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

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

May 7, 2008

MEMORANDUM

SUBJECT: **Naphthalene**: Phase 2 Amendment: Revisions Required to Update Hazard Characterization.

PC Code: 055801	**DP Barcode:** 352389
MRID No.: 43716501	**Registration No.:** N/A
Petition No.: N/A	**Regulatory Action:** Phase 2
Risk Assessment Type: Response to Error Only Comments	**Case No.:** 0022
T**XR No.:** N/A	**CAS No.:** 91-20-3
MRID No.: 43716501	**40 CFR:** N/A (Non-Food/ Non-Feed)

FROM: Wade Britton, MPH, Industrial Hygienist
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This document serves a revision of the April 10, 2008 naphthalene occupational and residential exposure assessment chapter, "Phase 2 Amendment: Response to Registrant Submitted Error Only Comments in Reference to "Naphthalene: Occupational and Residential Exposure Assessment and Recommendations for the Reregistration Eligibility Decision Document." An update of this chapter is required to address the following hazard characterization language:

- Executive Summary, Residential Indoor Postapplication Noncancer Exposure and Risk Estimates, Second Paragraph has been revised to read:

Since the data available to date indicate that rodents are more likely to be susceptible to the respiratory effects of naphthalene than humans, the use of rodents as a model without application of species scaling accounting for species differences in dosimetry and metabolism would likely result in inaccurate estimates of human risk. Therefore, rather than quantifying inhalation risks to humans, the levels of ambient naphthalene measured in the human exposure study were compared directly to the levels resulting in a 1) no adverse effects in the rodent studies (NOAELs) and 2) a toxic effect in rodents (LOAELs). This comparison provides a sense of the difference between actual naphthalene concentrations that a human may encounter and the doses which elicit either no adverse response or a toxic response in rodents.

- 1.2 Toxicological Endpoints, Second Paragraph has been revised to read:

The toxicological endpoints used to complete the residential exposure assessment are summarized in Table 2. The rationale for endpoints selected for the assessment of residential risk can be referenced in the document, Naphthalene: Phase 2 Amendment: Response to Registrant Submitted Error Only Comments in Reference to "Naphthalene: HED Chapter of the Reregistration Eligibility Decision Document (RED)," (D. Drew, D335941).

- 1.2 Toxicological Endpoints, descriptor following Table 2. Toxicological Doses and Endpoints for Naphthalene for Use in Human Health Risk Assessments has been revised to read:

* Since the data available to date indicate that rodents are more likely to be susceptible to the respiratory effects of naphthalene than humans, the use of rodents as a model without application of species scaling accounting for species differences in dosimetry and metabolism would likely result in inaccurate estimates of human risk.. Therefore, rather than quantifying inhalation risks to humans, the levels of ambient naphthalene measured in the human exposure study were compared directly to the levels resulting in a 1) no adverse effects in the rodent studies (NOAELs) and 2) a toxic effect in rodents (LOAELs).

- 2.2.1 Residential Postapplication Inhalation Exposure and Risk, Second Paragraph has been revised to read:

Since the data available to date indicate that rodents are more susceptible to the respiratory toxicity of naphthalene, the use of rodents as a model without the appropriate species scaling accounting for species differences in dosimetry would likely result in an inaccurate estimation of human risk. Therefore, rather than quantifying inhalation risks to humans, the levels of ambient naphthalene measured in the human exposure study were compared directly to the levels resulting in a 1) no adverse effects in the rodent studies (NOAELs) and 2) a toxic effect in rodents

(LOAELs). This comparison provides a sense of the difference between actual naphthalene concentrations that a human may encounter and the doses which elicit either no adverse response or a toxic response in rodents.

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Executive Summary

Background and Purpose

This occupational and residential exposure and risk assessment is being conducted as part of EPA's human health risk assessment for the naphthalene Reregistration Eligibility Decision (RED). This document addresses the exposures and risks associated with occupational and residential exposure to naphthalene based upon prescribed label uses.

Naphthalene Use Summary

According to the 3/28/2007 SMART meeting and EPA databases, registrants are supporting two pesticide uses of naphthalene registered in the U.S. These are a moth treatment for the protection of woolen clothing (indoor) and an animal repellant against nuisance vertebrate pests (indoor and outdoor). All registered products of naphthalene are intended for residential uses only. Residential products for use within the home are formulated as mothballs or flakes, while outdoor products are formulated as dusts, flakes, and granules.

Occupational Exposure and Risk Estimates

Naphthalene products are not registered for occupational use and, therefore, occupational exposure and risk is not anticipated and has not been assessed.

Residential Applicator Exposure and Risk Estimates

HED has determined that there is potential for short-term (1-30 days) exposure in residential settings during the application process for homeowners who purchase and use naphthalene-containing products. HED anticipates handler dermal and inhalation exposure during the application process; however, appropriate inhalation handler exposure data are not available to assess this scenario, therefore, only dermal exposure was assessed. Applications of naphthalene can be made indoors and outdoors and are expected to be short-term in duration due to the intermittent nature of use associated with these products.

Margins of Exposure (MOEs) for residential handlers were calculated using standard assumptions and the results of an exposure study, "Estimation of Homeowner Exposure to LX1298-01 (Naphthalene) Resulting from Simulated Residential Use as an Insect Repellent (MRID 43716501)," in which dermal handler exposure data was derived from the monitoring of a person weighing out and placing mothballs in a closet and dresser at three different locations.

Residential handler MOEs (indoor and outdoor) are > 100 and, therefore, not of concern to HED.

Residential Indoor Postapplication Noncancer Exposure and Risk Estimates

HED has determined that there is potential for adult and toddler exposure from naphthalene applications made indoors for moth treatments and indoors/outdoors for animal repellency. While labels specify that treated indoor areas should be airtight to be effective, HED anticipates that naphthalene will volatilize and be inhaled by adults accessing treated areas (i.e., containers, dresser drawers, closets, etc.) and by adults and toddlers that inhabit treated areas exposed to ambient concentrations of naphthalene. Exposures from accessing treated areas are expected to be acute in duration and exposures from inhabiting treated areas are short-, intermediate- (1-6 months), and long-term (>6 months) in duration.

Since the data available to date indicate that rodents are more likely to be susceptible to the respiratory effects of naphthalene than humans, the use of rodents as a model without application of species scaling accounting for species differences in dosimetry and metabolism would likely result in inaccurate estimates of human risk. Therefore, rather than quantifying inhalation risks to humans, the levels of ambient naphthalene measured in the human exposure study were compared directly to the levels resulting in a 1) no adverse effects in the rodent studies (NOAELs) and 2) a toxic effect in rodents (LOAELs). This comparison provides a sense of the difference between actual naphthalene concentrations that a human may encounter and the doses which elicit either no adverse response or a toxic response in rodents.

Comparisons for acute and short-term exposure durations were estimated using standard assumptions and the results of the aforementioned exposure study (MRID 43716501). Inhalation exposure data from the study applies to exposure durations ranging from 15 minutes (person accessing treated closets and dresser drawers) to 24 hours (average air concentration surrounding treated closets, dresser drawers, and beds). Based upon direct comparison, acute and short-term inhalation exposures to naphthalene in residences are 60X and 80X, respectively, below the animal dose (LOAEL) resulting in respiratory toxicity (olfactory epithelium lesions) and are 20X and 30X below the animal dose (NOAEL), respectively.

A direct comparison of intermediate- and long-term exposure durations was also performed using standard assumptions; however, due to the lack of a naphthalene-specific study of an appropriate duration, a different exposure study was used to assess these durations of exposure (Polycyclic Aromatic Hydrocarbon Exposure of Children in Low-Income Families, Chuang et al., 1999). This study was conducted to observe exposures to polycyclic aromatic hydrocarbons (PAHs) inside of 24 homes from air, dust, soil, and food. For the purposes of this risk assessment, only those results which pertain to the indoor ambient concentrations of naphthalene were used estimate postapplication inhalation (intermediate- and long-term) exposure. Intermediate- and long-term exposures to naphthalene in residences are 1000X and 5400X, respectively, below the animal dose (LOAEL) resulting in respiratory toxicity (olfactory epithelium lesions) and intermediate-term exposure is 540X below the animal dose (NOAEL). A NOAEL was

not identified for long-term inhalation exposure and, therefore, this duration was not assessed.

Residential Indoor Postapplication Cancer Risk Estimates

Residential handler cancer exposure and risk estimates were not assessed due to the uncertainty of whether naphthalene poses a human cancer concern at ambient or environmental levels of exposure because of potential species differences in rates of metabolism leading to its toxicity.

Residential Episodic Ingestion Postapplication Exposure and Risk Estimates

HED has determined there is potential that a toddler may ingest formulations used for indoor or outdoor treatments of naphthalene. In order to assess this exposure route, HED estimated the risk of a toddler ingesting a single mothball. In addition, HED estimated the amount of a single mothball that a toddler could ingest to result in an MOE = 100.

Toddler episodic ingestion of one naphthalene mothball results in an MOE < 100 and, therefore, is of concern to HED. An oral dose of 0.5 mg/kg/day would be required to result in an MOE = 100. This dose is equivalent to toddler episodic (incidental) ingestion of 0.32% of one mothball (7.5 of 2350 total mg).

Recommendations and DCI Rationale

HED recommends that the registrant conduct an exposure study to determine levels of naphthalene in indoor air resulting from simulated residential mothball use over intermediate- and long-term durations. Intermediate- and long-term residential indoor postapplication exposure and risk was estimated using surrogate data from an exposure study which was conducted to determine indoor ambient levels of naphthalene. Since the surrogate exposure study was not duration- or use-specific, it may potentially underestimate naphthalene exposure and risk. An appropriate study is required to confirm that the estimation of residential postapplication inhalation exposure is protective of human health.

Review of Human Research

This risk assessment relies in part on data from studies in which adult human subjects were intentionally exposed to a pesticide or other chemicals. It was determined that the study, "Estimation of Homeowner Exposure to LX1298-01 (Naphthalene) Resulting from Simulated Residential Use as an Insect Repellent (MRID 43716501)," required review of its ethical conduct, and has received that review. It was concluded that "there are no regulatory barriers to EPA's reliance on this study in its actions under FIFRA" (memorandum, J. Carley to Molly Clayton, 4/24/07). The study, "Polycyclic Aromatic Hydrocarbon Exposure of Children in Low-Income Families, Chuang et al., 1999," was also reviewed for its ethical conduct. It was concluded that it "does not meet the regulatory definition of research involving intentional human exposure and is therefore

not required to undergo ethical review" and that "there are no regulatory, ethical, or policy barriers" to using this study in the risk assessment (electronic communication, J. Carley to Catherine Eiden, 2/20/08).

1.0 Background Information

1.1 Purpose and Criteria for Conducting Exposure Assessments

A residential exposure assessment is required for an active ingredient if (1) certain toxicological criteria are triggered and (2) there is a potential for exposure to handlers during use or to persons entering treated sites after application is complete. Naphthalene meets both criteria. There is potential for residential exposure to naphthalene from application, inhabiting previously treated homes, and the episodic (incidental) ingestion of the product.

1.2 Toxicological Endpoints

A summary of the acute toxicity data is included in Table 1. Naphthalene is acutely toxic in the rat via the oral (Category III) and inhalation (Category II) routes of exposure. In the rabbit, it is a moderate acute dermal toxicant (Category III). It is a moderate (Category III) skin and eye irritant in the rabbit. Naphthalene is not a dermal sensitizer.

Table 1. Acute Toxicity of Naphthalene

GDLN	Study Type	MRID	Results	Tox Category
870.11	Acute Oral - rat	257224	LD_{50}: 2649 mg/kg (♂+♀)	III
870.12	Acute Dermal	257229	LD_{50} >2000 mg/kg (♂+♀)	III
870.13	Acute Inhalation	257902	LC_{50} > 0.4 mg/L (77.7 ppm) (♂+♀)	II
870.24	Primary Eye Irritation	257228	Slight-moderate irritation	III
870.25	Primary Skin Irritation	257227	Moderate irritation	III
870.26	Dermal Sensitization	00148173	Nonsensitizer – guinea pig	N/A

The toxicological endpoints used to complete the residential exposure assessment are summarized in Table 2. The rationale for endpoints selected for the assessment of residential risk can be referenced in the document, Naphthalene: Phase 2 Amendment: Response to Registrant Submitted Error Only Comments in Reference to "Naphthalene: HED Chapter of the Reregistration Eligibility Decision Document (RED)," (D. Drew, D335941).

Table 2. Toxicological Doses and Endpoints for Naphthalene for Use in Human Health Risk Assessments				
Exposure/ Scenario	**Point of Departure**	**Uncertainty/ Safety Factors**	**Level of Concern for Risk Assessment**	**Study and Toxicological Effects**
Incidental Oral Exposures (Postapplication)				
Incidental Oral (Short-term)	NOAEL= 50 mg/kg/day	UF_A= 10x UF_H= 10x	MOE= 100	**NTP Developmental Rat Study** NOAEL = 50 mg/kg/day LOAEL= 150 mg/kg/day based on maternal effects – persistent clinical signs of lethargy, slow breathing, rooting behavior, and significant decreases in body weights/body weight gains and decreased food and water consumption.
Dermal Exposures				
Dermal (Short-Term)	Dermal NOAEL= 300 mg/kg/day	UF_A= 10x UF_H= 10x	MOE= 100	**90-Day Dermal Toxicity Study –Rat** NOAEL = 300 mg/kg/day LOAEL = 1000 mg/kg/day based on atrophy of seminiferous tubules in males, and nonneoplastic lesions in the cervical lymph node (hyperplasia), liver (hemosiderosis), thyroid thyroglossal duct cysts), kidneys (pyelonephritis), urinary bladder (hyperplasia) and skin (acanthosis, hyperkeratosis) in females.
Inhalation Exposures				
*Inhalation (Short-term)	Inhalation LOAEL = 10 ppm or 52 mg/m^3 NOAEL = 3 ppm or 16 mg/m^3	N/A	N/A	**4-Week (Nose-Only) Inhalation – Rat** NOAEL = 3 ppm LOAEL = 10 ppm based increased incidence and severity of nasal lesions (slight disorganization, rosette formation, basal cell hyperplasia, erosion, atrophy, and degenerate cells in the olfactory epithelium; loss of bowman's glands; respiratory epithelium hypertrophy; rosette formation in the septal organ of Masera and fusion of the turbinates).

Table 2. Toxicological Doses and Endpoints for Naphthalene for Use in Human Health Risk Assessments				
Exposure/ Scenario	**Point of Departure**	**Uncertainty/ Safety Factors**	**Level of Concern for Risk Assessment**	**Study and Toxicological Effects**
*Inhalation (Intermediate-term; 1-6 months)	Inhalation LOAEL = 2 ppm or 10 mg/m^3 NOAEL = 1 ppm or 5.2 mg/m^3	N/A	N/A	**13-Week (nose-only) Inhalation Rat Study; Subchronic (nose-only) Neurotoxicity Rat Study** NOAEL = 1 ppm (Subchronic neurotoxicity study) NOAEL (13 week inhalation study) – not identified. LOAEL = 2 ppm (13 week inhalation study) based on increased incidence and severity of nasal lesions (degeneration, atrophy and hyperplasia of basal cells of the olfactory epithelium; rosette formation of olfactory epithelium; loss of Bowman's glands; hypertrophy of respiratory epithelium). LOAEL = 10 ppm (subchronic neurotoxicity study) based on atrophy/disorganization of the olfactory epithelium and hyperplasia of the respiratory and transitional epithelium.
*Inhalation (Long-term)	Inhalation LOAEL = 10 ppm or 52 mg/m^3	N/A	N/A	**NTP ChronicToxicity and Carcinogenicity Studies in the Rat and Mouse** NOAEL – not identified. LOAEL (rat study) = 10 ppm based on increased incidence and severity of atypical (basal cell) hyperplasia, atrophy, chronic inflammation, and hyaline degeneration of the olfactory epithelium; hyperplasia, squamous metaplasia, hyaline degeneration, and goblet cell hyperplasia of the respiratory epithelium; and glandular hyperplasia and squamous metaplasia.
All Routes of Exposure				
Cancer (inhalation)	Cancer was not assessed due to the uncertainty of whether naphthalene poses a human cancer concern at ambient or environmental levels of exposure because of potential species differences in rates of metabolism leading to its toxicity.			

Point of Departure (POD) = A data point or an estimated point that is derived from observed dose-response data and used to mark the beginning of extrapolation to determine risk associated with lower environmentally relevant human exposures. NOAEL = no observed adverse effect level. LOAEL = lowest observed adverse effect level. UF = uncertainty factor. UF_A = extrapolation from animal to human (interspecies). UF_H = potential variation in sensitivity among members of the human population (intraspecies). MOE = margin of exposure. LOC = level of concern. N/A = not applicable.
* Since the data available to date indicate that rodents are more likely to be susceptible to the respiratory effects of naphthalene than humans, the use of rodents as a model without application of species scaling accounting for species differences in dosimetry and metabolism would likely result in inaccurate estimates of human risk. Therefore, rather than quantifying inhalation risks to humans, the levels of ambient naphthalene measured in the human exposure study were compared directly to the levels resulting in a 1) no adverse effects in the rodent studies (NOAELs) and 2) a toxic effect in rodents (LOAELs).

1.3 Incident Report

In order to complete the incident report for naphthalene (M. Hawkins and H. Allender, D336085), four databases were consulted for poisoning incident data. These include: OPP Incident Data System (IDS), Poison Control Centers (PCC), California Department of Pesticide Regulation, and National Institute of Occupational Safety and Health's Sentinel Event Notification System for Occupational Risks (NIOSH SENSOR). The summary findings from the incident report for the period 1993 to 2005 for naphthalene are:

- Naphthalene produces a higher proportion of acutely toxic incidents requiring medical attention when compared to the composite average of all other pesticides. There is a pattern of statistically significant results in cases seen in a health care facility. This pattern observed in the combined population (occupational, non-occupational, children) is largely due to the frequency and severity of pesticide poisoning among children less than 6 years;
- Exposure to children is much higher than a typical pesticide;
- Naphthalene PCC data show average results of about 11,647 exposures/year, 133 symptomatic cases/year, and 310 cases/year seen in a heath care facility;
- No apparent annual trend is evident in the 13 year-span of data collected; and
- NIOSH/SENSOR data indicate that indoor uses of naphthalene are responsible for a large number of cases.

Recommendations from the incident report for residential naphthalene use are as follows:

- In order to prevent exposures to children, actions restricting the access to the active ingredient should be taken. This could include packaging changes and other limitations to block children from coming into contact with the active ingredient. Note: This will not address inhalation concerns.

1.4 Summary of Use Patterns, Formulations, and Application Methods

Uses

Naphthalene is used as a moth treatment for the protection of woolen clothing and as an animal repellant against nuisance vertebrate pests. All registered products of naphthalene are intended for residential uses only. The moth treatment use is registered for indoor only and is labeled for treatment of indoor storage areas (containers, drawers, and storage closets). The animal repellant use is labeled for indoor (attics and wall voids) and outdoor (around the perimeter of domestic dwellings, ornamental gardens, flower beds, lawns, or any area to be protected such as wood piles, utility houses, barns, and trash cans) use.

Mode of Action and Targets Controlled

Naphthalene is a white, crystalline solid which volatilizes to create a characteristic odor. In a sealed container, naphthalene vapors build up to levels toxic to both the adult and larval forms of many moths destructive to wool clothing. In addition, naphthalene's odor can be used to repel vertebrate animals.

Application Rates, Formulation Types, and Percent Active Ingredient

Naphthalene products for use within the home are formulated as mothballs or flakes, while outdoor products are formulated as dusts, flakes, and granules. Percent active ingredient of indoor-use products range from 99.7-100%, and from 7-99.9% for outdoor-use products.

Table 3 summarizes registered naphthalene products by formulation, use site, formulation, percent active ingredient, and application rate.

Table 3. Summary of Registered Naphthalene Uses

Indoor Use				
Product	**Use Site**	**Formulation**	**% A.I.**	**App. Rate for the Area to be Treated**
ENOZ® Old Fashioned Mothballs (1475-74)	Indoor storage areas (containers and storage closets)	Mothball	99.95	1 ounce per 3 ft^3 - 0.25 lb ai / Average Garment Bag (12 ft^3) 0.33 lb ai / Large Trunk (15 ft^3) 1 lb ai / Small Closet (50 ft^3)
ENOZ® Old Fashioned Moth Flakes (1475-75)	Indoor storage areas (containers and storage closets)	Flake	99.95	1 ounce per 3 ft^3 - 0.25 lb ai / Average Garment Bag (12 ft^3) 0.33 lb ai / Large Trunk (15 ft^3) 1 lb ai / Small Closet (50 ft^3)
ENOZ® Cedar Pine Mothballs (1475-120)	Indoor storage areas (containers and storage closets)	Mothball	99.85	1 ounce per 3 ft^3 - 0.25 lb ai / Average Garment Bag (12 ft^3) 0.33 lb ai / Large Trunk (15 ft^3) 1 lb ai / Small Closet (50 ft^3)
Chaperone Squirrel and Bat Repellant (2724-685)	Attics and wall voids and indoor storage areas (containers and storage closets)	Flake	100	1 pound per 400 ft^3 1 ounce per 3 ft^3 - 0.25 lb ai / Average Garment Bag (12 ft^3) 0.33 lb ai / Large Trunk (15 ft^3)

Table 3. Summary of Registered Naphthalene Uses				
Indoor Use				
Product	**Use Site**	**Formulation**	**% A.I.**	**App. Rate for the Area to be Treated**
				1 lb ai / Small Closet (50 ft^3)
Dr. T's Rabbit, Squirrel, Bat & Bird Repellant (58630-2)	Attics and wall voids	Flake	99.95	1 pound per 400 ft^3
I-Ching Naphthalene Moth Balls (80305-1)	Indoor storage areas (containers and storage closets)	Mothball	99.9	1 ounce per 3 ft^3 - 0.25 lb ai / Average Garment Bag (12 ft^3) 0.33 lb ai / Large Trunk (15 ft^3) 1 lb ai / Small Closet (50 ft^3)
IMS Old Fashioned Moth Balls (81433-6)	Indoor storage areas (containers and storage closets)	Mothball	99.95	1.5 ounces per 3 ft^3 - 0.37 lb ai / Average Garment Bag (12 ft^3) 0.36 lb ai / Large Trunk (15 ft^3) 1.1 lb ai / Small Closet (50 ft^3)
Moth Avoid Brand Traditional Moth Balls (83424-2)	Indoor storage areas (containers and storage closets)	Mothball	99.7	1 ounce per 3 ft^3 - 0.25 lb ai / Average Garment Bag (12 ft^3) 0.33 lb ai / Large Trunk (15 ft^3) 1 lb ai / Small Closet (50 ft^3)
Outdoor Use				
F&B Rabbit and Dog Chaser (4-465)	Soil treatment on ornamental plants, paved areas	Dust	15	0.45 lb ai/ treated area (3 lb container) (assuming entire contents used to treat area)
ENOZ® Skat! (1475-146)	Around the perimeter of ornamental plants	Flake	99.45	2.5 lb ai/ treated area (2.5 lb container) (assuming entire contents used to treat area)
Dr. T's Snake-A-Way Snake Repellant (58630-1)	Around the perimeter of domestic dwellings (outdoors), wood piles, utility houses, barns, trash cans, flower beds, and gardens	Granule	7	0.28 lb ai/treated area (4 lb container) 2 lb ai/ treated area (28 lb container) (assuming entire contents used to treat area)
Dr. T's Rabbit, Squirrel, Bat & Bird Repellant (58630-2)	Around the perimeter of ornamental plants	Flake	99.95	4 lb ai/ treated area (4 lb container) 24 lb ai/ treated area (24 lb container) (assuming entire contents used to treat area)

Timing of Applications

Registered labels for indoor, moth treatment use recommend keeping the product in an airtight space for a minimum of seven days. Re-treatment is recommended when the mothballs have dissipated. Since moths are active all year, there is the potential for continual treatment indoors. One moth control label recommends re-treatment twice per year. Re-treatment for indoor/outdoor repellant uses are recommended as needed to maintain odor intensity. Hot weather, wind, and rain may diminish the effectiveness of the product and necessitate re-treatment.

Application Methods

Naphthalene treatments for indoor moth treatment use and indoor/outdoor repellant use are labeled for application by hand.

2.0 Residential Exposure and Risk

HED has determined that there is a potential for exposure in residential settings during the application process for homeowners who purchase and use products containing naphthalene. There is also a potential for postapplication exposure from inhabiting indoor areas previously treated with naphthalene, as well as, incidental toddler ingestion of formulations used for indoor/outdoor treatments. The exposure and risk for homeowners applying naphthalene in the residential environment is discussed in section 2.1.

A direct comparison of human exposure study results and points of departure (LOAEL/NOAEL) from animal studies were estimated for adult and toddler exposure from accessing (i.e., dresser drawers and closets) and inhabiting indoor areas previously treated with naphthalene and are discussed in Section 2.2. Exposure and risk from toddler incidental ingestion of naphthalene formulations used for indoor/outdoor treatments is discussed in section 2.3.

2.1 Residential Handler Noncancer Exposure and Risk

The Agency uses the term "handlers" to describe those individuals who are involved in the pesticide application process. The Agency believes that there are distinct tasks related to applications and that exposures can vary depending on the specifics of each task. Job requirements (e.g., the amount of chemical to be used in an application), the method of application, and the target being treated can cause exposure levels to differ in a manner specific to each application event.

HED has determined that there is potential for exposure in residential settings during the application process for homeowners who purchase and use naphthalene-containing products. According to label instructions, homeowners must physically place naphthalene formulations into indoor storage areas (containers and storage closets) and around the perimeter of outdoor areas to be protected. HED anticipates handler dermal exposure during the application process; however, appropriate inhalation handler exposure data are not available to assess this scenario and, therefore, only dermal exposure was assessed.

Data for acute (15 minute) exposure were used in conjunction with animal studies to derive a direct comparison for postapplication inhalation exposure to areas treated with naphthalene. HED assumes that the acute postapplication inhalation assessment is protective for handler inhalation exposure since measured concentrations of naphthalene would likely be greater due to the time allotted in the exposure study (4-6 days) for the product to accumulate in the enclosed areas that were accessed.

Applications of naphthalene are expected to be short-term in nature due to the intermittent uses associated with the residential products. As a result, no intermediate-term or long-term assessments were assessed for handlers.

2.1.1 Residential Handler Noncancer Exposure and Risk Estimates

The residential handler exposure and noncancer risk calculations are presented in this section. Noncancer risks were calculated using the MOE as described in Appendix A, Section B. The following scenarios were assessed for handlers of naphthalene:

1. Hand application of naphthalene formulations for indoor moth treatments
2. Hand application of naphthalene formulations for indoor/outdoor animal repellent treatments

Data Sources

Exposure data for acute and short-term residential handler exposure durations were taken from the study, "Estimation of Homeowner Exposure to LX1298-01 (Naphthalene) Resulting from Simulated Residential Use as an Insect Repellent (MRID 43716501)." Dermal handler exposure data was derived from the result of monitoring a person weighing out and placing mothballs in a closet and dresser at three different locations.

A summary of the exposure study is provided below with dermal handler results presented in Table 4. The following is a summary of naphthalene exposure study, including the handler dermal and indoor air concentration data sources used within for quantitative risk assessment purposes. The summary also encompasses the inhalation portion of the exposure study with results presented in Tables 5 and 6.

MRID 43716501: Estimation of Homeowner Exposure to LX1298-01 (Naphthalene) Resulting from Simulated Residential Use as an Insect Repellent. Review: W. Britton, D340008

LX1298-01, a mothball formulation, containing 99.5% (0.995 g ai/g product) of the active ingredient (ai) naphthalene, was applied as an insect repellent by placing mothballs in a closet and a dresser drawer at the maximum application rate of 1.0 lb ai/50 ft^3 in designated bedrooms at three different locations near Valdosta, Georgia. The person weighing out the mothballs and placing them in the closet and dresser drawer at each location was monitored for inhalation exposure and dermal exposure of naphthalene to the hands. After the application, the treated room was closed and not entered for three days. At the beginning of the fourth day, indoor air concentration sampling at three locations within the treated room was monitored continuously for 8-hour intervals for three consecutive days. During a 12-hour period of each sampling day (4, 5 and 6 days after treatment (DAT)) a worker wearing a personal air sampling device (two-stage charcoal filter cartridge) entered the treated room every two hours for a 15-minute sampling duration to simulate a homeowner's or worker's daily activities in the room.

Indoor air concentration samples were also collected at three, 15-minute intervals during this same 12-hour period inside the treated closet and inside the treated drawer. Dermal exposure to the applicator was determined by analysis of gloves worn when weighing out and applying the test product. The results of inhalation exposure (15 minute) to the applicator were not written into the Study Report.

The overall average naphthalene applicator hand exposure (dermal) was 0.053 mg/lb ai, as summarized in Table 4. Post-application inhalation exposure and air concentration was monitored on Days 4, 5 and 6 after the application. The overall average post-application inhalation exposures (daily activities) for Days 4, 5 and 6 were 0.77 mg /m^3, 0.87 mg /m^3 and 0.90 mg /m^3, respectively, as summarized in Table 5. Results of the air monitoring took place within the treated zones (dresser drawer and closed closet); however, the Study Author only provided naphthalene air concentrations for Hour 0, Hours 4-8, and Hour 12. These concentrations ranged for all three trials from 2.37 to 10.3 mg/m^3 in the dresser drawer and from 1.49 to 12.29 mg/m^3 in the closet for all three days. The air sampling devices monitoring the areas outside the treated zone were placed just outside the closet, on top of the dresser and adjacent to the head of the bed. The average 24-hour naphthalene air concentration on top of the dresser at all three test sites on Days 4, 5 and 6 ranged from 0.39 to 0.89 mg/m^3. The average 24-hour naphthalene air concentration adjacent to the closet at all three test sites on Days 4, 5 and 6 ranged from 0.43 to 0.81 mg/m^3. The average 24-hour naphthalene air concentration at the head of the bed at all three test sites on Days 4, 5 and 6 ranged from 0.39 to 0.86 mg/m^3. A summary of all average 24-hour air concentrations are summarized in Table 6.

Table 4. Applicator Hand Exposure (mg/cm^2) Based on Cotton Glove Dosimeters			
Trial	Naphthalene Residue - Both Hands (mg/lb ai)	Contact Surface Area of Both Gloves (cm^2)	Naphthalene Hand Exposure (mg/cm^2)
92-298-01-21H-02	0.00807	407	1.98E-05
92-298-01-21H-03	0.104	407	2.56E-04
92-298-01-21H-04	0.0465	407	1.14E-04
Mean	**0.053**	407	1.30E-04

Table 5. Post-Application Inhalation Exposure (Acute) – (mg/m^3)			
Site #	Average Day 4 Air Concentration (mg/m^3)	Average Day 5 Air Concentration (mg/m^3)	Average Day 6 Air Concentration (mg/m^3)
92-298-01-21H-02	0.49	0.48	0.63
92-298-01-21H-03	0.85	1.1	1.3
92-298-01-21H-04	0.98	1.0	0.74
Overall Average	0.77	0.87	0.90

Mean	**0.85 mg/m^3**

Table 6. Postapplication Air Concentration of Naphthalene (Short-Term) - (mg/m^3)									
Hours	Average Day 4 Naphthalene Air Concentration Adjacent to Dresser Drawer (mg/m^3)	Average Day 5 Naphthalene Air Concentration Adjacent to Dresser Drawer (mg/m^3)	Average Day 6 Naphthalene Air Concentration Adjacent to Dresser Drawer (mg/m^3)	Average Day 4 Naphthalene Air Concentration Adjacent to Closet (mg/m^3)	Average Day 5 Naphthalene Air Concentration Adjacent to Closet (mg/m^3)	Average Day 6 Naphthalene Air Concentration Adjacent to Closet (mg/m^3)	Average Day 4 Naphthalene Air Concentration Adjacent to Bed (mg/m^3)	Average Day 5 Naphthalene Air Concentration Adjacent to Bed (mg/m^3)	Average Day 6 Naphthalene Air Concentration Adjacent to Bed (mg/m^3)
92-298-01-21H-02									
0 – 8	0.48	0.41	0.36	0.50	0.44	0.64	0.52	0.37	0.64
8 – 16	0.45	0.50	0.69	0.53	0.53	0.72	0.39	0.46	0.66
16 - 24	0.24	0.52	0.92	0.27	0.61	0.81	0.25	0.58	0.83
Avg.	0.39	0.48	0.66	0.43	0.53	0.72	0.39	0.47	0.71
92-298-01-21H-03									
0 – 8	0.76	0.93	1.10	0.73	0.86	0.98	0.68	0.87	1.03
8 – 16	0.94	1.05	1.02	0.95	0.95	0.91	0.99	1.05	0.98
16 - 24	0.73	0.66	0.55	0.71	0.60	0.54	0.58	0.66	0.57
Avg.	0.81	0.88	0.89	0.80	0.80	0.81	0.75	0.86	0.86
92-298-01-21H-04									
0 – 8	0.65	0.64	0.57	0.73	0.91	0.63	0.65	0.60	0.56
8 – 16	0.71	0.63	0.47	0.92	0.69	0.56	0.72	0.54	0.43
16 - 24	0.55	0.49	0.50	0.77	0.67	0.62	0.52	0.47	0.41
Avg.	0.64	0.59	0.51	0.81	0.76	0.60	0.63	0.54	0.47
Day/Site Avg.	0.61	0.65	0.69	0.68	0.70	0.71	0.59	0.62	0.68

Geometric Mean	**0.66 mg/m^3**

Assumptions Regarding Residential Applicator Exposure

- Homeowner handlers are expected to complete all tasks associated with the use of a pesticide product (e.g., application);
- The maximum application rate of 14.4 lb ai/ treated area was used for indoor moth treatment risk calculations, assuming that 3 closets (600 ft^3) and 3 dresser drawers (90 ft^3) are treated at 0.0625 lb ai/ 3 ft^3;
- The maximum application rate of 24 lb ai/ treated area was used for outdoor repellant treatment risk calculation, assuming the entire contents of a 24 lb container is used for treatment at 99.95% ai;
- A body weight of 70kg was assumed because the endpoint is not gender specific;
- Dermal absorption is assumed to be 100%, which is representative of a conservative assumption of risk; and
- Areas for chemical used in the risk assessment are based on Agency guidance specific to residential use patterns.

Risk Summary

Table 7 presents the quantitative risks associated with both scenarios considered for the residential handler noncancer assessment. Both dermal handler scenarios assessed resulted in MOEs > 100 and, therefore, are not of concern to HED.

Table 7. Naphthalene Noncancer Risks Attributable to Homeowner Handler Exposures

Exposure Scenario	Total Applied (lb ai)	Daily Exposure (mg/ lb ai)	MOE (LOC = 100)
1 - Apply Moth Treatment by Hand	14.4	0.053	28000
2 – Apply Animal Repellant Treatment by Hand	24	0.053	17000

2.1.2 Residential Handler Cancer Exposure and Risk

Residential handler cancer exposure and risk estimates were not assessed due to the uncertainty of whether naphthalene poses a human cancer concern at ambient or environmental levels of exposure because of potential species differences in rates of metabolism leading to its toxicity.

2.2 Residential Postapplication Exposure and Risks

The Agency uses the term “postapplication” to describe exposures to individuals that occur as a result of working in an environment that has been previously treated with a pesticide (also referred to as re-entry exposure). HED has determined that there is potential for adult exposure from accessing treated areas and adult and toddler exposure

from inhabiting homes previously treated with naphthalene, as well as, toddler exposure from the episodic (incidental) ingestion of formulations used for indoor/outdoor animal repellency.

2.2.1 Residential Postapplication Inhalation Exposure and Risk

As previously described, naphthalene applications are made indoors for moth treatments. While labels specify that treated indoor areas (i.e., containers, dresser drawers, and storage closets) should be airtight to be effective, HED anticipates that naphthalene will volatilize and be inhaled by adults accessing treated areas (acute exposure) and by adults and toddlers that inhabit treated areas exposed to ambient concentrations of naphthalene (short-, intermediate-, and long-term exposures).

Since the data available to date indicate that rodents are more susceptible to the respiratory toxicity of naphthalene, the use of rodents as a model without the appropriate species scaling accounting for species differences in dosimetry would likely result in an inaccurate estimation of human risk. Therefore, rather than quantifying inhalation risks to humans, the levels of ambient naphthalene measured in the human exposure study were compared directly to the levels resulting in a 1) no adverse effects in the rodent studies (NOAELs) and 2) a toxic effect in rodents (LOAELs). This comparison provides a sense of the difference between actual naphthalene concentrations that a human may encounter and the doses which elicit either no adverse response or a toxic response in rodents.

In lieu of an appropriate inhalation study for comparison to anticipated acute (15 minute) exposures, HED used the short-term inhalation endpoint. The pairing of an acute inhalation exposure with a short-term toxicity endpoint is likely to be conservative and protective of human health for this route of exposure. HED used appropriate endpoints from short-, intermediate-, and long-term inhalation toxicity studies to estimate risks for individuals inhabiting treated homes.

2.2.2 Residential Postapplication Inhalation Exposure and Risk Estimates

The residential indoor postapplication inhalation exposure comparisons (human exposure study results and points of departure (LOAEL/NOAEL) from animal studies) are presented in this section. The following scenarios were assessed:

Adult

1. Acute inhalation from accessing treated areas

Adult/Toddler

2. Short-/intermediate-/long-term inhalation from inhabiting treated area

Data Sources

Exposure data for acute and short-term residential postapplication inhalation was taken from the exposure study, "Estimation of Homeowner Exposure to LX1298-01 (Naphthalene) Resulting from Simulated Residential Use as an Insect Repellent (MRID 43716501)." Inhalation exposure data was derived for accessing treated areas (15-minute duration) from the results of air sampling of an individual accessing treated a treated drawer and closet, and performing household tasks (i.e., dusting, sitting in a chair, etc) in a treated room. A summary of the exposure study data is provided in Table 6. Inhalation exposure data was derived for inhabiting a treated area (short-term) was derived from the results of indoor air sampling in enclosed rooms in 3 different locations. Air samples were collected continuously (in 8-hour intervals) for 3 consecutive days from devices surrounding treated closets, dresser drawers, and beds. A summary of the exposure study data is provided in Table 5.

Results of the registrant-submitted exposure study indicate that indoor air concentrations of naphthalene range between 0.85 and 0.66 mg/m^3 for acute and short-term durations of exposure, respectively. These results fall well within the range (0.23 – 7.5 mg/m^3) of naphthalene concentrations observed in indoor air from mothball sources (acute-/short-term duration) in the open literature and, therefore, are not likely to underestimate naphthalene exposure for acute and short-term durations. The following open literature sources were identified for comparison:

- 0.35 mg/m^3 in a cupboard containing mothballs (Lau et al., 1995);
- 7.5 mg/m^3 in a closet, 1.2 in a bedroom, 0.90 mg/m^3 in a living room, 0.35 mg/m^3 in a garage, and 0.23 mg/m^3 outdoors of a home which had closets treated liberally with mothballs (Gammage and Matthews, 1987); and
- 0.68 mg/m^3 from a living room of a home containing mothballs (Hawthorne et al., 1985).

HED determined that the exposure data used to assess acute and short-term exposure to indoor postapplication inhalation exposure to naphthalene from mothball sources was not appropriate to assess intermediate- and long-term exposure durations. As described previously, naphthalene volatilizes into the treated area and it is assumed that adults and toddlers who inhabit these areas are potentially exposed. Based upon label application timing recommendations for moth control, it is likely that re-treatment could occur, at a minimum, once every 1-6 months. The continued volatilization of naphthalene over time results in a reduced concentration of the chemical and, likewise, reduced potential for inhalation exposure. Therefore, the exposure data used for the acute and short-term duration likely overestimates the concentration of naphthalene available for inhalation over longer term durations. HED was unable to identify an exposure data source which was appropriate to assess intermediate- and long-term exposure to naphthalene from a mothball source. Exposure data was extrapolated, however, from a study in the open literature which observed indoor ambient concentrations of naphthalene in 24 homes. This study is not duration-specific, nor does naphthalene originate from a mothball

source; however, it has been identified as the best data source to account for naphthalene volatilization over time.

The following is a summary of the exposure study, "Polycyclic Aromatic Hydrocarbon Exposure of Children in Low-Income Families," with indoor air naphthalene concentration results presented in Table 8.

J. Chuang et al. Polycyclic Aromatic Hydrocarbon Exposure of Children in Low-Income Families. ***Journal of Exposure Analysis and Environmental Epidemiology.*** **(1999) 2, pp. 85-98.**

Humans can be exposed to polycyclic aromatic hydrocarbons (PAHs) by inhaling contaminated air, by ingesting tainted food, by non-dietary ingestion of contaminated dust or soil, or by dermal ingestion. Children of inner-city families are likely exposed to greater levels of PAHs than children in rural areas based upon household proximity to heavier traffic and more industrial sources. A two-home pilot study (1994) and a nine-home winter and summer study (1995) were conducted in Durham and the NC Piedmont area with the following objectives: to establish methods for measuring total PAH exposure of children in low-income families, to estimate the PAH exposures to these children, and to estimate the relative importance of the environmental pathways for PAH exposure. In each study multimedia samples were collected and analyzed for PAH or hydroxy-PAH. For the purposes of this risk assessment, HED used only the resulting concentrations of PAH (specifically, naphthalene) of indoor, ambient air observed in the 24 low-income homes sampled.

A total of 14 inner city and 10 rural homes were sampled in the study. All inner city homes were located in downtown Durham, NC, close to either freeways and/or busy streets. The rural homes were located away from heavy traffic areas. Homes were recruited on the basis of the presence of an adult and a preschool, toilet-trained child living at home; unvented combustion space heating; and family income below the US Department of Health and Human Services (DHHS) poverty guidelines. The heating systems of the 24 homes were noted and included central electric and gas heating, kerosene heaters, open-flame gas heaters, and fireplaces. Cooking appliances were electric and gas. For the two-home pilot study conducted in Durham, the field sampling activities were completed in a 3-day period. One home was occupied by nonsmokers, the other by smokers. The nine-home study was carried out using a revised study protocol that monitored two home in 2 days and the summer studies monitored three homes in 2 days. Five inner city and four rural homes inhabited by nonsmokers were recruited for the winter study. Nine nonsmokers' (five inner city and four rural) and four smokers homes (two inner city and two rural) were recruited for the summer study.

In order to assess indoor concentrations of PAHs, indoor air samplers and real-time PAH monitors were installed and a capillary adsorption tube sampler (CATS) was deployed to measure air exchange rate. Outdoor air samples, as well as occupant food and urine sample collection took place, but are not of significance to the current risk assessment. The indoor sampler was placed in either the living room or the family room and was

sampled for a 24 hour period within each home. The PAH in air were collected by passing air at 20 liters/minute through a sampling cartridge containing a quartz fiber filter and XAD-2 resin in series. After sampling, the filter and XAD-2 samples were wrapped in clean aluminum foil, placed in a clean container, sealed, and stored in a freezer until being sent back to the laboratory for analysis. The flow rate of each sampler was checked and recorded at the initiation and at the conclusion of the air sampling period.

The mean, standard deviation, minimum and maximum values of naphthalene concentrations in indoor air samples from the 24 low-income homes are summarized in Table 8. Of all PAH concentrations resulting, naphthalene was the most abundant target PAH identified. Results from the overall study including indoor and outdoor air, and food and urine samples indicated that inhalation is the most important pathway for adults' and childrens' exposure to total PAH and that levels of PAH in indoor air were higher than in corresponding outdoor air in most households. Due to the uncertainty associated with the use of an exposure study which is not duration- or use-specific, HED selected the most conservative exposure value (i.e., maximum concentration observed) for risk assessment purposes.

Table 8. Summary of Naphthalene Concentrations (mg/m^3) in Indoor Air of the 24 Low-Income Homes

Mean	Standard Deviation	Minimum	Maximum
0.0022	0.0019	0.00033	**0.0097**

Assumptions Regarding Postapplication Inhalation

- HED assumes that an individual could access treated areas (i.e., containers, dresser drawers, and storage closets) for an exposure duration of 15 minutes; and
- HED assumes that an individual could be exposed continually within their home (i.e., 24 hours per day) for short-/intermediate-/long-term duration.

Risk Summary

A comparison was performed of points of departure (LOAEL/NOAEL) from animal studies resulting in toxic outcomes in the rodents and human exposure studies. For acute- and short-term exposure scenarios, the results of an exposure study, "Estimation of Homeowner Exposure to LX1298-01 (Naphthalene) Resulting from Simulated Residential Use as an Insect Repellent (MRID 43716501)" were used. The 15 minute (acute) and 24 hour (short-term) samples resulted in average concentrations of 0.85 and 0.66 mg/m^3 of naphthalene, respectively. These values were compared directly to the animal LOAEL (10 ppm or 52 mg/m^3) and NOAEL (3 ppm or 16 mg/m^3) selected for acute and short-term exposure durations.

Acute and short-term exposures to naphthalene in residences are 60X and 80X, respectively, below the animal dose (LOAEL) resulting in respiratory toxicity (olfactory epithelium lesions) and 20X and 30X below the animal dose (NOAEL), respectively.

For intermediate- and long-term durations, the results of an exposure study, "Polycyclic Aromatic Hydrocarbon Exposure of Children in Low-Income Families (Chuang et al., 1999) were utilized." The indoor ambient samples which pertain to the air concentrations of naphthalene resulted in a maximum level of 0.0097 mg/m^3. This exposure value was directly compared to the animal LOAEL for olfactory epithelium lesions selected for intermediate- (2 ppm or 10 mg/m^3 identified in a nose-only study) and long-term (10 ppm or 52 mg/m^3 identified in an exposure chamber study) durations, as well as, the NOAEL selected for the intermediate-term duration (1 ppm or 5.2 mg/m^3). A NOAEL was not identified for long-term inhalation exposure.

Intermediate- and long-term exposures to naphthalene in residences are 1000X and 5400X, respectively, below the animal dose (LOAEL) resulting in respiratory toxicity (olfactory epithelium lesions) and intermediate-term exposure is 540X below the animal dose (NOAEL). The long-term duration was not assessed since a NOAEL was not identified.

2.2.3 Residential Postapplication Cancer Exposure and Risk

Residential postapplication cancer exposure and risk estimates were not assessed due to the uncertainty of whether naphthalene poses a human cancer concern at ambient or environmental levels of exposure because of potential species differences in rates of metabolism leading to its toxicity.

2.2.4 Residential Postapplication Episodic Ingestion Exposure and Risk

As previously described, naphthalene applications are made indoors for moth treatments and indoors/outdoors for animal repellency. HED anticipates that toddlers could come in contact with naphthalene formulations inside a treated home or in treated outdoor areas. While labels specify that indoor moth treatments be made in airtight containers, it is assumed that a toddler could potentially access these areas and ingest naphthalene products. Outdoor applications of naphthalene are labeled for use around the perimeter of areas to be protected. While a toddler could potentially access outdoor treated areas, HED believes that toddler episodic (incidental) ingestion exposure is more likely to occur indoors. Results of the incident report support this belief (D336085). In order to assess postapplication episodic (incidental) ingestion of naphthalene, a potential dose was derived from the assumption of a toddler ingesting one mothball. HED also estimated the amount of the mothball that could be ingested by a toddler to result in an MOE = 100.

Inhalation and episodic (incidental) ingestion routes of exposure were not combined for toddlers in order to differentiate the occurrence of a discrete accidental event (assessed to give a worst-case estimate of risk) from the expected daily exposure via the inhalation route. It would not be appropriate to combine episodic exposure for comparison to a short- (or longer) term endpoint.

2.2.5 Residential Postapplication Episodic Ingestion Exposure and Risk Estimates

The residential indoor/outdoor postapplication episodic (incidental) ingestion exposure risk calculations are presented in this section. Noncancer risks were calculated using the approach described in the *Standard Operating Procedures (SOPs) for Residential Exposure Assessments, Section: 2.3.1, Postapplication – Incidental Nondietary Ingestion*. SOPs were used to derive the potential dose rate of a toddler ingesting one mothball, which was then compared to the incidental oral endpoint to calculate an MOE. In addition, HED estimated the amount of a single mothball that a toddler could ingest to result in an MOE = 100. Appendix A, Section C presents the algorithms used to determine these values.

The following scenario was assessed for episodic (incidental) ingestion of naphthalene formulations:

Toddler

1. Episodic (incidental) ingestion of naphthalene formulation from indoor/outdoor exposure

Assumptions Regarding Toddler Episodic Ingestion

- One mothball weighs 2.35 grams (or 2350 mg) and the maximum labeled percent active ingredient is 99.95%;
- For the purposes of this risk assessment, HED is assuming that a child is only ingesting one mothball; and
- 3 year old toddlers are expected to weigh 15 kg.

Episodic Ingestion Summary

Toddler episodic (incidental) ingestion of one naphthalene mothball results in an MOE < 100 and, therefore, is of concern to HED. An oral dose of 0.5 mg/kg/day would be required to result in an MOE = 100. This dose is equivalent to toddler incidental ingestion of 0.32% of one mothball (7.5 of 2350 mg).

References

1. U.S. EPA 2007. Naphthalene SMART Meeting, March 28, 2007

2. U.S. EPA 1997. "Draft Standard Operating Procedures for Residential Exposure Assessments" U.S. Environmental Protection Agency, Office of Pesticide Programs. December 19, 1997.

3. EPA MRID 43716501 – "Estimation of Homeowner Exposure to LX1298-01 (Naphthalene) Resulting from Simulated Residential Use as an Insect Repellent," T. Bill Waggoner, October 7, 1994.

4. W. Britton, 2007. Naphthalene: Review of "Estimation of Homeowner Exposure to

LX1298-01 (Naphthalene) Resulting from Simulated Residential Use as an Insect Repellent (MRID 43716501)" (D340008) June 21, 2007.

5. J. Chuang et al. Polycyclic Aromatic Hydrocarbon Exposure of Children in Low-Income Families. *Journal of Exposure Analysis and Environmental Epidemiology*. (1999) 2, pp. 85-98.

6. M. Hawkins and H. Allender, 2007. Review of Naphthalene Incident Reports (D336085) June 25, 2007.

APPENDIX A

STANDARD FORMULAS USED FOR CALCULATING RESIDENTIAL EXPOSURES TO NAPHTHALENE

A. Introduction

This section summarizes the algorithms used to calculate risk estimates from residential exposures to naphthalene. These formulas and a basic description of how they are used were taken from Reference 2. These references also contain more detailed information on the rationale behind these formulas. Only those formulas that are pertinent to naphthalene exposures are discussed in this document.

B. Residential Applicator Exposure and Risk

The basic rationale for this algorithm is that the daily exposure is the product of the amount of active ingredient (ai) handled per day times a unit exposure value. The amount of ai handled per day is the product of the application rate times the area treated. For example, if 0.0625 lbs of naphthalene are required to treat 3 ft^3, and 3 closets and 3 dressers drawers total 690 ft^3, then the amount of naphthalene handled would be 14.4 lbs that day. The unit exposure value is the amount of exposure that results from handling a given amount of active ingredient by a certain method. The unit exposure value, 0.053 mg/lb ai, used for dermal applicator exposure of naphthalene was derived from the previously described exposure study (MRID 43716501). In this example, the daily exposure would be 14.4 lbs ai handled multiplied by 0.053 mg unit exposure per pound of ai handled which equals 0.763 mg per day. The daily absorbed dose (mg/kg BW) is calculated from the exposure by multiplying the exposures times an absorption factor (1.0) and dividing the result by the body weight (70 kg). In this example the daily dose would be (0.763 mg/day *1.0)/ 70 kg which would equal 0.011 mg/kg/day. An MOE is calculated by dividing the endpoint for dermal exposure (300 mg/kg/day) by the daily dose (0.011 mg/kg/day), which would equal 28,000.

Daily dermal exposure is calculated**:**

Daily dermal exposure	=	Unit exposure	x	Application rate	x	Area Treated
(mg/day)		(mg/ lb ai)		(lb ai/ ft^3)		(ft^3/day)

Where:

Unit exposure =	normalized exposure value (mg exposure per pound ai handled) derived from exposure study (MRID 43716501) (0.053 mg/lb ai)
Application rate =	normalized application rate (0.625 lb ai/ ft^3)
Area treated =	normalized application area (690 ft^3/day)

Absorbed Daily Dose is calculated**:**

Absorbed daily dermal dose	=	(Daily dermal exposure	x	absorption factor)	/	body weight
(mg/kg/day)		(mg/day)		(unitless)		(kg)

MOE Calculations for the Dermal Pathway:

The MOEs are calculated for each individual pathway using the MOE formula:

MOE (unitless) = NOAEL / (Dose /BW)

Where:

NOAEL = 300 mg/kg/day (short-term)
Dose = 0.011 mg/kg/day
BW = 70 kg (adult)

The level of concern for residential handlers is an MOE = 100. Scenarios with MOEs ≥ 100 are not of concern to HED for the residential population.

C. Residential Postapplication Episodic Ingestion Exposure and Risk

The formula used to estimate residential postapplication episodic (incidental) ingestion in this instance is based upon the assumption that a toddler accidentally ingests an entire mothball. In order to assess the risk of this exposure route, a dose is estimated from ingestion and compared to the incidental oral endpoint. A potential dose rate (PDR) is calculated using the ingestion rate (g/day) multiplied by the fraction of ai in the mothball (unitless) and a conversion factor (1000 mg/g). For example, a mothball weighs 2.35 grams and contains 99.95% active ingredient. Multiplying all the factors together gives a PDR of 2349 mg/day. The PDR is normalized by body weight of the toddler (15 kg), which gives a value of 156.6 mg/day. The normalized PDR value is then used in conjunction with the endpoint for incidental oral exposure (50 mg/kg/day) to give an MOE.

The PDR value was calculated using the following equation:

PDR = IgR * F * CF1

PDR = 2.35 g/day x 0.9995 x 1,000 mg/g
PDR = 2349 mg/day

The PDR_{norm} value was then calculated using the following equation:

$PDR_{norm} = PDR / BW$

$PDR_{norm} = (2349 \text{ mg/day}) / (15 \text{ kg})$
$PDR_{norm} = 156.6 \text{ mg/kg/day}$

The MOEs for episodic ingestion are calculated for using the MOE formula:

MOE (unitless) = NOAEL / (Dose)

Where:

NOAEL = 50 mg/kg/day (short-term)
Dose = 156.6 mg/kg/day