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

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

OFFICE OF PESTICIDE PROGRAMS
REGISTRATION DIVISION (7505P)

March 14, 2018

MEMORANDUM

SUBJECT: N,N-dimethyltetradecanamide; Human Health Risk Assessment and Ecological Effects Assessment to Support Proposed Exemption from the Requirement of a Tolerance When Used as an Inert Ingredient in Pesticide Formulations.

All PC Code: 800306
Decision No.: D-502315

Petition No: IN-10805

DP Barcode: N/A
Regulatory Action: Inert Tolerance Exemption; 40 CFR 180.910
All CAS Reg. No.: 3015-65-4

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EXECUTIVE SUMMARY

The EPA (Agency) received a petition (IN-10805) from Technology Sciences Group, (1150 18th Street, NW, Suite 1000 Washington, DC 20036) Bergeson & Campbell PC (2200 Pennsylvania Avenue, N.W. Suite 100W Washington, D.C. 20037) on behalf of Stepan Company (22 West Frontage Road, Northfield, Illinois 60093) requesting that the Agency establish a tolerance exemption for residues of N,N-dimethyltetradecanamide (CAS Reg No. 3015-65-4) when used as an inert ingredient (surfactant and solvent) on pre- and post-harvest crops under 40 CFR Part 180.910. EPA published the notice of filing for this petition in the Federal Register on November 23, 2015 (80 FR 72941). One comment was received in response to this notice.

This chemical is very similar in structure to two other compounds that EPA has established tolerance exemptions as inert ingredients in food use pesticide formulations under 40 CFR 180.920. These two inert ingredients are: N,N-dimethyldecanamide (decanamide, N, N-dimethyl-) and N,N-dimethyloctanamide (octanamide, N,N-dimethyl), which differ from the proposed inert only in the number of carbons. Therefore, data to support N,N-dimethyldecanamide and N,N-dimethyloctanamide are considered suitable surrogates to characterize toxicity due to exposure to N,N-dimethyltetradecanamide.

N,N-dimethyltetradecanamide is not a sensitizer. Based on the acute toxicity data on surrogate chemicals N,N-dimethyldecanamide (decanamide, N,N-dimethyl-) and N,N-dimethyloctanamide (octanamide, N,N dimethyl), it is expected to be of low oral acute toxicity; the lethal dose, LD_{50} in rats is 1770 milligrams/kilogram (mg/kg). The acute dermal LD_{50} is greater than 400 mg/kg and the acute inhalation lethal concentration, LC_{50} is greater than 3.55 milligrams/liter (mg/l). It is expected to be a severe irritant to the skin and corrosive to the eyes.

A ninety-day oral toxicity study is available in rats. In the rat, toxicity is manifested as an increased incidence of basophilic regenerative tubules in the renal cortex as well as a slight increase in the amount of protein excreted in the urine at 10,000 parts/per/million (ppm) (787.6 mg/kg/day). The no-observed-adverse effect level (NOAEL) is 2000 ppm (136.8 mg/kg/day). The chronic reference dose (cRfD) is based on this study.

A 6-week toxicity study in dogs via gavage is available. In this study, decreased food consumption is seen at 1,000 mg/kg/day, the highest dose tested. The NOAEL is 500 mg/kg/day.

Developmental toxicity studies are available on rats and rabbits. Fetal susceptibility is not observed in either study. In rats, maternal and developmental toxicity are observed at 450 mg/kg/day. Maternal toxicity is manifested as clinical signs, food consumption and increased post-implantation loss. Developmental toxicity is manifested as decreased fetal body weight, increased incidence of skeletal malformations/variations. In the rabbit, neither maternal nor developmental toxicity is observed at dose levels up to 1,000 mg/kg/day.

In a 5-day repeat dose inhalation toxicity study in rats (nose only, 6-hour exposure per day), marginally reduced body weight gains and goblet cell hyperplasia in the nasal and paranasal

cavities were seen at 521.2 mg/m^3 (approximately 426.8 mg/kg/day), the highest dose tested. The NOAEL is 111.2 mg/m^3(approximately 135.8 mg/kg/day).

N,N-dimethyltetradecanamide is negative for gene mutations and clastogenicity in the Ames test and the micronucleus assay, respectively.

Carcinogenicity studies with N,N-dimethyltetradecanamide are not available. However, a Derek Nexus structural alert analysis was conducted with N,N-dimethyl 9-decenamide and indicated no structural alerts for carcinogenicity or mutagenicity. Therefore, N,N-dimethyl tetradecanamide is not expected to be carcinogenic.

Neurotoxicity and immunotoxicity studies with N,N-dimethyl tetradecanamide are not available for review. However, evidence of potential neurotoxicity or immunotoxicity was not observed in the submitted studies.

Metabolism studies with N,N-dimethyltetradecanamide are not available for review. However, based on the chemical structure and known mammalian enzymatic activities, N,N-dimethyltetradecanamide is expected to undergo carboxyamide hydrolysis by amidase enzymes that have broad substrate specificity.

A dermal penetration study with N,N-dimethyl 9-decenamide was conducted in rats. Following 10 hours of exposure, the average amount absorbed was 75% of the 3.24 mg/cm^2, 46% of the 0.108 mg/cm^2, and 57% of the 0.00808 mg/cm^2 doses. An *in vitro* dermal absorption study with N,N-dimethyl 9-decenamide was conducted with human skin. The percentage of the concentration absorbed after 24 hours of exposure ranged from 70.198% (19.2% formulation) to 86.852% (0.192% formulation). The dermal absorption factor is 85%.

The chronic reference dose (cRfD) as well as all exposure scenarios is based on the 90-day toxicity study in the rat. In this study, the LOAEL is 10,000 ppm (equivalent to 787.6 mg/kg/day) based on an increased incidence of basophilic regenerative tubules in the renal cortex as well as a slight increase in the amount of protein excreted in the urine. The NOAEL is 2000 ppm (equivalent to 136.8 mg/kg/day). The standard uncertainty factors are applied to account for interspecies (10x) and intraspecies (10x) variations. The FQPA safety factor for the protection of infants and children is reduced to 1X. An additional 3X FQPA safety factor was applied to account for the extrapolation from subchronic to chronic exposures scenarios. This results in a level of concern (LOC) for the margin of exposure (MOE) of 300 for the dietary scenario only. The LOC for the MOE is 100 for short- and intermediate-term dermal and inhalation exposure scenarios. The chronic population adjusted dose (cPAD) = 0.456 mg/kg/day (cPAD =POD/300). A dermal absorption factor of 85% was applied based a dermal penetration study in rats. A default value of 100% absorption was used for the inhalation absorption factor.

There was no hazard attributable to a single exposure seen in the toxicity database for N,N-dimethyltetradecanamide. Therefore, it is not expected to pose an acute risk.

Chronic dietary risk assessments were conducted on N,N-dimethyltetradecanamide using the Dietary Exposure Evaluation Model software with the Food Commodity Intake Database

(DEEM-FCID™, Version 3.16). One hundred percent crop treated was assumed, default processing factors and tolerance-level residues for all foods and use limitations of not more than 20 % by weight in pesticide formulations. Conservative estimated drinking water concentrations of 100 ppb were incorporated directly into the dietary assessment. The chronic dietary risk assessment shows that the chronic dietary risk estimates are not of concern (i.e., <100% cPAD). For the U.S. population, the exposure for food and water utilized 16.9 % of the cPAD. The chronic dietary risk estimate for the highest exposed population subgroup, children 1-2 years old, is 62.3 % of the cPAD.

Short- and intermediate term aggregate exposures take into account short- and intermediate-term residential exposure plus chronic exposure to food and water (considered to be a background exposure level). EPA concluded that the combined short- and intermediate-term aggregated food, water, and residential pesticidal exposures result in MOEs of 680 and 1475, respectively, for both adult males and females. Adult residential exposure combines high end dermal and inhalation handler exposure from liquids/trigger sprayer/home garden and indoor hard surface, wiping with a high end post application dermal exposure from contact with treated lawns. As the level of concern is for MOEs that are lower than 100, these MOEs are not of concern. The combined short- and intermediate-term aggregated food, water, and residential pesticidal exposures result in MOEs of 359 and 394, respectively, for children. Children's residential exposure includes total exposures associated with contact with treated lawns and surfaces (dermal and hand-to-mouth exposures). As the level of concern is for MOEs that are lower than 300, these MOEs are not of concern.

Occupational handler risks are not of concern provided that protective gloves are worn except for mixer/loader/applicators applying wettable powder with a low pressure hand wand. Occupational post-application exposures are not of concern.

N,N-dimethyltetradecanamide is not acutely toxicity to the fathead minnow but is acutely toxic to *Daphnia magna*. It is readily biodegradable in a CO_2 evolution test. Based on EPI Suite TM 4.11, it is not expected to bioaccumulate.

Taking into consideration all available information on N,N-dimethyltetradecanamide (CAS Reg. No. 3015-65-4), EPA is establishing an exemption from the requirement of a tolerance for residues of N,N-dimethyltetradecanamide when used in pesticide formulations as an inert ingredient (surfactant/solvent), not to exceed 20% of the formulation. The limitation is applied as a result of aggregate risks of concern when considering the unlimited use of N,N-dimethyltetradecanamide as was initially requested. Consequently, EPA concludes that there is a reasonable certainty that no harm will result to the general population or to infants and children from aggregate exposure to N,N-dimethyltetradecanamide. Therefore, the establishment of an exemption from tolerance as an inert ingredient (surfactant/solvent) in or on raw agricultural commodities and growing crops under 40 CFR Part 180.910 and limited to a maximum concentration of 20% in the end-product formulation can be considered safe under section 408 of the FFDCA.

1. BACKGROUND

The EPA (Agency) received a petition (IN-10805) from Technology Sciences Group, (1150 18th Street, NW, Suite 1000 Washington, DC 20036) Bergeson & Campbell PC (2200 Pennsylvania Avenue, N.W. Suite 100W Washington, D.C. 20037) on behalf of Stepan Company (22 West Frontage Road, Northfield, Illinois 60093) requesting that the Agency establish a tolerance exemption for residues of N,N-dimethyltetradecanamide (CAS Reg No. 3015-65-4) when used as an inert ingredient (surfactant and solvent) on pre- and post-harvest crops under 40 CFR Part 180.910. EPA published the notice of filing for this petition in the Federal Register on November 23, 2015 (80 FR 72941). One comment was received in response to this notice.

This document provides an assessment of the risk to human health and the environment for N,N-dimethyltetradecanaimde when used as an inert ingredient (surfactant) in pesticide formulations used on pre- and post-harvest crops limited to 20% in the end-use formulation. Information from the submitter's petition is reproduced and referenced in this assessment.

I. INERT INGREDIENT PROFILE

Table 1. Physical and Chemical Properties of N,N-dimethyltetradecanamide

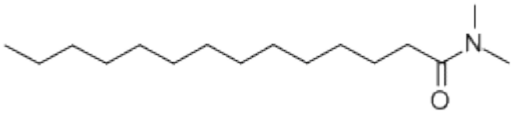
Parameter	Values	Reference
Structure		
CAS #	3015-65-4	
Molecular Formula	$C_{16}H_{33}NO$	
Molecular Weight (g/mol)	255.443	
Common Names	N,N-dimethylmyristamide	
Log Kow	5.41	
BP (ºC)	343.66	
MP (ºC)	99.14	
VP (mmHg at 25ºC)	0.000187	
Water Solubility (mg/L)[a]	0.93364[b]	
Henry's Law Constant atm-m^3/mole at 25ºC (Bond)	1.62 E-006	
Log Koc	3.672[c]; 3.870[d]	
Probability of Rapid Biodegradation (BIOWIN)	0.9445[e] 0.9805[f] 2.8788[g] 0.6730[h] 0.7772[i]	

Table 1. Physical and Chemical Properties of N,N-dimethyltetradecanamide		
Parameter	**Values**	**Reference**
BCF (L/kg wet-wt)	72.62	
Atmospheric Oxidation Half Life (hr)	3.616	
Fugacity Model Compartment/Mass Amount (%)	Air: 0.643 Water: 23.4 Soil: 72.6 Sediment: 3.35	
Fugacity Model Compartment/Half Life (hr)	Not Provided [j] Not provided [k]	

[a] WSKOW result; not appropriate for estimation of water solubility of dispersible compounds, including surfactants
[b] Fragment results
[c] MCI method results
[d] Kow method results
[e] Kow method results
[f] Biowin1 (linear model)
[g] Biowin2 (non-linear model)
[h] Biowin3 (Ultimate survey model)
[i] Biowin5 (MITI linear model)
[j] Biowin6 (MITI non-linear model)
[l] Model River
[k] Model Lake

II. HUMAN HEALTH ASSESSMENT

The following studies were reproduced and referenced from the petition submitted by the registrant. Studies were conducted with either Steposol MET-10U (N,N dimethyl 9-decenamide), Hallcomid M-8-10 (mixture containing the surrogate chemicals N,N dimethyl decanamide and octanamide, N,N-dimethyl) or N,N dimethyloctanamide.

Acute Toxicity Studies

Table 2. Acute Toxicity Profile of N,N-dimethyltetradecanamide

Guideline No.	Study Type	Results
870.1100	Acute-Oral-rats	LD_{50} = 1770 mg/kg
870.1200	Acute-Dermal-rats	Female LD_{50} > 400 and < 2,000 mg/kg Male LD_{50} > 2,000 mg/kg
	Acute inhalation-rats	LC_{50} > 3.55 mg/L
870.2500	Acute-Dermal Irritation-rabbits	Severe Irritation
870.2500	Acute-Eye Irritation-rabbits	Corrosive
870.2400	Dermal sensitization-guinea pig	Not a sensitizer

Acute Toxicity Studies

N,N dimethyloctanamide:

Skin Irritation:

Skin irritation potential of N,N dimethyloctanamide was evaluated in the in vitro Epiderm ™ Skin Model. This test determines irritation potential based upon the relative conversion of MTT (3-[4 ,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) in tissues that had been treated with the test substance for 60 minutes, followed by a 42-hour post-exposure expression period. The irritation potential is determined by the relative viability of the skin with and without test substance exposure, as measured by absorbance at 570 nm. In this test, the mean viability of the positive control, 5% SLS, was 3.27%. The mean viability of the neat test substance was 3.26%. Because the mean viability was less than 50%, N,N dimethyloctanamide is considered a potential skin irritant (Costin and Krawiec, 2014).

Hallcomid M-8-10 (Decanamide, N,N-dimethyl-, and octanamide, N,N-dimethyl mixture):

Oral:

An acute oral toxicity study was conducted with Hallcomid M-8-10. This study was conducted initially as a limit dose study by administration of undiluted test material to 5 male and 5 female rats at a dose of 5,000 mg/kg. These initial groups all died and an LD_{50} was determined for males and females combined using groups of 2 males and 2 females per dose at doses of 2,500, 1,250 and 625 mg/kg. The calculated LD_{50} for males and females combined was 1,770 mg/kg. A female-only LD_{50} for the mixture would have been lower than 1, 770 mg/kg because both females died following administration of the 2,500 mg/kg dose, and one of two females died following administration of the 1,250 mg/kg dose of the mixture. In contrast, one of two males died following administration of the 2,500 mg/kg dose and no males died following administration of the lower doses. Thus female rats are more sensitive acutely than males, and the LD_{50} for the mixture would have been closer to the LD_{50} determined for N,N dimethyloctanamide if the LD_{50} for females had been determined. Decanamide, N,N-dimethyl-, and octanamide, N,N-dimethyl mixture is classified as EPA Toxicity Category III for acute oral toxicity (MRID 45369714).

Dermal:

The potential for Hallcomid M-8-10 to cause toxicity following acute dermal exposure was evaluated under 24 hour occlusion. Test material was applied under occlusion to 5 rats/dose/sex at doses of 50, 200, 2,000 and 5,000 mg/kg to males and 50, 200, 400, and 2,000 mg/kg to females. The LD_{50} for males was approximately 2,000 mg/kg and for females, between 400 and 2,000 mg/kg. Decanamide, N,N-dimethyl-, and octanamide, N,N-dimethyl mixture is classified as EPA Toxicity Category II for acute dermal toxicity (MRID 45369716).

Inhalation:

The potential toxicity of Hallcomid M-8-10 following acute inhalation exposure was evaluated in rats exposed to the test article as an aerosol. Briefly, groups of 5 male and 5 female rats were exposed in nose/head only inhalation chambers to aerosol concentrations of: 0.118, 0.586, 2.008, or 3.550 mg/L decanamide, N,N-dimethyl-, and octanamide, N,N-dimethyl mixture. The aerosol particulate size for all exposure concentrations were 99 to 100% ~ 3µm in size. Exposure duration was 4 hours. Clinical signs of toxicity were reported for the groups exposed to 0.586 mg/l and higher, and a single male rat died at the highest exposure. The LC_{50} was determined to be > 3.550 mg/L. Decanamide, N,N-dimethyl-, and octanamide, N,N-dimethyl mixture is classified as EPA Toxicity Category IV for acute inhalation toxicity (MRID 45369717).

Skin Irritation:

The potential of decanamide, N,N-dimethyl-, and octanamide, N,N-dimethyl mixture to cause dermal irritation was evaluated in a single New Zealand white rabbit. The rabbit received a

dermal dose of 0.5 ml of the undiluted test article covering an area of one square inch of intact skin, covered by gauze. Severe irritation was noted 1/2 to one hour after test article application to skin that persisted through 72 hours. Due to the effects reported in the first animal, the study was terminated without testing additional animals. Decanamide, N,N-dimethyl-, and octanamide, N,N-dimethyl mixture is classified as EPA Toxicity Category I for dermal irritation (MRID 45369722).

Eye Irritation:

The potential of decanamide, N,N-dimethyl-, and octanamide, N,N-dimethyl to cause ocular irritation was evaluated in a single New Zealand white rabbit. The rabbit received a dose of 0.1 ml of the undiluted test article in one eye that was rinsed after 24 hours. The exposure produced corneal opacity, iritis, and conjunctival irritation that persisted throughout the four-day study. Due to the severity of the effects reported in the first animal, the study was terminated without testing additional animals. Decanamide, N,N-dimethyl-, and octanamide, N,N-dimethyl mixture is classified as EPA Toxicity Category I for primary eye irritation (MRID 45369721).

Dermal Sensitization:

The potential for decanamide, N,N-dimethyl-, and octanamide, N,N-dimethyl to produce delayed contact hypersensitivity in guinea pigs was evaluated following exposure to a 5% solution in 80% ethanol 20% distilled water according to an adaptation of the Buehler method. There were no grade 1 responses in the treated or control subjects following the primary challenge. The incidence of +/- responses in the test article treated group was comparable to that of the naive control group, indicating that sensitization had not occurred (MRID # 45369724).

Repeated Dose Toxicity studies with Decanamide, N,N-dimethyl-, and Octanamide, N,N-dimethyl

6-Week Oral-gavage:

Dog:

A 6-week range-finding study in dogs that received gavage doses of Hallcomid-M-8-10 was conducted to characterize the effects from repeated exposure to 0, 20, 100 or 500 mg/kg/day test material. After 2 weeks, the 500 mg/kg/day dose was increased to 1,000 mg/kg/day due to a lack of toxicity in the high dose group. A decrease in food consumption was observed in the high dose group, and clinical signs of toxicity were observed in the high dose group after the dose was increased to 1,000 mg/kg/day. An increase in liver N-demethylase and cytochrome P450 activity was observed in the liver in the high dose group in addition to increased liver weight. Both are expected as an adaptive response to the high dose of test material. Histopathologic findings in the high dose group were changes in the lungs that correlated with aspiration during gavage of the test material. Other histopathologic findings were considered by the pathologist to be of spontaneous origin. The LOAEL is 1,000 mg/kg/day based on decreased food consumption. The NOAEL was identified as 100 mg/kg/day, but no clinical signs were identified during the 500 mg/kg/day dosing, so the NOAEL is 500 mg/kg/day (MRID 45369727).

90-Day oral-Diet

Rat:

In a 90-day oral study (OECO TG 406), Hallcomid-M-8-10 was administered in the diet of 10 Wistar rats per sex at 0, 400, 2000, or 10,000 ppm for 13 weeks, and at 0 or 10,000 ppm for 13 weeks followed by a 28-day recovery period. Corresponding mg/kg/day doses for males were: 0, 27.4, 136.8, and 787.6, and for females: 0, 35.2, 178, and 894.6 mg/kg/day. Endpoints monitored during the study included survival, appearance, feed/water consumption, and body weight. The study animals were inspected at least twice daily and a detailed assessment of findings for individual animals was performed once weekly. The routine assessments included evaluation of general behavior, posture, breathing and excretions. Examination of hematological endpoints, clinical chemistry, and urinalysis were carried out on all animals throughout the study. After sacrifice, rats underwent gross pathology and histopathology examinations. The adrenals, heart, testes, brain, liver, lung, spleen, and kidneys were weighed, and all organs specified in the guideline were fixed and subjected to histopathological evaluation.

The test substance had no effect on survival in males or females. In addition, no treatment related abnormalities were observed in general behavior, posture, breathing or excretions in any dose group. Some males (5/20) in the high dose groups appeared emaciated during weeks 11 and/or 12, while the appearance of females was unaffected at any dose. Body weight gain among the males in the main mid and high dose groups was significantly lower (6-8% and 7-11%, respectively) than controls beginning in week 3. Body weight gain in the high dose females of the recovery group was significantly lower (6-12%) than the control group during weeks 2-13. There was no toxicologically significant difference between the body weights of the treated and control animals after the recovery period. There was no difference in feed and water consumption in any dosed group compared to controls. Absolute liver weights (high dose female) and relative liver weights (high dose, both sexes) were slightly but statistically significantly increased at the end of treatment. Of these effects, only the female relative liver weights were still elevated after the recovery period. The outcome of the clinical chemistry, gross pathological and histopathological examinations did not support a test article related effect on liver function that was toxicologically significant. Effects on liver function at the high dose included increased plasma cholesterol levels in both sexes, which may suggest slightly impaired fat metabolism in the liver. The lack of histological findings in the liver precludes definitively linking fat metabolism to slightly increased absolute liver weights (female) and relative liver weights (male and female). The impaired metabolism may be a non-specific adaptation to higher metabolic demands, hence the toxicological importance of this finding was impossible to determine. Cholesterol levels were not elevated after the recovery period. The relative spleen weights among females were also significantly higher even after the recovery period. There were no accompanying changes in spleen morphology. Higher relative brain weights in high dose females were not considered toxicologically relevant because they were thought to be the result of lower body weights. Finally, high dose males showed an increased incidence of basophilic regenerative tubules in the renal cortex as well as a slight increase in the amount of protein excreted in the urine. These effects were not statistically significant after the recovery period. The NOAEL for decanamide, N,N-dimethyl-, and octanamide, N,N-dimethyl in this study was

2000 ppm in males based on reversible kidney effects, and 10,000 ppm in females, equivalent to approximately 136.8 mg/kg/day in males and 894.6 mg/kg/day in females (MRID 45369715).

Developmental Toxicity Studies

Rat:

A study was conducted to evaluate the effects of Hallcomid-M-8-10 on the embryonic and fetal development of Wistar rats by Becker & Biedermann. Groups of 25 pregnant female rats received gavage doses of 0, 50, 150, or 450 mg/kg/day of decanamide, N,N-dimethyl-, and octanamide, N,N-dimethyl day gestation days 6-15. On gestation day 21, dams were sacrificed and fetuses were removed by Caesarean section and examined. Dams in the high dose group exhibited clinical signs of toxicity during the exposure period, including ruffled fur, recumbency, apnea and in 4 dams, a comatose state. No clinical signs were reported in dams of the two lower dose groups. A significant decrease in food consumption was reported in the dams of the 450 mg/kg/day treatment group during the dosing period, while no significant decreases in food consumption were reported for the lower dose groups. The dams in the high dose group gained less body weight during gestation than the controls such that the difference in body weight between the high dose group and controls became significant on days 18 and 19 of gestation. The corrected weight gain in controls throughout gestation was 7.8%, and in the high dose group the corrected weight gain was 4.9%. No effects of test article on body weight in the lower dose groups were identified. There was a significant decrease in fetal body weight in the 450 mg/kg/day group and an increased incidence of fetuses with common skeletal abnormalities and delayed developmental growth. The maternal and developmental NOAEL from this study are both 150 mg/kg/day. The maternal LOAEL of 450 mg/kg/day is based on clinical signs of toxicity and post-implantation loss. The developmental LOAEL of 450 mg/kg/day is based on decreased body weight and an increased incidence of skeletal variations. The maternal NOAEL = 150 mg/kg/day. The developmental LOAEL of 450 mg/kg/day is based on decreased body weight and an increased incidence of skeletal variations. The developmental NOAEL = 150 mg/kg/day (MRID 45369719).

Rabbit:

In an embryotoxicity/teratogenicity study (OECD TG 414), pregnant Chinchilla Rabbits (Chbb: CH, Hybrids, SPF quality; n=16/group) received Hallcomid-M-8-10 at doses of 100, 300, or 1,000 mg/kg/day by gavage in a vehicle of bi-distilled water and 0.5% Cremophor. A vehicle control group was run concurrently. Rabbits received doses on post-coitum days 6-18. Throughout the study, regular observations were made of mortality, food consumption, and body weight. Sacrifice took place on day 28 post-coitum. Post mortem examination included gross macroscopic examination of organs, particularly uterus, uterine contents, position of fetuses, and number of corpora lutea. Fetuses were removed, weighed and examined for gross abnormalities. Further fetal examinations were carried out on viscera, heads, and skeletons. Reproductive endpoints evaluated were pre- and post-implantation loss, mean number of live fetuses per dam, and sex ratio.

There were no deaths throughout the study that were attributed to the test substance. The food consumption of high dose animals was reduced during the dosing period (post-coitum days 6-19); this difference was statistically significant during post-coitum days 11-15. Mean body weight gain during this period was slightly but not statistically significantly reduced in high dose animals. The mean body weight gain corrected for uterus weight was similar across dose groups. There was no significant difference from controls on any reproductive endpoint. There was no statistically significant difference in any fetal endpoint of treated fetuses versus controls. The maternal NOAEL = 1,000 mg/kg/day, the highest dose tested. The maternal NOAEL = 300 mg/kg/day. The developmental NOAEL = 1,000 mg/kg/day, the highest dose tested.

Inhalation Toxicity Study-Rat

Male and female Wistar BorWISW SPF-CPB rats (10/sex/group) were exposed nose only to target concentrations of 0, 100, 500 or 2500 mg/m3 of aerosols of the test material for 6 hours /day for five consecutive days followed by a recovery period which ended on study day 22. Actual concentrations were 0, 24.5, 111.2 and 521.2 mg/m3, respectively. The average MMAD and GSD of the aerosols at each concentration were approximately 1.4 microns and 1.5, respectively. Half of the animals were killed on study day 7 and the remainder on study day 22. Animals exposed to the high dose exhibited labored breathing, wheezing, serous nasal discharge and reduced motility from study days 2 to 7. Body weights of males and females were lower than initial values on days 4 and 7 of the test. Rectal temperatures of males were slightly lower than control on the first day of the test. Rectal temperatures of females were lower than control on the first day of the test and on day 7. An increased incidence of goblet cell hyperplasia in the nasal and paranasal cavities on days 7 (5/5) and 22 (4/5) compared to the control (0/5 and 1/5, respectively). The NOAEL was considered to be 111.2 mg/m^3 (approximately 135.8 mg/kg/day) based on reduced body weight gain and histopathology of the nasal cavity observed at 521.2 mg/m^3 (approximately 426.8 mg/kg/day)(MRID 45369720).

Chronic/Carcinogenicity Study-Rat

Carcinogenicity studies with N,N-dimethyltetradecanamide are not available. However, a Derek Nexus structural alert analysis was conducted with N,N-dimethyl 9-decenamide and indicated no structural alerts for carcinogenicity or mutagenicity. Therefore, N,N-dimethyl tetradecanamide is not expected to be carcinogenic.

Genotoxicity Studies

Hallcomid M-8-10 was evaluated for mutagenic activity in the *in vitro Salmonella typhimurium - E. coli* reverse mutation assay. Tester strains used were *Salmonella typhimurium* strains: TA1537, TA98, TA100, and TA1535. Testing was performed in triplicate at each concentration both with and without an S9 metabolic activation system of rat liver induced by Aroclor™. Hallcomid M-8-10 was tested using the plate incorporation method at 8, 40, 200, and 5000 μg/plate without S9 and 0, 25, 50, 100, 200, 400 and 800 μg/plate with activation. Cytoxicity was observed either in one or more strains at ≥ 200 μg/plate with and without metabolic activation. Criteria for a negative response were met for all tester strains with and

without metabolic activation in both the initial and confirmatory assays. The data from the positive control substances demonstrated the sensitivity of the assay for detecting chemical mutagens with and without S9. The study data support the conclusion that Hallocmid M-8-10 is negative for mutation in the bacterial reverse mutation assay (Herbold 1992; MRID 45369728).

Hallcomid M-8-10 was evaluated for mutagenic activity in the HGPRT assay in Chinese Hamster lung cells (V79). Hallcomid M-8-10 did not induce forward mutations at the HGPRT locus at concentrations of 25- 250 µg/mL in the presence or absence of metabolic activation. In the pre-test, cytotoxicity was noted to increase in a dose-dependent manner starting at a concentration of 200 µg/mL. The positive control substance for the non-activated condition was ethylmethanesulfonate and for the S-9 activated condition, methylbenzanthracene. The test material induced significant concentration-related cytotoxic reflected in decreases in relative survival and population growth but not in cloning efficiency (Brendler-Schwaab 1994; MRID 45369729).

Hallcomid M-8-10 was evaluated for clastogenicity in Chinese Hamster Ovary (CHO) cells. CHO cells were exposed to 10-160 µg/mL Hallcomid M-8-10 in the absence of metabolic activation and 7.2-180 µg/mL with metabolic activation. Cells were harvested after 8, 24, or 30 hours. Cytotoxicity was observed at the highest doses under each metabolic condition. The mitotic indices were reduced to 66.7 and 43.2 % of solvent controls. The number of cells with chromosomal aberrations was not significantly higher in the presence of Hallcomid M-8-10 under any experimental condition except one. At 180 µg/mL Hallcomid with metabolic activation, there was a significant increase in the number of cells with chromosomal aberrations at the 8-hour harvest time compared with control cells. However, the difference was not significant in the context of historical control aberration frequency in that laboratory. Study authors did not consider the difference to be biologically significant. The positive control compounds mitomycin C and cyclophosphamide induced clear clastogenic effects, demonstrating the sensitivity of the test system. Under the conditions of this study. Hallcomid M-8-10 was not considered to be clastogenic with or without metabolic activation (Gahlmann 1995, MRID 45369730).

Metabolism:

There are no published mammalian metabolism studies conducted on N,N-dimethyl tetradecanamide. Based on the chemical structure and known mammalian enzymatic activities, N,N-dimethyl tetradecanamide is expected to undergo carboxamide hydrolysis by amidase enzymes that have broad substrate specificity. This results in a carboxylic acid with a fatty acid structure and terminal double bond (9-decenoic acid). The surrogate chemicals will be similarly metabolized by amidase enzymes, resulting in fatty acids 8 and 10 carbons in length (octanoic and decanoic acids). Fatty acids are products of digestion that are metabolized by beta oxidation in the mitochondria to produce acetyl-CoA, which can enter the citric acid cycle to produce energy. Beta oxidation is a process that begins at the carboxylic acid end of the molecule and cleaves two carbons at a time from the activated fatty acid. Beta oxidation requires a double bond at even numbered carbons on the fatty acid, such that these bonds are generated by acylCoA dehydrogenase if the double bond is not naturally occurring. If a double bond is located at an odd number carbon, as it is for the proposed inert, the double bond is converted from *cis*- to

trans- by the enzyme, enoyl-CoA, essentially moving the bond from the number 9 carbon to the number 8 carbon. Thus, the product of beta oxidation metabolism of the proposed inert and the surrogate inert compounds is essentially identical (Mayes & Botham, 2003).

Dermal Absorption:

Rats:

In a dermal penetration study radiolabeled and unlabeled STEPOSOL MET-10U (^{14}C-methyl-MET-10U, Lot number 84463-1-17-1, purity 100%; MET-10U, Lot number S63455701, purity 99.1%) was dermally applied to a shaved area of ~ 10 cm^2 on the back to groups of 12 male Sprague Dawley rats at concentrations of 3.24, 0.108, or 0.00808 mg/cm^2. Four rats/group were sacrificed 10, 24, and 120 hours after application. Urine, feces and expired air were collected at 0-10, 10-24, and daily up to 120 hours after dermal application.

The mean recovery of the radiolabel was acceptable, being 96% of the applied dose. The majority of the dose was absorbed by 10 hours post-dose; however, low but measurable amounts of radioactivity were associated with the application site at all time points. At each subsequent time point, the percent of dose absorbed generally increased as the low levels of absorbable residues remaining in the exposed skin were made available. Following 10 hours of exposure, the average amount absorbed was 75% of the 3.24 mg/cm^2, 46% of the 0.108 mg/cm^2, and 57% of the 0.00808 mg/cm^2 doses. Following 120 hours of exposure, the average amount absorbed was 82% of the 3.24 mg/cm^2 dose, 68% of the 0.108 mg/cm^2 dose, and 67% of the 0.00808 mg/cm^2 dose. As a percentage of absorbable dose, 97% to 99% of the amount available for absorption was found in the urine, cage rinse, cage wash, feces, and expired air. The percent of total absorbed dose present in urine and feces collected at each time point for each dose group were comparable regardless of dose concentration, suggesting that excretion was not saturated. By 120 hours post-dose, ~83% of the absorbed dose was present in urine (including cage rinse), and up to 9% of the absorbed dose was present in feces. As a percent of absorbable dose, ~ 87% to 91% of the available dose was excreted in urine and feces by 120 hours post-dose. The remaining amount of absorbed radioactivity was recovered in the carcass, expired air, and cage wash. The rate, route, or extent of elimination was not dependent on dose (MRID 50248101).

Human skin:

In an *in vitro* dermal absorption study STEPOSOL® MET-10U (MET-10U; 99.2%, Lot No. S53427601) was applied *in vitro* to four replicate 2.5 cm^2 slices of human skin/applied dose at applied doses of 2.679, 0.2679, and 0.02679 mg/cm^2. In addition, ^{14}C-labeled reference materials (benzoic acid; mannitol) were applied to four replicate 2.5 cm^2 slices of human skin/reference material each at 1 mM concentrations (500 µL). The exposure duration was 24 hours and absorption was evaluated by sampling the receiver fluid (50% ethanol/50% ultrapure water for the test material) at 1, 2, 4, 8, and 24 hours of exposure.

The percentage of the initial dose that was absorbed into the receiver (Cumulative % Initial Dose Absorbed) after 24 hours of exposure from Franz Cells with acceptable mass balance

values ranged from 70.198% (19.2% formulation) to 86.852% (0.192% formulation). The cumulative percent absorption for ^{14}C-Benzoic Acid was 96.4% ±0.6%, and for ^{14}C-Mannitol was 95.8% ±1.2%. The overall flux (total amount of material permeating through a cm^2 of skin per hour) increased with an increase in MET-10U formulation concentration. The mean flux values for the 0.192%, 1.92%, and 19.2% MET-10U formulations were 2.01 ±0.64 $\mu g/cm^2/h$, 32.99 ±7.75 $\mu g/cm^2/h$, and 90.54 ±45.77 $\mu g/cm^2/h$, respectively. Results for the ^{14}C-Benzoic Acid and ^{14}C-Mannitol reference materials indicated the assay was properly performed and the skin used performed within expected parameters (MRID 50248103).

Table 3. Toxicology Profile for N,N-dimethyltetradecanamide

Study Type	Doses	Results
6-week oral gavage dog	0, 20, 100, or 500 mg/kg/day	NOAEL = 500 mg/kg/day. LOAEL = 1,000 mg/kg/day based on decreased food consumption.
90-day dietary rat	0, 400, 2,000, or 10,000 ppm equivalent to 27.4/35.2, 136.8/178.5, 787.5/894.6 (M/F) mg/kg/day.	NOAEL = 2,000 ppm (136.8 mg/kg/day). LOAEL = 10,000 (787.6 mg/kg/day) based on an increased incidence of basophilic regenerative tubules in the renal cortex as well as a slight increase in the amount of protein excreted in the urine.
Developmental toxicity-rat	0, 50, 150, or 450 mg/kg/day	Maternal NOAEL = 150 mg/kg/day Maternal LOAEL = 450 mg/kg/day based on clinical signs and increased post-implantation loss. Developmental NOAEL = 150 mg/kg/day Developmental LOAEL = 450 mg/kg/day based on decreased fetal body weight, increased incidence of skeletal malformations/variations.
Developmental toxicity-rabbit	0, 100, 300, or 1,000 mg/kg/day	Maternal NOAEL = 1,000 mg/kg/day Maternal LOAEL = was not established. Developmental NOAEL = 1,000 mg/kg/day. Developmental LOAEL was not established.
Inhalation toxicity-rat	0, 24.5, 111.2 and 521.2 mg/m^3	NOAEL = 111.2 mg/m^3 (approximately 426.8 mg/kg/day). LOAEL = 521.2 mg/m^3 (approximately 426.8 mg/kg/day) based on reduced bodyweight gain and goblet cell hyperplasia in the nasal and paranasal cavities.
Reverse Mutation Assay	0-5000 µg/plate	Negative
HGPRT Assay	25-250 µg/mL	Negative
Chromosomal Aberrations	7.2-180 µg/mL	Negative

Table 3. Toxicology Profile for N,N-dimethyltetradecanamide		
Study Type	**Doses**	**Results**
In vivo Dermal Penetration-Rat	3.24, 0.108, or 0.00808 mg/cm^2	Following 10 hours of exposure, the average amount absorbed was 75% of the 3.24 mg/cm2, 46% of the 0.108 mg/cm2, and 57% of the 0.00808 mg/cm2 doses.
In vitro Dermal Absorption-Human	2.679, 0.2679, and 0.02679 mg/cm^2	Percentage absorbed ranged from 70.198% (19.2% formulation) to 86.852% (0.192% formulation)

A. Toxicity Endpoint Selection

The chronic reference dose (cRfD) as well as all exposure scenarios was based on the 90-day toxicity study in the rat. In this study, the LOAEL was 10,000 ppm (equivalent to 787.6 mg/kg/day) based on an increased incidence of basophilic regenerative tubules in the renal cortex as well as a slight increase in the amount of protein excreted in the urine. The NOAEL was 2000 ppm (equivalent to 136.8 mg/kg/day). This represents the lowest NOAEL in the most sensitive species in the toxicity database. The standard uncertainty factors were applied to account for interspecies (10x) and intraspecies (10x) variations. An additional 3X uncertainty factor was applied to account for the extrapolation from subchronic to chronic exposures scenarios because the kidney effects were reversible and observed in male rats only. Additionally, in the dog following 6 weeks of oral exposure, no signs of toxicity were observed up to 500 mg/kg/day and the only sign of toxicity (decreased food consumption) was observed at the limit dose of 1,000 mg/kg/day. The 5-day inhalation toxicity study in rats was not selected for inhalation exposure assessment because the oral endpoint and inhalation endpoint yielded comparable NOAELs. In addition, the nasal effects seen in this study is primarily due to irritation and the marginal reduction body weight would have observed in the oral study. A dermal absorption factor of 85% was applied based on a dermal penetration study in rats and an *in vitro* dermal absorption study with human skin. The default value of 100% absorption was used for the inhalation absorption factor. The resultant cPAD is 0.456 mg/kg/day and acceptable MOEs for residential and occupational exposures are 300.

B. Special Considerations for Infants and Children

Section 408 of the FFDCA provides that EPA shall apply an additional margin of safety for infants and children in the case of threshold effects to account for prenatal and post natal toxicity and the completeness of the database on toxicity and exposure unless EPA determines that a different margin of safety will be safe for infants and children. EPA concludes that the FQPA safety factor could be reduced to 1X for N,N-dimethyl tetradecanamide for the following reasons:

i. The database is considered adequate for FQPA assessment. The following acceptable studies are available:

Subchronic toxicity (Rat)
Developmental toxicity (Rat, Rabbit)

ii. Developmental toxicity studies are available on rats and rabbits. Fetal susceptibility was not observed in either study. In rats, maternal and developmental toxicity were observed at 450 mg/kg/day. Maternal toxicity was manifested as clinical signs, food consumption and increased post-implantation loss. Developmental toxicity was manifested as decreased fetal body weight, increased incidence of skeletal malformations/variations. In the rabbit, neither maternal nor developmental toxicity was observed up to 1,000 mg/kg/day. Reproduction toxicity studies were not available; however, increased post-implantation loss is observed at 450 mg/kg/day in the developmental toxicity study in rats. The concern is low for post-implantation loss because there is a well-established NOAEL in the study and the established cRfD will be protective of the observed effects.

iii. Neurotoxicity studies were not available for review. However, evidence of neurotoxicity was not observed in the submitted studies.

iv. Immunotoxicity studies were not available for review. However, evidence of immunotoxicity was not observed in the submitted studies.

v. The dietary food exposure assessment utilizes proposed tolerance level or higher residues and 100% CT information for all commodities. By using these screening-level assessments, chronic exposures/risks will not be underestimated.

III. EXPOSURE ASSESSMENT

The Agency assessed the dietary exposures to N,N-dimethyltetradecanamide as an inert ingredient used in pesticide formulations applied to growing crops.

In estimating total dietary (food and drinking water) exposures to N,N-dimethyltetradecanamide, estimated dietary exposures (food and drinking water) resulting from the its use as an inert ingredient in pesticide formulations applied to growing crops and raw agricultural commodities after harvest. The exposure estimates for its use as an inert ingredient in pesticide formulations applied to growing crops and raw agricultural commodities after harvest are derived using the Agency's DEEM-FCID model for chronic dietary exposures and are in the DEEM analysis (attached for reference). The DEEM analysis was conducted using the cPAD of 0.456 mg/kg/day. EPA assessed dietary exposures from N,N-dimethyltetradecanamide in food as follows:

A. Dietary Exposure:

i. Acute exposure. No adverse effects attributable to a single exposure of N,N-dimethyl 9-decenamide was seen in the toxicity databases. Therefore, an acute dietary risk assessment is not necessary.

ii. Chronic exposure. In conducting the chronic dietary exposure assessment, EPA used food consumption information from the U.S. Department of Agriculture's (USDA's) 2003-2008 National Health and Nutrition Examination Survey, What We Eat in America (NHANES/WWEIA). As to residue levels in food, no residue data were submitted for N,N-dimethyltetradecanamide. In the absence of specific residue data, EPA has developed an approach which uses surrogate information to derive upper bound exposure estimates for the subject inert ingredient. Upper bound exposure estimates are based on the highest tolerance for a given commodity from a list of high use insecticides, herbicides, and fungicides. A complete description of the general approach taken to assess inert ingredient risks in the absence of residue data is contained in the memorandum entitled ''Alkyl Amines Polyalkoxylates (Cluster 4): Acute and Chronic Aggregate (Food and Drinking Water) Dietary Exposure and Risk Assessments for the Inerts,'' (D361707, S. Piper, 2/25/09) and can be found at http://www.regulations.gov in docket ID number EPA–HQ–OPP–2008–0738.

In the dietary exposure assessment, the Agency assumed that the residue level of the inert ingredient would be no higher than the highest tolerance for a given commodity. Implicit in this assumption is that there would be similar rates of degradation (if any) between the active and inert ingredient and that the concentration of inert ingredient in the scenarios leading to these highest levels of tolerances would be no higher than the concentration of the active ingredient.

The Agency believes the assumptions used to estimate dietary exposures lead to an extremely conservative assessment of dietary risk due to a series of compounded conservatisms. First, assuming that the level of residue for an inert ingredient is equal to the level of residue for the active ingredient will overstate exposure. The concentrations of active ingredient in agricultural products are generally at least 50 percent of the product and often can be much higher. Further, pesticide products rarely have a single inert ingredient; rather there is generally a combination of different inert ingredients used which additionally reduces the concentration of any single inert ingredient in the pesticide product in relation to that of the active ingredient. In the case of N,N-dimethyltetradecanamide, EPA made a specific adjustment to the dietary exposure assessment to account for the use limitations of the amount of N,N-dimethyltetradecanamide that may be in pesticide formulations (limited to no more than 20%) present at the maximum limitation rather than at equal quantities with the active ingredient.

Second, the conservatism of this methodology is compounded by EPA's decision to assume that, for each commodity, the active ingredient which will serve as a guide to the potential level of inert ingredient residues is the active ingredient with the highest tolerance level. This assumption overstates residue values because it would be highly unlikely, given the high number of inert ingredients, that a single inert ingredient or class

of ingredients would be present at the level of the active ingredient in the highest tolerance for every commodity. A third compounding conservatism is EPA's assumption that all foods contain the inert ingredient at the highest tolerance level. In other words, EPA assumed 100 percent of all foods are treated with the inert ingredient at the rate and manner necessary to produce the highest residue legally possible for an active ingredient. In summary, EPA chose a very conservative method for estimating what level of inert residue could be on food, then used this methodology to choose the highest possible residue that could be found on food and assumed that all food contained this residue. No consideration was given to potential degradation between harvest and consumption even though monitoring data shows that tolerance level residues are typically one to two orders of magnitude higher than actual residues in food when distributed in commerce.

Accordingly, although sufficient information to quantify actual residue levels in food is not available, the compounding of these conservative assumptions will lead to a significant exaggeration of actual exposures. EPA does not believe that this approach underestimates exposure in the absence of residue data.

iii. Dietary exposure from drinking water. For the purpose of the screening level dietary risk assessment to support this request for an exemption from the requirement of a tolerance for N,N-dimethyltetradecanamide, a conservative drinking water concentration value of 100 parts per billion (ppb) based on screening level modeling was used to assess the contribution to drinking water for chronic dietary risk assessments for N,N-dimethyltetradecanamide. These values were directly entered into the dietary exposure model.

iv. Cancer exposure. *Cancer*. A Derek Nexus structural alert analysis was conducted with N,N-dimethyl 9-decenamide and indicated no structural alerts for carcinogenicity or mutagenicity. Therefore, N,N-dimethyltetradecanamide is not expected to be carcinogenic.

B. Residential (Non-Occupational) Exposure:

The term ''residential exposure'' is used in this document to refer to non-occupational, non-dietary exposure (e.g., for lawn and garden pest control, indoor pest control, termiticides, and flea and tick control on pets). N,N-dimethyltetradecanamide may be used as an inert ingredient in products that are registered for specific uses that may result in residential exposure. A screening level residential exposure and risk assessment was completed for products containing N,N-dimethyltetradecanamide as an inert ingredient. The Agency selected representative scenarios, based on end-use product application methods and labeled application rates. The Agency conducted an assessment to represent worst-case residential exposure by assessing N,N-dimethyltetradecanamide in pesticide formulations (outdoor scenarios) and N,N-dimethyltetradecanamide in disinfectant-type uses (indoor scenarios). The Agency assessed the disinfectant-type products containing N,N-dimethyltetradecanamide using exposure scenarios used by OPP's Antimicrobials Division to represent worst-case indoor residential handler

exposure. Further details of the residential exposure and risk analysis can be found at http://www.regulations.gov in the memorandum entitled: ‘‘JITF Inert Ingredients. Residential and Occupational Exposure Assessment Algorithms and Assumptions Appendix for the Human Health Risk Assessments to Support Proposed Exemption from the Requirement of a Tolerance When Used as Inert Ingredients in Pesticide Formulations,’’ (D364751, 5/7/09, Lloyd/LaMay in docket ID number EPA–HQ–OPP–2008–0710.

IV. AGGREGATE RISK ASSESSMENT

EPA determines whether acute and chronic pesticide exposures are safe by comparing aggregate exposure estimates to the acute population adjusted dose (aPAD) and chronic population adjusted dose (cPAD). The aPAD and cPAD represent the highest safe exposures, taking into account all appropriate safety factors (SFs). EPA calculates the aPAD and cPAD by dividing the point of departure (POD) by all applicable UFs. For linear cancer risks, EPA calculates the probability of additional cancer cases given the estimated aggregate exposure. Short-, intermediate-, and chronic-term risks are evaluated by comparing the estimated aggregate food, water, and residential exposure to the POD to ensure that the MOE called for by the product of all applicable UFs is not exceeded.

i. Acute Dietary Risk.

There was no hazard attributable to a single exposure seen in the toxicity database for N,N-dimethytetradecanamide. Therefore, N,N-dimethyltetradecanamide is not expected to pose an acute risk.

ii. Chronic Dietary Risk.

A chronic aggregate risk assessment takes into account exposure estimates from chronic dietary consumption of food and drinking water using the exposure assumptions discussed in this unit for chronic exposure. Using the exposure assumptions discussed above for chronic exposure and the use limitations of not more than 20% by weight in pesticide formulations, the chronic dietary exposure to food and water to N,N-dimethyltetradecanamide is 16.8 % of the cPAD for the U.S. population and 62.3 % of the cPAD for children 1-2 years old, the most highly exposed population subgroup (See appendix A).

iii. Short-term Aggregate Risk.

Short-term aggregate exposure takes into account short-term residential exposure plus chronic exposure to food and water (considered to be a background exposure level).

N,N-dimethyltetradecanamide may be used as an inert ingredient in pesticide products that could result in short-term residential exposure and the Agency has determined that it is appropriate to aggregate chronic exposure through food and water with short-term residential exposures to N,N-dimethytetradecanamide. Using the exposure assumptions described above, EPA has concluded that the combined short-term aggregated food,

water, and residential exposures result in MOEs of 680 for both adult males and females. Adult residential exposure combines high end dermal and inhalation handler exposure from liquids/trigger sprayer/home garden and indoor hard surface, wiping with a high end post application dermal exposure from contact with treated lawns. As the level of concern is for MOEs that are lower than 100, this MOE is not of concern. EPA has concluded the combined short-term aggregated food, water, and residential exposures result in an aggregate MOE of 359 for children. Children's residential exposure includes total exposures associated with contact with treated lawns and surfaces (dermal and hand-to-mouth exposures). As the level of concern is for MOEs that are lower than 100, this MOE is not of concern.

iv. Intermediate-Term Aggregate Risk.

Intermediate-term aggregate exposure takes into account intermediate-term residential exposure plus chronic exposure to food and water (considered to be a background exposure level).

N,N-dimethyltetradecanamide is currently registered for uses that could result in intermediate -term residential exposure and the Agency has determined that it is appropriate to aggregate chronic exposure through food and water with intermediate-term residential exposures to N,N-dimethytetradecanamide. Using the exposure assumptions described above, EPA has concluded that the combined intermediate-term aggregated food, water, and residential exposures result in aggregate MOEs of 1475 for adult males and females. Adult residential includes high end post application dermal exposure from contact with treated lawns. As the level of concern is for MOEs that are lower than 100, this MOE is not of concern. EPA has concluded the combined intermediate-term aggregated food, water, and residential exposures result in an aggregate MOE of 394 for children. Children's residential exposure includes total exposures associated with contact with treated lawns and surfaces (dermal and hand-to-mouth exposures). As the level of concern is for MOEs that are lower than 100, this MOE is not of concern. (short- and intermediate-term aggregate risk calculations can be found in Table 7.3 in appendix B).

v. Aggregate Cancer Risk for U.S. Population.

The EPA has not identified any concerns for carcinogenicity relating to N,N-dimethyltetradecanamide.

V. OCCUPATIONAL EXPOSURE/RISK PATHWAY

The representative occupational scenarios selected by the Agency for assessment were assessed based on likely maximum application rates for products which may contain N,N-dimethyltetradecanamide as inert ingredients for the short-term exposure assessment, and average application rates for products likely to contain N,N-dimethyltetradecanamide as inert ingredients for intermediate- and long-term exposure durations. Active ingredient application rates were corrected for the maximum amount of N,N-dimethyltetradecanamide likely to be in the final formulations to determine exposure and risk from exposure to N,N-dimethyltetradecanamide grouped by fungicide/insecticide or herbicide.

RD traditionally considers a level of concern (LOC) for risk assessments to be an MOE of 100 based on the standard 10X inter and 10X intra species extrapolation safety factors. Therefore, the LOC was for MOEs below 100.

The occupational exposure assessments are based upon a toxicological no-observed-adverse-effect level (NOAEL) from a 90-day toxicity study in the rat. A dermal absorption factor of 85% was applied based on a dermal penetration study in rats. The default value of 100% absorption is used for assessing risks associated with inhalation exposures.

A. Occupational Handler Risk

Dermal and inhalation exposure was estimated using the Pesticide Handlers Exposure Database (PHED). The quantitative exposure/risk assessment developed for occupational handlers to support the requested exemption for N,N-dimethyltetradecanamide is based on scenarios that represent the highest potential exposure (mixers, loaders, applicators). Occupational handler risks are not of concern for all scenarios provided that protective gloves are worn.

B. Occupational Post-Application Risk

The Agency expects human exposure as a result of agricultural activities related to post-application exposure. The estimated Margins of Exposure for activities known typically to result in high occupational exposures are all >100 and therefore do not exceed the Agency's level of concern.

VI. CUMULATIVE EXPOSURE

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

EPA has not found N,N-dimethyltetradecanamide to share a common mechanism of toxicity with any other substances, and that N,N-dimethyltetradecanamide do not appear to produce a toxic metabolite produced by other substances. For the purposes of this tolerance action, therefore, EPA has assumed that N,N-dimethyltetradecanamide do not have a common mechanism of toxicity with other substances. For information regarding EPA's efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see EPA's website at *http://www.epa.gov/pesticides/cumulative*.

VII. ENVIRONMENTAL JUSTICE STATEMENT

Potential areas of environmental justice concerns, to the extent possible, were considered in this human health risk assessment, in accordance with U.S. Executive Order 12898, "Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations," http://www.eh.doe.gov/oepa/guidance/justice/eo12898.pdf.

As a part of every pesticide risk assessment, OPP considers a large variety of consumer subgroups according to well-established procedures. In line with OPP policy, RD estimates risks to population subgroups from pesticide exposures that are based on patterns of that subgroup's food and water consumption, and activities in and around the home that involve pesticide use in a residential setting. Extensive data on food consumption patterns are compiled by the USDA under CSFII and are used in pesticide risk assessments for all registered food uses of a pesticide. These data are analyzed and categorized by subgroups based on age, season of the year, ethnic group, and region of the country. Additionally, OPP is able to assess dietary exposure to smaller, specialized subgroups and exposure assessments are performed when conditions or circumstances warrant. Whenever appropriate, non-dietary exposures based on home use of pesticide products and associated risks for adult applicators and for toddlers, youths, and adults entering or playing on treated areas post-application are evaluated. Further considerations are currently in development as OPP has committed resources and expertise to the development of specialized software and models that consider exposure to bystanders and farm workers as well as lifestyle and traditional dietary patterns among specific subgroups.

VIII. ENVIRONMENTAL FATE CONSIDERATIONS

Ready Biodegradability

The probability of rapid biodegradation of the dimethyl amides was evaluated using EPI Suite™ 4.11 in the BIOWIN module. The biodegradation model probabilities for the two surrogate compounds and for N,N-dimethyltetradecanamide indicate "rapid biodegradation" and "readily biodegradable" for all three compounds. The probability outputs from the Biowinl (linear model) and Biowin2 (non-linear model) are used to determine the speed of biodegradation such that a biodegradation probability >0.5 for both models indicates rapid biodegradation, while a biodegradation probability < 0,5 for both models indicates "not rapid biodegradation" (EPA, 2005). The dimethyl amide biodegradation probabilities in Biowinl for all three dimethyl amides were greater than 0.94 and in Biowin2 all probabilities were at least 0.98, indicating rapid biodegradation. Similarly, probability outputs from the Biowin5 (MITI linear model) and Biowin6 (MITI non-linear model) are used to determine the ease of biodegradation such that a biodegradation probability >0.5 for both models indicates readily degradable, while a biodegradation probability < 0.5 for both models indicates not readily degradable (EPA, 2005), The dimethyl amide biodegradation probabilities for all three compounds in Biowin5 were all greater than 0.62 and in Biowin6 the probabilities were ail greater than 0.75, indicating ready degradation. The Biowin3 model result for N,N-dimethyItetradecanamide indicates that biodegradation for all three compounds is expected to take place in a matter of weeks.

A similar biodegradability study was performed on Hallcomid -8-10. Evaluation of the biodegradation of Hallcomid-8-10 using the CO_2 evolution test (OECD 301 B) resulted in a net cumulative percent CO_2 production greater than 60% at day 29, demonstrating the test material was "readily biodegradable" (Mclaughlin, 2009).

Bioconcentration

EPI Suite™ 4.11 was used to determine the potential for the dimethyl amides to bioconcentrate in aquatic organisms. The estimated bioconcentration factor (BCF) for the proposed inert dimethyl amide, N,N-dimethyltetradecanamide indicated a low bioconcentration potential. The BCF is reported as the ratio (in L/kg) of a chemical's concentration in the tissue of an aquatic organism to its concentration in the ambient water, when exposure of the organism is to waterbome chemicals, not including dietary intake (EPA, 2005). BCFs considered high are >5,000, moderate BCFs are in the range of 1,000 to 5,000, and low BCFs are < 1,000. The BCF for each of the modeled dimethyl amides is between 19.55 and 86.94, indicating that the dimethyl amides are not expected to bioconcentrate in aquatic organisms (EPI Suite™, 2009).

Hydrolysis

Radiolabeled N,N-dimethyldecanamide was used to evaluate potential for degradation by various mechanisms in water and soil. Recovery of radioactivity was high in all studies. A hydrolysis study was carried out at pH 5, 7, and 9 (Burri 1995a, MRID 45369732). Radiolabeled N,N-dimethyldecanamide was incubated at concentrations of 0.79-0.81 µg/mL for 30 days at 25ºC. Hydrolysis was negligible at each pH.

Photodegradation in water

Photodegradation of N,N-dimethyldecanamide was assessed at pH 5 in water. A concentration of 0.94 µg/mL 14C-labeled N,N-dimethyldecanamide in water was illuminated under sterile conditions for 30 days at 25ºC. Degradation during that time was negligible, with a half-life of >30 days indicating that this compound is stable against direct photolysis (Burri 1995b, MRID 45369734).

Photodegradation in soil

^{14}C-Labeled N,N-dimethyldecanamide was applied to soil at an average dose of 4.1 mg/kg and exposed to artificial light under a 12-hour light/dark cycle. The half-life of N,Ndimethyldecanamide was calculated to be 33 days. The primary degradates were identified as N,N-dimethylsuccinic acid monoamide and, ultimately, CO2. Unilluminated samples hardly degraded at all in the 30-day experiment (reduced by 13.4%) (Burri 1996, MRID 45369737).

Aerobic soil metabolism

The aerobic degradation and metabolism of N,N-dimethyldecanamide was evaluated and shown to rapidly degrade (Wyss-Benz & Tschech, 1995, MRID 45369735). Radiolabeled test article was applied to 108.57 g soil, corresponding to 100g dry soil equivalent at an initial

concentration of 40.07 µg/100g dry soil, equal to an application rate of 536 lbs/acre. The test article was metabolized completely and rapidlv. One day after application, 33.5% of the radioactivity of the labeled test article was found as ' CO2. Two days after application, 63.5% of the radioactivity was found as $^{14}CO_2$. A DT-50 value of 2.2 hours and a DT-90 value of 7.5 days were calculated based on the data from the 154-day incubation period.

Environmental Fate

The Fugacity model module of EPI Suite™ 4.11, LEV3EPI is a multimedia fate model that provides predictions of environmental partitioning of chemicals between air, soil, sediment, and water under steady state conditions for a default model "environment". The output provides percent of the modeled compound in each media, and corresponding half-life. The fugacity model indicates that once released to the environment, 72.6% of the proposed inert N,N-dimethyltetradecanamide would reside in the soil, 23.4% would reside in the water, 3.35% would reside in the sediment and a very small percent, 0.643%, would be in the air. The estimated percentages of the two proposed surrogates in each compartment are very similar to the percentages of the proposed new inert ingredient, N,N-dimethyltetradecanamide. The overall persistence time estimated in EPI Suite is not long: 483 hours (~20 days).

N,N-dimethyltetradecanamide, proposed for use as an inert ingredient in food use pesticide formulations, is expected to have a minimal impact on the environment. The physical and chemical properties of this dimethyl amide indicate it will degrade rapidly in the environment. The dimethyl amides are expected to partition into the soil, but some may also remain in or enter the water where it may readily biodegrade. N,N-dimethyltetradecanamide is not expected to bioconcentrate in aquatic organisms. The dimethyl amides are not particularly volatile, and so will not partition into the air.

IX. ECOTOXICITY

There were no aquatic ecotoxicity studies available for N,N-dimethyltetradecanamide. ECOSAR, a modeling program that is a component of EPI-Suite (US EPA 2009), estimated the acute toxicity of this amide to aquatic organisms based on a log Kow of 5.408 (Kowwin v 1.68) and water solubility of 0.5309 mg/L (WSKowwin v 1.43). The LC_{50} values of N,Ndimethyltetradecanamide for fish (96-hour), daphnid (48-hour), and algae (96-hour) were estimated to be 0.279, 0.064, and 0.018 mg/L, respectively. These values suggest N,Ndimethyltetradecanamide is highly toxic (LC_{50} >0.1-1 mg/L) to very highly toxic (LC_{50} <0.1 mg/L) to aquatic organisms. The full output from the ECOSAR model is appended in Appendix III.

Based on the ready biodegradability of N,N-dimethyltetradecanamide and the relatively low partitioning of the proposed inert into water, effects of concern to nontarget aquatic species resulting from the use of N,N-dimethyltetradecanamide as an inert ingredient are anticipated to be low.

X. RISK CHARACTERIZATION

The EPA (Agency) received a petition (IN-10806) from Bergeson & Campbell PC (2200 Pennsylvania Avenue, N.W. Suite 100W Washington, D.C. 20037) on behalf of Stepan Company (22 West Frontage Road, Northfield, Illinois 60093) requesting that the Agency establish a tolerance exemption for residues of N,N-dimethyltetradecanamide (CAS Reg No. 3015-65-4) when used as an inert ingredient (surfactant and solvent) on pre- and post-harvest crops under 40 CFR Part 180.910. EPA published the notice of filing for this petition in the Federal Register on November 23, 2015 (80 FR 72941). One comment was received in response to this notice.

This chemical is very similar in structure to two other compounds that EPA has established tolerance exemptions as inert ingredients in food use pesticide formulations under 40 CFR 180.920. These two inert ingredients are: N,N-dimethyldecanamide (decanamide, N, N-dimethyl-) and N,N-dimethyloctanamide (octanamide, N,N-dimethyl), which differ from the proposed inert only in the number of carbons. Therefore, data to support N,N-dimethyldecanamide and N,N-dimethyloctanamide are considered suitable surrogates to characterize toxicity due to exposure to N,N-dimethyltetradecanamide.

N,N-dimethyltetradecanamide is not a sensitizer. Based on the acute toxicity data on surrogate chemicals N,N-dimethyldecanamide (decanamide, N,N-dimethyl-) and N,N-dimethyloctanamide (octanamide, N,N dimethyl), it is expected to be of low acute oral, dermal and inhalation toxicity. It is expected to be a severe irritant to the skin and corrosive to the eyes.

Subchronic exposure in rats causes an increased incidence of basophilic regenerative tubules in the renal cortex as well as a slight increase in the amount of protein excreted in the urine at 10,000 ppm (787.6 mg/kg/day). The NOAEL is 2000 ppm (136.8 mg/kg/day). Fetal susceptibility is not observed in developmental studies in rats and rabbits. N,N-dimethyltetradecanamide is not mutagenic or clastogenic. It is not expected to be carcinogenic, neurotoxic or immunogenic.

Based on the chemical structure and known mammalian enzymatic activities, N,N-dimethyltetradecanamide is expected to undergo carboxyamide hydrolysis by amidase enzymes that have broad substrate specificity.

The dermal absorption factor is 85% based on an *in vivo* dermal penetration study in rats and an *in vitro* dermal absorption study conducted with human skin.

The chronic reference dose (cRfD) as well as all exposure scenarios is based on the 90-day toxicity study in the rat. The standard uncertainty factors are applied to account for interspecies (10x) and intraspecies (10x) variations. The FQPA safety factor for the protection of infants and children is reduced to 1X. An additional 3X FQPA safety factor was applied to account for the extrapolation from subchronic to chronic exposures scenarios. This results in a level of concern (LOC) for the margin of exposure (MOE) of 300 for the dietary scenario only. The LOC for the MOE is 100 for short- and intermediate-term dermal and inhalation exposure scenarios. The chronic population adjusted dose (cPAD) = 0.456 mg/kg/day (cPAD =POD/300).

A dermal absorption factor of 85% was applied based a dermal penetration study in rats. A default value of 100% absorption was used for the inhalation absorption factor.

N,N-dimethyltetradecanamide is not expected to pose an acute risk. The chronic dietary risk assessment shows that the chronic dietary risk estimates are not of concern (i.e., <100% cPAD). For the U.S. population, the exposure for food and water utilized 16.9 % of the cPAD. The chronic dietary risk estimate for the highest exposed population subgroup, children 1-2 years old, is 62.3 % of the cPAD.

Combined short- and intermediate term aggregated food, water, and residential pesticidal exposures result in MOEs of 680 and 1475, respectively, for both adult males and females and 359 and 394, respectively, for children. As the level of concern is for MOEs that are lower than 300, these MOEs are not of concern.

Occupational handler risks are not of concern provided that protective gloves are worn except for mixer/loader/applicators applying wettable powder with a low pressure hand wand. Occupational post-application exposures are not of concern.

Taking into consideration all available information on N,N-dimethytetradecanamide, EPA concludes that there is no reasonable certainty that no harm will result to the general population or to infants and children from aggregate exposure to N,N-dimethyltetradecanamide. Therefore, the establishment of an exemption from tolerance under 40 CFR 180.910 for residues of N,N-dimethyltetradecanamide as an inert ingredient for use as a surfactant and solvent in pesticide formulations used on pre- and post-harvest crops at a concentration of no more than 20% in the end-product formulation cannot be considered safe under section 408 of the FFDCA.

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APPENDICES

APPENDIX A

DEEM

US EPA Ver. 3.16, 03-08-d
DEEM-FCID Chronic analysis for INERTS- DECENAMIDE
NHANES 2003-2008 2-day
Residue file name: C:\Users\laustin\Documents\DEEM Version 3.16\Decenamide\Decenamide 20% INERTS_57ACTIVE_100PPBH2OREV.R08
Adjustment factor #2 used. (0.4 (wt % in decimal) for all commodities)
Analysis Date 12-09-2015/11:21:07
Residue file dated: 12-09-2015/11:20:21
Reference dose (RfD, Chronic) = .456 mg/kg bw/day
COMMENT 1: Inert 57 active ingredients + drinking water (100ppb)

Total exposure by population subgroup

Population Subgroup	Total Exposure mg/kg body wt/day	Percent of Rfd
Total US Population	0.076994	16.9%
Hispanic	0.083904	18.4%
Non-Hisp-White	0.075612	16.6%
Non-Hisp-Black	0.071417	15.7%
Non-Hisp-Other	0.090790	19.9%
Nursing Infants	0.100418	22.0%
Non-Nursing Infants	0.188072	41.2%
Female 13+ PREG	0.067278	14.8%
Children 1-6	0.220278	48.3%
Children 7-12	0.092011	20.2%
Male 13-19	0.054368	11.9%
Female 13-19/NP	0.055341	12.1%
Male 20+	0.057569	12.6%
Female 20+/NP	0.062584	13.7%
Seniors 55+	0.062290	13.7%
All Infants	0.161011	35.3%
Female 13-50	0.059811	13.1%
Children 1-2	0.284309	62.3%
Children 3-5	0.195781	42.9%
Children 6-12	0.101323	22.2%
Youth 13-19	0.054835	12.0%
Adults 20-49	0.059149	13.0%
Adults 50-99	0.061954	13.6%
Female 13-49	0.059782	13.1%

APPENDIX B

Residential Exposure Assessment

1.0 Executive Summary

A screening level residential exposure and risk assessment was completed for products containing N,N-dimethyl tetradecanamide as inert ingredients. For all residential handler and post application scenarios, risk estimates are not of concern.

Provided that N,N-dimethyl tetradecanamide is limited to no more than 20% by weight in the final formulation, aggregate risks are not of concern for the U.S. population and all subpopulations, including children 1 – 2 years of age, the most highly exposed subgroup.

This assessment relies in part on data from studies in which adult human subjects were intentionally exposed to a pesticide. These studies have received the appropriate ethical review for use in risk assessment.

6.0 Residential (Non-Occupational) Exposure/Risk Characterization

A screening level residential exposure and risk assessment was completed for products containing N,N-dimethyl tetradecanamide inert ingredients. A summary of the residential exposure and risk assessment is presented below.

The LOC for these risk assessments is an MOE of 300 based on the standard 10X inter-species and 10X intra-species extrapolation safety factors and a 3X uncertainty factor to account for extrapolation from subchronic to chronic exposure scenario.

6.1 Residential Handler Exposure

<u>Exposure Scenarios</u>

The Agency selected representative scenarios, based on end-use product application methods and labeled application rates. N,N-dimethyl tetradecanamide is used in pesticide formulations that may be used around the home in pesticide formulations used on lawn, turf, or gardens. In addition, this inert may be present in home cleaning products. CITAB conducted an assessment to represent conservative residential exposure by assessing:

- N,N-dimethyl tetradecanamide in pesticide formulations (fungicides/insecticides/herbicides); (Outdoor Scenarios)
- N,N-dimethyl tetradecanamide in disinfectant-type uses; (Indoor Scenarios)

Based on use information, N,N-dimethyl tetradecanamide can be present in consumer cleaning products. Therefore, HED assessed the disinfectant-type products containing the N,N-dimethyl tetradecanamide inerts using exposure scenarios used by OPP's Antimicrobials Division to represent conservative residential handler exposure.

Mixer/Loader/Applicator High Exposure Outdoor Scenarios:

The mixer/loader/applicator high exposure outdoor scenarios use data from the Outdoor Residential Exposure Task Force:

- Liquid products: Low Pressure Handwand (ORETF data)
- Liquid products: Hose End Sprayer (ORETF data)
- Ready to Use (RTU): Trigger Pump Sprayer Applications (ORETF data)

Exposure Data and Assumptions:

A series of assumptions and exposure factors served as the basis for completing the residential handler risk assessments for N,N-dimethyl tetradecanamide. Each assumption and factor is detailed below. In addition to these factors, unit exposures were used to calculate risk estimates.

Unit Exposure Values: Unit Exposure values were taken from exposure data on outdoor exposure scenarios available from the ORETF Handler Studies (MRID 449722-01 and MRID 444598-01): A report was submitted by the ORETF (Outdoor Residential Exposure Task Force).

The Agency used assumptions based on the Residential Exposure Assessment Standard Operating Procedures (Residential SOPs). Key assumptions used in this assessment are summarized below.

- The maximum application rate for the inert based on its use in a class of pesticide (herbicide/insecticide/fungicide) has been assessed for the short-term exposure duration.
- Residential risk assessments are based on high-end estimates of what homeowners would typically treat. Per HED's Residential SOPs (1997 & 2001 revision), residential pesticide handlers are assumed to mix and use a volume of 5 gallons of product per day.
- For outdoor pesticide applications, residential handlers are assumed to use a total of 0.09 lbs N,N-dimethyl tetradecanamide per day. This estimate is based on the following assumptions:
    - Five (5) gallons of formulated pesticide solution are assumed to be used per day by a residential handler (Revised Residential SOPs Area Treated, February, 2001). Consistent with the residential SOPs, the density of the formulated pesticide solution is assumed to be 9 lbs/gallon. The proposed limit to the amount of N,N-dimethyl tetradecanamide in the pesticide products is 20%. Therefore 20% of any pesticidal product is assumed to be N,N-dimethyl tetradecanamide. Product concentrates are assumed to be diluted at a 1 to 10 ratio with water.

> 5 gallons formulated pesticide solution*(9 lbs/gallon)*(20% N,N-dimethyl tetradecanamide)*(1 part product concentrate/10 parts water) = 0.9 lbs N,N-dimethyl tetradecanamide in formulated pesticide solutions per day.

- Residential exposure is assessed assuming clothing consisting of a short-sleeved shirt, short pants and no gloves or respiratory protection, the typical clothing for a home applicator.
- The dermal absorption factor of 85% was applied based on a dermal penetration study in rats.

CITAB believes the duration of exposure for most homeowner applications of home garden and lawn care products is best represented by the short-term duration (1 to 30 days). These exposure scenarios include the application of herbicides to lawns and insecticides/fungicides to gardens, ornamental plants, or lawns. While these types of applications may be applied on consecutive days, they are not likely to exceed 30 consecutive application days.

Mixer/Loader/Applicator High Exposure Indoor Scenarios:

The mixer/loader/applicator high exposure outdoor scenarios use data from the proprietary Chemical Manufacturers Association (CMA) antimicrobial exposure study, and the Pesticide Handlers Exposure Database:

- Liquid Products: Mopping Use (CMA data)
- Liquids Products: Wiping Use (CMA data)
- Aerosol Spray/Trigger pump/Air Deodorization Use (PHED data)

Exposure Data and Assumptions:

The Agency used assumptions based on methodology developed by the Antimicrobial Division (AD) of the Office of Pesticide Programs and the Residential SOPs to assess exposure and risk from indoor use of household cleaning products containing N,N-dimethyl tetradecanamide. Based on information from RD, the Agency assumed that the maximum percentage by weight in indoor products would be 5% N,N-dimethyl tetradecanamide.

Unit Exposure Values: Unit exposure values were taken from the proprietary Chemical Manufacturers Association (CMA) antimicrobial exposure study (USEPA, 1999: DP Barcode D247642) or from the PHED data presented in HED's Residential SOPs (USEPA, 1997).

Appendix A contains additional information about the disinfectant-type exposure scenarios assessed in this document.

The following key assumptions were used in this assessment:

- For the mopping scenario, the CMA dermal and inhalation unit exposure values for ungloved mopping were used (71.6 mg/lb inert. and 2.38 mg/lb inert, respectively). These values are based on data collected from six replicates mopping floors and receiving exposure via contact with the mop or with the bucket.
- For the wiping scenario, the CMA dermal and inhalation unit exposure values for ungloved wiping were used (2,870 mg/lb inert and 67.3 mg/lb inert, respectively). These values are based on data collected from six replicates (dental technicians) who used a finger pump sprayer to apply the product and then wiped the surfaces with a paper towel.
- For aerosol spray, trigger pump and air deodorization scenarios, the PHED dermal and inhalation unit exposure values are 220 mg/lb inert and 2.4 mg/lb inert, respectively. The values are based on homeowners applying an aerosol insecticide to baseboards in kitchens and are representative of a handler wearing short pants and a short sleeve shirt, with no gloves.

The quantities handled/treated were estimated based on information from various sources and assumptions.

- For the mopping scenarios, it was assumed that 1 gallon of diluted solution is used. HED assumes that cleaning products are assumed to have the same density as water (8.34 lbs/gallon). While typical product concentrate directions indicate that 1 oz concentrated product per 1 gallon of water should be used, HED followed the AD SOP and assumed a dilution factor of 2 oz concentrated product/128 oz (1 gallon) of water for the residential handler risk assessment to represent heavy-duty cleaning formulations. This is comparable to the one quarter cup of cleaner diluted in one gallon of water as stated in AD's SOP. Based on information from RD, the Agency assumed that the maximum percentage by weight in indoor products would be 5% N,N-dimethyl tetradecanamide.

1 gallon formulated pesticide solution*(8.34 lbs/gallon)*(5% N,N-dimethyl tetradecanamide)*(2 oz/128 oz dilution factor) = 0.0065 lbs N,N-dimethyl

- For the wiping and trigger pump spray scenarios, it was assumed that 0.5 liter (0.13 gal) of ready-to-use (RTU) solution is used. For anti-microbial products, 5% N,N-dimethyl tetradecanamide in product is assumed.

0.13 gallon formulated pesticide solution*(8.34 lbs/gallon)*(5% N,N-dimethyl tetradecanamide) = 0.0542 lbs N,N-dimethyl tetradecanamide in formulated pesticide

- For the aerosol foam spray and air deodorization scenarios, it is assumed that one can of product is used. For the aerosol spray/trigger pump/air deodorization scenario, it is assumed that a 12 oz net weight product is used (0.094 gallons). 5 % N,N-dimethyl tetradecanamide in antimicrobial product assumed.

0.094 gallon formulated pesticide solution*(8.34 lbs/gallon)*(5% N,N-dimethyl tetradecanamide) = 0.0392 lbs N,N-dimethyl tetradecanamide in formulated

The dermal absorption factor of 85% was applied based on a dermal penetration study in rats..

HED believes the duration of exposure for most homeowner applications of indoor cleaning products is believed to be best represented by the short-term duration (1 to 30 days) because the different scenarios (i.e. methods of application) are assumed to be episodic, not daily. In addition, homeowners are assumed to use different cleaning products with varying active and inert ingredients.

Risk Summary

For all residential handler scenarios, risk estimates are not of concern (i.e., MOEs are greater than 300) for both the route-specific (dermal or inhalation) assessment and for the total MOE

(dermal and inhalation combined). A summary of the results are provided below in Tables 6.1, below.

The Agency believes that the handler scenarios assessed represent worse-case exposures and risks resulting from use of indoor and outdoor pesticide products and cleaning products containing the N,N-dimethyl tetradecanamide in residential environments.

Table 6.1. Short-term Exposure and Risks for N,N-Dimethyl tetradecanamide Residential Handlers

Exposure Scenario (Formulation/ Application)	Application Rate[1] (lb inert/ gallon)	Quantity Handled/ Treated per day[2]	Dermal Unit Exposure (mg/lb inert)[3]	Inhalation Unit Exposure (mg/ lb inert)[3]	Dermal Dose (mg/kg /day)[4]	Inhalation Dose (mg/kg/ day)[5]	Baseline Dermal MOE[6]	Baseline Inhalation MOE[7]	Total MOE[8]
Outdoor Products									
Liquids/ Low Pressure Handwand (ST) (ORETF data)	0.011 lb/gal	5 gallons	38	0.003	0.0353	1.187E-05	3900	12000000	3900
Liquids/ Hose End Sprayer, Lawn (ST) (ORETF data)	0.011 lb/gal	5 gallons	11	0.017	0.0075	1.450E-05	18000	9400000	18000
Liquids/ Trigger Sprayer/ Home Garden (ST) (ORETF data)	0.011 lb/gal	5 gallons	54	0.0019	0.0728	9.229E-05	1900	1500000	1900
Indoor Products									
Indoor hard surface, Mopping (ST) (CMA data)	0.0065 lb/gal	1 gallon	71.6	2.38	0.0050	0.0002	28000	710000	27000
Indoor hard surface, Wiping (ST) (CMA data)	0.0065 lb/gal	0.13 gallons	2870	67.3	0.0258	0.0007	5300	190000	5200
Indoor hard surface, Aerosol spray (ST) (PHED data)	0.417 lb/gal	0.094 gallons (12 oz)	220	2.4	0.0916	0.0012	1500	120000	1500

[1]Application rates are based on maximum application rates of products containing N,N-dimethyl tetradecanamide multiplied by 20% for outdoor products and 5% for indoor products to convert from product application rate to inert application rate.
[2]Quantity treated daily values are back-calculated from 5 gallons of product used per day (Revised Residential SOPs 2001) for outdoor products. Indoor products are assumed to be used at 1 gallon of solution for the mopping scenario, 0.5 L (0.13 gallon) of solution for the wiping scenario, and a 12 oz (0.094 gallon) can of spray for the aerosol spray/air deodorization scenario.
[3]Unit Exposure data sources are identified in the exposure scenario column. All exposure scenarios assess exposure reflecting applicators wearing short-sleeved shirts and shorts and no respiratory protection.

[4]Daily Dermal Dose = (Dermal Unit Exposure (mg inert /lb inert) * Application Rate (lb /gal) * Quantity handled (gallons/day))/ Body Weight (80 kg) * Dermal Absorption Factor of 85%.
[5] Daily Inhalation Dose = (Inhalation Unit Exposure (mg inert / lb inert) * Application Rate (lb /gal) * Quantity handled (gallons/day)) / Body Weight (80 kg)
[6] Dermal MOE = PoD (NOAEL of 136.8 mg/kg/day)/ Daily dermal dose (mg/kg/day)
[7] Inhalation MOE = PoD (NOAEL of 136.8 mg/kg/day) / Daily inhalation dose (mg/kg/day)
[8] Total MOE = (NOAEL of 136.8 mg/kg/day)/ [Daily dose dermal + Daily dose inhalation (mg/kg/day)]

6.2 Residential Postapplication Exposure

Exposure Scenarios

Residential postapplication exposures result when bystanders, such as children come in contact with the N,N-dimethyl tetradecanamide in areas where end-use products have recently been applied (e.g., treated lawns, gardens or recently cleaned surfaces). The Agency selected representative scenarios, based on end-use product application methods and labeled application rates. HED conducted an assessment to represent worst-case residential exposure by assessing post application exposures and risks from:

- N,N-dimethyl tetradecanamidein pesticide formulations (fungicides/ insecticides/ herbicides); (Outdoor Scenarios)
- N,N-dimethyl tetradecanamide in disinfectant-type uses; (Indoor Scenarios)

The Agency considers dermal (adults and children) or incidental oral (children only) the primary exposure routes for the N,N-dimethyl tetradecanamide. Inhalation exposures are not typically calculated for postapplication scenarios because inhalation exposures generally account for a negligible percentage of the overall body burden for most pesticide chemicals. Any inhalation exposure through the postapplication route will be less than the inhalation exposures assessed by residential handlers above in section 6.1.

For all postapplication exposure scenarios, exposures are assessed at short- and intermediate-term exposure durations because residues may be present on treated lawns or indoor treated surfaces for lengths of time consistent with short- and intermediate-term exposure. Additionally, residential postapplication exposure can occur in commercially treated environments (e.g., schools, child care facilities, hospitals). If the products are used on a routine basis (i.e., daily), exposures may occur over an intermediate-term time duration (30 days – 6 months).

Postapplication High End Outdoor Exposure Scenarios

- Dermal exposure to treated lawns (adults/children)
- Hand-to-Mouth activity for toddlers on treated lawns (children)
- Object-to-Mouth activity for toddlers on treated lawns (children)
- Soil ingestion from treated soil (children)

The exposures from these routes and scenarios were considered individually and were also added together, where appropriate, to determine a total dose for children exposure to treated lawns. Residential postapplication exposure is assessed on the day of application, typically referred to as Day 0.

Exposure Data and Assumptions

A series of assumptions and exposure factors served as the basis for completing the residential postapplication risk assessments. The assumptions and factors used in the risk calculations are consistent with current HED policy for completing residential exposure assessments (i.e., *SOPs for Residential Exposure Assessment [1997 and 2001 revision]*).

Exposures to adults/children after contact with treated lawns have been addressed using the latest approaches for this scenario including:

- For adult exposure, the mean for US males and females was used to estimate exposure (80 kg). For child exposure, the mean of median values for male and female 3 year olds was used to estimate exposure (15 kg).
- HED has developed standard transfer coefficient (TC) values for residential postapplication scenarios to ensure consistency in exposure assessments. For the short-term assessment, TC values of 14,500 cm^2/hr (adults) and 5,200 cm^2/hr (children) were used. For intermediate-term risk assessment, TC values of 7,300 cm^2/hr (adults) and 2,600 cm^2/hr (children) were used. These default transfer coefficients, found in the 2001 Residential SOPs, were used to calculate postapplication exposures.
- Based on HED's Residential SOPs, it was assumed that the surface area used for each hand-to-mouth event is 20 cm^2 (based on the surface area of three fingers of a toddler's hand). For short-term exposures, it is assumed that there were 20 events per hour (90^{th} percentile, according to the SOP) and for intermediate-term exposures, it was assumed that there were 9.5 event/hour (mean value).
- The exposure time used is 2 hours a day (USEPA, 2000 and 2001).
- The saliva extraction efficiency used is 50% (USEPA, 2000 and 2001).
- Pesticidal products are assumed to contain a maximum of 20% N,N-dimethyl tetradecanamide by weight in the end use outdoor products.
- The relevant application rates for N,N-dimethyl tetradecanamide containing products are derived above in Section 6.1
- A dermal absorption factor of 85% was applied based a dermal penetration study in rats.

Postapplication High End Indoor Exposure Scenarios

Standard methodologies based on HED's Residential SOPs were used to assess residential postapplication exposure to hard surface cleaners.

The Agency assumed that the maximum percentage by weight in indoor products would be 5% N,N-dimethyl tetradecanamide. Based on an overall query of products that contain N,N-dimethyl tetradecanamide, this reflects a high-end concentration.

Typically, the Agency assesses disinfectant-type products for the short-term exposure duration (1 to 30 days). This assumption is supported by the fact that the different scenarios (i.e. methods of application) are episodic, not daily. In addition, homeowners are assumed to use different cleaning products with varying active and inert ingredients. However, intermediate-term exposure is assessed for children because disinfectant products are used frequently in schools and day care centers where children can spend significant amounts of time. In those environments, cleaning products can be used on a daily basis.

The Agency used assumptions based on the Residential SOPs. The following key assumptions were used in this assessment:

- Toddlers (3 years old) were used to represent the 1 to 6 year old age group and are assumed to weigh 15 kg, the mean of median values for male and female toddlers (USEPA, 2000 and 2001).

- Based on HED's Residential SOPs, it was assumed that the surface area used for each hand-to-mouth event is 20 cm^2 (based on the surface area of three fingers of a toddler's hand). For short-term exposures, it is assumed that there were 20 events per hour (90^{th} percentile, according to the SOP) and for intermediate-term exposures, it was assumed that there were 9.5 event/hour (mean value).
- The exposure time was 4 hours a day (USEPA, 2000 and 2001).
- The saliva extraction efficiency was 50% (USEPA, 2000 and 2001).
- No label information was available to represent the volume of disinfectant to be used for cleaning surfaces such as floors. It was assumed that the diluted treatment solution was applied at a rate of 1 gallon per 1,000 sq. ft.
- The maximum application rate on the product labels for application to hard surfaces is 8.34 lbs product/gal, based on the density of water. The amount of product used is assumed to be 0.5 gallons per day at a rate of 1 gallon/1000 ft^2, (i.e., 0.5 gallons for 500 ft^2). Therefore, the application rate used for the hard surface cleaner scenario in the post application scenario was $5.2x10^{-6}$ lbs inert/ft^2 [(1 gallon of product used * 8.34 lbs/gallon)/1000 ft^2 cleaned = 0.008 lb product/ft^2); (0.008 lb product/ ft^2 * 4% inert in a given disinfectant formulation * 2 oz/128 oz dilution factor= $5.2x10^{-6}$ lb/ft^2 /per day)] (See Table 6.2: Indoor Cleaning Products).
- No data is available regarding the quantity of solution residue left on the floor after treatment. As a conservative measure, it was assumed that 25% of the cleaner remains after the final mopping. This assumption has been used by the AD for other Office of Pesticide Program risk assessments.
- No transferable residue data were available that could be used to estimate the transfer factor from the floor to skin. Therefore, it is assumed that 20% of the deposition rate is available for dermal transfer (USEPA, 2000 and 2001).
- A dermal absorption factor of 85% was applied based a dermal penetration study in rats.

Risks were calculated using the Margin of Exposure (MOE) approach, which compares a toxicological PoD to an exposure estimate.

Risk Summary

A summary of the residential postapplication exposure and risk estimates are presented in Table 6.2, below. Short- and intermediate-term post application risks for children are not of concern. The individual route-specific and combined non-dietary risks from dermal exposure and hand-to-mouth exposure for the outdoor scenarios and indoor scenarios do not demonstrate risks of concern for toddlers (i.e., the MOEs for the assessed scenarios are greater than 300) for both the short- and intermediate-term exposure durations.

Risk Characterization

At this time, residue dissipation data or reliable use pattern data are not available, including the frequency and duration of use of antimicrobial products in the residential setting. The Agency does not believe that the use patterns of many residential products result in intermediate-term exposure. However, the Agency notes that intermediate-term exposure to children may occur in areas where disinfecting products are used more frequently (i.e., schools and day care centers).

Table 6.2. Residential Postapplication Short- and Intermediate-term Exposures and Risks for N,N-dimethyl tetradecanamide				
Exposure Scenario	Application Rate[1]	Exposed Population & Exposure Duration[2]	Daily Dose (mg/kg/day)[3]	MOE[4]
Outdoor Lawn Products				
Dermal Exposure to Treated Lawns	0.18 lb/day	Adult ST	0.0311	4400
		Adult IT	0.0157	8700
		Child ST	0.0595	2300
		Child IT	0.0297	4600
Hand-to-Mouth from Treated Lawn		Child ST	0.0027	51000
		Child IT	0.0013	110000
Object-to-Mouth from Treated Lawn		Child ST	0.0007	200000
		Child IT		
Soil Ingestion		Child ST	9.016E-06	15000000
		Child IT		
Total Lawn Combined Exposures*		Child ST	0.0622	2200
		Child IT	0.0310	4400
Indoor Cleaning Product				
Dermal Exposure to Treated Indoor Surface	6.49E-6 lb/ft^2	Child ST	0.0297	4600
		Child IT		
Hand-to-Mouth from Treated Indoor Surface		Child ST	0.0042	32200
		Child IT	0.0020	67800
Total Surface Combined Exposures*		Child ST	0.0339	4035
		Child IT	0.0317	4300

[1] Application rates for outdoor products are derived in Section 6.1 Application rates for indoor products are derived in Section 6.2.
[2] ST and IT indicate short- or intermediate-term exposure durations
[3] Daily Dose = Daily Dose algorithms for various residential postapplication scenarios outlined in Appendix B
[4] MOE = PoD (NOAEL of 136.8 mg/kg/day)/ Daily dose (mg/kg/day)
[5] Combined exposures reflect the aggregation of dermal exposure to treated areas and HTM exposure from treated areas (for children). *Total Combined Exposures = (NOAEL of 136.8 mg/kg/day)/ [Daily dose dermal + Daily dose HTM (mg/kg/day)]

7.0 Aggregate Risk Assessments and Risk Characterization

7.1 Acute Aggregate Risk

There was no hazard attributable to a single exposure seen the in the toxicity database for the N,N-dimethyl tetradecanamide; therefore, an acute aggregate risk assessment is not required.

7.2 Short-Term/Intermediate-Term Aggregate Risk

Short-term and intermediate-term aggregate risk assessments for the N,N-dimethyl tetradecanamide inert ingredients combine high end residential short- or intermediate-term exposures with average food and drinking water exposures, and compare this total to a short- or intermediate term PoD.
Short- and intermediate term residential exposures are summarized in Table 7.2.

Table 7.2. Short- and Intermediate-Term Residential Exposures for the N,N-dimethyl tetradecanamide Aggregate Risk Calculations			
Population	Handler Exposure (mg/kg/day)[1]	Postapplication Exposure (mg/kg/day)[2]	Residential Exposure (mg/kg/day)[3]
Short-Term			
Adult Male	0.0928 Source: Table 6.1 Indoor hard surface, Wiping (ST)	0.0311 Source: Table 6.2 ST Dermal Exposure to Treated Lawn	0.1239
Adult Female	0.0928 Source: Table 6.1 Indoor hard surface, Wiping (ST)	0.0311 Source: Table 6.2 ST Dermal Exposure to Treated Lawn	0.1239
Child	N/A	0.0622 Source: Table 6.2 ST Total Lawn Combined Exposures + 0.0339 ST Total Surface Combined Exposures	0.0961
Intermediate-Term			
Adult Male	N/A	0.0157 Source: Table 6.2 IT Dermal Exposure to Treated Lawn	0.0157
Adult Female	N/A	0.0157 Source: Table 6.2 IT Dermal Exposure to Treated Lawn	0.0157
Child	N/A	0.0310 Source: Table 6.2 IT Total Lawn Combined Exposures + 0.0317 IT Total Surface Combined Exposures	0.0627

1 – Handler exposure combines high end dermal and inhalation handler exposure, where the exposure duration is appropriate to assess

2 – Postapplication exposure combines high end dermal exposure to outdoor lawn products or indoor cleaning products with high end incidental oral exposure to outdoor or indoor products for the relevant exposure duration

3 - Residential exposure combines high end dermal and inhalation handler exposure (Table 6.1) with high end post application dermal and incidental oral exposure (Table 6.2).

Short- and intermediate-term aggregate risks are summarized in Table 7.3. Short- and intermediate-term aggregate risks are not of concern for adults or children.

Table 7.3. Short- and Intermediate-Term Aggregate Risk Calculations for N,N-dimethyl tetradecanamide						
Population	PoD mg/kg/day	LOC[1]	Max Allowable Exposure[2] mg/kg/day	Average Food & Water Exposure	Residential Exposure[3] mg/kg/day	Aggregate MOE (food and residential)[4]

				mg/kg/day		
Short-Term						
Adult Male	136.8	300	0.456	0.0770	0.1239	680
Adult Female	136.8	300	0.456	0.0770	0.1239	680
Child	136.8	300	0.456	0.2843	0.0961	359
Intermediate-Term						
Adult Male	136.8	300	0.456	0.0770	0.0157	1475
Adult Female	136.8	300	0.456	0.0770	0.0157	1475
Child	136.8	300	0.456	0.2843	0.0627	394

[1] The LOC (Level of Concern) is based on the standard inter- and intra-species uncertainty factors totaling 100 and an additional 3X to account for the extrapolation from subchronic to chronic exposure scenario.
[2] Maximum Allowable Exposure (mg/kg/day) = PoD (Point of Departure)/LOC
[3] Residential Exposure = [Oral exposure + Dermal exposure + Inhalation Exposure]. Sources identified above in Table 7.2
[4] Aggregate MOE = [PoD/ (Avg Food & Water Exposure + Residential Exposure)]

10.0 Human Studies

This assessment relies in part on data from studies in which adult human subjects were intentionally exposed to a pesticide. These studies, listed below, have received the appropriate ethical review for use in risk assessment.

The PHED Task Force, 1998. The Pesticide Handler Exposure Database (PHED), Version 1.1. Task Force members: Health Canada, U.S. Environmental Protection Agency, the California Department of Pesticide regulation, and the American Crop Protection Association; released August 1998.

ORETF Handler Studies (MRID 44972201): Outdoor Residential Exposure Task

Chemical Manufacturers Association (CMA) antimicrobial exposure study (USEPA, 1999: DP Barcode D247642).