Reregistration Eligibility Decision

Exposure and Risk Assessment on Lower Risk Pesticide Chemicals

Naptalam Sodium

CASE 0183

Special Review and Reregistration Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
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Background:

The Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) was amended in 1988 to accelerate the reregistration of products with active ingredients registered prior to November 1, 1984. The amended Act calls for the development and submission of data to support the reregistration of an active ingredient, as well as a review of all submitted data by the U.S. Environmental Protection Agency (referred to as EPA or the Agency). Reregistration involves a thorough review of the scientific database underlying a pesticide's registration. The purpose of the Agency's review is to reassess the potential hazards arising from the currently registered uses of the pesticide; to determine the need for additional data on health and environmental effects; and to determine whether or not the pesticide meets the "no unreasonable adverse effects" criteria of FIFRA.

On August 3, 1996, the Food Quality Protection Act (FQPA) was signed into law. This Act amends FIFRA to require tolerance reassessment during reregistration. It also requires that by 2006, EPA must review all tolerances in effect on the day before the date of the enactment. FQPA also amends the Federal Food, Drug, and Cosmetic Act (FFDCA) to require a safety finding in tolerance reassessment based on factors including an assessment of cumulative effects of chemicals with a common mechanism of toxicity.

This document represents the Reregistration Eligibility Decision (RED) document for naptalam sodium. This assessment summarizes available information on the use, physical/chemical properties, toxicological effects, occupational exposure profile, dietary assessment, tolerance reassessment, and the environmental fate and ecotoxicity for naptalam sodium. EPA established a tolerance for residues of naptalam sodium when used on cantaloupe, cucumber, muskmelon and watermelon. The Agency has considered any new data generated after the tolerance exemption was issued, new Agency guidance or other federal regulations, as well as previously available information in this assessment. Currently, there are no homeowner products, so there are no use-patterns that are likely to result in residential handler or postapplication exposures, and the only use-patterns are for occupational use in non-residential settings. A review meeting for an earlier draft of this document was conducted by the Lower Risk Pesticide Chemical Focus Group (LRPCFG) on August 25, 2004.

I. Executive Summary:

Naptalam sodium is registered for use as a pre-emergent herbicide for control of broadleaf weeds in cucurbits and woody nursery stock. There is currently only one end-use product for naptalam sodium, a liquid concentrate. The product label indicates that for its usage for weed control in cucurbits, it may be applied as a broadcast application at planting and/or over the top of the cucurbits in the early season before they begin to vine. For weed control in woody nursery stock, the product label indicates that it may be applied as a broadcast spray prior to transplanting or as a soil-directed spray around established stock. For both cucurbits and woody nursery stock application, the product label recommends watering-in following application.

A chronic dietary exposure assessment was conducted for naptalam sodium using the Dietary Exposure Evaluation Model. There was no acute endpoint identified for conducting dietary assessments. The chronic dietary (food only) assessment shows that the estimated risks for naptalam sodium are very low, less than 0.1% of the cPAD for the most sensitive age groups and for the general U.S. population. In addition, the estimated drinking water concentrations (EDWCs) were also calculated by utilizing models. The EDWCs are low for naptalam sodium, 658.2 ppb for the annual peak concentrations, and 188.7 ppb for the annual mean concentrations for surface waters, and 3.3 ppb for groundwater.

An oral NOAEL (29.7 mg/kg/day) was selected as the toxicological endpoint of concern for assessing short- and intermediate-term dermal and inhalation occupational exposures. The dermal and inhalation doses were converted to an equivalent oral dose using a default value of 100% absorption, since no data are available on dermal or inhalation absorption. The toxicological endpoint was based on reduced body weight gain, reduced food efficiency, and increased organ weights in dogs from a 90-day oral toxicity study. Since the toxicological endpoint is the same for dermal and inhalation, total risks (dermal plus inhalation) must be estimated. The Agency determined that an uncertainty factor of 100 (10 for interspecies extrapolation and 10 for intraspecies variation) was appropriate for occupational risks.

Occupational handler and postapplication exposures and risks were assessed in this document. Naptalam sodium may be applied with groundboom equipment to cucurbits, and with groundboom, low-pressure handwand or handgun equipment to the soil around woody nursery stock. The exposure scenarios and application rate chosen for this risk assessment were based on the current label for the naptalam sodium end-use product.

For handlers mixing/loading liquid concentrates to support groundboom applications, risks did not exceed the level of concern with the addition of chemical-resistant gloves to baseline attire (long-sleeve shirt, long pants, shoes, socks, and no respirator). Risks to handlers applying liquids with open-cab groundboom equipment did not exceed the level of concern at baseline attire. Risks to mixers/loaders/applicators using low-pressure handwand or handgun equipment did not exceed the level of concern with the addition of chemical-resistant gloves to baseline attire.

The Agency uses transfer coefficients and dislodgeable foliar residues (DFRs) or soil transferrable residues to assess occupational postapplication exposures to agricultural workers entering treated areas to perform various tasks after applications are complete, and mitigates these postapplication risks using a restricted entry interval (REI). The REI is the time period following a pesticide application during which entry into the treated area is restricted. The Agency has received a chemical-specific DFR study which shows a foliar half-life of less than 3 days. The Agency does not have default transferrable residue values for contact with soil, but postapplication exposures and risks to workers who contact the soil subsurface are also unlikely to exceed the level of concern at the REI for other handlers. The Agency has determined that the postapplication risks are adequately mitigated by retaining the 48 hour REI specified on the current label; due to the eye irritation study showing severe opacity continuing until day 7, the REI is 48 hours, and protective eyewear will remain on the label for pesticide handlers.

As further risk mitigation, the registrant has voluntarily agreed to place a restriction on the label to prevent aerial applications, and will retain label restrictions against greenhouse use as well as applications through any type of irrigation system. In addition, the registrant will incorporate label language to insure that ground applications will be made with equipment placed as close to the ground as feasible, that droplet sizes will be as large as possible (no fine droplets), and that watering-in will be clearly stated on the label directions. In addition, the registrant has voluntarily agreed to remove nursery stock/woody ornamentals from their label. The registrant has also agreed to include language on their revised label, that the maximum application rate will remain at 4 pounds active ingredient per acre per application, that two applications per year are permitted, and that the total applications annually may not exceed 8 pounds per acre per year.

The environmental fate and mobility of naptalam sodium is pH dependent. Naptalam sodium will readily dissociate, and exists predominantly as the sodium cation and the acidic anion in the environment. Anions often possess high mobility in soils, tend to have significant leaching potential, and will not volatilize from water or soil surfaces. The hydrolysis of naptalam appears to occur slowly under alkaline and neutral conditions, but proceeds rapidly under acidic conditions with a half-life on the order of a few days. Biodegradation appears to be insignificant under anaerobic conditions, but may be an important environmental fate process in soil and water under aerobic conditions.

Results of acute toxicity studies suggest that naptalam is practically nontoxic to freshwater fish and invertebrates. No chronic toxicity data were submitted for freshwater organisms and no acute or chronic testing of marine/estuarine fish or invertebrates was submitted. A Tier 1 screening level risk assessment focusing on maximum proposed uses of naptalam sodium on cucumber, watermelon, honeydew and cantaloupe suggests that concentrations of naptalam in the environment, when compared with minimum toxicity values, are unlikely to result in acute adverse effects to freshwater aquatic organisms. Adequate toxicity data are not available to characterize the risk of chronic adverse effects to freshwater organisms, and no data are available to characterize the risk to marine/estuarine fish and invertebrates.

Naptalam is categorized as slightly toxic to small mammals on an acute oral basis and the potential for chronic reproductive effects appears to be low. However, there is a potential for risks to terrestrial and avian species, but the risk assessment procedure is a screening level and/or qualitative assessment, and does not constitute any findings under the Endangered Species Act. Results of acute oral toxicity studies suggest that naptalam is practically non-toxic to birds. Results of reproductive studies of naptalam in birds are not available. Based on contact LD_{50} studies for the honey bee (*Apis mellifera*), naptalam is classified as practically nontoxic on an acute contact basis.

Based on the data from the plant metabolism and crop field trials studies, the tolerances have also been reassessed for naptalam sodium. The tolerances for some commodities (i.e., cantaloupe, muskmelon, and watermelon) will be revoked, and in their place, a tolerance will be established for the melon subgroup (Crop Group 9A).

II. Use Information:

Naptalam sodium (OPP Chemical Code 030703; CAS Reg. No. 132-67-2) was first developed by the Uniroyal Chemical Company in 1949; therefore, its first registration was with the U.S. Department of Agriculture, and predates the Environmental Protection Agency. It is a List A reregistration chemical, and was the subject of a Registration Standard document, Guidance for the Reregistration of Pesticide Products Containing Naptalam/Naptalam Sodium as the Active Ingredient, dated March 30, 1985. The current registrant is a successor company to its parent Uniroyal, Crompton Manufacturing Company, Inc. Crompton applied for a low volume/minor use waiver in 1993, and on May 5, 1994, the Agency granted this waiver and applied a somewhat reduced set of guideline requirements.

Naptalam sodium is registered for use as a pre-emergent herbicide for control of broadleaf weeds in cucumbers and the melons subgroup (with the following crops listed on the current label: cucumber, watermelon, muskmelon, cantaloupe, honeydew melon, Persian melon, and casaba are) and woody nursery stock (transplants and established plants, with use in greenhouses prohibited). It had previously been registered for applications to soybeans, peanuts, and cranberries, but uses on these crops have now been cancelled. According to the BEAD Quantitative Usage Analysis (QUA), the weighted average amount applied is about 84,000 pounds of active ingredient used per year in the United States, with an estimated maximum of about 149,000 pounds per year. (See Appendix A for additional details concerning the BEAD QUA, and other label information). Naptalam sodium controls weeds at germination and early growth, but is ineffective against emerged weeds. The sole end-use product formulation (EPA Registration Number: 400-49) is a liquid concentrate (23.7% active ingredient), although in the past, there had also been registrations for soluble liquid concentrate and granular formulations. There is no technical product registration.

Naptalam is the common name of the acid from which the subject sodium salt is derived, the scientific name of this acid being 2-((1-naththalenyl-amino)carbonyl)-benzoic acid (also know as *N*-1-naphthylphthalamate). The OPP Chemical Code of naptalam is 030702, and its CAS Reg. No. is 132-66-1. According to the OPP REFS database (and its successor database, OPPIN), there have never been any registered products for naptalam. Note that some of the Agency documents which refer to naptalam (and are listed as having MRIDs associated with naptalam) are actually for the sodium salt, and will be included herein under the assumption as referring to naptalam sodium.

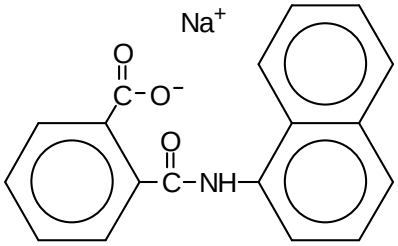
III. Physical/Chemical Properties:

Naptalam sodium is highly soluble (Table 1). It is a solid, since it has a melting point in excess of 185 °C. Its molecular weight is 313.3 (EPA Reg. Standard, 1985), and it has a multi-ring structure (Figure 1), thus, naptalam sodium exhibits only limited volatility, with a vapor pressure of 9.1×10^{-11} mm Hg.

Table 1. General Physical and Chemical Properties for Naptalam Sodium				
Chemical	Molecular formula	Molecular weight	Solubility in Water	Density/Specific Gravity
Naptalam sodium	$C_{18}H_{13}NO_3.Na$	313.30	230,800 ppm @ 25°C	1.386

Reference: Toxnet (2004).

Figure 1. Molecular Structure of Naptalam Sodium



IV. Hazard Assessment:

Key toxicological data for naptalam sodium are provided in Tables 2 and 3. These data were obtained from EPA reviewed toxicological studies (EPA, 1994, 1996) and from a recent toxicity overview (EPA, 2004).

Table 2. Acute Toxicity Profile - Naptalam Sodium				
Study Type	Species	MRID	Results	Toxicity Category
Acute oral	Rat	29172	LD_{50} = 1,700 mg/kg	III
		76205	(Naptalam acid: no deaths at 8192 mg/kg)	(IV)
Acute dermal	Rat	60402	LD_{50} > 2,000 mg/kg	III
	Rabbit	427397-01	LD_{50} > 5,000 mg/kg	IV
Acute inhalation	Rat	439364-01	LC_{50} > 2.0 mg/L	IV
Acute eye irritation	Rabbit	78530	slight irritation (liquid: Alanap [product])	III (or II)
		60404	severe opacity (granular: Alanap [Tech.])	I
Acute dermal irritation	Rabbit	060408	non-irritant	IV
Skin sensitization	Guinea Pig	15185	dermal sensitizer	

Naptalam sodium has low toxicity via the inhalation route, and is not dermally irritating to the skin (Toxicity Category IV for both), but is in Toxicity Category III for oral and dermal toxicity to the rat. (Note that testing with naptalam acid in the rat indicates Toxicity Category IV.) For dermal toxicity and inhalation testing in the rat, Limit Dose tests were performed, with no deaths observed in either study. In a Limit Dose dermal toxicity study in the rabbit, no mortality was observed; thus, results in the rabbit indicate acute dermal is Toxicity Category IV. Alanap liquid

was found to be slightly irritating to the eye (Toxicity Category III) or moderately irritating (II, as reported in MRID 78530), but "Alanap (Tech.)", described as a granular material, was found to cause severe irritation in the rabbit eye, accompanied by corneal opacity which had not recovered by day 7 after instillation, in 6 of 6 rabbits tested. Naptalam sodium is a dermal sensitizer.

Table 3. Subchronic, Chronic and Other Toxicity Profile - Naptalam Sodium

Study Type (species) [Accession or MRID No.]	Classification/Doses	Results
90-Day: oral toxicity (rat) [106276; 410575-01]	Acceptable - Non-Guideline 0, 500, 1000, 5000 ppm 0, 25, 50, 250 mg/kg/day	NOAEL = 1000 ppm (50 mg/kg/day) LOAEL = 5000 ppm (250 mg/kg/day) based on reduced body weight gain, reduced food efficiency, decreased organ weights.
90-Day: oral toxicity (dog) [106277]	Acceptable - Non-Guideline 0, 300, 1000, 3000, 5000 ppm Males: 0, 11.4, 29.7, 124.7 mg/kg/day Females: 0, 9.7, 29.9, 123.6 mg/kg/day	NOAEL = 1000 ppm (29.7-29.9 mg/kg/day) LOAEL = 3000 ppm (123.6-124.7 mg/kg/day) based on reduced body weight gains, reduced food efficiency, increased absolute and relative liver weights.
1-Year: oral toxicity (dog) [410575-01]	Acceptable - Non-Guideline 0, 200, 1000, 5000 ppm 0, 5.3, 25.8, 121 mg/kg/day	NOAEL = 1000 ppm (25.8 mg/kg/day) LOAEL = 5000 ppm (121 mg/kg/day) based on liver weights, increased enzyme activity and bilirubin
Prenatal developmental (rat) [106320; 437671-01; 437744-01]	Acceptable 0, 15, 115, 500 mg/kg/day	**Maternal** NOAEL = 15 mg/kg/day LOAEL = 115 mg/kg/day based on reduced body weight gain. **Developmental** NOAEL = 115 mg/kg/day LOAEL = 500 mg/kg/day based on reduced fetal weights, increased skeletal observations.
Prenatal developmental (rabbit) [157186]	Core - Minimum 0, 50, 200, 650 mg/kg/day	**Maternal** NOAEL = 200 mg/kg/day LOAEL = 650 mg/kg/day based on reduced body weight gain, mortality, clinical observations. **Developmental** NOAEL = 200 mg/kg/day LOAEL = 650 mg/kg/day based on increased skeletal observations.
Reproduction and fertility effects (rat) [31684]	Core - Minimum 0, 120, 600, 3000 ppm 0, 6, 30, 150 mg/kg/day	**Parental/Systemic** NOAEL = 600 ppm (30 mg/kg/day) LOAEL = 3000 ppm (150 mg/kg/day) based on reduced body weights. **Reproductive** NOAEL >= 3000 ppm (150 mg/kg/day) LOAEL > 3000 ppm (150 mg/kg/day). **Offspring** NOAEL = 600 ppm (30 mg/kg/day) LOAEL = 3000 ppm (150 mg/kg/day) based on reduced mean pup body weights.
Chronic toxicity (rat) [77053; 418388-01; 418600-01]	Acceptable - Guideline 0, 120, 600, 3000 ppm 0, 5.6, 27, 140 mg/kg/day	NOAEL >= 140 mg/kg/day LOAEL > 140 mg/kg/day.

Table 3. Subchronic, Chronic and Other Toxicity Profile - Naptalam Sodium		
Study Type (species) [Accession or MRID No.]	Classification/Doses	Results
Chronic toxicity (dog) [410575-01]	Acceptable - Guideline 0, 200, 1000, 5000 ppm 0, 5.3, 25.8, 121 mg/kg/day	NOAEL = 1000 ppm (25.8 mg/kg/day) LOAEL = 5000 ppm (121 mg/kg/day) based on increased liver weights, increased levels of alkaline phosphatase and bilirubin.
Carcinogenicity (rat)	Unacceptable - Guideline see chronic toxicity - rat	study classified as Unacceptable-Guideline; thus, cancer potential could not be addressed based on this study.
Carcinogenicity (mouse) [119003]	Minimum 0, 50, 2500, 5000 ppm Males: 0, 8, 376, 737 mg/kg/day Females: 0, 9, 437, 870 mg/kg/day	NOAEL = 50 ppm (Males: 8 mg/kg/day; Females: 9 mg/kg/day) LOAEL = 2500 ppm (Males: 376 mg/kg/day; Females: 437 mg/kg/day) based on decreased body weight gain in both sexes, liver hypertrophy of the centrilobular parenchymal cells in males.
Gene Mutation: CHO/HGPRT [400691-03; 427397-03]	Acceptable	Negative
Cytogenetics: CHO [400691-04]	Acceptable	Positive
Cytogenetics: Micronucleus [400691-05]	Unacceptable	Positive; repeat assay requested
Cytogenetics: UDS [401498-01]	Acceptable	Negative
Metabolism and Pharmacokinetics (rat) [402745-02; 418600-03; 438818-01]	Acceptable - Non-Guideline	^{14}C-labeled naptalam was rapidly absorbed, distributed, and then excreted, with 7-day recovery of the radiolabeled material being reported as 85%.

The primary target organ for the effects of naptalam sodium is the liver. These toxic effects on the liver were noted in the rat, mouse, and dog involving changes in liver weight and liver enzyme activities (Table 3). In some of the repeated dose studies, body weights were observed to be somewhat reduced, but without concomitant observations of clinical signs, tissue/organ effects on microscopic examination, or adverse effects based on clinical chemistry observations. In addition, in some studies there were wide spacings in the dosage groupings; for example, the differences between NOAELs and LOAELs were 7.67-fold in one study and 50-fold in another study. In general, regardless of the NOAEL doses reported in the various studies conducted, adverse effects were not observed unless the administered doses were in excess of 115 mg/kg/day.

The absorption, distribution, metabolism, and excretion of naptalam were studied in groups of

male and female rats administered a single oral gavage or injected dose of radiolabeled naptalam. Naptalam was rapidly absorbed, distributed, and excreted in rats. Naptalam and/or its metabolites do not bioaccumulate to an appreciable extent following oral exposure since all tissues contained negligible levels of radioactivity at 7 days post-exposure. The elimination data suggest that absorption of naptalam is rapid, bioaccumulation is low, and excretion occurs in the feces and urine. Based on the study results, absorption, distribution, and elimination of naptalam did not appear to be sex or dose related.

In the various studies reported, there were no significant developmental or reproductive toxicity noted in the development effects studies in the rat and rabbit, and a reproductive and fertility effects study in the rat (Table 3). All effects on the offspring (fetuses and pups) occurred above the levels of maternal/paternal toxicity and were not different from what was seen in the adult animal. For example, in a prenatal developmental study in the rat (MRID 106320, 4376710-01, and 437744-01) developmental toxicity was noted in the 500 mg/kg/day dose group, based on lower mean fetal weight compared to the control group and an increased incidence of unspecified missing sternebrae, incomplete ossification of unspecified vertebrae, unspecified skull bones, unspecified extremities and increased missing or reduced hyoid bone in the 500 mg/kg/day group; however, maternal toxicity was noted in the 115 mg/kg/day dose group and above in the form of reduced body weight gain during the dosing period (gestation days 6-15), the post dosing period (gestation days 15-20), for the combined dosing plus post dosing period (gestation days 6-20) and for the entire gestation period (except 115 mg/kg/day). Therefore, the Agency has concluded that there was no indication of offspring (fetus/pup) susceptibility or sensitivity.

Naptalam sodium was positive in 2 mutagenicity studies, and negative in 2 studies. Based on these various genotoxicity/mutagenicity assays, the weight-of-evidence for naptalam sodium being characterized as genotoxic and/or mutagenic is equivocal. In addition, naptalam sodium showed no carcinogenic effects in any studies, and is classified by the Agency as a Group “D” carcinogen, which means there is inadequate data for assessing potential human carcinogenicity.

Special Considerations for Infants and Children:
Based on the results of prenatal developmental studies in the rat and the rabbit and a reproductive and fertility effects study in the rat, the fetuses and offspring do not exhibit more sensitivity than the maternal dams. Thus, at this time, there is no concern for potential sensitivity to infants and children resulting from exposure to naptalam sodium. Therefore, a safety factor analysis has not been used to assess the risk. For the same reason, the additional tenfold FQPA safety factor (SF 10X) is unnecessary, and has been removed (equivalent to 1x).

Toxicological Endpoint Selection:
For dietary exposures for naptalam sodium, there was no single dose (i.e., acute) effect endpoint identified. For chronic dietary exposures, the toxicological endpoint of concern selected was a NOAEL of 25.8 mg/kg/day from the 1-year oral toxicity study in the dog (Table 4).

Table 4. Summary of Toxicological Endpoints and Other Factors Used in Human Dietary Risk Assessment for Naptalam Sodium			
Exposure	Dose	Endpoint	Study (Accession or MRID No.)
Acute	NOAEL = none identified	None identified.	None identified.
Chronic (Non-Cancer)	NOAEL = 25.8 mg/kg/day	LOAEL = 121 mg/kg/day, based on increased liver weights, and increased levels of alkaline phosphatase and bilirubin.	1 Year Oral Toxicity Dog (410575-01)
	UF = 100 FQPA SF = 1 cPAD = 0.258 mg/kg/day		
Chronic (Cancer)	Classified as a **"**Group "D" carcinogen, which means there is inadequate data for assessing potential human carcinogenicity for naptalam sodium.		

For the occupational handlers, inhalation and dermal exposure were examined, as well as postapplication dermal exposures. Inhalation exposures are thought to be negligible in outdoor postapplication scenarios due to the dilution expected outdoors. As such, inhalation postapplication exposures are not considered in this assessment. Since there are no inhalation or dermal toxicological studies available, a subchronic oral NOAEL was used to assess short- and intermediate-term dermal and inhalation exposures (Table 5). The dermal and inhalation doses were converted to an equivalent oral dose using a 100% absorption factor, since no dermal or inhalation absorption data are available. The oral toxicological endpoint (NOAEL) of 29.7 mg/kg/day was used, as being the most appropriate health protective value. This NOAEL was based on reduced body weight gain, reduced food efficiency, and increased organ weights in the dog from a 90-day oral toxicity study (EPA, 1994, 1996, 2004). According to the data listed in Table 4, there are studies listed with lower NOAEL values, but the Agency has determined that this is the most reliable, most toxicologically justifiable NOAEL for use in short- and intermediate-term assessments, and not ones from these other studies. (See the recent Agency Toxicity Overview for details.) For example, there is a reported NOAEL in the prenatal developmental study in the rat, in which the dams were dosed at 15 mg/kg/day from gestation day 6 to 15, but the Agency has determined that "the maternally toxic effects noted in this study (MRID# 00106320) at 115 mg/kg/day are minimal at best and not supported by any other observations. The actual NOAEL is probably much higher. The rabbit teratology study had effects at a much higher dose levels. This dose (from the rat teratology study) should not be used for short term risk assessments." Thus, the Agency has utilized a weight-of-evidence approach to identify the best supported toxicity endpoint for short- and intermediate-term exposures of 29.7 mg/kg/day, the NOAEL from the 90-day oral toxicity study in the dog.

Table 5. Summary of Occupational Toxicological Endpoints for Naptalam Sodium				
Exposure	Dose	Endpoint	Study (Accession or MRID No.)	UF
Short- and Intermediate-Term Dermal [1]	Oral NOAEL = 29.7 mg/kg/day	LOAEL = 3000 ppm (123.6 mg/kg/day), based on reduced body weight gains, reduced food efficiency, increased absolute and relative liver weights.	90-Day: oral toxicity (dog) (106277)	100
Short- and Intermediate Term Inhalation [2]	Oral NOAEL = 29.7 mg/kg/day	LOAEL = 3000 ppm (123.6 mg/kg/day), based on reduced body weight gains, reduced food efficiency, increased absolute and relative liver weights.	90-Day: oral toxicity (dog) (106277)	100
Long-Term Dermal or Inhalation	N/A [3]	There are currently no long-term exposures, so these risk assessments are not required for non-cancer risk assessments.	None	N/A
Chronic (Cancer)	N/A	Classified as "Group "D" carcinogen, which means there is inadequate data for assessing potential human carcinogenicity for naptalam sodium.	N/A	N/A

[1] Dermal absorption is assumed to be equivalent to oral absorption (100%) for risk assessment purposes.

[2] Inhalation absorption is assumed to be equivalent to oral absorption (100%) for risk assessment purposes.

[3] N/A = Not Applicable.

A toxicological endpoint of concern was also selected for long-term dermal and inhalation exposures, specifically a NOAEL of 25.8 mg/kg/day from a 1-year oral toxicity study in the dog. However, long-term (chronic) exposures (>180 days) are not anticipated with the current use patterns for naptalam sodium.

V. Dietary (Food) Exposure:

The Population Adjusted Dose (PAD) characterizes the dietary risk of a chemical, and reflects the Reference Dose (RfD), either acute or chronic, that has been adjusted to account for the FQPA SF. The acute PAD (aPAD) is an estimate of the one-day dietary exposure to a pesticide residue which is believed to have no significant deleterious effects. The chronic PAD (cPAD) is an estimate of the level of daily dietary exposure to a pesticide residue which, over a 70-year human life span, is believed to have no significant deleterious effects.

As indicated above, the FQPA Safety Factor has been removed, and in addition, there is no identified acute RfD. For chronic dietary exposures, the chronic RfD is 0.258 mg/kg/day, based on the selected toxicological endpoint of concern, a NOAEL of 25.8 mg/kg/day from the 1-year oral toxicity study in the dog, and based a total uncertainty factor (UF) of 100x, based on the uncertainty factor of 10x for interspecies extrapolation and the 10x for intraspecies variability. A dietary risk estimate of less than 100% of the aPAD or cPAD is not of concern to the Agency.

The Agency usually prefers to utilize data from USDA's Pesticide Data Program (PDP) for the dietary risk assessments. However, for naptalam sodium, these data could not be quantitatively used in the risk assessment, because the Agency usually requires that there be at least 100 samples for each commodity to incorporate the USDA PDP monitoring data into risk assessments. Not enough samples were monitored among the crops for which the Agency needed to establish naptalam sodium tolerances, and many of the commodity groups for which the Agency has tolerances were not even included in the USDA PDP monitoring program. For naptalam sodium, field trial data have been utilized to estimate residues in the respective food commodities (MRID 402745-04). These data were developed for the following crops: cantaloupe treated at 4 lb ai/A and harvested 47-54 days after treatment; cucumbers treated at 4 lb ai/A preemergent; and watermelon treated at 4 lb ai/A and harvested 33-68 days after treatment. All residues reported in field trials were non-detectable (<0.1 ppm). Based on these non-detectable data, the amounts of naptalam in each commodity were estimated to be 0.1 ppm. This value represents a high-end estimate for each commodity, based on utilizing the limit of quantification (LOQ) from the naptalam analytical method.

The chronic dietary risk assessment for naptalam sodium was conducted using the Dietary Exposure Evaluation Model software with the Food Commodity Intake Database (DEEM-FCID™, Version 2.03), which incorporates consumption data from US Department of Agriculture (USDA) Continuing Surveys of Food Intakes by Individuals (CSFII), 1994-1996 and 1998. These CSFII data are based on the reported consumption of more than 20,000 individuals over two non-consecutive survey days. For the chronic exposure assessment, consumption data are averaged for the entire U.S. population and within population subgroups. Based on an analysis of these CSFII consumption data, which took into account dietary patterns and survey respondents, the Agency concluded that it is most appropriate to report risk for the following population subgroups: the general U.S. population, all infants (<1 year old), children 1-6 years old, children 7-12, youth 13-19, adults 20-49, females 13-49, and adults 50+ years old.

For chronic dietary exposure assessment, an estimate of the residue level in each food or food-form (e.g., fresh cucumbers or pickles) on the food commodity residue list is multiplied by the average daily consumption estimate for that food/food form. The resulting residue consumption estimate for each food/food form is summed with the residue consumption estimates for all other food/food forms on the commodity residue list to arrive at the total average estimated exposure. The exposure is expressed in mg/kg body weight/day, and as a percent of the chronic Population Adjusted Dose (cPAD). The value for the PAD was taken as equal to the Reference Dose (RfD) of 0.258 mg/kg/day, and the exposure estimation procedure for dietary exposures is performed for each population subgroup.

The Agency is generally not concerned when exposure estimates are less than 100% of the cPAD. The estimates for naptalam sodium are less than 0.1% of the cPAD for each population subgroup (Table 6). Note that no acute dietary (food) exposures have been estimated for naptalam sodium, because there has been no acute toxicological endpoint identified, and similarly, no cancer dietary (food) exposures have been estimated because the Agency have classified naptalam sodium (and naptalam) as a Group "D" carcinogen, which means there is inadequate data for assessing potential human carcinogenicity.

Table 6. Summary of Chronic Dietary (Food) Exposure and Risk for Naptalam Sodium.		
	Dietary Exposure (mg/kg/day)	% cPAD*
General U.S. Population	0.000040	< 0.1
All Infants (< 1 year old)	0.000045	< 0.1
Children 1-6 years old	0.000077	< 0.1
Children 7-12 years old	0.000051	< 0.1
Youth 13-19 years old	0.000032	< 0.1
Adults 20-49 years old	0.000029	< 0.1
Adults 50+ years old	0.000043	< 0.1
Females 13-49 years old	0.000032	< 0.1

VI. Drinking Water Exposure:

Tier I Estimated Drinking Water Concentrations (EDWCs) for naptalam were calculated by utilizing the FIRST V. 1.0 (surface water) and SCIGROW V. 2.3 (ground water) models for use in the human health risk assessment, following applications of naptalam sodium. For surface waters, the estimated peak concentration of naptalam was 658.2 ppb, and the annual average concentration was 188.7 ppb (Table 7). The estimated ground water concentration, suitable for both peak and annual average concentrations, was 3.31 ppb for naptalam. These values represent "conservative" (i.e., high-end) estimates of the concentrations of naptalam that could be found in surface and ground water following the applications to cucurbits and ornamentals, the crop sites on the current label. There are no available monitoring data for assessing these EDWCs in either surface waters or ground water.

Table 7. Estimated Environmental Concentrations (ppb) of Naptalam Sodium in Surface and Groundwater at Two Applications of 4.0 lb/acre with 14-day Intervals.				
Scenario	**Peak (ppb)**	**Long-Term Average, Peak (ppb)**		
		Annual	**21-day**	**60-day**
Surface water drinking water (FIRST)	658.2	188.7		
Ambient surface water (GENEEC)	435.5		421.4	395.3
Groundwater drinking water (SCI-GROW)	3.31			

VII. Aggregate Assessment:

The Food Quality Protection Act amendments to the Federal Food, Drug, and Cosmetic Act [FFDCA, Section 408(b)(2)(A)(ii)] require "that there is a 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 are reliable information." Aggregate exposure

typically includes exposures from food, drinking water, residential uses of a pesticide, and other non-occupational sources of exposure. For an aggregate assessment of naptalam sodium, the only significant exposure routes are oral exposure through food and water consumption, because there are no registered residential uses or other non-occupational sources of exposure.

To determine the maximum contribution allowed from water in the diet, the Agency first looks at how much of the overall allowable risk is contributed by food to determine a "drinking water level of comparison" (DWLOC). The modeled drinking water estimates are then compared to the DWLOC to ensure that they do not exceed this level. A chronic dietary exposure assessment was conducted, which shows that naptalam sodium represents an extremely small percent of the PAD, specifically, less than 0.1% of the cPAD for all population subgroups. The Agency is generally not concerned when dietary exposure estimates are less than 100% of the PAD. As discussed above, the estimated peak concentration of naptalam in surface waters was 658.2 ppb, and the annual average surface water concentration was 188.7 ppb. The estimated ground water concentration, suitable for both peak and annual average concentrations, was 3.31 ppb for naptalam.

Since the dietary contribution is significantly below the PAD and the estimated drinking water exposure levels are in the moderate range, the Agency considers it very unlikely that levels of concern would be reached from the combination of these two exposure sources. As support for this position, the chronic risk estimates for exposure to food and drinking water sources for two population subgroups, children 1-6 years old and for the general U.S. population, have been determined (Table 8). Considering that the conservatively estimated environmental concentrations of naptalam are significantly below the DWLOC for the most sensitive population subgroup (children 1-6) and for the general population, and the relatively low production volume and total amount applied of this chemical, the risks associated with food and drinking water exposures to naptalam are not of concern to the Agency.

Table 8. Summary of Aggregate Risk Estimates for Chronic Food and Water Exposures to Naptalam

Population Subgroup	Chronic PAD (mg/kg/d)	Food Exposure (mg/kg/d)	Allowable Water Exposure (mg/kg/d)	Annual Peak in Drinking Water (ppb)	Annual Mean in Drinking Water (ppb)	DWLOC (ppb)
Children 1-6 yrs. old	0.258	0.000077	0.257923	658.2	188.7	2580
General U.S. Population	0.258	0.000040	0.25796	658.2	188.7	9029

VIII. Occupational Exposure Assessment:

Naptalam sodium is formulated as liquid concentrate for use as a pre-emergent broadleaf herbicide on cucurbit crops and woody nursery stock. It may be applied with groundboom equipment to cucurbits and with groundboom, low-pressure handwand, and handgun equipment

to the soil around established or transplanted woody nursery stock. The current label does not specify whether aerial applications are permitted, but the registrant has indicated they know of no current aerial applications, and are willing to place such restrictions on their revised label. In addition, the registrant has recently placed a restriction against use in greenhouses on their label. The label also prohibits use through any type of irrigation system.

Table 9 provides the acres treated per day and the maximum application rates. The daily areas treated were defined for each handler scenario (in appropriate units) by determining the amount that can be reasonably treated in a single day (e.g., acres). It was assumed that the average occupational workday is 8 hours. Since the toxicological endpoint is the same for dermal and inhalation, total risks (dermal plus inhalation) must be estimated. An uncertainty factor of 100 (10 for interspecies extrapolation and 10 for intraspecies variation) was used for this assessment. Since the toxicological endpoint of concern is not sex-specific, the average body weight of an adult (70 kg) was used to calculate doses.

Table 9: Summary of Maximum Application Rates for Naptalam Sodium

Crop Type/ Use Site	Maximum Application Rate	Application Equipment	Acres Treated Per Day
Cucurbits (i.e., cucumber, watermelon, muskmelon, cantaloupe, honeydew melon, Persian melon, and casaba)	4 lb ai/acre[a]	groundboom	80
Woody nursery stock transplants or established plants (The label indicates "Not for use in a greenhouse.")	8 lb ai/acre[b]	groundboom	40
		handgun	5
		low-pressure handwand	2

a From product label, 2 lbs of naptalam sodium per gallon of product; apply 2 gallons/acre maximum

b From product label, 2 lbs of naptalam sodium per gallon of product; apply 4 gallons/acre maximum

The Agency has determined that there is a potential for exposure to naptalam sodium in occupational scenarios from handling naptalam sodium products during the application process (i.e., mixer/loaders, applicators, and mixers/loaders/applicators) and a potential for postapplication worker exposure from entering into areas previously treated with naptalam sodium. As a result, risk assessments have been completed for occupational handler scenarios as well as occupational postapplication scenarios. The label lists the various cucurbit crops, with the possibly of staggered plantings of the different species in the same area, and with the applications to both pre-emergent (immediately after planting) and pre-vining plants listed on the label. The registrant has provided information that usually a grower would utilize only a single treatment (immediately after planting or pre-vining), but since the label permits a second treatment, both treatment have been assessed. The registrant also indicates that the time period between these two treatments may be between 2 to 6 weeks apart. Therefore, the Agency has included assessments for both short- and intermediate-term exposures, with short-term exposures being 1 to 30 days, and intermediate-term being 1 to 6 months duration. In addition, the label lists treatment for broadleaf weed control in nursery stock transplants or established plants, without any restrictions on the time of year of treatment, except for conditions of extreme temperatures.

The exposure scenarios and application rates chosen for this risk assessment were based on the anticipated use patterns and the current label for the naptalam sodium product (see Table 9).

Occupational Handler Exposures and Risks:
The occupational handler exposure assessments were completed considering different levels of possible risk mitigation. A tiered approach was used, with the lowest tier represented by the baseline attire exposure scenario (i.e., long-sleeve shirt, long pants, shoes, socks, and no respirator), followed by increasing levels of personal protective equipment or PPE (e.g., gloves, double-layer body protection, and/or respirators) and engineering controls (e.g., enclosed cabs, enclosed cockpits, and closed mixing/loading systems). Occupational handler exposure estimates were based on surrogate data from the Pesticide Handlers Exposure Database (PHED) and the Outdoor Residential Exposure Taskforce (ORETF). (See Appendix 2 for additional details concerning PHED and ORETF studies.)

Based on the exposure assessments reported in Table 10, the results of the occupational handler exposure and risk assessment indicate that total (dermal + inhalation) risks did not exceed the level of concern:

- For handlers mixing/loading liquid concentrates to support aerial and groundboom applications, with the addition of chemical-resistant gloves to baseline attire.
- For handlers applying liquids with enclosed-cockpit aerial and open-cab groundboom equipment with baseline attire.
- For handlers mixing/loading/applying with low-pressure handwand or handgun equipment with the addition of chemical-resistant gloves to baseline attire.

Table 10. Short- and Intermediate Term Dermal and Inhalation Handler Risks - Naptalam Sodium											
Exposure Scenario	Crop or Target	Application Rate[a] (lb ai/acre)	Area Treated Daily[b] (acres)	Unit Exposures			Dermal MOEs[f]		Inhalation MOE[g]	Combined Dermal + Inhalation MOEs	
				Dermal Baseline Attire[c] (mg/lb ai)	Inhalation Baseline[d] (µg/lb ai)	Dermal PPE[e] (baseline plus gloves) (mg/lb ai)	Baseline	PPE- (baseline plus gloves)	Baseline	Baseline Dermal + Baseline Inhalation	PPE Dermal (baseline plus gloves) + Baseline Inhalation
Mixer/Loader											
Mixing/Loading Liquid Concentrates for Groundboom Applications	nurseries	8	40	2.9	1.2	0.023	2.3	290	5400	2.3	270
	cucurbits	4	80	2.9	1.2	0.023	2.3	290	5400	2.3	270
Applicator											
Applying Liquid Sprays via Groundboom Equipment	nurseries	8	40	0.014	0.74	0.014	460	460	8900	440	440
	cucurbits	4	80	0.014	0.74	0.014	460	460	8900	440	440
Mixer/Loader/Applicator											
Mixing/ Loading/ Applying Liquid Concentrates with Low Pressure Handwand (PHED)	nurseries	8	2	100	30	0.43	1.3	300	4300	1.3	290

Table 10. Short- and Intermediate Term Dermal and Inhalation Handler Risks - Naptalam Sodium											
Exposure Scenario	Crop or Target	Application Rate[a] (lb ai/acre)	Area Treated Daily[b] (acres)	Unit Exposures			Dermal MOEs[f]		Inhalation MOE[g]	Combined Dermal + Inhalation MOEs	
				Dermal Baseline Attire[c] (mg/lb ai)	Inhalation Baseline[d] (µg/lb ai)	Dermal PPE[e] (baseline plus gloves) (mg/lb ai)	Baseline	PPE- (baseline plus gloves)	Baseline	Baseline Dermal + Baseline Inhalation	PPE Dermal (baseline plus gloves) + Baseline Inhalation
Mixing/ Loading/ Applying Liquid Concentrates with a Handgun Sprayer (LCO ORETF data)	nurseries	8	5	No Data	1.8	0.45	No Data	113	29000	No Data	113

a Application rates are the maximum application rates determined from the EPA registered label for naptalam sodium.

b Amount handled per day values are estimates of acres treated daily.

c Dermal baseline attire is long-sleeve shirt, long pants, and no gloves.

d Inhalation baseline is no respirator.

e PPE-single layer plus gloves is baseline attire plus chemical-resistant gloves.

f Dermal MOE = NOAEL (29.7 mg/kg/day) / dermal daily dose (mg/kg/day), where dermal dose = daily unit exposure (mg/lb ai) x application rate x amount handled per day / body weight (70 kg adult).

g Inhalation MOE = NOAEL (29.7 mg/kg/day) / inhalation daily dose (mg/kg/day), where inhalation dose = daily unit exposure (µg/lb ai) x application rate x amount handled per day x conversion factor (1mg/1,000 µg) / body weight (70 kg adult).

Occupational Postapplication Exposures and Risks:
Occupational postapplication exposures to agricultural workers are estimated, in general, using transfer coefficients and dislodgeable foliar residue values or soil transferrable residue values to estimate the postapplication exposures. Transfer coefficients are linked to specific worker tasks, such as irrigating, scouting, weeding, harvesting, etc. These tasks are typically crop-specific and may involve light to heavy contact with the crop at various stages of growth, depending on the timing of application. Dislodgeable foliar residues (DFRs) are the amounts of pesticide available on the leaf surface that can potentially be transferred to the skin of agricultural workers who contact treated foliage or other surfaces. DFRs are measured using techniques that specifically determine the amount of residues on the surface treated leaves or other plant surfaces. Soil transferrable residues (STRs) are the amounts of pesticide active ingredient available in the soil that can potentially be transferred to the skin of agricultural workers who contact treated soil.

The product label indicates that for weed control in cucurbits, naptalam sodium may be applied as a broadcast application at planting and/or over the top of the cucurbits in the early season before they begin to vine. For weed control in woody nursery stock, the product label indicates that it may be applied as a broadcast spray prior to transplanting or as a soil-directed spray around established stock. For both cucurbits and woody nursery stock application, the product label recommends watering-in following application. For the over-the-top application to cucurbits, residues would be on plant foliage; therefore, a DFR value would be used in the postapplication risk assessment. The registrant submitted a study (MRID 449725-01) designed to fulfill the requirements under Occupational and Residential Exposure Test Guidelines: 875.2100, Dislodgeable Foliar Residue Dissipation. Based on the information available in this DFR study, the data indicate that the calculated dissipation half-lives for naptalam sodium ranged from 1.45 to 1.66 days for the portion of the study conducted in Indiana, and from 2.82 to 2.88 days for the portion of the study conducted in Washington State. Since the foliar applications are made only in early season before the cucurbits begin to vine, and exposures would be limited to immature crops, so it was considered there to be the potential for only low exposure activities.

It should be noted that the current label for the naptalam sodium product recommends that soil watering regimen after application is very important for the proper use of this product. Water is needed to carry this product to the seeds or roots of the weeds. Irrigation therefore, may be needed in dry conditions.

The Agency generally mitigates postapplication risks to agricultural workers using a restricted entry interval (REI), which is a period of time following a pesticide application during which entry into the treated area is restricted. The naptalam sodium product is intended for early-season applications to cucurbits, both soil-directed and foliar, with watering-in, to control preemergent weeds. The Agency has determined that there is a low potential for occupational post-application exposure when a pre-emergent herbicide is used, since most pre-emergent herbicides are applied to the soil directly and/or are soil-incorporated well before the crops are mature. This is the situation for the naptalam sodium product. In addition, the timing of the applications, relative to harvest activities, can greatly reduce the potential for post-application exposure. With applications to high acreage field crops, mechanically planted early in the season, there is a minimal potential for dermal contact. But there is a somewhat greater concern for the post-application exposure when a pre-emergent herbicide is used on crops that must be hand-planted or transplanted, such as the cucurbits. However, most of the activities associated with these crops are low contact.

The Agency has decided to use a qualitative approach to address the post-application exposures for naptalam sodium, based on several key factors: the pre-emergent use pattern of this chemical; the label recommends that soil watering regimen is very important for watering-in the herbicide, thus limiting DFR residues; and, worker exposure would be limited to immature crops. For naptalam sodium, a pre-emergent herbicide used on crops that are hand planted or transplanted, the postapplication assessment on the exposure through the treated soil has been considered in this qualitative approach, and an REI is not being assessed for postapplication exposures. The decision not to assess an REI is based on the low potential for occupational post-application exposure when pre-emergent herbicides are used. Naptalam sodium is applied to the soil directly and the label recommends watering-in, so the product is soil incorporated well before the crops are mature. The timing of the application of naptalam sodium can greatly reduce the potential for post-application exposure. Also, most agricultural operations mechanically plant the cucurbits early in the season, which minimizes the potential for dermal contact. Minimal exposure during harvesting or any other late season activities is expected since naptalam sodium is applied early in the growing season to control pre-emergent weeds.

For consistency of establishing a postapplication REI, the current product label lists an REI of 48 hours. This REI was based on the eye irritation study (MRID 60404), which determined that naptalam sodium causes severe eye irritation. Consequently, this RED now finds that the REI of 48 hours should be retained, and that the stipulation that PPE for applicators and other handlers must include protective eyewear is also retained.

IX. Environmental Fate and Ecotoxicity:

Environmental Fate and Transport:

The environmental fate database for naptalam sodium is sufficient to conduct a preliminary assessment. The physical and chemical properties important in assessing the environmental fate and transport of naptalam sodium are listed in Table 11. The environmental fate and mobility of naptalam sodium is pH dependent. The herbicide is formulated as a sodium salt, and will dissociate readily and will predominantly exist as the sodium cation and acid anion in the environment. Anions often possess high mobility in soils, tend to have significant leaching potential and will not volatilize from water or soil surfaces. The hydrolysis of naptalam appears to occur slowly under alkaline and neutral conditions, but proceeds rapidly under acidic conditions with a half-life on the order of a few days. Biodegradation appears to be insignificant under anaerobic conditions, but may be an important environmental fate process in soil and water under aerobic conditions. A major degradation product of naptalam is 1-naphthylamine which has been classified as a carcinogen by the Occupational Safety and Health Administration (OSHA), although this degradate was not detected in the submitted plant metabolism studies.

Table 11. Physical and Chemical Properties Important for the Environmental Fate and Transport of Naptalam Sodium.		
Parameter	**Value**	**Source**
Scientific name	2-((1-naththalenyl-amino)carbonyl)-benzoic acid, sodium salt	
Molecular formula	$C_{18}H_{13}NO_3.Na$	Toxnet (2004)
Molecular weight	313.3	Toxnet (2004)
Melting Point	greater than 185 °C	Toxnet (2004)
Density/Specific Gravity	1.386	Toxnet (2004)
Vapor Pressure (25 °C)	$9.1x10^{-11}$ mm Hg	EPIWIN
Henry's Law Coeffiicient	$2.4x10^{-15}$ atm-m^3/mol	EPIWIN
Estimated Octanol/Water Partition Coefficient (log K_{ow})	5.42 (naptalam) -0.39 (sodium salt)	Tomlin, 1997 EPIWIN
Dissociation Constant (pK_a)	4.6	Tomlin, 1997
Water Solubility (mg/L at 25°C)	200 mg/L (naptalam) 300,000 mg/L (sodium salt) 249,000 mg/L (sodium salt)	Tomlin, 1997 Tomlin, 1997 Weed Science Society of America, 7th edition, 1994
Hydrolysis Half-life (days)	2.9 (at pH 5) No data at pH 7 and 9	MRID 436477-01
Aerobic Soil Metabolism Half-life (days)	36.7	MRID 414272-01
	< 3	MRID 00145416
Anaerobic Soil Metabolism Half-life (days)	246	MRID 414272-02
Aerobic Aquatic Metabolism Half-life (days)	"137.25"	No study; value calculated as 3x the aerobic soil $t_{½}$ from MRID 416477-01, in accordance with EFED policy (2002)
Aqueous Photolysis Half-life (days)	6.2-6.9 10.3	MRID 413854-01 MRID 413854-01
Soil photolysis half-life	15.9 days	MRID 413854-02
Estimated Soil Sorption Coefficient (Adsorption coefficient, K_{oc}[2])	20	Weber 1994

Ecotoxicity and Environmental Risk Assessment:

Results of acute toxicity studies suggest that naptalam is practically nontoxic to freshwater fish and invertebrates. No chronic toxicity data were submitted for freshwater organisms and no acute

or chronic testing of marine/estuarine fish or invertebrates was submitted. A Tier 1 screening level risk assessment focusing on maximum proposed uses of naptalam on cucumber, watermelon, honeydew and cantaloupe suggests that concentrations of naptalam in the environment, when compared with minimum toxicity values, are unlikely to result in acute adverse effects to freshwater aquatic organisms. Insufficient toxicity data are available to characterize the risk of chronic adverse effects to freshwater organism, and no data are available to characterize the risk to marine/estuarine fish and invertebrates.

Naptalam is categorized as slightly toxic to small mammals on an acute oral basis and the potential for chronic reproductive effects appears to be low. Risks to terrestrial and avian species may occur, but are expected to be unlikely due to the rapid breakdown of the naptalam acid in soils and the surfaces of plants, and due to the label-mediated practice of watering-in the naptalam into the soil following application.

Results of acute oral toxicity studies suggest that naptalam is practically non-toxic to birds. Results of reproductive studies of naptalam in birds are not available. Based on contact LD_{50} studies for the honey bee (*Apis mellifera*), naptalam is classified as practically nontoxic on an acute contact basis. Because naptalam is an herbicide, it is anticipated that non-target plants might be susceptible to adverse effects; however, no data were submitted to assess the toxicity of naptalam toward aquatic or terrestrial non-target plants.

The Agency's ecological risk assessment compares toxicity endpoints from ecological toxicity studies to estimated environmental concentrations (EECs) based on environmental fate characteristics and pesticide use data. To evaluate the potential risk to nontarget organisms from the use of naptalam sodium products, the Agency calculates Risk Quotient (RQ) values, which are the ratio of the EEC to the most sensitive toxicity endpoint value, such as the median lethal dose (LD_{50}) or the median lethal concentration (LC_{50}). These RQ values are then compared to the Agency's level of concern (LOC) values to estimate whether a chemical, when used as directed, has the potential to cause adverse effects on nontarget organisms. When the RQ exceeds the LOC for a particular category, the Agency presumes a potential risk of concern to that category of organisms.

A Tier 1 screening level risk assessment focusing on maximum proposed uses of naptalam sodium on cucumber, watermelon, honeydew and cantaloupe has been conducted. The results suggest that concentrations of naptalam in the environment, when compared with minimum toxicity values, are unlikely to result in acute adverse effects to freshwater aquatic organisms. Insufficient toxicity data are available to characterize the risk of chronic adverse effects to freshwater organisms, and no data are available to characterize the risk to marine/estuarine fish and invertebrates.

Naptalam sodium is absorbed by seeds and primary roots, and interferes with normal growth, but it exhibits minimal foliar activity and minimal activity on grassy weeds. Thus, while no data were submitted to assess the toxicity of naptalam toward aquatic or terrestrial non target plants, it is expected that there are minimal adverse risks to terrestrial non-target plants. In addition, the results indicate that there are no risk concerns for avian species.

Screening level risk estimates have been conducted for terrestrial mammalian species, and the acute, chronic, endangered species, and restricted use triggers are summarized below:

- In mammalian species, acute exposure to naptalam under maximum residues conditions on short grass to small mammals (15 g) indicates a potential for acute risk, because the RQ is 0.58, as well as five other potential exceedances of acute restricted use LOCs in tall grass and in broadleaf plants and small insects, as well as three potential exceedances of the endangered species LOC.

- In mammalian species, chronic exposure to naptalam on short grass for maximum residue conditions also indicates the potential for chronic risk to mammals, because the RQ of 1.74 exceeds the LOC of 1.

Note that with respect to endangered species, this is only a screening level and/or qualitative assessment, and does not constitute any findings by the Agency with regard to specifications under the Endangered Species Act.

X. Cumulative Exposure:

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." If chemicals are structurally related and all are low toxicity chemicals, then the risks either separately or combined should also be low.

EPA does not have, at this time, available data to determine whether naptalam sodium 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 naptalam sodium and any other substances, and naptalam sodium does not appear to produce toxic metabolites produced by other substances.

For the purposes of this tolerance action, therefore, EPA has not assumed that naptalam sodium has a common mechanism of toxicity with other substances. For information regarding the Agency'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/.

XI. Risk Mitigation/Management:

The assessments of occupational handler and postapplication exposures to naptalam sodium indicate that there are risks associated with its use as an herbicide on cucurbits and nursery stocks. Risks to handlers can be mitigated with baseline attire, and for mixer/loader and mixer/loader/application scenarios, with the addition of chemical-resistant gloves. Thus, the revised label for the end-use product will now include chemical-resistant gloves for mixer/loaders and mixer/loader/applicators. Due to lack of exposure data, the only mitigation for aerial

applications would have been engineering controls (enclosed cockpit and probably closed transfer mixing and loading systems); however, due to these factors and apparently minimal usage of aerial applications, the registrant has agreed to place label restrictions against aerial applications on their revised label. Postapplication risks to agricultural workers can be mitigated with a restricted-entry interval, with an REI of 24 hours, which actually is a shorter time interval than the 48 hours on the current label. In addition, soil exposures were also unlikely to exceed the level of concern at an REI conservatively estimated to be 24 hours after application. However, due to an eye irritation study showing severe opacity continuing until day 7, both the REI of 48 hours and the requirement for protective eyewear will remain on the label.

In addition to the risk mitigation of the registrant voluntarily agreeing to place a restriction on the label to prevent aerial applications, the registrant will retain label restrictions against greenhouse use, as well as applications through any type of irrigation system. In addition, the registrant will incorporate label language to insure that ground applications will be made with equipment placed as close to the ground as feasible, that droplet sizes will be as large as possible (no fine droplets), and that the watering-in requirement will be clearly stated on the label directions. In addition, the registrant has voluntarily agreed to remove nursery stock/woody ornamentals from their label. The registrant has also agreed to include on the revised label that the maximum application rate will remain at 4 pounds active ingredient per acre per application, that two applications are permitted (a first may be made immediately after planting and a second may be made before the plants start to vine but before weeds have emerged), and that the total applications annually may not exceed 8 pounds per acre per year.

The Agency's screening level risk assessment for naptalam sodium indicated the possibility of risks to endangered species. Note, however, that with respect to endangered species, this is only a screening level and/or qualitative assessment, and does not constitute any findings by the Agency with regard to specifications under the Endangered Species Act.

The Agency is not requiring specific mitigation at the present time relative to threatened and endangered species. However, the general risk mitigation required through this RED will serve to reduce exposures somewhat, until such time as the Agency completes a full endangered species risk assessment. If in the future specific measures are necessary for the protection of listed species, the Agency will implement them through the Endangered Species Protection Program.

XII. Endocrine Disruptor Effects:

The Agency 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), the Agency determined that there were scientific bases for including, as part of the program, the androgen and thyroid hormone systems, in addition to the estrogen hormone system. The Agency also adopted EDSTAC's recommendation that the Program include evaluations of potential effects in wildlife. For pesticide chemicals, the Agency 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, naptalam sodium may be subjected to additional screening and/or testing to better characterize effects related to endocrine disruption.

XIII. Tolerance Reassessment:

"Risk Cup" Determination:
As part of the FQPA tolerance reassessment process, the Agency assessed the risks associated with the naptalam sodium. FQPA requires the Agency to evaluate food tolerances on the basis of cumulative risk from substances sharing a common mechanism of toxicity, such as the toxicity expressed through a common biochemical interaction. The Agency does not know of any cumulative risk posed by an entire class of chemicals including naptalam sodium.

Thus, the Agency has determined that the dietary risk from exposure to naptalam sodium is within its own "risk cup." In other words, if naptalam sodium did not share a common mechanism of toxicity with other chemicals, the Agency would be able to conclude today that the food tolerances for naptalam sodium meet the FQPA safety standards. In reaching this determination concerning the FQPA safety standards, the Agency has considered the available information on the special sensitivity of infants and children, as well as both the chronic and acute food exposure. An aggregate assessment was conducted for exposures through food and drinking water. Based on the results of this aggregate assessment, the Agency has determined that the human health risks from these combined exposures are within acceptable levels, because the combined risks from all exposures to naptalam sodium do not "fill" the aggregate risk cup.

Residue Analytical Methods:
PAM II lists two colorimetric methods: (1) Smith and Stone (Method A), and (2) Lane, et. al. (Method B). Recovery of the parent acid of naptalam sodium using FDA PAM I protocols A, D, and E is unlikely. FDA has not reported any analyses for the parent acid of naptalam sodium from 1999 to 2002.

Tolerance Reassessment:
Due to various recent changes in the Agency commodity definitions, the Agency is revoking the current tolerances for cantaloupe, muskmelon, and watermelon. Instead of these three commodities, the Agency is now establishing a single tolerance for the Melon subgroup (Crop Group 9A). In addition, the "(N)" designation for negligible residues, as listed in the current 40 CFR §180.279 entries, is now being deleted from all the entries.

The current tolerance expression for residues is expressed at 40 CFR 180.297 as "established for residues of the herbicide *N*-1-naphthyl phthalamic acid from application of its sodium salt in or on the following raw agricultural commodities." This RED has reassessed these tolerances and has determined that the tolerances should now be expressed as in Table 12.

Table 12. The reassessed Tolerance Summary will now be as follows: "Residues of the herbicide Naptalam Sodium, as established for residues of *N*-1-naphthyl phthalamic acid, from application of its sodium salt in or on the following raw agricultural commodities:"

Commodity	Current Tolerance (ppm)	Tolerance Reassessment (ppm)	Comments [*Correct Commodity Definition*]
Tolerances Listed Under 40 CFR § 180.297			
Cantaloupe	0.1 (N) [a]	Revoke	While this tolerance should be maintained at 0.1 ppm, based on available field trial data for cantaloupe that indicate all measured residues of naptalam are less than the detection limit of 0.1 ppm, the Agency determined that cantaloupe should be combined into a group tolerance at 0.1 ppm for Melon Subgroup. [*Melon Subgroup, Crop Group 9A*]
Cucumber	0.1 (N)	0.1	
Muskmelon	0.1 (N)	Revoke	While this tolerance should be maintained at 0.1 ppm, based on available field trial data for surrogate crops (cantaloupe and watermelon) that indicate all their measured residues of naptalam are less than the detection limit of 0.1 ppm, the Agency determined that muskmelon should be combined into a group tolerance at 0.1 ppm for Melon Subgroup. [*Melon Subgroup, Crop Group 9A*]
Watermelon	0.1 (N)	Revoke	While this tolerance should be maintained at 0.1 ppm, based on available field trial data for watermelon that indicate all measured residues of naptalam are less than the detection limit of 0.1 ppm, the Agency determined that cantaloupe should be combined into a group tolerance at 0.1 ppm for Melon [*Melon Subgroup, Crop Group 9A*]
Melon subgroup (Crop Group 9A)		0.1	The Agency intends to establish this new tolerance with the concomitant revocation of the tolerances for Cantaloupe, Muskmelon, and Watermelon.

a: (N) = Negligible residue

There are no established Codex maximum residue limits (MRLs) or tolerances for residues of naptalam. Therefore, international harmonization is not an issue.

XIV. References:

Environmental Protection Agency (EPA). 1994,1996. Toxicological Reviews for Naptalam, Sodium Salt. TX0012040, TX0011972, TX0011936, TX0010989, TX0010741.

Environmental Protection Agency (EPA). 2004. Toxicology Overview: Naptalam and Sodium

Naptalam. Stephen Dapson, August 12, 2004.

Science Advisory Council (SAC) for Exposure (2000) Policy Memo #003.1: Agricultural Transfer Coefficients (August 17, 2000).

Toxnet. 2004. Hazardous Substances Data Bank. Sodium N-1-Naphthylphthalamate. National Library of Medicine. http://www.toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB.

Appendix 1. BEAD Screening Level Estimate of Agricultural Uses and Other Information

The tables below contain “screening level” usage data for agricultural crops. This information is retrieved from our principal agricultural pesticide usage databases. At the present time data from 1998 to 2002 is being used.

All numbers reported are rounded.
'<500' indicates less than 500 pounds of active ingredient.
'<2.5' indicates less than 2.5 percent of crop is treated.

Maximum percent of crop treated is the highest **observed** percent crop treated during this time period. For some crops there may have been only one or two observations and it is quite possible that if usage information had been available for more years that higher usage might have been observed. This situation is more likely to occur with low acreage crops.

'(CA only)' indicates information was available only for California. California requires reporting of all agricultural pesticide use. Their database may indicate small amounts of usage of a pesticide on crops on which the pesticide is not registered. Possible reasons for this include:
- This use may actually have occurred either as an unregistered use or as an experimental or other use in which the crop was not intended for consumption.
- Data input errors may have occurred and either the crop or the pesticide is incorrect in the database.

Use of the chemical on crops for which only California use is reported may possibly have occurred in other states.

In some cases the percent crop treated column is blank. This is because information on acres grown was not readily available.

Some of the numbers may be based on information that does not cover all 50 states. Therefore, it is possible that if the remaining (usually minor states for the crop) had been included that pounds of active ingredient would be slightly higher.

Last revised by BEAD: Feb 06, 2004

Screening Level Estimates of Agricultural Uses of naptalam
Sorted Alphabetically

OBS	Crop	Pounds Active Ingredients	Percent Crop Treated Typical Average	Likely Maximum
1	Cantaloupes	3,000	<1	5
2	Cucumbers	30,000	10	15
3	Pumpkins	2,000	<1	5
4	Soybeans	80,000	<1	<2.5
5	Squash	1,000	<1	<2.5
6	Sweet Corn	<500		
7	Watermelons	20,000	5	10

All numbers rounded.
'<500' indicates less than 500 pounds of active ingredient.
'<2.5' indicates less than 2.5 percent of crop is treated.
'(CA only)' indicates information was available only for California.
Use of naptalam on this crop may also have occurred in other states.

(slua0001.sas naptalam)

Screening Level Estimates of Agricultural Uses of naptalam
Sorted by descending quantity of naptalam applied to each crop

OBS	Crop	Pounds Active Ingredients	Percent Crop Treated Typical Average	Likely Maximum
1	Soybeans	80,000	<1	<2.5
2	Cucumbers	30,000	10	15
3	Watermelons	20,000	5	10
4	Cantaloupes	3,000	<1	5
5	Pumpkins	2,000	<1	5
6	Squash	1,000	<1	<2.5
7	Sweet Corn	<500		

All numbers rounded.
'<500' indicates less than 500 pounds of active ingredient.
'<2.5' indicates less than 2.5 percent of crop is treated.
'(CA only)' indicates information was available only for California.
Use of naptalam on this crop may also have occurred in other states.

(slua0001.sas naptalam)

Screening Level Estimates of Agricultural Uses of naptalam
Sorted by descending percent of crop treated with naptalam

OBS	Crop	Pounds Active Ingredients	Percent Crop Treated Typical Average	Likely Maximum
1	Cucumbers	30,000	10	15
2	Watermelons	20,000	5	10
3	Soybeans	80,000	<1	<2.5
4	Cantaloupes	3,000	<1	5
5	Pumpkins	2,000	<1	5
6	Squash	1,000	<1	<2.5
7	Sweet Corn	<500		

All numbers rounded.
'<500' indicates less than 500 pounds of active ingredient.
'<2.5' indicates less than 2.5 percent of crop is treated.
'(CA only)' indicates information was available only for California.
Use of naptalam on this crop may also have occurred in other states.

(slua0001.sas naptalam)

Prepared by: BEAD
September 10, 2004

Appendix 2. Naptalam Sodium: Chronic Dietary (Food) Exposure Assessment

U.S. Environmental Protection Agency Ver. 2.00
DEEM-FCID Chronic analysis for NAPTALAM (1994-98 data)
Residue file name: H:\Briefcase\Chemistry Reviews\DEEM Runs\Naptalam.R98
Adjustment factor #2 NOT used.
Analysis Date 09-27-2004/10:18:18 Residue file dated: 09-27-2004/10:17:56/8
Reference dose (RfD, Chronic) = 25.8 mg/kg bw/day

Total exposure by population subgroup

Population Subgroup	Total Exposure mg/kg body wt/day	Total Exposure Percent of Rfd
U.S. Population (total)	0.000040	0.0%
U.S. Population (spring season)	0.000044	0.0%
U.S. Population (summer season)	0.000077	0.0%
U.S. Population (autumn season)	0.000022	0.0%
U.S. Population (winter season)	0.000015	0.0%
Northeast region	0.000043	0.0%
Midwest region	0.000037	0.0%
Southern region	0.000033	0.0%
Western region	0.000050	0.0%
Hispanics	0.000043	0.0%
Non-hispanic whites	0.000039	0.0%
Non-hispanic blacks	0.000027	0.0%
Non-hisp/non-white/non-black	0.000084	0.0%
All infants (< 1 year)	0.000045	0.0%
Nursing infants	0.000044	0.0%
Non-nursing infants	0.000046	0.0%
Children 1-6 yrs	0.000077	0.0%
Children 7-12 yrs	0.000051	0.0%
Females 13-19 (not preg. or nursing)	0.000027	0.0%
Females 20+ (not preg. or nursing)	0.000038	0.0%
Females 13-50 yrs	0.000035	0.0%
Females 13+ (preg./not nursing)	0.000028	0.0%
Females 13+ (nursing)	0.000073	0.0%
Males 13-19 yrs	0.000038	0.0%
Males 20+ yrs	0.000030	0.0%
Seniors 55+	0.000045	0.0%
Children 1-2 yrs	0.000072	0.0%

Children 3-5 yrs	0.000083	0.0%
Children 6-12 yrs	0.000054	0.0%
Youth 13-19 yrs	0.000032	0.0%
Adults 20-49 yrs	0.000029	0.0%
Adults 50+ yrs	0.000043	0.0%
Females 13-49 yrs	0.000032	0.0%

Appendix 3. Details Regarding PHED, ORETF Studies, and Dislodgeable Foliar Residue (DFR) Studies

Pesticide Handler Exposure Database (PHED) Version 1.1 (August 1998): 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.

ORETF Handler Studies (MRID 449722-01): 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 LCO exposure scenarios using a low pressure, high volume turf handgun (ORETF Study OMA002) is summarized below.

LCO Handgun Sprayer: 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 "handgun" 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 liters per minute for light work (NAFTA,1999), the actual sampling time for each individual, and the pump flow rate. All results were normalized for pounds active ingredient handled. A total of 90 replicates were monitored using 17 different subjects. Four different formulations of dacthal [75% wettable powder (packaged in 4 and 24 pound bags), 75% wettable powder in water soluble bags (3 pound bag), 75% water dispersable granules (2 pound bag) and 55% liquid flowable (2.5 gallon 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 using only the 75 percent wettable powder formulation. A target application rate of 2 pounds active ingredient was used for all replicates (actual rate achieved was about 2.2 pounds active ingredient per 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 exposures are presented below. [Note the data were found to be lognormally distributed. As a result, all exposures are geometric means.]