	4.2	42,000
	container grown, field grown and landscape ornamentals	3 lb ai/acre	10 acres	4.2	56,000
	ornamental bulbs	1.5 lb ai/acre	10 acres	4.2	110,000
Loading/Applying Granulars with a Gravity Feed Backpack Granular Spreader (MRID 452507-01) (9)	Christmas trees	4 lb ai/acre	10 acres	44	4,000
	container grown, field grown and landscape ornamentals	3 lb ai/acre	10 acres	44	5,300
	ornamental bulbs	1.5 lb ai/acre	10 acres	44	11,000
Loading/Applying Granulars with a Belly Grinder (10)	Christmas trees	4 lb ai/acre	1 acres	62	28,000
	turf	3 lb ai/acre	1 acres	62	38,000
	container grown, field grown and landscape ornamentals	3 lb ai/acre	1 acres	62	38,000
	ornamental bulbs	1.5 lb ai/acre	1 acres	62	75,000
Loading/Applying Granulars with a Push Type Spreader (ORETF) (11)	Christmas trees	4 lb ai/acre	5 acres	7.3	48,000
	turf: residential areas, commercial areas, and golf courses; and ornamentals: container grown, field grown, and landscape	3 lb ai/acre	5 acres	7.3	64,000
	ornamental bulbs	1.5 lb ai/acre	5 acres	7.3	130,000
Loading/Applying Granulars with a Bucket and Spoon (MRID 452507-01) (12)	Christmas trees	0.0918 lb ai/1000 sq ft	5000 sq ft	45	340,000
	ornamentals: container grown, field grown and landscape	0.0689 lb ai/1000 sq ft	5000 sq ft	45	450,000
	ornamental bulbs	0.0344 lb ai/1000 sq ft	5000 sq ft	45	900,000
Loading/Applying Granulars with a Shaker Can (PHED) (13)	Christmas trees	0.0918 lb ai/1000 sq ft	5000 sq ft	470	32,000
	ornamentals: container grown, field grown and landscape	0.0689 lb ai/1000 sq ft	5000 sq ft	470	43,000
	ornamental bulbs	0.0344 lb ai/1000 sq ft	5000 sq ft	470	87,000

Footnotes

a Application rates are the maximum application rates determined from EPA registered labels for cypermethrin.

b Amount handled per day values are EPA estimates of acreage treated or gallons applied based on Exposure SAC Policy #9 "Standard Values for Daily Acres Treated in Agriculture".

c Baseline inhalation unit exposure values from PHED Surrogate Exposure Guide and represent no respiratory protection.

d Baseline inhalation MOE = short-term NOAEL (100 mg/kg/day) / baseline inhalation dose (mg/kg/day), where baseline inhalation dose = baseline inhalation unit exposure (µg/lb ai) x application rate x amount handled per day x 1mg / 1000µg) / body weight (70 kg).

Table 12. Occupational Handler Risk Summary / Intermediate-Term

Exposure Scenario	Crop or Target	Application Rate[a]	Area Treated Daily[b]	Baseline Inhalation Unit Exposure (ug/lb ai)[c]	Baseline Inhalation MOE[d]
Mixer/Loader					
Mixing/Loading Dry Flowables for Groundboom Application	alfalfa, birdsfoot trefoil, clover	1.5 lb ai/acre	200 acres	0.77	2,200
	lettuce	1.5 lb ai/acre	80 acres	0.77	5,500
	turf: golf courses	3 lb ai/acre	40 acres	0.77	5,500
	turf: residential and commercial areas	3 lb ai/acre	5 acres	0.77	44,000
Loading Granulars for Drop Type Tractor (or ATV) Drawn Spreader Application	turf: commercial areas and golf courses; and ornamentals: container grown, field grown and landscape	3 lb ai/acre	40 acres	1.7	2,500
	Christmas trees	4 lb ai/acre	40 acres	1.7	1,900
	non-crop land, rights-of-way	6 lb ai/acre	80 acres	1.7	620
	ornamental bulbs	1.5 lb ai/acre	5 acres	1.7	40,000
Applicator					
Applying Sprays with Groundboom Application	alfalfa, birdsfoot trefoil, clover	1.5 lb ai/acre	200 acres	0.74	2,300
	lettuce	1.5 lb ai/acre	80 acres	0.74	5,700
	turf: golf courses	3 lb ai/acre	40 acres	0.74	5,700
	turf: residential and commercial areas	3 lb ai/acre	5 acres	0.74	45,000
Applying Granulars with Drop Type Tractor (or ATV) Drawn Spreader	turf: commercial areas and golf courses; and ornamentals: container grown, field grown and landscape	3 lb ai/acre	40 acres	1.2	3,500
	Christmas trees	4 lb ai/acre	40 acres	1.2	2,600
	non-crop land, rights-of-way	6 lb ai/acre	80 acres	1.2	880
	ornamental bulbs	1.5 lb ai/acre	5 acres	1.2	56,000
Mixer/Loader/Applicator					
Mixing/Loading/Applying Dry Flowables with a Low Pressure Handwand	turf	3 lb ai/acre	5 acres	30	1,100
Mixing/Loading/Applying Dry Flowables with a Backpack Sprayer	turf	3 lb ai/acre	5 acres	30	1,100
Mixing/Loading/Applying Dry Flowables with a Handheld Handgun (ORETF)	turf	3 lb ai/acre	5 acres	2.2	15,000

Exposure Scenario	Crop or Target	Application Rate[a]	Area Treated Daily[b]	Baseline Inhalation Unit Exposure (ug/lb ai)[c]	Baseline Inhalation MOE[d]
Loading/Applying Granulars with a Pump Feed Backpack Granular Spreader (MRID 451672-01)	Christmas trees	4 lb ai/acre	10 acres	4.2	3,000
	container grown, field grown and landscape ornamentals	3 lb ai/acre	10 acres	4.2	4,000
	ornamental bulbs	1.5 lb ai/acre	10 acres	4.2	8,000
Loading/Applying Granulars with a Gravity Feed Backpack Granular Spreader (MRID 452507-01)	Christmas trees	4 lb ai/acre	10 acres	44	290
	container grown, field grown and landscape ornamentals	3 lb ai/acre	10 acres	44	380
	ornamental bulbs	1.5 lb ai/acre	10 acres	44	760
Loading/Applying Granulars with a Belly Grinder	Christmas trees	4 lb ai/acre	1 acres	62	2,000
	turf	3 lb ai/acre	1 acres	62	2,700
	container grown, field grown and landscape ornamentals	3 lb ai/acre	1 acres	62	2,700
	ornamental bulbs	1.5 lb ai/acre	1 acres	62	5,400
Loading/Applying Granulars with a Push Type Spreader (ORETF)	Christmas trees	4 lb ai/acre	5 acres	7.3	3,500
	turf: residential areas, commercial areas, and golf courses; and ornamentals: container grown, field grown, and landscape	3 lb ai/acre	5 acres	7.3	4,600
	ornamental bulbs	1.5 lb ai/acre	5 acres	7.3	9,200
Loading/Applying Granulars with a Bucket and Spoon (MRID 452507-01)	Christmas trees	0.0918 lb ai/1000 sq ft	5000 sq ft	45	24,000
	ornamentals: container grown, field grown and landscape	0.0689 lb ai/1000 sq ft	5000 sq ft	45	33,000
	ornamental bulbs	0.0344 lb ai/1000 sq ft	5000 sq ft	45	65,000
Loading/Applying Granulars with a Shaker Can (PHED)	Christmas trees	0.0918 lb ai/1000 sq ft	5000 sq ft	470	2,300
	ornamentals: container grown, field grown and landscape	0.0689 lb ai/1000 sq ft	5000 sq ft	470	3,100
	ornamental bulbs	0.0344 lb ai/1000 sq ft	5000 sq ft	470	6,200

Footnotes

a Application rates are the maximum application rates determined from EPA registered labels for cypermethrin.

b Amount handled per day values are EPA estimates of acreage treated or gallons applied based on Exposure SAC Policy #9 "Standard Values for Daily Acres Treated in Agriculture".

c Baseline inhalation unit exposure values from PHED Surrogate Exposure Guide and represent no respiratory protection.

d Baseline inhalation MOE = intermediate-term NOAEL (7.2 mg/kg/day) / baseline inhalation dose (mg/kg/day), where baseline inhalation dose = baseline inhalation unit exposure (µg/lb ai) x application rate x amount handled per day x 1mg / 1000µg) / body weight (70 kg).

7.2.4 Summary of Risk Concerns and Data Gaps for Handlers

Margin of Exposure estimates for occupational handler scenarios are greater than 100 at the baseline level of risk mitigation. There is a data gap identified for evaluating exposure when mixing/loading/applying benfluralin using backpack equipment. However, estimates based on low pressure handwand equipment is considered a reasonable surrogate to evaluate this risk.

7.3 Occupational Postapplication Exposures and Risk

Benfluralin uses are varied, since it is used in agriculture, on ornamentals, and on turf (lawns, golf courses). As a result, a wide array of individuals can potentially be exposed by working in areas that have been previously treated. However, since no dermal endpoint has been identified for systemic toxicity, no occupational post-application exposure and risk assessment is required.

7.4 Skin Sensitization Concerns

The Agency is concerned about dermal sensitization reactions in persons occupationally exposed to benfluralin. At present, EPA has no method for determining a quantitative endpoint for skin sensitization and, therefore, has no means of quantitatively assessing the risk resulting from benfluralin's sensitization potential. The HIARC concluded (4/3/03) that risks from dermal exposure cannot be adequately quantified because benfluralin is a dermal sensitizer and a NOAEL for dermal toxicity could not be established from the 21-day dermal study. *Formulated* products showed no evidence of sensitization in Beuhler's assays, when tested concentrations range from 19% to 60% benfluralin. The lack of sensitization potential for the formulated products possibly occurred because the tests on the formulations were conducted with water as a vehicle, and/or benfluralin in the formulated product was not of sufficient concentration, did not penetrate the skin or material in formulation interfered with the test. However, it is noted that the skin lesions found in 21-day rabbit dermal study, were with the technical grade and a water vehicle. Therefore potential skin sensitization of products containing benfluralin is not eliminated. The technical grade caused typical delayed hypersensitivity in guinea pigs. Repeated dermal applications to rabbits resulted in skin lesions that progressed in severity and therefore may have the potential for adverse effects.

Therefore, as a risk mitigation measure, EPA will require a sensitization warning statement on all benfluralin end-use product labels and a recommendation that contact with the skin be avoided (the HIARC recommends that the products containing benfluralin should be labeled as SENSITIZER and contact should be avoided). In addition, EPA has determined that long-sleeved shirts, long pants, shoes, socks, and chemical-resistant gloves will be required on all occupational end-use products

containing benfluralin.

8.0 Human Incident Data Review

Relatively few incidents of illness have been reported due to benfluralin. There was some evidence of dermal effects, but these cases may be due to not wearing required personal protective equipment. The following data bases have been consulted for the poisoning incident data on the active ingredient benfluralin.

OPP Incident Data System (IDS): Reports of incidents from various sources, including registrants, other federal and state health and environmental agencies and individual consumers, submitted to OPP since 1992. Reports submitted to the Incident Data System represent anecdotal reports or allegations only, unless otherwise stated. Typically no conclusions can be drawn implicating the pesticide as a cause of any of the reported health effects. Nevertheless, sometimes with enough cases and/or enough documentation risk mitigation measures may be suggested. Please note that the following cases from the IDS do not have documentation confirming exposure or health effects unless otherwise noted: 1) a pesticide incident occurred in 1994, when a law enforcement officer reported respiratory injury, sore throat, coughing, and burning eyes after investigating a transportation spill. No further information on the disposition of the case was reported; and 2) an incident occurred in 1995 in California involving 7 persons. See summary of this incident under California data.

Poison Control Centers: As the result of a data purchase by EPA, OPP received Poison Control Center data covering the years 1993 through 1998 for all pesticides. Most of the national Poison Control Centers (PCCs) participate in a national data collection system, the Toxic Exposure Surveillance System which obtains data from about 65-70 centers at hospitals and universities. PCCs provide telephone consultation for individuals and health care providers on suspected poisonings, involving drugs, household products, pesticides, etc.

Results for the years 1993 through 1998 are presented below for occupational cases, non-occupational involving adults and older children, and for children under age six. Cases involving exposures to multiple products are excluded. Too few cases were reported to warrant presenting the information in tabular form except in summary form. There was only one occupational report reported that experienced a moderate medical outcome due to flushing, skin irritation or pain, and itching sufficient to require medical attention. Two other non-occupational reports involved similar dermal symptoms. There were a total of 46 non-occupational exposures, 31 of which were children under six years of age. However, only about half of the children received follow-up and just one of those experienced symptoms classified as minor. Seventy-two percent of the 22 non-occupational reports that received follow-up did not report any symptoms. For adults and older children, there were five cases involving minor symptoms, mostly

dermal in nature among the eight cases receiving follow-up. Except for the one moderate case, none of the reports appear to result in serious outcome. Only 3 of the 47 cases were seen in a health care facility and none were hospitalized.

Table 13. Poison Control Center data for 1993-98

Occup./Age Group	Number exposed	Outcome determine	Minor outcome	Moderate outcome	Seen in health care facility/hospitalized
Occupational	1	1	0	1	1/0
Non-Occup. and 6-19 years	15	8	5	0	1/0
Child < 6 years	31	13	1	0	1/0

California Department of Pesticide Regulation: California has collected uniform data on suspected pesticide poisonings since 1982. Physicians are required, by statute, to report to their local health officer all occurrences of illness suspected of being related to exposure to pesticides. The majority of the incidents involve workers. Information on exposure (worker activity), type of illness (systemic, eye, skin, eye/skin and respiratory), likelihood of a causal relationship, and number of days off work and in the hospital are provided.

Detailed descriptions of 10 cases submitted to the California Pesticide Illness Surveillance Program (1982-2001) were reviewed. In 7 of these cases, benfluralin was used alone or was judged to be responsible for the health effects. Only cases with a definite, probable or possible relationship were reviewed. Six of the seven cases occurred in a single incident in 1995 when residents, the responding police officer, and fire fighter sought medical evaluation following exposure to benfluralin, which was applied to a front yard without permission. Symptoms reported included headache, raspy throat, light headedness, dizziness, and nausea. In all six cases the relationship between benfluralin exposure and symptoms was judged possible.

In a probable case, a worker developed a rash and itching on the trunk and extremities while mixing and loading. Wind blew the material onto him while he was pouring it into the mixtank. A notice of violation was issued for inadequate training, lack of soap, water or towels available and for not wearing protective gloves. This worker was off work for five days.

National Pesticide Telecommunications Network: NPTN is a toll-free information service supported by OPP. A ranking of the top 200 active ingredients for which telephone calls were received during calendar years 1984-1991, inclusive, has been

prepared. The total number of calls was tabulated for the categories human incidents, animal incidents, calls for information, and others.

9.0 DATA REQUIREMENTS

Toxicology: A subchronic inhalation study is required on a solution of benfluralin. The Agency should be contacted prior to conducting the study.

Another study of carcinogenicity in the male mouse is necessary. The CARC determined that the male mouse was not dosed sufficiently high to test the carcinogenic potential of benfluralin.

Product Chemistry: UV/Visible absorption; 830.7050.

Residue Chemistry: A limited rotational field trial study with analysis for trifluoroacetic acid.

LABEL REVISIONS

The registrant must modify their product label to specify a 12-month plant-back interval for crops that may be rotated, and to make it clear that rotational crop restrictions apply to all regions of the U.S.

As a risk mitigation measure, EPA will require a sensitization warning statement on all (occupational) benfluralin end-use product labels and a recommendation that contact with the skin be avoided (the HIARC recommends that the products containing benfluralin should be labeled as SENSITIZER and contact should be avoided). In addition, EPA has determined that long-sleeved shirts, long pants, shoes, socks, and chemical-resistant gloves will be required on all occupational end-use products.

Appendix A. Pesticide Handler Exposure Database (PHED) Version 1.1 (8/98):

PHED was designed by a task force of representatives from the U.S. EPA, Health Canada, the California Department of Pesticide regulation, and member companies of the American Crop Protection Association. PHED is a software system consisting of two parts -- a database of measured exposure values for workers involved in the handling of pesticides under actual field conditions and a set of computer algorithms used to subset and statistically summarize the selected data. Currently, the database contains values for over 1,700 monitored individuals (i.e., replicates)

Users select criteria to subset the PHED database to reflect the exposure scenario being evaluated. The subsetting algorithms in PHED are based on the central assumption that the magnitude of handler exposures to pesticides are primarily a function of activity (e.g., mixing/loading, applying), formulation type (e.g., wettable powders, granulars), application method (e.g., aerial, groundboom), and clothing scenarios (e.g., gloves, double layer clothing).

Once the data for a given exposure scenario have been selected, the data are normalized (i.e., divided by) by the amount of pesticide handled resulting in standard unit exposures (milligrams of exposure per pound of active ingredient handled). Following normalization, the data are statistically summarized. The distribution of exposure values for each body part (e.g., chest upper arm) is categorized as normal, lognormal, or "other" (i.e., neither normal nor lognormal). A central tendency value is then selected from the distribution of the exposure values for each body part. These values are the arithmetic mean for normal distributions, the geometric mean for lognormal distributions, and the median for all "other" distributions. Once selected, the central tendency values for each body part are composited into a "best fit" exposure value representing the entire body.

The unit exposure values calculated by PHED generally range from the geometric mean to the median of the selected data set. To add consistency and quality control to the values produced from this system, the PHED Task Force has evaluated all data within the system and has developed a set of grading criteria to characterize the quality of the original study data. The assessment of data quality is based on the number of observations and the available quality control data. These evaluation criteria and the caveats specific to each exposure scenario are summarized in Appendix A, Table A1. While data from PHED provide the best available information on handler exposures, it should be noted that some aspects of the included studies (e.g., duration, acres treated, pounds of active ingredient handled) may not accurately represent labeled uses in all cases. HED has developed a series of tables of standard unit exposure values for many occupational scenarios that can be utilized to ensure consistency in exposure assessments. Unit exposures are used which represent

different levels of personal protection as described above. Protection factors were used to calculate unit exposure values for varying levels of personal protection if data were not available.

APPENDIX B. Outdoor Residential Exposure Task Force (ORETF) Studies

A report was submitted by the ORETF (Outdoor Residential Exposure Task Force) that presented data in which the application of various products used on turf by homeowners and lawncare operators (LCOs) was monitored. All of the data submitted in this report were completed in a series of studies. The study that monitored homeowner exposure scenarios using a push-type spreader (ORETF Study OMA003) and using a hose-end sprayer (ORETF Study OMA004) are summarized below.

Homeowner Push-Type Spreader (OMA003): A mixer/loader/applicator study was performed by the Outdoor Residential Exposure Task Force (ORETF) using Dacthal (active ingredient DCPA, dimethyl tetrachloroterephthalate) as a surrogate compound to determine "generic" exposures of individuals applying a granular pesticide formulation to residential lawns. A total of 30 volunteers were monitored using passive dosimetry (inner and outer whole body dosimeters, hand washes, face/neck wipes, and personal inhalation monitors). Each volunteer carried, loaded, and applied two 25-lb bags of fertilizer (0.89% active ingredient) with a rotary type spreader to a lawn covering 10,000 ft^2. The target application rate was 2 lb ai/acre (actual rate achieved was about 1.9 lbs ai/acre). The average application time was 22 minutes, including loading the rotary push spreader and disposing of the empty bags. Each replicate handled approximately 0.45 lbs ai. Dermal exposure was measured using inner and outer whole body dosimeters, hand washes, face/neck washes, and personal air monitoring devices with OVS tubes. The study results are normalized to kg ai handled. The US EPA HED typically assumes that residential applicators wear short pants and short-sleeved shirts, as described in the Residential SOPs (1997). Therefore, the table reports the dermal exposures for the short pants and short-sleeve shirt clothing scenario only.

Garden Hose-end Sprayer OMA004: A mixer/loader/applicator study was performed by the Outdoor Residential Exposure Task Force (ORETF) using diazinon (25% EC) as a surrogate compound to determine "generic" exposures to individuals applying a pesticide to turf with a garden hose-end sprayer. Surrogate chemicals were chosen by the Task Force for their representativeness based on physical chemical properties and other factors. The study was designed to simulate a typical application event for a homeowner applying pesticides to home lawns via a hose-end sprayer. Each replicate monitored the test subject treating 5,000 ft^2 of turf at a nominal application rate of 4 lb ai/acre and handling a total of 0.5 lb ai/replicate. The average time per replicate was 75 minutes. A total of 60 replicates were monitored using 30 test subjects (two replicates each). Thirty applicator replicates were monitored using a ready-to-use (RTU) product (Bug-B-Gon) packaged in a 32 fl. oz. screw-on container.

These containers were attached to garden hose-ends. An additional 30 mixer/loader/applicator replicates were monitored using Diazinon Plus also packaged in 32 fl. oz. plastic bottles. This product required the test subjects to pour the product into dial-type sprayers (DTS) that were attached to garden hose-ends. Dermal and inhalation exposures were monitored using passive dosimetry (inner and outer whole body dosimeters, hand washes, face/neck wipes, and personal inhalation monitors with OVS tubes). The inner samples represent a single layer of clothing. Inhalation exposure was calculated using an assumed respiratory rate of 17 Lpm for light work (NAFTA,1999), the actual sampling time for each individual, and the pump flow rate. No gloves were worn in any replicate. All results were normalized for the amount of active ingredient handled. The QA/QC data are within an acceptable range and the study results are corrected for field recoveries. The unit exposure values are presented in the table below.

LCO Push-Type Spreader (OMA001): A loader/applicator study was performed by the Outdoor Residential Exposure Task Force (ORETF) using Dacthal (active ingredient DCPA, dimethyl tetrachloroterephthalate) as a surrogate compound to determine "generic" exposures of lawn care operators (LCOs) applying a granular pesticide formulation to residential lawns. Surrogate chemicals were chosen by the Task Force for their representativeness based on physical chemical properties and other factors. Dacthal, which was the surrogate chemical used for the granular spreader and low-pressure hand gun sprayer studies, has a molecular weight of 331.97 and a vapor pressure of 1.6×10^{-6}, and is believed to be an appropriate surrogate for many relatively nonvolatile pesticides. The study was designed to simulate a typical work day for a LCO applying granular pesticide formulation to home lawns. Each LCO replicate involved loading and applying approximately 3.3 lb ai (360 lb formulated product) over a period of about 4 hours to 15 simulated residential lawns (6480 ft^2 each) with a rotary type spreader. The average industry application rate of 2 lb ai/acre was simulated (actual rate achieved was about 1.9 lb ai/acre). The monitoring period included driving, placing the spreader onto and off of the truck, carrying and loading the formulation in the spreader, and the actual application. Incidental activities such as repairs, cleaning up spills, and disposing of empty bags were monitored. A total of 40 replicates (individual application events) were monitored using passive dosimetry (inner and outer whole body dosimeters, hand washes, face/neck wipes, and personal inhalation monitors with OVS tubes). The inner samples represent a single layer of clothing. Inhalation exposure was calculated using an assumed respiratory rate of 17 Lpm for light work (NAFTA,1999), the actual sampling time for each individual, and the pump flow rate. In 20 of the replicates, the subjects wore chemical-resistant gloves while in the remaining replicates, no gloves were worn. No gloves were worn in any replicate while driving. All results were normalized for the amount of active ingredient handled. Nearly all samples (for every body part and for inhalation) were above the level of quantitation (LOQ) for dacthal. Where results were less than the reported LOQ, ½ LOQ value was used for calculations, and no recovery corrections were applied. The

overall laboratory recoveries (83-101%) and field recoveries (73-98%). The unit exposure values are presented in Table 9 below. [Note the inhalation exposure value is a median because the data were found to be neither normally nor lognormally distributed. All dermal values are geometric means as the data were lognormally distributed.]

LCO Handgun Sprayer (OMA002): A mixer/loader/applicator study was performed by the Outdoor Residential Exposure Task Force (ORETF) using Dacthal as a surrogate compound to determine "generic" exposures to individuals applying a pesticide to turf with a low-pressure "nozzle gun" or "hand gun" sprayer. Dermal and inhalation exposures were estimated using whole-body passive dosimeters and breathing-zone air samples on OVS tubes. Inhalation exposure was calculated using an assumed respiratory rate of 17 Lpm for light work (NAFTA,1999), the actual sampling time for each individual, and the pump flow rate. All results were normalized for lb ai handled. A total of 90 replicates were monitored using 17 different subjects. Four different formulations of dacthal [75% wettable powder (packaged in 4lb and 24 lb bags), 75% wettable powder in water soluble bags (3 lb bag), 75% water dispersable granules (2 lb bag) and 55% liquid flowable (2.5 Gal container)] were applied by five different LCOs to actual residential lawns at each site in three different locations (Ohio, Maryland, and Georgia) for a total of fifteen replicates per formulation. An additional ten replicates at each site were monitored while they performed spray application only using the 75 percent wettable powder formulation. A target application rate of 2 lb ai/acre was used for all replicates (actual rate achieved was about 2.2 lb ai/acre). Each replicate treated a varying number of actual client lawns to attain a representative target of 2.5 acres (1 hectare) of turf. The exposure periods averaged five hours twenty-one minutes, five hours thirty-nine minutes, and six hours twenty-four minutes, in Ohio, Maryland and Georgia, respectively. Average time spent spraying at all sites was about two hours. All mixing, loading, application, adjusting, calibrating, and spill clean up procedures were monitored, except for typical end-of-day clean-up activities, e.g. rinsing of spray tank, etc. Dermal exposure was measured using inner and outer whole body dosimeters, hand washes, face/neck washes, and personal air monitoring devices. All test subjects wore one-piece, 100 percent cotton inner dosimeters beneath 100 percent cotton long-sleeved shirt and long pants, rubber boots and nitrile gloves. Gloves are typically worn by most LCOs, and required by many pesticide labels for mixing and loading. Overall, residues were highest on the upper and lower leg portions of the dosimeters In general, concurrent lab spikes produced mean recoveries in the range of 78-120 percent, with the exception of OVS sorbent tube sections which produced mean recoveries as low as 65.8 percent. Adjustment for recoveries from field fortifications were performed on each dosimeter section or sample matrix for each study participant, using the mean recovery for the closest field spike level for each matrix and correcting the value to 100 percent. The unit exposure values are presented in Table 9 below. [Note the data were found to be lognormally distributed. As a result, all exposure values are geometric means.]

APPENDIX C. Proprietary Studies

Two proprietary studies were used to obtain unit exposure values for handlers loading/applying with a pump-type backpack granular spreader and with a gravity-feed backpack granular spreader. In addition, a proprietary study on applying granules with a bucket and spoon was used to obtain surrogate unit exposure values for applying granules by hand. The studies are summarized below.

Worker Exposure Study During Application In Banana Plantation With Temik 10G, EPA MRID 451672-01: EPA used data from the aldicarb (Temik) study to assess exposures and risks to handlers applying granulars with a pump feed backpack sprayer. Exposure during the application of a granular formulation of the insecticide, aldicarb (i.e., Temik 10G), was monitored during granular backpack application to bananas for control of insects, mites, and nematodes. A total of 12 mixer/loader/applicator events during granular backpack (i.e., a specialized pump-feed device manufactured by Swissmex Rapid) application to bananas were monitored during August of 1998 on the island of Martinique is in the French West Indies. Weather was typical of the application season in that it was hot, humid, and rainy at points.

Monitoring was completed using whole body dosimeters, handwashes, facial wipes, and personal sampling pumps equipped with XAD resin/filter combination samplers. Temik 10G was supplied in 22 pound boxes which was loaded directly into the backpack devices (i.e., 4 to 8 boxes were used per replicate). The application rate for aldicarb used in this study is 20 grams of Temik 10G (i.e., 2 grams ai/plant) which is equivalent to about 3.56 lb ai/acre at approximately 2000 plants per acre. The numbers of acres treated ranged from approximately 2.5 to 5 acres. The pounds of active ingredient handled ranged from 8.8 up to 17.6 per replicate. Each applicator wore the whole body dosimeters covered by a cotton coverall, Tyvek gloves supplied with the Temik 10G formulation, and an apron on their backs between their backs and the backpack applicator. The Tyvek gloves were changed with each box of Temik 10G used. In many instances, the gloves were compromised because they were ripped. In one case, the gloves filled with rainwater. In many other cases, when the whole body dosimeters were removed, they were found to be wet and muddy.

Analysis of aldicarb and its sulfoxide and sulfone degradates was completed. The residue levels were added together to obtain total exposure levels. The limits of quantification (LOQ) were 1.0 µg per sample for the whole-body dosimeters and handwashes (600 mL volume). The LOQ for the facial wipes was 0.10 µg per sample and 0.05 to 0.10 µg per sample for the air filters. Field and laboratory recovery data were generated for all media for all residues measured (i.e., parent and metabolites). Field recovery data were generated in a manner that addressed field sampling, field storage, transport, laboratory storage, and analysis. Residues were corrected for the overall average field recovery for each residue/matrix combination. Generally, recovery

data were adequate for all media/residue combinations. If the PHED grading criteria are applied all residue/matrix combinations (except facial wipes with sulfone residues) have at least grade "B" data and in many cases the data meet the grade "A" criteria. The grade "B" criteria require laboratory recovery data with an average of at least 80 percent and a coefficient of variation of 25 or less accompanied with field recoveries that are at least 50 percent but not exceeding 120 percent. The grade "A" criteria require laboratory recovery data with an average of at least 90 percent and a coefficient of variation of 15 or less accompanied with field recoveries that are at least 70 percent but not exceeding 120 percent.

Unit exposure values were calculated using the data from the study and a commercial spreadsheet program. The exposures that were calculated were normalized by the amount of chemical used, the duration of the application interval, and by the body weight of the individual applicators. For each calculation, the arithmetic mean, geometric mean, and various percentiles were calculated. No analyses were completed with these data to ascertain the exact type of distribution. The Agency typically uses the best fit values from the Pesticide Handlers Exposure Database which are representations of the central tendency. Considering the standard practice, the Agency will use the geometric mean for risk assessment purposes.

Worker Exposure Study During Application of Regent 20GR In Banana Plantation, EPA MRID 452507-02: EPA used data from the fipronil (Regent 20 GR) study to assess exposures and risks to handlers loading and applying granulars with a gravity feed backpack sprayer. In addition, EPA used data from loading and applying granulars using a scoop and bucket from the fipronil study to assess exposures and risks to occupational handlers applying granules by hand.

Exposure during the application of a granular formulation of the insecticide, fipronil (i.e., Regent 20GR), was monitored during granular gravity-feed backpack (i.e., Horstine Farmery Microspread®) applications and spoon applications to bananas for control of insects, mites, and nematodes. A total of 18 mixer/loader/applicator events during granular backpack (i.e., a specialized gravity-feed device manufactured by Horstine Farmery) or spoon application to bananas were monitored during applications on three different days in June, 1994 on the same banana plantation in Cameroon. The 18 replicates were distributed over the 3 sampling days as follows: 6 spoon/hand applications on day 1; 4 spoon/hand applications on day 2; and 8 backpack events on day 3. Weather was typical of the application season in that it was hot and humid. Monitoring was completed using whole body dosimeters, cotton gloves, cotton caps, and personal sampling pumps equipped with filters. Regent 20GR was supplied in 22 pound boxes which was loaded directly into the backpack devices or buckets for the spoon applicators. The application rate for fipronil used in this study is 7.5 grams of Regent 20GR (i.e., 0.15 grams ai/plant) which is equivalent to about 0.26 lb ai/acre (0.00033 lb ai/plant) at approximately 800 plants per acre. The numbers of acres

treated ranged from approximately 0.75 to 1 acre. The pounds of active ingredient handled ranged from about a quarter to half a pound per replicate.

Each applicator wore whole body dosimeters that also served as the normal work clothing. PVC gloves were also worn over cotton gloves which served as the dosimeters. A protection factor of 50 percent was used by the Agency to calculate exposure levels under a layer of normal work clothing. Dosimeter samples were segmented into arms, legs, and torso for analysis.

Analysis of fipronil residues was completed with gas chromatography and electron capture detection. The limits of quantification (LOQ) were 9.7 µg per sample for all media used. The limit of detection (LOD) varied for each media. The LOD for the cotton gloves was 0.5 µg per sample, 0.10 µg per sample for the air filters, and 2.0 to 4.0 µg per sample for the whole body dosimeters depending upon the sample analyzed. Field and laboratory recovery data were generated for all media. Field recovery data were generated in a manner that addressed field sampling, field storage, transport, laboratory storage, and analysis. However, the laboratory recovery data were indeterminate because the sample media could not be identified for each reported result. The overall recovery values do appear to be quantitative. Residues were corrected for the overall average field recovery for each residue/matrix combination. Generally, recovery was adequate for all media/residue combinations (i.e., all correction factors were greater than 85 percent). If the PHED grading criteria are applied and the overall laboratory recovery averages are used all residue/matrix combinations are considered grade "A" data. The grade "A" criteria require laboratory recovery data with an average of at least 90 percent and a coefficient of variation of 15 or less accompanied with field recoveries that are at least 70 percent but not exceeding 120 percent.

Unit exposure values were calculated using the data from the study and a commercial spreadsheet program. The exposures that were calculated were normalized by the amount of chemical used, the duration of the application interval, and by the body weight of the individual applicators (see table below). The values are based on a 50 percent clothing penetration factor and are separated for each equipment type monitored in this study. For each normalization factor, the arithmetic mean, geometric mean, and various percentiles were calculated. No analyses were completed with these data to ascertain the exact type of distribution. The Agency typically uses the best fit values from the Pesticide Handlers Exposure Database which are representations of the central tendency. Considering the standard practice, the Agency will use the geometric mean for risk assessment purposes.

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