HUMAN PESTICIDE EXPOSURE ASSESSMENT

HYDRAMETHYLNON

(An Insecticide for the Control of Ants and Cockroaches Primarily in Nonfood Areas in Domestic Dwellings and Commercial Establishments)

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HS-1804 February 26, 2004

ABSTRACT

Hydramethylnon (CAS name: tetrahydro-5,5-dimethyl-2(1*H*)-pyrimidinone [3-[4-(trifluoromethyl)phenyl]-1-[2-[4-(trifluoromethyl)phenyl]ethenyl]-2-propenylidene]hydrazone) is a trifluoromethyl aminohydrazone insecticide of low acute mammalian toxicity. It is a slow activating stomach toxicant registered for the control of a variety of ants (including fire ants) and cockroaches, primarily in noncrop and nonfood areas. From 1982 through 1998, a total of 2 illnesses/injuries occurring in California were reported to have been associated with exposure to hydramethylnon used alone, or used in combination with other pesticides. As of September 2001, 47 hydramethylnon products were actively registered in California, including the 4 allowed for use on container or field-grown ornamentals, non-bearing fruit, berries, and the like. Of the hydramethylnon active ingredient used in California today, more than 97% is for structural pest control. Despite this current use pattern, the present exposure assessment was performed to calculate the absorbed daily dosages (ADD) for (potential or actual) users and residents or bystanders of all groups, to the extent necessary. It is written to be an integral part (Volume 2) of the risk characterization document prepared by the Department of Pesticide Regulation for all legal uses of hydramethylnon. The toxicological endpoints for the risk assessment include developmental and male reproductive adverse effects. The best conservative estimate of (acute) ADD calculated for aerial or ground loaders working with hydramethylnon granules was 0.05 μg/kg BW/day. This was the highest calculated among the agricultural handlers. The highest ADD (from the dose range finder list) calculated for reentry exposure of fieldworkers, and for that of non-user residents as well, was 2.0 μg/kg BW/day; this was for individuals assumed to be involved in very high crop-contact or high exposure (post-application) activities. For homeowner users and non-agricultural handlers working in the industrial, institutional, or residential setting, the highest ADD observed was 0.24 μg/kg BW/day, that for pest control operators applying granules by (bare) hand. The results of two rat studies indicated that dermal absorption of hydramethylnon is likely to be less than 5% over a 10- or 24-hour exposure period. A review of the available animal metabolism studies revealed that once absorbed, hydramethylnon is excreted rapidly as unchanged parent compound (>70% of applied dose in 36 hours) primarily via the (rat) feces.

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I. INTRODUCTION

Hydramethylnon is a tri-fluoromethyl aminohydrazone insecticide of low acute mammalian toxicity. It is a slow activating stomach toxicant registered for the control of a variety of ants and cockroaches, primarily in noncrop and nonfood areas. Over the years, 62 products have been registered in California that contain hydramethylnon as the active ingredient (AI). As of September 2001, 47 hydramethylnon products were actively registered, including the 4 allowed for use on field-grown ornamentals, non-bearing fruit, berries, and the like. Of the hydramethylnon AI used in California today, more than 97% is for structural pest control. Despite this current use pattern showing little or no use in agricultural fields, all potential exposures from all legal uses were considered in this exposure assessment as common practice. This practice is meant to address potential use pattern changes. For example, red imported fire ants are known to inhabit agricultural fields. These pests, which have been observed in the southern part of California, may migrate to the agricultural regions.

Introduced as an insecticide by American Cyanamid Company, hydramethylnon was first registered with the U.S. Environmental Protection Agency (U.S. EPA, 1999) in August 1980. In April 1991, U.S. EPA issued a Phase 3 Data Call-In (DCI) to require further registration data on product chemistry, on environmental fate, on toxicology, and on worker exposure. In 1995, U.S. EPA issued additional DCIs to require the submission of data on foliar residue dissipation, on dermal passive dosimetry exposure, and on inhalation passive dosimetry exposure. American Cyanamid subsequently also committed to amend their product labels to comply with state restrictions dealing primarily with labeling requirements (as outlined in Section V of the RED mentioned below). Upon reviewing some of the DCI data and the new labels, U.S. EPA (1999) prepared a Reregistration Eligibility Decision (RED) document for hydramethylnon. Although U.S. EPA has not yet made a determination regarding the common mode or mechanism of toxicity of hydramethylnon, they have concluded that the residential and occupational exposures involved are minimal.

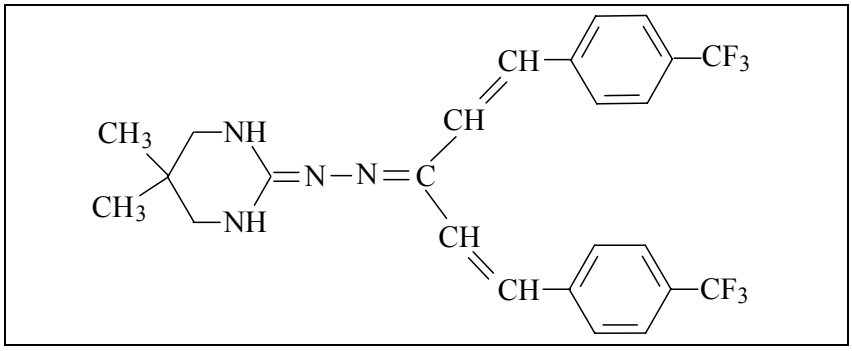
In spite of its relatively low acute toxicity observed in animals, hydramethylnon is currently among the Proposition 65 list of chemicals known to the state of California to cause cancer or reproductive toxicity. Hydramethylnon was first listed in California both as a developmental toxicant and as a male reproductive toxicant on March 5, 1999. According to the summary of toxicology data prepared by the Medical Toxicology Branch (MedTox) for hydramethylnon (Aldous, 1993), possible adverse effects were identified in chronic, oncogenicity, and reproduction studies. In part due to its low volatility, currently hydramethylnon is not included in the list of chemicals to be regulated by the Department of Pesticide Regulation (DPR) as toxic air contaminants.

A risk characterization document (RCD) is currently being prepared by DPR for all uses of hydramethylnon, partly in response to the insecticide's adverse developmental and male reproductive effects. The present human exposure assessment by the Worker Health and Safety Branch (WH&S) is written to be an integral part of this RCD.

II. EXPOSURE-RELATED FACTORS

1. Physical and Chemical Properties

Hydramethylnon (CAS name: tetrahydro-5,5-dimethyl-2(1*H*)-pyrimidinone [3-[4-(trifluoro-methyl)phenyl]-1-[2-[4-(trifluoromethyl)phenyl]ethenyl]-2-propenylidene]hydrazone); CAS Registry No. 67485-29-4; molecular formula $C_{25}H_{24}F_6N_4$; molecular weight 494.50) is a non-systemic insecticide. According to U.S. EPA (1999) and the open literature (e.g., Tomlin, 1994), technical grade hydramethylnon is a yellow to orange crystalline solid with a characteristic vegetable oil odor and a melting point of 189 – 191°C. It is insoluble in water (0.005 – 0.007 mg/L at 25°C), slightly to moderately soluble in alcohols, and soluble in acetone, chlorobenzene, and 1,2-dichloroethane. The vapor pressure is 2 x 10^{-8} mm of Hg at 25°C. The average partition coefficient (K_{ow}) of hydramethylnon between η-octanol and water was determined to be 27,965 (log K_{ow} = 4.45). It undergoes photolysis in sunlight. The following is the chemical structure of hydramethylnon:



2. Formulations and Label Uses

Technical hydramethylnon currently available in the United States is manufactured by American Cyanamid Company, under the trade name Amdro Technical Insecticide (EPA

Reg. No. 241-270). This product contains 95% AI and is intended only for use in the formulation of other end-use hydramethylnon insecticide products. As of September 2001, 47 hydramethylnon end-use products registered in California. These 47 end-use products were available in 4 formulations, as summarized in Table 1. The granular formulation may be applied via broadcast or to individual mounds for control of a variety of ants, including fire ants. Both the impregnated gel formulation and the tablet/cake/pellet type are ready-to-use (RTU) products intended to be indoor bait stations for the control of (primarily household) ants and cockroaches. Hydramethylnon is also used for the control of subterranean termites in a bait package that is sold to and only for use by certified Pest Control Operators (PCOs).

Table 1. Uses/Formulations of Hydramethylnon Products Registered in California

Uses	Formulations[a]	Crop Types/Sites
Greenhouse	granular (0.73%)	mushroom house, ornamentals, non-bearing fruit/nuts, etc.
Nursery (including non-commercial)	granular (1.0%, 0.73%); bait cartridge (0.3%); RTU bait (0.9%, 1.0%, 1.65%, 2.0%)	ornamentals, field crops, hobby greenhouse, refuge sites, etc.
Forests/NonCrop	granular (0.73%)	trees, tree plantations, etc.
Rights-of-Way	bait cartridge (0.3%) granular (0.73%)	windbreaks, utility poles, fences, retaining walls, etc.
Conservation Lands	granular (0.73%)	protected grasslands/forests, etc.
Parks/Paths	gel (2.0%); bait cartridge (0.3%) granular (0.73%, 1.0%)	recreation areas, camps, golf courses, landscape plants, etc.
Animal Premises/ Cemeteries	gel (2.0%, 2.15%); bait cartridge (0.3%); granular (0.73%, 1.0%)	dairy barns, poultry houses, grassy areas, refuge sites, etc.
Waterways	granular (0.73%)	ant mounds
Abatement	granular (0.73%)	ant mounds
Structural (residential or industrial)	bait cartridge (0.3%); RTU bait (1%, 1.65%); gel (2.0%, 2.15%); granular (1.0%, 0.73%)	porches, driveways, sidewalks, garbage, buildings, homes, crawl spaces, attics, windowsills, etc.

[a] RTU = ready-to-use (in child-resistant disc); in parentheses are percent of active ingredient.

Use of hydramethylnon on pasture and rangeland grasses is permitted in some other states but not in California. For nonfood uses, the indoor and outdoor sites are rather broad. These

areas include in and around homes, on lawns, in and around outside buildings/barns, rights-of-way/uncultivated lands, agricultural soils/crops, golf courses, animal sleeping quarters, non-critical premises in hospitals or clinics, indoor and outdoor commercial/industrial equipment or establishment, and much more. In essence, the nonfood use sites cover just about all noncrop or nonfood areas where ants and roaches (of any type) frequent or colonize.

3. Label Precautions

The hydramethylnon products registered in California are all classified as having Category III toxicity (with the signal word CAUTION). The hazards from ingestion and dermal contact are indicated on the labels for all formulations other than the RTU type; and a statement of practical treatment or at least a contact number is included on all the 47 labels.

The labels for the four broader-use, 0.73% granular products (EPA Reg. Nos. 241-322-AA; 241-322-ZA; 241-322-ZB; and 241-322-ZC) specify that applicators wear waterproof gloves, long pants, a long-sleeved shirt, and shoes plus socks when working with the granules. These personal protective equipment (PPE) and clothing requirements are consistent with the Worker Protection Standard (WPS) set forth for agricultural pesticides [40 CFR 170.240(d)(4-6)]; the four products are allowed to be used on container or field-grown ornamentals, non-bearing fruit, berries, and the like. The restricted entry interval (REI) for use of these four products on agricultural commodities is 12 hours.

There are 6 other granular formulations among the 47 end-use products. These 6 other granule products are intended to be sprinkled or spread to small noncrop or nonfood areas. Of these 6, 4 (EPA Reg. Nos. 64240-1-ZA, 64240-25-AA, 64248-6-ZA, and 64248-19-AA) require the use of gloves when handling the granules.

No PPE or (specific) clothing requirements are indicated on the labels for the other two granule products, or for the rest of the non-granular formations (i.e., those used as bait stations). None of the 47 product labels contains any statement about dermal sensitization.

4. California Requirements

California Code of Regulations (2001) requires that employees wear protective eyewear when engaged in certain handling tasks, including many of those considered in this exposure assessment. Other special requirements are already covered on the product labels.

5. Usage in California

The use of hydramethylnon in California was not included in the 1994 or the 1995 Pesticide Use Report (PUR). The PUR for 1996 (DPR, 1999a), 1997 (DPR, 1999b), and 1998 (DPR, 2000) indicated that over 97% of the hydramethylnon AI used in each of these three years was for structural pest control. The remaining 1 to 3% was primarily for public health or regulatory pest control, landscape maintenance, rights-of-way, and research commodity. The annual usages of hydramethylnon in 1996, 1997, and 1998 were 1,741, 5,456, and 3,183 lbs, respectively.

6. Sales in California

The PURs do not cover pesticide uses in all residential areas, such as those by homeowners or

non-licensed persons. To some extent, the annual usage for these unreported sites can be approximated from the mill assessment data, which are confidential information where fewer than 4 registrants are involved. Nonetheless, at the time of this documentation, these sales data cannot be made available for internal review (due to some sales reporting errors to be corrected by the registrants).

7. Reported Illnesses in California

The Pesticide Illness Surveillance Program database maintained in WH&S indicated that from the first available year 1982 through 1998, a total of 2 cases occurring in California were reported to have been probably associated with exposure to hydramethylnon used alone (Mehler, 2000). Both cases, one (a bystander office worker) occurring in 1996 and the other (a bystander convalescent hospital employee) in 1998, were classified as having a probable association with hydramethylnon used for structural pest control treatment. The 1996 case was reported as having respiratory symptoms only, whereas the 1998 case involved skin and systemic effects. Neither case resulted in hospitalization or in any days lost from work.

8. Significant Exposure Scenarios

According to the RED (U.S. EPA, 1999), hydramethylnon has established tolerances from use on grasses in pastures and rangeland. However, the use of the insecticide on these two commodities is not permitted in California. U.S. EPA has also concluded that exposure of hydramethylnon to drinking water is not likely, given that this insecticide hydrolyzes rapidly, especially under sunlight. Consumer use in residential settings thus appears to be the greatest source of potential exposure to children or non-user adult residents.

Based on current registered uses and in accordance with the RED, 6 major exposure scenarios were identified for hydramethylnon users or handlers. These exposure scenarios are: (1) loading granular for aerial or ground application; (2) flagging for granular aerial application; (3) application of granular by aerial equipment; (4) application of granular by ground equipment (e.g., tractor-drawn, gandy type spreader); (5) loading and application of granular by hand-held equipment; and (6) hand broadcast (distribution) of granular.

The potential for post-application (reentry) occupational and residential exposures also exists. As pointed out in the RED, there could be some exposure to hydramethylnon for golf-course maintenance workers, for mowers on sod farms, and for persons in buildings following indoor applications. Four granular product labels (EPA Reg. Nos. 241-322-AA; 241-322-ZA; 241-322-ZB; and 241-322-ZC) permit the use of hydramethylnon in and around field-grown or container ornamentals in California. Therefore, flower cutters and the like could be exposed to hydramethylnon in greenhouses or open fields where ornamentals were treated.

The exposure scenario that involves occupational or residential handling of the RTU type, child-resistant bait stations was not included in this exposure assessment. Such exposure was expected to be biologically insignificant, or to be much less than that from hand broadcasting the granular products under scenario 6 above. Also excluded from consideration was the use scenario involving applications of gel bait to cracks and crevices by syringe dispenser. Although inadvertent exposure to the dispenser or treated surface may result in some gel on the hand surface, it is expected that either this gel layer should soon be wiped off by the

applicator, or the gel would get on to only a small part of the hand.

III. ACUTE TOXICITY AND PHARMACOKINETICS

1. Acute Toxicity and Dermal Sensitization

Acute toxicity has been investigated in animals for technical (≥ 95% AI) hydramethylnon. According to U.S. EPA (1999), the acute dermal LD_{50} for this technical grade was >2,000 mg/kg in rabbits (Toxicity Category III). The acute inhalation LC_{50} for 4 hours of whole-body exposure to this technical grade was 2.9 mg/L in male and female rats combined (Toxicity Category IV). The acute oral LD_{50} for this technical grade was 1,146 mg/kg in male and female rats combined (Toxicity Category III). U.S. EPA considered the eye and the dermal irritation observed from exposure to this technical grade in rabbits to be, respectively, moderate (Toxicity Category IV) and none (Toxicity Category IV). For other formulations, especially those of 2% gel, the acute toxicities were concluded by MedTox (Rubin, 1993), by U.S. EPA (Dykstra, 1988), and by WH&S (Knaak, 1983) to be generally less severe than those observed for this technical grade. Based upon the findings of a study using both a technical formulation of slightly lower grade (92%) and a 3.2% concentrate (Siglin and Becci, 1982), U.S. EPA also determined that hydramethylnon is not a dermal sensitizer.

2. Dermal and Inhalation Absorption

There are no human data for dermal absorption of hydramethylnon. Nor is there any human or animal dermal absorption study available for the technical grade. Two animal dermal absorption studies are available, however, with the gel formulations.

In one study (Frantz and Beskitt, 1993), young adult (approximately 8 weeks old) male Sprague-Dawley rats were dosed topically with a 2.15% (by weight) gel preparation of ^{14}C-hydramethylnon. A preliminary review of the data indicated that as much as 2.0% of the radioactivity might have been absorbed from a 10- or 24-hour exposure, if the residues bound to the skin at the application site were included.

The skin of young male Sprague-Dawley rats was also used in another absorption study (Sharp, 1993). The test material used was from a slightly different gel preparation containing 2.16% AI (by weight) of ^{14}C-hydramethylnon. In this second study, the amount of radioactivity absorbed appeared to be slightly higher than that observed in the first study; it might have been as much as 3% for a 10-hour exposure, again if the amount of radioactivity in the skin of the test site were included.

Based on the results of these two animal studies, and on the fact that no dermal absorption data were available for the technical or the granular formulations, a dermal absorption of 5% was used in this exposure assessment. This determination was based on the concern that gel inert ingredients might *retard* the percutaneous absorption of hydramethylnon to a greater extent than the granular inerts would. There is indication (Dugard, 1977) that percutaneous absorption of chemicals varies with the substance (vehicle) in which the active chemical is suspended or contained. Another more important reason for doubling the observed dermal absorption is that the applied doses in the above two studies were over 100 $\mu g/cm^2$, a level typically many times above the range of human doses encountered in pesticide exposure assessment. There is some indication (Wester and Maibach, 1976; Thongsinthusak *et al.*,

1999) that as the amount of test material on the skin increases (10- to 100-fold), the efficiency of absorption decreases (2- to 5-fold) although the total amount absorbed always increases. U.S. EPA used 1% in their RED for hydramethylnon (1999). Their value was derived from the same two studies but without accounting for the residues bound to the skin.

No inhalation absorption studies were available for hydramethylnon. Because inhalation exposures from the various label uses of hydramethylnon were considered to be insignificant compared to dermal exposure, no attempts were made to determine inhalation absorption in this exposure assessment. U.S. EPA (1999) also reached the same conclusion regarding inhalation exposure to hydramethylnon. Otherwise, the default values used by WH&S for inhalation uptake and intake for most (especially for non-volatile) chemicals, including hydramethylnon, would be 50% and 100%, respectively (Thongsinthusak *et al*., 1993).

3. Animal and Human Metabolism

Human Studies. No metabolism or pharmacokinetic studies were available or submitted by the registrants for evaluation of hydramethylnon's biotransformation directly in humans, as such human studies apparently had never been conducted or reported.

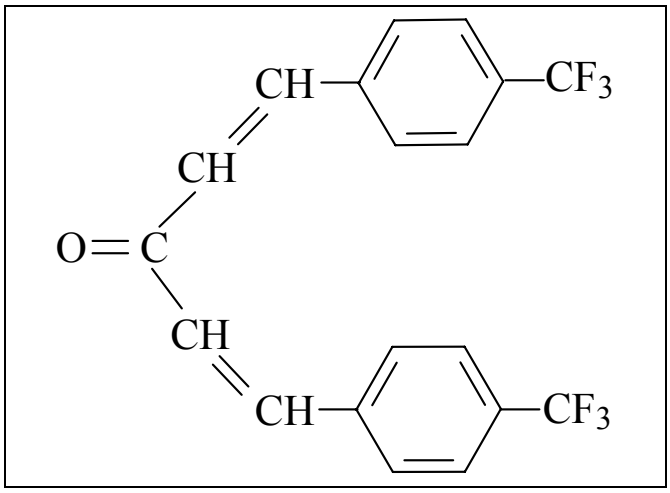
Animal Studies. In a metabolism study by Zdybak and Robinson (1992), five young male and five young female Sprague-Dawley rats were dosed by gavage with ^{14}C-labeled hydramethylnon in either the phenyl or the pyrimidinyl ring. These rats received a single low dose of approximately 3 mg/kg rat body weight, a single high dose of approximately 100 mg/kg, or an *un*labeled low dose (i.e., ~ 3 mg/kg) once daily for 14 consecutive days followed by a single *labeled* low dose on day 15. Urine and feces were collected over 7 days. The collection of expired carbon dioxide and volatile organic compounds was not attempted on grounds that a 3-day preliminary study had shown no exhalation of such materials. More than 89% (after adjustment to 100% recovery) of the applied dose was recovered in feces over the 7-day period, with most of the radioactivity (≥95%) being the unchanged parent compound. In contrast, the urine contained only a small amount (<5%) of parent compound and a variety of minor polar (e.g., benzoate and cinnamate) metabolites combined. Most of the elimination occurred within the first 24 to 36 hours after dosing. There was no significant sex or dose-related variation observed in these urine and fecal eliminations.

In another radiobalance study (Hussain *et al*., 1979), five groups of 3 Sprague-Dawley male rats each were given a single oral dose equivalent to 10 ppm of the benzylic, ^{14}C-labeled hydramethylnon in their daily diet, plus an additional group serving as controls. These animals were sacrificed in groups at 24, 48, 96, 144, or 216 hours following dosing. Approximately 90% of the radioactivity was found to have been excreted within 9 days. Of this amount, 88.4% was in feces and 1.7% in urine. The radioactivity eliminated in the feces during the first 24 hours, which amounted to 71.5% of the oral dose, contained 92.7% of the unchanged parent compound. The urine contained mostly polar metabolites but no parent compound.

In order to elucidate the metabolic pathways beyond the excretion pattern, in the second study additional male Sprague-Dawley rats were treated with a higher oral dose of hydramethylnon labeled ^{14}C in either the benzylic (equivalent to 74 ppm in diet) or the

pyrimidinyl (equivalent to 79 ppm in diet) ring, plus a control group. These rats were sacrificed in groups at 24, 48, and 96 hours. Analysis of tissue extracts from rats treated with these high doses showed that in the fat and kidney, most of the radioactivity was again associated with the unchanged parent compound.

There were 18 or more hydramethylnon metabolites identified in the liver from the tissue extraction analysis. Of these, the most significant other than the parent compound was 1,5-bis(α,α,α-trifluoro-*p*-tolyl)-1,4-pentadien-3-one. The following is the chemical structure of this significant metabolite.



IV. ENVIRONMENTAL CONCENTRATIONS

1. Ambient Air

No data on ambient air concentration of hydramethylnon were submitted to WH&S. Ambient air data for this chemical are not anticipated to be available any time soon, especially when the insecticide is not on the list of toxic air contaminants and is not considered a volatile or a semi-volatile compound.

2. Dislodgeable Foliar Residues

Despite the DCI (Data Call-In) issued in 1995 by U.S. EPA (1999) requiring the submission of foliar residue data, there were no chemical-specific dislodgeable foliar residues (DFR) studies available for hydramethylnon. Surrogate residue data and assumptions were hence used to estimate post-application exposure from dermal contact with foliar residues.

3. Turf and Other Surface Residues

There were also no chemical-specific data on other surface residues such as those on sod-farm or golf course turfgrass, which may not be considered as the same type of foliar residues as those present on foliage of more common agricultural commodities. Surrogate residue data and assumptions were hence also used to estimate post-application exposure from dermal contact with surface residues.

V. EXPOSURE ASSESSMENT

To facilitate discussion, the exposure scenarios identified in Section II-8, which were based on formulations and use patterns summarized in Table 1, were subsumed into three groups: (1) working with hydramethylnon for agricultural use; (2) working with hydramethylnon for non-agricultural use; and (3) children and adult non-user residents or passers-by. These three user groups are not necessarily mutually exclusive in terms of the types of exposure potential involved. For example, hydramethylnon may also be applied to airports, corrals, forests, or uncultivated areas in a relatively large operation via ground or even aerial equipment. Another point noteworthy is that those working with hydramethylnon for non-agricultural use may include both PCOs and resident users. Both residents and PCOs may apply granular bait by hand or via a hand-held spreader. In accordance with U.S. EPA (1999), inhalation exposures to hydramethylnon in all cases were estimated to be insignificant (compared to dermal exposure) partly due to its low vapor pressure and the size of the granules involved (which are oily in nature and larger than 140 microns, and hence less inhalable). No chemical-specific data on worker exposure were available for any of the use scenarios.

1. Agricultural Use

Handlers. The exposures to granular hydramethylnon for applicators, loaders, and flaggers are summarized in Table 2. The basic assumptions used in the calculations are footnoted in the table. The baseline dermal exposure rates used for these workers were based on the arithmetic means derived from the Pesticide Handlers Exposure Database (PHED, 1995) surrogate subsets appended to this document. The subsets were not limited to A or B grade quality data (as common practice), but in a couple of cases here extended to lower grades due to scarcity of data. Several worker exposure studies were evaluated by WH&S (Formoli and Fong, 1995), in which exposures were monitored for pilots, aerial flaggers, and aerial loaders handling the 10G formulation of molinate. The dermal exposure rates derived from these formulation-specific studies (as well as from their evaluations by WH&S) were not used as surrogate here because molinate is a much more volatile chemical and available in 50- and up to 1,500-lb bulk bags. In contrast, the 0.75% hydramethylnon granules are available in 4.5-lb bags. In addition to the differences in loading and application equipment involved, the exposure rates reported for molinate were all per hour, not per pound of AI handled (thus further making it not a good surrogate to use). The basic assumption is that more work and time will be required to fill up, say, a 500-lb hopper if much smaller bags are used.

As reflected in Section II-5, to this date hydramethylnon has not been truly used on agricultural crops. However, the exposures to hydramethylnon were considered here for agricultural workers because agricultural uses are allowed by four product labels registered in California (EPA Reg. Nos. 241-322-AA; 241-322-ZA; 241-322-ZB; and 241-322-ZC). It is important to note that certain fire ants species such as red imported fire ants are known to inhabit fields where their large above-ground mounds can become a pest problem in planting and harvesting crops. For example, this species will feed on wheat, corn and sorghum seed, and the like. These ants are exothermic (i.e., cold-blood) creatures. Their body temperatures and physiological functions thus necessarily depend on the outside temperature, meaning that they are unlikely a year-long pest in (the same) agricultural fields. In short, because outdoor fire ants and the kind are seasonal pest problems typically lasting no more than 3 months per

year, and for lack of specific use data, the seasonal exposure frequencies for these agricultural handlers were assumed to be roughly 60 days (less weekends and reapplication intervals). *As footnoted in Table 2, the upper-bound and the average absorbed dosages were estimated for acute and subchronic or chronic exposures, respectively.*

Table 2. Upper-bound and Average Daily Exposures Estimated for Agricultural Handlers Working with Hydramethylnon Granules[a].

Work Task	Exposure[b] (µg/lb AI)	Maximum Label Rate[c] (lb AI/acre)	Acres/Day[d] upper	Acres/Day[d] ave.	Daily Exposure (µg/person)[e] upper	Daily Exposure (µg/person)[e] average	Absorbed Dosage (µg/kg/day)[f] upper	Absorbed Dosage (µg/kg/day)[f] average
1. aerial								
loader	7.2	0.015	600	300	64.8	32.4	0.05	0.023
applicator	2.0	0.015	600	300	18.0	9.0	0.01	0.006
flagger	1.3	0.015	600	300	11.7	5.9	0.01	0.004
2. ground								
applicator[g]	10.5	0.015	100	50	15.8	7.9	0.01	0.005

[a] upper-bound and average are for acute and subchronic or chronic exposures, respectively; workers were assumed to wear long pants, a long-sleeved shirt, shoes plus socks, and waterproof gloves, as per label requirements; exposure frequencies for these work groups were all assumed to be 60 days per season as well as per year (*see* text for justification).

[b] dermal exposure rate from PHED (*see* Appendix for subsets attached and the Exposure Appraisal subsection for further discussion).

[c] maximum label rate, as based on the four 0.73% granular products discussed in Section II-3.

[d] the upper (bound) is the default maximum assumed for lack of specific use data; this default maximum is not unreasonable, in that 15 of the 97 aerial applicators (replicates) in PHED treated more than 600 acres per monitoring duration, with the highest total daily usage observed being 1,061 acres (*see* Dong, 1999; Dong and Haskell, 1999 for further discussion); the average (ave.) value is assumed to be half of the maximum used here, and is the maximum used by U.S. EPA (1999) in their RED for hydramethylnon (based on information submitted to them by registrants).

[e] daily exposure (µg/person) = (dermal exposure rate) x (maximum label rate) x (daily acreage).

[f] absorbed dosage (µg/kg/day) = (daily exposure) x (5% dermal absorption) x (70 kg body weight)$^{-1}$; *see* Section III-2 for dermal absorption, and the 70 kg body weight is the average for male and female adults combined (U.S. EPA, 1997), as for a hypothetical person.

[g] including loading (i.e., exposure rate = 10.5 µg/lb AI handled = [7.2 µg/lb AI handled from mixing/loading] + [3.3 µg/lb AI handled from using a drop-type tractor-drawn spreader]).

Fieldworkers. Harvesters and other fieldworkers are subject to exposure from contact with dislodgeable hydramethylnon residues present on treated foliage. Data on reentry exposure to hydramethylnon for these workers were not available to WH&S. For these fieldworkers, it

is thus necessary to extrapolate the dermal exposure from a dermal transfer rate or factor, which is defined here simply as the ratio (or sometimes some other relation, such as linear regression) of hourly dermal exposure typically in μg/hr to DFR in μg/cm^2. Both of these variables should be measured more or less at the same time. The term DFR is defined as the amount of residues that can be removed from both sides of treated foliage surfaces using aqueous surfactant. When multiplied with a proper dermal transfer rate, the DFR under study may be readily converted to hourly dermal exposure of workers entering a treated area. This conversion is based on the common assumption that *(dermal exposure) = (dermal contact or transfer rate)* x *(surface concentration)*.

Table 3. Upper-bound Range Finder Daily Reentry Exposure to Hydramethylnon for Fieldworkers (and Residents) Engaged in Low, Medium, and High Crop Contact/High Exposure Activities[a].

Exposure[b] Activities	DFR (μg/cm^2)[c] (at 0.015 lb AI/acre)	Dermal Transfer[d] (μg/hr per μg/cm^2)	Daily Exposure[e] (μg/person)	Absorbed Dosage[f] (μg/kg/day)
low	0.035	2,000	560	0.4
medium	0.035	5,000	1,400	1.0
high	0.035	10,000	2,800	2.0

[a] workers were assumed to wear long pants, a short-sleeved shirt without gloves; ***these range finder post-application exposures were also intended for residents reentering treated sites*** (*see* discussion in text).

[b] as examples, low exposure crops/activities include mostly row crops, low-growing ornamentals, established turf, and (cotton) scouting; medium exposure crops/activities include some row crops, mostly field crops, and mostly fruit trees, such as ornamental trees, shrubs, and sod farm turf; high exposure crops/activities include mostly labor- and contact-intensive activities, such as grape girdling and harvesting of greenhouse roses (*see*, e.g., Dong, 1994, 1995, 1999; Dong and Haskell, 1999 for more specific examples).

[c] estimates for DFR (dislodgeable foliar residues) were based on an upper confidence limit (UCL) for the generic *mean* initial deposition generalized from 21 foliar residue studies on 14 pesticides (Dong, 1993; *see* also the section on Exposure Appraisal). This UCL value (2.36 μg/cm^2 per lb AI sprayed before adjustment for the maximum label rate of 0.015 lb hydramethylnon AI/acre) was calculated from the algorithm for upper confidence limit for the mean, as outlined in Appendix 6 (*see* text for further discussion).

[d] these upper-bound dermal transfer rates (μg/hr per μg/cm^2) were based primarily on those observed or used in earlier pesticide exposure assessments (*see* Dong, 1994, 1995, 1999; Dong and Haskell, 1999; Haskell, 1995); they are consistent with those used in the RED by U.S. EPA (1999).

[e] daily exposure (μg/person) = (DFR) x (dermal transfer rate) x (8 hours/day).

[f] absorbed dosage (μg/kg/day) = (daily exposure) x (5% dermal absorption) x (70 kg body weight)$^{-1}$; *see* Section III-2 for dermal absorption, and the 70 kg body weight is the average for male and female adults combined (U.S. EPA, 1997), as for a hypothetical person.

There were no chemical-specific DFR data available to WH&S. A conservative or *first-tier* range finder approach was thus used to assess the reentry exposures in question. This approach involved the use of dermal transfer rates at three exposure activity levels and an

upper confidence limit for the generic *mean* initial deposition of DFR. The three dermal transfer rates (factors) used were 2,000, 5,000, and 10,000 μg/hr per μg/cm^2, representing typically as the maximum for low, medium, and high crop contact or high exposure activities, respectively, as reflected in earlier pesticide exposure assessments (e.g., Dong, 1994, 1995, 1999; Dong and Haskell, 1999; Haskell, 1995). This range of dermal transfer rates is also consistent with that used by U.S. EPA (1999) in their RED for hydramethylnon.

The upper-bound *mean* initial deposition (2.36 μg/cm^2 per lb AI sprayed) was generalized from 21 foliar residue studies on 14 liquid pesticides (Dong, 1993), following the algorithm presented in Appendix 6 (*see* also the section on Exposure Appraisal for use of liquid formulations as surrogate). It was calculated from the arithmetic mean of 2.0 μg/cm^2/lb AI sprayed + [(2 standard deviations) ÷ (sample size of 21)$^{-1/2}$] in an attempt to represent a 95% upper confidence limit for the mean initial deposition. This upper-bound mean initial deposition rate (which later applied to hydramethylnon's maximum label rate) again is comparable to that used by U.S. EPA, after taking into account the potential for residue build-up due to carry-over from reapplication. U.S. EPA assumed a rate estimate of 20% of the AI applied as their agency's default, yielding 2.2 μg/cm^2 per lb AI sprayed. The reentry exposures estimated from using the surrogate rates and DFR are summarized in Table 3 above. For reasons given earlier for handlers, the exposure frequencies for all fieldworkers were also assumed to be 60 days.

It is important to note that the estimations presented in Table 3 are solely for the purpose of finding the range of acute and long-term reentry exposures involved. The intention was to determine if upon a preliminary assessment based on an array of conservative assumptions, there is still a concern with reentry exposure and hence a need for the provision of use- and chemical-specific data on the dissipation of hydramethylnon DFR. Since there were no chemical-specific data on DFR dissipation, the dose range as estimated was deemed sufficient and necessary for both the acute and the subchronic or chronic reentry exposures. Otherwise, the DFR used for estimation of subchronic or chronic reentry exposures typically should be based on those specific to the *average* reentry days, not to day 0 post-application (*see* the Exposure Appraisal section for further discussion).

2. Non-Agricultural Use

Potential handler exposures from the use of granular hydramethylnon in *large* non-agricultural operations (if any in future) were assumed to be similar to those presented in Table 2. (That is, the exposures estimated for Scenarios 1 and 2 in Table 4 below were actually reproduced from those presented in Table 2.) For application of the granular bait in small operations, such as when applying the granules in or around homes or commercial establishments, two surrogate exposure rates were used. The dermal exposure rate calculated for granular diazinon (Dong, 1999), after adjustment for maximum label rate, was used for loading and applying hydramethylnon with a hand-held rotary or push-type granular spreader

For dispersion by hand, the PHED exposure rate (taking into account the small contribution from inhalation) based on arithmetic mean was used (as used in Dong, 2001). The exposures calculated with these two surrogate exposure rates are summarized in Table 4. As footnoted in this table, the commercial operators (i.e., the PCOs) were assumed to apply the granules

Table 4. Upper-bound and Average Daily Exposures Estimated for Non-Agricultural Handlers Working with Hydramethylnon Granules[a].

Work Task	Exposure[b] (mg/lb AI)	Maximum Label Rate[c] (lb AI/acre)	Acres/Day[d] upper	Acres/Day[d] ave.	Daily Exposure[e] (µg/person) upper	Daily Exposure[e] (µg/person) average	Absorbed Dosage[f] (µg/kg/day) upper	Absorbed Dosage[f] (µg/kg/day) average
1. aerial								
loader	0.0072	0.015	600	300	64.8	32.4	0.05	0.023
applicator	0.002	0.015	600	300	18.0	9.0	0.01	0.006
flagger	0.0013	0.015	600	300	11.7	5.9	0.01	0.004
2. ground								
applicator[g]	0.0105	0.015	100	50	15.8	7.9	0.01	0.005
3. via spreader[h]								
residents					3.8	NA	0.003	NA
PCOs					18.8	18.8	0.01	0.01
4. by bare hand[i]								
residents	200.0	0.015	0.02	0.02	66.0	NA	0.05	NA
PCOs	200.0	0.015	0.11	0.11	330.0	330.0	0.24	0.24

[a] upper-bound and average are for acute and subchronic or chronic exposures, respectively; for scenarios 1 and 2 dealing with large non-agricultural operations, workers were assumed to wear long pants, a long-sleeved shirt, shoes plus socks, and waterproof gloves (as would agricultural workers); users in scenarios 3 and 4 are not required to wear additional clothing or personal protective equipment; and exposure frequencies for these worker groups (excluding residents) were all assumed to be 60 days per season as well as per year (*see* text for justification).

[b] dermal exposure rates were from PHED and, for scenarios 1 and 2, identical to those listed in Table 2 (*see* Appendix for subsets attached and the Exposure Appraisal subsection for further discussion).

[c] maximum label rate, as was based on the four 0.73% hydramethylnon granular products discussed in Section II-3; for some uses, the 1.0% granular is also available but for smaller operations leading to lower daily usage.

[d] except otherwise noted, the upper (bound) is the default maximum assumed for lack of specific use data; this default maximum is not unreasonable, in that 15 of the 97 aerial applicators (replicates) in PHED treated more than 600 acres per monitoring duration, with the highest total daily usage observed being 1,061 acres (*see* Dong, 1999; Dong and Haskell, 1999 for further discussion); the average (ave.) value is assumed to be half of the maximum used here and is the maximum used by U.S. EPA (1999) in their RED for hydramethylnon.

[e] except otherwise noted, daily exposure (µg/person) = (dermal exposure rate) x (maximum label rate) x (daily acreage/usage).

[f] absorbed dosage (µg/kg/day) = (daily exposure) x (5% dermal absorption) x (70 kg body weight)$^{-1}$; *see* Section III-2 for dermal absorption, and the 70 kg body weight is the average for male and female adults combined (U.S. EPA, 1997), as for a hypothetical person.

[g] including mixing/loading (i.e., exposure rate = 10.5 µg per lb AI handled = [7.2 µg/lb AI handled from mixing/loading] + [3.3 µg/lb AI handled from ground application using a drop-type tractor-drawn spreader]).

[h] based on the diazinon dermal exposure rate (Dong, 1999) used as surrogate (*see* text for discussion); exposure for residents is assumed to be 5 times less than that for PCOs (*see* text for justification), NA = not applicable; exposure for PCOs was calculated as follows: 18.8 µg/person/day = (7.0 mg/day per 5.6 lb diazinon AI/acre) x (0.015 lb/acre for hydramethylnon); *no data could be used to yield a lower, average daily exposure*.

[i] exposure for residents is assumed to be 5 times less than that for PCOs (*see* text for justification); NA = not applicable; note that 0.11 acre ≈ 5,000 ft^2, as used in the RED (U.S. EPA, 1999*); no data could be used to yield a lower, average daily exposure*.

five times more often than residents would during each workday, under the assumption that the treatment for each site amounts to 1 to 2 hours of work and that PCOs work 8 hours a day. This five-fold assumption is largely consistent with that made by U.S. EPA (1999) in their RED for hydramethylnon.

As footnoted in Table 4, the upper-bound and the average absorbed dosages were estimated for acute and subchronic or chronic exposures, respectively. (Note that for Scenarios 3 and 4 involving small operations, no data could be used to yield a lower, average daily dosage for subchronic or chronic exposures.) It was expected that, like agricultural workers, PCOs would handle hydramethylnon granules no more than 60 days per *severe* ant season (and hence per year as well). Although roaches and non-fire ants can be a pest problem that in some places occurs all year long, the short- or long-term exposure to the bait placed indoors is expected to be insignificant for PCOs or resident users. There should be no direct hand or dermal contact with the hydramethylnon AI when applying the RTU roach or ant killer bait products which are child-resistant.

3. Non-User Residents and Passers-by

As first-tier range finder estimates (*see* Section V-1 under Fieldworkers for specific intention discussed), the reentry exposures presented in Table 3 for fieldworkers were also used for residential post-application exposure to hydramethylnon. These range finders were primarily for exposures from outdoor uses of hydramethylnon, from which children's exposure may be considered insignificant. Rarely are ant killers used for prophylactic purposes, especially in a relatively large area such as lawns or recreational areas. If hydramethylnon is applied to an outdoor place where ants actually exist, children normally are reluctant to play there for fear of ants. Children are not expected to have dermal contact with outdoor surface residues for 8 hours long per day. In accordance with more recent practice within WH&S (*see*, e.g., Dong, 1999; Formoli, 1996), one hour per day was assumed to be a reasonable estimate of the time that a child's full body would exert some type of aerobic contact with a treated surface. Although their body weight can be 7 times less than that of adults, children's body surface will also be 3 times smaller (thus resulting in a smaller dermal transfer rate). Also, as pointed out in Section II-8, this aminohydrazone insecticide hydrolyzes rapidly, especially in sunlight. The post-application exposures presented in Table 3 are thus more than enough as estimates for children. Children's exposure to the indoor bait is expected to be insignificant, given that the bait stations are child-resistant. *In short, as indicated in Table 3, the acute or long-term dosage for residents, including children, at most would range from 0.4 to 2.0 μg/kg/day*.

As stated in Section IV-1, no data on ambient air concentration of hydramethylnon were available. Ambient air data for this chemical are not anticipated to be available any time soon, however, especially when the insecticide is not on the list of toxic air contaminants. It was also justified earlier in this exposure assessment section that inhalation exposure to hydramethylnon was considered to be insignificant (especially when compared to the dermal exposure involved).

4. Exposure Appraisal

In using the absorbed dosages estimated in this exposure assessment, it is important to note

that there were uncertainties built into the process that might not be immediately apparent to the risk assessor or the risk manager. Many of these uncertainties tend to overestimate the exposure involved, but are typically hidden and therefore seldom acknowledged. Below is a brief account of the uncertainties associated with the factors used here that tend to have a critical impact on the exposures estimated.

Exposure Rates from PHED. The Pesticide Handlers Exposure Database (PHED) is a generic database for pesticide applicator, flagger, and mixer/loader exposures that contains measured values of inhalation and dermal exposure rates (e.g., μg per lb AI handled or per hour worked). Built into this database is the well-received, but not fully validated, concept that worker exposure is proportional to the amount of AI handled or the work time spent. WH&S has been using the exposure rates in terms of the amount of AI handled, primarily because the total work time spent within each handling task is not as well defined.

It is important to note that due to small sample size and for the statistical reasons given in Appendix 6 of this document, the PHED exposure rates (and hence the dosages as well) listed in Table 2 (and Table 4) might have been underestimated by approximately two-fold. Another alternative may be to increase the usual margin of exposure benchmark from 100 to 200 for this group of workers, for which the exposures were estimated using the PHED data. As explained in Appendix 6, the more correct approach may be to adjust the PHED mean exposure rates using the associated sample standard deviation and the sample size. However, the calculation of these sample statistics is difficult and complex, if not impossible.

In calculating the absorbed dosage in this exposure assessment, the average body weight assumed for workers and adults was 70 kg. The use of this default value might have overestimated slightly the dosage of hydramethylnon for those work groups whose exposure rates were calculated from PHED. The exposure rates calculated from PHED were based on exposure monitoring studies in which the volunteers were primarily male workers. The average body weight for the male volunteers is approximately 10% higher than the average of 70 kg assumed here for male/female adults (U.S. EPA, 1997; Thongsinthusak *et al.*, 1993), as for a hypothetical person. In addition, the total body surface area used for the PHED rate estimates was 21,760 cm^2, which is about 15% higher than that later re-calculated by U.S. EPA (1997) for an average male adult of 78 kg. In short, the dermal exposures calculated for these work groups were likely based on a somewhat higher ratio of body surface to body weight than should be, thus on this ratio alone possibly overestimating the exposures by 15 to 20%.

Other factors related to the use of PHED were discussed in a paper by Ross *et al.* (2000) and in the exposure assessment document for naled (Dong and Haskell, 1999). Included in the discussions in these two documents were the concerns or uncertainties with the use of non-detects, passive patch dosimetry data, data from partial vs. full workday exposure monitoring, and the arithmetic mean.

Exposure Frequencies (Seasonal Exposure). The annual or seasonal exposure frequencies (60 days) that were assumed for all commercial (agricultural and PCO) workers were likely to have been overestimated. It is unlikely for the same worker or same work crew to deal

with severe (fire) ant problems every day in a season that typically lasts no more than 90 days. Yet due to the lack of more specific data, such a conservative default was assumed. Such uncertainty might lead to an overestimation of the subchronic or long-term risks estimated in the risk characterization document for these workers.

Other Surrogate Data. The diazinon exposure rate used as surrogate in Section V-2 was actually based on a worker exposure study (Weisskopf *et al.*, 1988) conducted a decade ago. In that study, 15 workers were monitored for exposure to diazinon during application of a 14% granular formulation to planters, pastures, lawns, and shrub areas at the rate of 5.6 lb AI per acre. The various types of application equipment used by these workers included a hand-held 5-lb coffee can (for planters and shrub areas), a gandy spreader (for most lawn areas), a Lesco broadcast type spreader (for high grass areas), and a belly grinder (for pastures or areas of weeds). As explained in the exposure assessment document for diazinon (Dong, 1999), the average total body dermal exposure extrapolated from head patches (for upper body), leg patches (for lower body), and hand rinses was approximately 3.5 mg per shift for all work crews. This estimate was then doubled to account for the total daily exposure potential from both the morning and the afternoon shift. Daily exposure can easily be overestimated from less than a full day of exposure monitoring, since saturation or overloading is not an uncommon effect or phenomenon with dermal contact (i.e., skin loading). Ross *et al.* (2000) recently have gathered some empirical evidence supporting such a possibility.

Dermal vs. Oral Plasma Levels. Dosage is expressed as a single static value both in worker exposure and animal toxicology studies. The rates of dermal absorption and of dermal acquisition are often seen or expected to be lower than the rates of oral absorption and oral acquisition in animals used for toxicology testing. In short, the dose via the nonbolus dermal route is likely to be less potent than the same amount administered orally. This factor was also discussed in Dong and Haskell (1999) and in Ross *et al.* (2000).

Dermal Absorption. The dermal absorption of 5% estimated (see Section III-2) and used in this exposure assessment might still be underestimated somewhat, considering the small human doses involved compared to the experimental doses used. There is also no concrete information on the actual impact of the vehicle (gel inerts) used. However, as pointed out in Ross *et al.* (2000), a review on a handful of compounds tested and available indicated that the rat overestimated human dermal absorption by two- to ten-fold.

Dislodgeable Foliar Residues (DFR). The upper confidence limit (UCL) for the mean DFR initial deposition, that of 2.36 $\mu g/cm^2$ presented in Section V-1, was calculated using the algorithm presented in Appendix 6. It was based on the assumption that the individual DFR initial depositions from the 21 studies were randomly selected. This is by no means the case, however, since the 21 studies represented only non-random data available opportunistically at the moment. At one point, it was thought that the UCL should be calculated as the sample mean plus 2 sample standard deviations in order to obtain a more confident UCL for the mean. The final decision was to treat the 21 initial depositions in the sample as randomly selected. Although the calculated UCL of 2.36 $\mu g/cm^2$ was with a confidence much lower than 95%, it is comparable to the default value of 20% of the AI applied (i.e., 2.2 $\mu g/cm^2$ per lb AI applied) that U.S. EPA (1999) used in their RED for hydramethylnon.

Initial deposition of DFR is not chemical-specific. It is primarily a function of the amount of chemical applied and the equipment used. For lack of chemical- and use-specific data on DFR, the UCL of 2.36 $\mu g/cm^2$ calculated in this exposure assessment was intended for use to estimate both the acute and the subchronic or chronic reentry exposures. Ideally, the mean DFR at average reentry days should be used to calculate the estimate for a subchronic or chronic reentry exposure where dermal transfer rate is used (in place of actual exposure monitoring data). In this exposure assessment, the use of an UCL for the mean initial deposition rate (i.e., the mean DFR immediately following application) was considered to be sufficient and necessary. It was considered necessary because data on mean DFR at average reentry days were not available.

The use of an UCL for the mean DFR initial deposition was also considered to be sufficient for the acute reentry exposures. According to the product labels, the restricted entry interval (REI) is 12 hours. In practice, the earliest reentry time for a full 8-hour work is likely close to 24 hours post-application. By that time, the DFR is likely to have dissipated substantially, especially since hydramethylnon hydrolyzes rapidly in sunlight. Another safeguard factor is that the hydramethylnon granules, though oily in nature, are not as adhesive to the foliage as the sprays that were used in the 21 studies, from which the mean DFR was derived. The use of an upper-bound initial deposition was thus considered not necessary for estimating the acute reentry exposure. The estimation of such an upper-bound DFR (for the population, not the sample) is also difficult, if not impossible, in that the sample distribution so derived from the 21 studies on hand could not be proven to represent closely the population distribution.

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VII. APPENDICES

Appendix 1: Subset from PHED for Dermal Exposure of (Agricultural) Mixer/Loaders Working with Granules under Open-Pour Loading.

Appendix 2: Subset from PHED for Dermal Exposure of (Agricultural) Flaggers from Aerial Application of Granules.

Appendix 3: Subset from PHED for Dermal Exposure of (Agricultural) Aerial Applicators (Pilots) Working with Granules.

Appendix 4: Subset from PHED for Dermal Exposure of (Agricultural) Applicators Using a Drop-Type Tractor-Drawn Spreader to Distribute Granules.

Appendix 5: Subset from PHED for Dermal Exposure of Applicators Dispersing Granular Bait by Hand.

(These PHED attachments are neither photocopies nor, due to system incompatibility, from imported files; they were reproduced using a not-so-perfect scanner and hence necessarily with some typing for touch-up. Nonetheless, the accuracy of their contents had been checked to the extent possible.)

Appendix 6: Statistical Justification for Doubling the Mean Exposure Values When the Sample Size Is Small.

APPENDIX 1
(Aerial and Ground Mixer/Loaders)

Name: HYDRAMN1.MLOD Subset Specifications for HYDRAMN1.MLOD

With Solid Type Equal to 4 (Granules) and
With Mixing Procedures Equal to 1 (Open) and
With Outdoor Equal to "X" and
With Dermal Grade Uncovered Equal to "A" "B" and
With Hand Grade Equal to "A" "B"
Subset originated from MLOD.FILE

SUMMARY STATISTICS FOR CALCULATED DERMAL EXPOSURES

SCENARIO: Long pants, long sleeves, gloves

PATCH LOCATION	DISTRIB. TYPE	MICROGRAMS PER LB AI MIXED Median	Mean	Coef of Var	Geo. Mean	Obs.
HEAD (ALL)	Lognormal	.39	1.43	142.007	.5761	3
NECK.FRONT	Lognormal	.87	1.27	114.3228	.5317	3
NECK.BACK	Lognormal	.011	.1063	155.3151	.033	3
UPPER ARMS	Lognormal	.4365	.582	63.2474	.4942	6
CHEST	Lognormal	.71	.71	50	.6451	3
BACK	Lognormal	.71	.71	50	.6451	3
FOREARMS	Lognormal	.242	.5647	151.3193	.2991	6
THIGHS	Lognormal	.382	.5093	43.2947	.4813	3
LOWER LEGS	Lognormal	.238	.6347	135.5444	.3921	6
FEET						0
HANDS	Lognormal	.17	.6464	288.0105	.126	18
TOTAL DERM:		4.2237	4.1595	**7.1634**	4.2237	

95% C.I. on Mean: Dermal: [-90.3058, 104.6326]

Number of Records: 18
Data File: MIXER/LOADER Subset Name: HYDRAMN1.MLOD

APPENDIX 2
(Aerial Flaggers)

Name: HYDRAMN1.FLAG Subset Specifications for HYDRAMN1.FLAG

With Solid Type Equal to 4 (Granules) and
Subset originated from FLAG.FILE

SUMMARY STATISTICS FOR CALCULATED DERMAL EXPOSURES

SCENARIO: Long pants, long sleeves, gloves

PATCH LOCATION	DISTRIB. TYPE	MICROGRAMS PER LB AI MIXED Median	Mean	Coef of Var	Geo. Mean	Obs.
HEAD (ALL)	Lognormal	.455	.4875	72.3282	.3785	20
NECK-FRONT	Lognormal	.0375	.042	73.8095	.0328	20
NECK.BACK	Lognormal	.033	.0396	97.9798	.0286	20
UPPER ARMS						0
CHEST	Other	.355	.355	0	.355	4
BACK	Other	.355	.355	0	.355	4
FOREARMS						0
THIGHS						0
LOWER LEGS						0
FEET						0
HANDS						0
TOTAL DERM:	1.1499	1.2355	**1.2791**		1.1499	

95% C.I. on Mean: Dermal: [-4.4386, 6.9968]

Number of Records: 20
Data File: FLAGGER Subset Name: HYDRAMN1.FLAG

APPENDIX 3
(Aerial Applicators)

Name: HYDRAMN1.APPL Subset Specifications for HYDRAMN1.APPL

With Solid Type Equal to 4 (Granules) and
With Application Method Equal to 5 (Fixed Wing) or Equal to 6 (Rotary Wing)
Subset originated from APPL.FILE

SUMMARY STATISTICS FOR CALCULATED DERMAL EXPOSURES

SCENARIO: Long pants, long sleeves, gloves

PATCH LOCATION	DISTRIB. TYPE	MICROGRAMS PER LB AI MIXED Median	Mean	Coef of Var	Geo. Mean	Obs.
HEAD (ALL)	Lognormal	.26	.38	77.0789	.2981	13
NECK.FRONT	Lognormal	.03	.0381	74.8031	.0312	13
NECK.BACK	Lognormal	.022	.0322	77.0186	.0252	13
UPPER ARMS	Other	.291	.291	0	.291	9
CHEST	Other	.355	.355	0	.355	13
BACK	Other	.355	.355	0	.355	13
FOREARMS	Other	.121	.121	0	.121	9
THIGHS						0
LOWER LEGS						0
FEET	Other	.131	.2911	164.9948	.1727	9
HANDS	Lognormal	.1015	.0906	55.5188	.0756	9
TOTAL DERM:	1.6831	1.6665	**1.954**		1.7248	

95% C.I. on Mean: Dermal: [-9.2094, 13.1174]
Number of Records: 13
Data File: APPLICATOR Subset Name: HYDRAMN1.APPL

APPENDIX 4
(Ground Applicators)

Name: HYDRAMN2.APPL Subset Specifications for HYDRAMN2.APPL

With Solid Type Equal to 4 (Granules) and
With Application Method Equal to 17 (Solid Broadcast Spreader, Tractor/Truck/ Agricultural Uses) and
With Cab Type Equal to 3 (Closed Cab/Window Closed)
Subset originated from APPL.FILE

SUMMARY STATISTICS FOR CALCULATED DERMAL EXPOSURES

SCENARIO: Long pants, long sleeves, gloves

PATCH LOCATION	DISTRIB. TYPE	MICROGRAMS PER LB AI MIXED Median	Mean	Coef of Var	Geo. Mean	Obs.
HEAD (ALL)	Lognormal	.52	1.872	150.5983	.6409	5
NECK.FRONT	Lognormal	.105	.168	108.3333	.0774	5
NECK.BACK	Lognormal	.044	.066	100	.0387	5
UPPER ARMS	Other	.291	.291	0	.291	2
CHEST						0
BACK						0
FOREARMS	Other	.484	.484	0	.484	1
THIGHS						0
LOWER LEGS	Other	.238	.238	0	.238	2
FEET						0
HANDS	Lognormal	.1994	.1994	10.1304	.1989	2
TOTAL DERM:	1.9689	1.8814	**3.3184**		1.9689	

95% C.I. on Mean: Dermal: [-74.9963, 81.6331]
Number of Records: 5
Data File: APPLICATOR Subset Name: HYDRAMN2.APPL

APPENDIX 5
(Applicators Dispersing Granular Bait by Hand)

Name: HYDRAMN3.APPL Subset Specifications for HYDRAMN3.APPL

With Solid Type Equal to 4 (Granules) and
With Application Method Equal to 22 (Others) and
With Study ID Equal to 520 (on Dispersion of Granular Bait by Hand)
Subset originated from APPL.FILE

SUMMARY STATISTICS FOR CALCULATED DERMAL EXPOSURES

SCENARIO: Long pants, long sleeves, no gloves (*to be back-calculated from gloved hands using a 90% protection factor for gloves*)

PATCH LOCATION	DISTRIB. TYPE	Median	MICROGRAMS PER LB AI MIXED Mean	Coef of Var	Geo. Mean	Obs.
HEAD (ALL)	Lognormal	5796.25	5911.864	65.7229	4628.645	16
NECK.FRONT	Lognormal	699.225	788.2688	56.8973	652.2670	16
NECK.BACK	Lognormal	490.452	500.2346	65.7229	391.6546	16
UPPER ARMS	Lognormal	12974.7	13233.48	65.7229	10361.05	16
CHEST	Lognormal	15828.2	16143.94	65.7229	12639.76	16
BACK	Lognormal	15828.2	16143.94	65.7229	12639.76	16
FOREARMS	Lognormal	5394.97	5502.581	65.7229	4308.201	16
THIGHS	Lognormal	17032.0	17371.78	65.7229	13601.10	16
LOWER LEGS	Lognormal	10611.6	10823.26	65.7229	8473.982	16
FEET						
TOTAL DERM:	67696.42	84655.6	**86419.34**		67696.4	

95% C.I. on Mean: Dermal: [-263592.6399, 436431.3225]

HANDS(**gloves**)	Lognormal	4555.6	**4660.951**	65.6070	3613.986	15
Inhalation	Lognormal	288.89	293.0964	68.6837	225.8441	16

Inhalation rate: 14 Liters/Minute
Number of Records: 16
Data File: APPLICATOR Subset Name: HYDRAMN3.APPL

APPENDIX 6

Statistical Justification for Doubling or Adjusting the Mean
Exposure Values When the Sample Size Is Small

This statistical argument is to justify that *whenever the sample standard deviation* is not available, the practice should be to double the *mean* exposure-related value derived from a set of data containing observations fewer than 5 or 6. The same approach is warranted for a sample size n between 6 and 15, if the associated coefficient of variation (CV) is expected to be greater than 100%.

When using the arithmetic mean of an exposure-related parameter in our exposure assessment, technically we should use the population mean μ, not the sample mean $\bar{u}$. In most cases, especially when both n is very large and CV is very small, $\bar{u}$ is close enough to μ with 95% or higher confidence that we can simply use the sample mean, and not the upper confidence limit (UCL) which otherwise would ensure that we are likely to have captured the *true* mean μ.

The UCL for μ, at $\alpha = 5\%$, is approximately equal to $\bar{u} + 1.96[s/(\sqrt{n})]$, where the sample standard deviation s is equal to $CV \cdot \bar{u}$. Note that when n is small (< 25 or so), the above z-value of 1.96 (at $\alpha = 5\%$, for a normal distribution) should be replaced with a slightly higher value from the Student t-distribution. The 95% UCL values calculated from assuming various values for CV and n are listed in Table A1 below.

In most cases, the CV on exposure and exposure-related variables are large, often in the range of 50 to 150%. This is the case with the exposure rates in U.S. EPA's Pesticide Handlers Exposure Database (PHED, 1995) calculated for the various body regions and for inhalation. The PHED subsets attached to the exposure assessment document for naled (Dong and Haskell, 1999), and to this exposure assessment document (as Appendices 1 through 4), readily demonstrate this range of CV. The exposure and field studies that WH&S staff have reviewed over the years also support such findings, as human factors are involved and many sample distributions that WH&S staff have encountered are closer to lognormal than normal. Based on the above CV range and when n is less than 5 or so, the 95% UCL listed in Table A1 are $> 1.5\bar{u}$.

It is important to note that in using or interpreting the values (factors) listed in Table A1 below, we assume that the subjects (observations) in the sample were randomly selected. Otherwise, for the same confidence level, the UCL in question would be larger than that derived from Table A1, although its exact value cannot be determined statistically.

Table A1. 95% Upper Confidence Limit (UCL) for the Population Mean Based on the Various Assumed Sample Size *n* and Coefficient of Variation (CV), Calculated as a Factor of the Sample Mean $\bar{u}$ [a]

Sample Size	CV = 10% factor of sample mean	CV = 20% factor of sample mean	CV = 50% factor of sample mean	CV = 75% factor of sample mean	CV = 100% factor of sample mean	CV = 150% factor of sample mean	CV = 200% factor of sample mean
3	1.12	1.29	**1.72**	**2.08**	**2.44**	**3.17**	**3.89**
4	1.10	1.25	**1.63**	**1.94**	**2.25**	**2.88**	**3.50**
5	1.09	1.22	**1.56**	**1.84**	**2.12**	**2.68**	**3.24**
6	1.08	1.20	**1.51**	**1.77**	**2.02**	**2.53**	**3.04**
7	1.08	1.19	1.47	**1.71**	**1.94**	**2.42**	**2.89**
8	1.07	1.18	1.44	**1.66**	**1.88**	**2.33**	**2.77**
9	1.07	1.17	1.42	**1.63**	**1.83**	**2.25**	**2.67**
10	1.06	1.16	1.40	**1.59**	**1.79**	**2.19**	**2.58**
11	1.06	1.15	1.38	**1.57**	**1.75**	**2.13**	**2.51**
12	1.06	1.14	1.36	**1.54**	**1.72**	**2.08**	**2.44**
13	1.06	1.14	1.35	**1.52**	**1.69**	**2.04**	**2.39**
14	1.05	1.13	1.33	1.50	**1.67**	**2.00**	**2.34**
15	1.05	1.13	1.32	1.48	**1.65**	**1.97**	**2.29**
16	1.05	1.13	1.31	1.47	**1.63**	**1.94**	**2.25**
17	1.05	1.12	1.30	1.45	**1.61**	**1.91**	**2.21**
18	1.05	1.12	1.29	1.44	**1.59**	**1.88**	**2.18**
19	1.05	1.11	1.29	1.43	**1.57**	**1.86**	**2.15**
20	1.04	1.11	1.28	1.42	**1.56**	**1.84**	**2.12**
21	1.04	1.11	1.27	1.41	**1.55**	**1.82**	**2.09**
22	1.04	1.11	1.27	1.40	**1.53**	**1.80**	**2.07**
23	1.04	1.10	1.26	1.39	**1.52**	**1.78**	**2.04**
24	1.04	1.10	1.26	1.38	**1.51**	**1.77**	**2.02**
25	1.04	1.10	1.25	1.38	1.50	**1.75**	**2.00**
26	1.04	1.10	1.25	1.37	1.49	**1.74**	**1.98**
27	1.04	1.10	1.24	1.36	1.48	**1.72**	**1.96**
28	1.04	1.09	1.24	1.35	1.47	**1.71**	**1.94**
29	1.04	1.09	1.23	1.35	1.46	**1.70**	**1.93**
30	1.04	1.09	1.23	1.34	1.46	**1.68**	**1.91**

[a] 95% UCL $\approx \bar{u} + (2.5 \cdot \mathrm{CV} \cdot \bar{u})/\sqrt{n}) = \bar{u}\,[1 + (2.5 \cdot \mathrm{CV})/(\sqrt{n})] = \bar{u}$ [factor], where 2.5 is an approximate global Student *t*-value; those estimated factors exceeding 1.50 are listed in bold.