# Final Amended Safety Assessment of the Cosmetic Ingredient Review Expert Panel

# Dimethyl Stearamine and Related Tertiary Aliphatic Amines as Used in Cosmetics

**December 16, 2009**

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**Cosmetic Ingredient Review**

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## ABSTRACT

Dimethyl stearamine and the additional tertiary aliphatic amines in this safety assessment, function in cosmetics as antistatic agents. Dimethyl stearamine can also function as a pH adjuster and as a corrosion inhibitor. Available safety and toxicity information are limited to dimethyl stearamine and dimethyl lauramine. Data on dermal penetration and metabolism are not available, but information from the FDA's VCRP indicates that dimethyl stearamine is currently used in hair sprays and fixatives and is not used in any leave-on products. The CIR Expert Panel determined that the available information could be used to support the safety of the additional tertiary aliphatic amines listed in this document. The CIR Expert Panel concluded that dimethyl stearamine and the other tertiary aliphatic amines in this safety assessment are safe in the present practices of use and concentration, as currently used in non-coloring hair care products.


## INTRODUCTION

The Cosmetic Ingredient Review (CIR) Expert Panel published a safety assessment on the use of dimethyl stearamine in cosmetics in 1995. The CIR Expert Panel concluded that " the available data are insufficient to support the safety of Dimethyl Stearamine and its hydrochloride salt as used in cosmetics."[1] A search for new published and unpublished information was conducted through October of 2009 and the results summarized in this document.

The ingredients dimethyl lauramine, dimethyl myristamine, dimethyl palmitamine, and dimethyl behenamine have been added to this safety assessment because of anticipated similarities to dimethyl stearamine in their conditions of use. The ingredient mixtures dimethyl cocamine, dimethyl tallowamine, dimethyl hydrogenated tallowamine and dimethyl soyamine have also been added to this safety assessment because of anticipated similarities to dimethyl stearamine in their conditions of use. The Cosmetic Ingredient Review (CIR) Expert Panel published a safety assessment on the use of dimethyl lauramine in cosmetics in 1995. The CIR Expert Panel concluded that " the data available are insufficient to support the safety of this ingredient as used in cosmetics."[2] A search for new published and unpublished information was conducted for dimethyl lauramine and the additional ingredients in this report through October of 2009 and the results were summarized in this document. The CIR Expert Panel concluded at the December 2009 meeting, that dimethyl stearamine, dimethyl lauramine, dimethyl myristamine, dimethyl palmitamine, dimethyl behenamine, dimethyl cocamine, dimethyl tallowamine, dimethyl hydrogenated tallowamine and dimethyl soyamine are safe in the present practices of use and concentration, as currently used in non-coloring hair care products as described in this safety assessment. Were ingredients in this group not in current use to be used in the future, the expectation is that they would be used in this product category and at concentrations comparable to others in the group.

## CHEMISTRY

### Definition and Structure

The structures of dimethyl stearamine and the additional ingredients in this assessment are in Figure 1. The registry numbers and definitions of dimethyl stearamine and the additional ingredients in this assessment are listed in Table 1. These ingredients are tertiary aliphatic amines or mixtures of tertiary aliphatic amines that can function in personal care products/cosmetics as antistatic agents. Antistatic agents are used to treat materials or their surfaces to reduce or eliminate the buildup of static electricity. Dimethyl stearamine is also used as a corrosion inhibitor in aerosol products that are stored in cans and as a pH adjuster.[3] Dimethyl stearamine is added to acrylate resins to neutralize the acidic groups on the resins thus increasing the water solubility of the product and promoting its removal upon washing the hair. The salt of dimethyl stearamine is formed in this process.[4]

The technical names for these ingredients are listed in Table 2.[5]

### Physical and Chemical Properties

The physical and chemical properties of the tertiary aliphatic amines listed in this safety assessment are shown in Table 3.[6] Values for the octanol-water partition coefficient ($LogK_{ow}$), water solubility and vapor pressure were calculated for

dimethyl lauramine, dimethyl myristamine, dimethyl palmitamine and dimethyl stearamine using the EPIWIN 3.05 program.[7] Limited information was available for dimethyl behenamine and no information was available for the ingredient mixtures.

### Manufacture and Production

In general, tertiary amines are formed via the reaction of a secondary amine with additional nitrile, imine, or alcohol at high temperatures and under hydrogenating conditions. They can also be produced by methylating primary or secondary fatty amines.[8]

Dimethyl cocamine is derived from coconut oil, which is about 50% lauric acid, 19% myristic acid and about 10% each palmitic, capric and caprylic acids.[9] Dimethyl tallowamine and dimethyl hydrogenated tallowamine are derived from tallow, which is about 40% oleic acid, 30% palmitic acid and 25% stearic acid.[10]

### Impurities

The typical alkyl composition of Armeen DM18D, the trade name for dimethyl stearamine as produced by Akzo Nobel, is 94% as the C18 tertiary amine (dimethyl stearamine), with 4% and 1% as the shorter C16 and C14 tertiary amines respectively and 1% as the longer C20 tertiary amine. Dimethyl stearamine as supplied by the manufacturer may contain up to 1% of the starting material.[3] A sample of Armeen DM18D, was analyzed using $^{1}H$ and $^{13}C$ NMR (LOD =0.1% w/w) for primary, secondary and tertiary amine content. The results found the sample to be 99.57% by weight tertiary amines (exact percentages of C18-C14 not provided) and 0.31% primary amines. No secondary amines were detected.[11] The typical alkyl composition of Armeen DM12D, the trade name for dimethyl lauramine as produced by Akzo Nobel, is 98% as the C12 tertiary amine (dimethyl lauramine), with 1% each as the C14 and the C10 tertiary amines.[3] Data generated using two commercially available mixtures of C12-C14 dimethyl amines were included in this safety assessment because dimethyl lauramine is a component of the mixtures. Genamin 12R 302 D is reportedly 95% dimethyl lauramine and Genamin LA 302D is reportedly 70% dimethyl lauramine.[12]

### Analytical Methods

Dimethyl steramine can be identified using gas chromatography.[13]

### Reactions

Dimethyl stearamine and the other aliphatic amines have the potential to form carcinogenic nitrosamines in the presence of N-nitrosating agents. When 19 hair-care products were analyzed for the presence of N-nitroso-N-methyloctadecylamine, no detectable levels (LOD, 20 ppb) of this nitrosamine were found in any of the products.[14] However, the authors cautioned that the number of products tested was small and could not be considered representative of dimethyl stearamine in general.

Dimethyl lauramine has the potential to form a carcinogenic nitrosamine when it is ingested with nitrite. A mixture of dimethyl lauramine and nitrite given orally in the drinking water to rats, induced neoplasms of the urinary bladder and nonglandular stomach.[15-17]

## USE

### Cosmetic

The product formulation data submitted to the Food and Drug Administration (FDA) as part of the Voluntary Cosmetic Registration Program (VCRP), indicates that the use of dimethyl stearamine has decreased from 55 uses in 1994 to 40 uses in 2009 (Table 4).[18,19] A survey of current use concentrations conducted by the Personal Care Products Council reported a use of 0.04% in hair conditioners and 4% in hair sprays.[20] Neither use nor concentration information was available for the other ingredients.

Dimethyl stearamine is used in hair sprays, and effects on the lungs that may be induced by aerosolized products containing this ingredient, are of concern.

The aerosol properties that determine deposition in the respiratory system are particle size and density. The parameter most closely associated with deposition is the aerodynamic diameter, $d_a$, defined as the diameter of a sphere of unit density possessing the same terminal settling velocity as the particle in question. In humans, particles with an aerodynamic diameter of $\leq 10$ µm are respirable. Particles with a $d_a$ from 0.1 – 10 µm settle in the upper respiratory tract and particles with a $d_a < 0.1$ µm settle in the lower respiratory tract.[21,22]

Particle diameters of 60-80 µm and ≥80 µm have been reported for anhydrous hair sprays and pump hairsprays, respectively.[23] In practice, aerosols should have at least 99% of their particle diameters in the 10 – 110 µm range and the mean particle diameter in a typical aerosol spray has been reported as ~38 µm.[24] Therefore, most aerosol particles are deposited in the nasopharyngeal region and are not respirable.

European Union

In the EU, trialkylamines and their salts may be used at maximum concentrations of 2.5% in finished, non-rinse off products. There is no concentration limit for use in rinse-off products. In all types of products, these ingredients should not be used in nitrosating systems and they must have a purity of 99% with a maximum secondary amine content of 0.5%. They must be kept in nitrite-free containers and can have a maximum nitrosamine content of 50 µg/kg .[25]

**Non-Cosmetic**

Dimethyl stearamine is used as a corrosion inhibitor.[3]

## GENERAL BIOLOGY

*Dimethyl Stearamine*

Dimethyl stearamine has antibacterial activity against *Streptococcus faecalis*. A concentration of 3.6 mol/L x $10^6$ caused 50% growth inhibition. The most active compound in this study was heptadecylamine, which inhibited growth by 50% at a concentration of 1.9 mol/L x $10^6$.[a] When structure-activity analyses were conducted, the authors noted that for tertiary amines, the bulk of the ammonium head along with the overall hydrophobic properties of the molecule appeared to determine activity.[26]

*Dimethyl Lauramine*

Dimethyl lauramine has antimicrobial, antibacterial, and fungicidal properties.[27] Its ability to inhibit is dependent on pH and temperature. In a study with *Streptococcus agalactiae* and *Escherichia coli*, the antimicrobial activity was greater at pH 7 than at pH 8, and at pH 6, a large decrease occurred in the ability of dimethyl lauramine to inhibit bacterial growth. Increasing the temperature from 20 to 40°C increased antimicrobial activity.[28] Dimethyl lauramine also inhibited the growth of *Streptococcus faecalis*.[26]

Absorption, Distribution, Metabolism, Excretion

No studies concerning the absorption, distribution, metabolism or excretion of dimethyl stearamine or the other related ingredients were found in the existing published literature.

Physical and chemical properties may be relevant to the question of dermal penetration. Table 3 presents the available physical and chemical properties of the individual ingredients presented in this report. No physical and chemical property data were available for the ingredient mixtures. The individual ingredients range from C12 to C22 in straight carbon chain length and have molecular weights > 200 g/mole. Values for the log $K_{ow}$, the water solubility and the vapor pressure were calculated for dimethyl lauramine, dimethyl myristamine, dimethyl palmitamine, and dimethyl stearamine. Dimethyl lauramine has a predicted water solubility of 8.58 mg/L. All of the other ingredients have predicted water solubility values of

[a] The CIR Expert Panel interpreted these values to be $10^{-6}$ concentrations.

< 1 mg/L with water solubility decreasing with increasing length of the alkyl chain. The predicted vapor pressure values are all < 0.1 hPa.

## ANIMAL TOXICOLOGY

### Acute Toxicity

Dermal

Rabbits (n=4; strain not specified) were treated dermally (surface area not specified) with 1, 4 and 16 g/kg dimethyl stearamine (as Armeen DM18D) for 24 h. Two rabbits per group received the test article on abraded skin. Weight loss was observed in some of the animals (number not specified). Mortality occurred in 0, 1 and 3 animals from the 1, 4 and 16 g/kg dose groups respectively. Other clinical signs included lethargy, diarrhea, ataxia, negative righting reflex, dyspnea, ptosis, emaciation, few feces, nasal discharge and mucous in the stool. Dermal reactions were observed and ranged from very slight to moderate erythema and very slight to severe edema. Abnormalities of the lungs, heart and skin were observed in necropsied animals that died on study. Surviving animals were not necropsied. The dermal $LD_{50}$ was 8.0 g/kg.[29]

Oral

*Dimethyl Stearamine*

An oral $LD_{50}$ of 780 mg/kg in rats (strain not specified) has been reported for dimethyl stearamine.[30]

Male rats (n=10/group; strain not specified) were given 0.96, 1.22, 1.54, 1.95, 3.12 and 5.0 g/kg of dimethyl stearamine (as Armeen DM18D; a clear liquid) via a single gavage dose and observed for 14 days. Three animals died over the course of the study at the 0.96 and 1.22 g/kg doses and all 10 animals died in each of the remaining dose groups. The $LD_{50}$ was determined to be 1.23 g/kg. Clinical signs included: lethargy, flaccidity, diarrhea, ataxia, piloerection, chromodacryorrhea, chromorhinorrhea, tremors, ptosis, emaciation, oily anogenital area, rough coat, hyperactivity, decreased respiration, and staining of the anogenital area. At necropsy, abnormalities of the heart, lung and GI tract were observed in the animals that died during the study. Body weight gains and necropsy were normal for animals that survived to the end of the study.[29]

Wistar rats (5/sex/group) were given a single 15 ml/kg dose (0.06 g/kg), via gavage, of a formulation containing 0.5% dimethyl stearamine. The animals were observed daily, and were killed on day 14. All animals survived to termination and no signs of toxicity were observed. No macroscopic changes were reported in any of the internal organs.[31]

*Dimethyl Lauramine*

No data are available for dimethyl lauramine alone, but two commercially sold mixtures of C12-14 alkyldimethylamines have been tested. Genamin 12 R 302 D has an $LD_{50}$ value after single gavage administration of 1890 and 1450 mg/kg bw for male and female rats respectively (strain not specified). Genamin LA 302 D has an $LD_{50}$ value after single gavage administration of 1200 mg/kg bw for female rats (strain not specified).[12]

### Dermal Irritation

*Dimethyl Lauramine*

No data are available for dimethyl lauramine alone, but two commercially sold mixtures of C12-14 alkyldimethylamines have been tested. Both Genamin 12 R 302 D and Genamin LA 302 D were labeled as corrosive after testing according to OECD Guideline 404. Briefly, albino rabbits (n=12; strain/sex not specified) were patch tested on abraded and intact skin using 0.5 ml of the test material with occlusion for 24 h. Animals were evaluated at patch removal and 48 h later.[12]

### Ocular Irritation

*Dimethyl Stearamine*

The ocular irritation potential of a formulation containing 0.5% dimethyl stearamine was evaluated by instilling 0.1 ml into the conjunctival sac of NZW rabbits (n=6/sex not specified). The eyes of 3 rabbits were rinsed with tap water after 1 min of exposure. The other 3 rabbits were treated for 24 h. Irritation was scored according to the Draize scale (maximum possible score: 110). Slight irritation of the conjunctivae was observed in all unrinsed eyes at the 24 and 48 h grading period. Rinsing prevented any irritation from occurring. No fluorescein retention was observed, and all eyes were clear after 72 h.[31]

*Dimethyl Lauramine*

A commercial mixture of C12-C14 alkyldimethylamines was classified according to the EC classification system, as irritating in ocular testing in the rabbit. No methodological details were available.[12]

### Short-Term Oral Toxicity

*Dimethyl Lauramine*

Sprague-Dawley rats (5/sex/group) were treated by gavage with dimethyl lauramine at dose levels of 0, 50, 150 and 300 mg/kg bw for 28 d. Body weights, feed consumption and clinical examinations were conducted on all animals.

The authors reported that no substance-related changes in body weight, feed consumption, hematology, clinical biochemistry, or organ weights were observed in animals in the 50 or 150 mg/kg dose group. In the 300 mg/kg bw group, 3 of the 5 females died during the study while all of the males survived to the end of the study. No other information is provided about effects observed in the highest dose group. Animals in the 150 mg/kg bw group were observed rubbing their snouts in the bedding material after dosing for approximately 5 minutes. This was not observed in the 50 mg/kg bw group. No mention is made regarding this behavior in the 300 mg/kg bw group. The authors concluded that 50 mg/kg bw is an oral NOEL based on this study.[12]

## REPRODUCTIVE AND DEVELOPMENTAL EFFECTS

*Dimethyl Lauramine*

Sprague-Dawley rats (10/sex/group) were treated by gavage with dimethyl lauramine at dose levels of 0, 50, 150, 300 and 450 mg/kg bw/day.[12] Males were treated 14 days prior to mating and during the 14-day mating period and females were treated 14 days prior to mating and throughout the mating, pregnancy and lactation periods. The highest dose group was discontinued due to the deaths of 3 animals (1 male and 2 females) on day 4 of the test and the poor health exhibited by the remaining animals in this treatment group. In the 300 mg/kg group, 1 male and 6 females died during the course of the treatment. Only 1 pup (female) was born alive in this group. In the 150 mg/kg dose group there were 2 deaths. The number of stillbirths was significantly increased and the birth weight of male pups was decreased (data not provided). The weight of the female pups was within the normal range. A significant increase in the mean post-implantation loss (50.4% vs. 13.3% in controls) and a significant decrease in the mean viability index (36.9% vs. 99.3% in controls), were observed.

In the 50 mg/kg dose group, no changes in behavior or external appearance were observed. No changes were observed in body weight gain or in feed consumption. There were no apparent effects on the reproductive parameters examined with post-implantation loss (~13%) and viability index (~99%) exhibiting values similar to control values. No changes in body weight or sex-ratio of the pups were observed in this dose group and the authors reported that these pups developed normally. The authors determined an oral NOEL of 50 mg/kg for reproductive/developmental toxicity based upon these findings.[12]

## GENOTOXICITY

In Vitro

*Dimethyl Stearamine*

Dimethyl stearamine (0.5 - 50 µg/plate) was tested in a reverse mutation assay with and without metabolic activation in *S. typhimurium* TA98 and TA100 strains. Dimethyl stearamine was not mutagenic with or without metabolic activation. Cytotoxicity was observed at 50 µg/plate.[32]

*Dimethyl Lauramine*

No data are available for dimethyl lauramine alone, but a commercial mixture of C12-14 alkyldimethylamines has been tested.

Genamin 12 R 302 D was found not mutagenic with or without metabolic activation in the Ames assay when tested at concentrations of 0.16 – 500 µg/plate in *S. typhimurium* (TA 98, TA100, TA1535, TA1537, and TA1538) and *E. coli* (WP2uvrA). Neither cytotoxicity nor negative and positive control data were reported.[12]

In Vivo

*Dimethyl Lauramine*

No data are available for dimethyl lauramine alone, but a commercial mixture of C12-14 alkyldimethylamines has been tested.

Genamin LA 302D was found not mutagenic in the micronucleus test in vivo. Male and female mice (number/species not specified) were treated by gavage with 0, 120, 400 and 1200 mg/kg bw/day of the test substance in sesame oil, for 2 days. No changes were observed in the number of polychromatic erythrocytes containing micronuclei or in the ratio of polychromatic erythrocytes to total erythrocytes in any of the animals.[12]

## CARCINOGENICITY

*Dimethyl Lauramine*

Lijinsky and Taylor (1977) examined the carcinogenicity of dimethyl lauramine and its nitrosated products in an oral drinking water study. Sprague-Dawley rats (15/sex/group) were given drinking water supplemented with either 0.18% dimethyl lauramine alone or with 0.18% dimethyl lauramine and 0.2% sodium nitrite 5 days/wk for 80 weeks. Positive control rats were given drinking water with 0.2% sodium nitrite and untreated control rats were given un-supplemented water. The authors reported that the total amine dose/rat was 14 g and the total nitrite dose/rat was 16 g over the 80 week study period. There were no significant differences in survival, feed consumption or weight gain, between the treated and untreated groups of rats. All of the male rats were necropsied at the end of the study, but 6 female rats died during the study due to a lack of water, and were not necropsied.

The authors reported a significant increase in the incidence of urinary bladder (2/15 in males; 1/9 in females) and forestomach tumors (3/15 in males; 1/15 in females) in rats receiving dimethyl lauramine plus nitrite. No significant increase in neoplasms was observed in rats receiving dimethyl lauramine alone. The authors concluded that dimethyl lauramine with sodium nitrite in the drinking water results in the formation of a carcinogenic nitrosamine.[16,17]

The carcinogenicity of a nitrosation product formed from the reaction of dimethyl lauramine with nitrous acid, nitrosomethyl-n-dodecylamine, has been documented. This compound has been found to cause urinary bladder tumors in Sprague-Dawley rats when administered via gavage.[15]

## CLINICAL ASSESSMENT OF SAFETY

### Dermal Irritation

The cumulative irritancy potential of a formulation containing 0.5% dimethyl stearamine was tested in 198 volunteer subjects. The test solution was applied to a ½ inch square gauze pad (vol not provided) and applied to the backs of the

volunteers for 48 h. Following removal of the patch, the volunteers were observed for an immediate reaction and 2 h later for a delayed reaction. The subjects received a total of 10 applications. No evidence of primary irritation or skin fatiguing was observed.[33]

The cumulative irritancy potential of dimethyl stearamine was tested in male (n=30) and female (n= 194) volunteer subjects (18-70 y old) using 4 different test substances. They were: a final hair spray formulation that contained dimethyl stearamine (concentration not provided), a final hair spray formulation that did not contain dimethyl stearamine, a 1% solution of dimethyl stearamine in denatured alcohol and a 1% solution of dimethyl stearamine in denatured alcohol with 0.25% citric acid. The test samples were selected to provide data on a use level of 1% dimethyl stearamine as well as a more representative use level found in a final formulation (% not provided). A total of 224 subjects were initially on study, with 215 subjects completing the study. The 9 subjects that left the study did so reportedly for reasons unrelated to the test material. Test sample (dose/unit area not provided) was applied, with occlusion, to the subjects' backs on Monday, Wednesday, and Friday (for a total of 9 applications) for 48 h and the sites were scored for dermal irritation 24 or 48 h after patch removal (by subjects) on Tuesday and Thursday or Saturday respectively. A few barely perceptible erythema reactions were recorded, but the study authors concluded that under the condition of this study, no clinically significant irritation occurred in this test population.[34-37]

### Dermal Sensitization

The cumulative irritancy study that included 198 subjects (see Dermal Irritation) was designed to also test for allergic contact sensitization potential using the formulation containing 0.5% dimethyl stearamine. A challenge patch (dose/unit area not provided) was applied for 48 h after a 2 week interval and a second challenge patch was applied for 48 h, 1 week after the first challenge. No evidence of sensitization reactions were observed in any of the test subjects.[33]

The cumulative irritancy study that included 215 subjects (see Dermal Irritation) was designed to also test for the allergic contact sensitization potential of the previously described formulations in the same test subjects. A challenge patch (dose/unit area not provided) was applied to a naive test site on the back, 2 weeks after the last cumulative irritation treatment. The test sites were evaluated for dermal reactions 24, 48 and 72 h after patch removal (by the study technician). No sensitization reactions were observed in any of the test subjects.[34-37]

## SUMMARY

Dimethyl stearamine is a tertiary amine that is used in cosmetic products as an antistatic agent and as a pH adjuster to neutralize the acidic groups on acrylate resins in hair sprays, to promote their water solubility. Dimethyl stearamine is also used as a corrosion inhibitor in aerosol products that are stored in cans. The reported uses of dimethyl stearamine have decreased from 55 uses in 1994 to 40 uses in 2009. It is used in hair sprays, hair tonics and other non-coloring hair care preparations at concentrations ranging from 0.04 – 4%. The additional ingredients in this assessment, dimethyl lauramine, dimethyl myristamine, dimethyl palmitamine, dimethyl behenamine, dimethyl cocamine, dimethyl tallowamine, dimethyl hydrogenated tallowamine and dimethyl soyamine are all tertiary amines or mixtures of tertiary amines that can function as antistatic agents, but are not currently reported as in use according to the FDA's VCRP. There is limited toxicological information available on dimethyl stearamine and dimethyl lauramine and no additional information was found for the other ingredients in this report.

No studies on the absorption, distribution, metabolism or excretion of these ingredients were found. Predicted values for the log $K_{ow}$, water solubility and vapor pressure were available for dimethyl lauramine, dimethyl myristamine, dimethyl palmitamine, and dimethyl stearamine. Dimethyl lauramine has a predicted water solubility of 8.58 mg/L. All of the other ingredients have predicted water solubility values of < 1 mg/L with water solubility decreasing with increasing length of the alkyl chain. The predicted vapor pressure values are all < 0.1 hPa.

For dimethyl stearamine, a dermal $LD_{50}$ of 8.0 g/kg was reported in rabbits and an oral $LD_{50}$ of 780 mg/kg was reported in rats.

No $LD_{50}$ data are available for dimethyl lauramine alone, but the oral $LD_{50}$ for two commercially sold mixtures of C12-14 alkyldimethylamines have been reported. The values range from 1200 – 1450 mg/kg bw for female rats and a value of 1890 mg/kg bw reported for male rats.

A NOEL of 50 mg/kg bw was reported for behavioral effects in a short-term study and for reproductive effects in a reproductive/developmental study of dimethyl lauramine in Sprague-Dawley rats.

Dimethyl stearamine, at 0.5% in a formulation, caused slight irritation in rabbits in an in vivo ocular irritation test.

Dimethyl stearamine was not mutagenic in a reverse mutation assay in TA98 and TA100 salmonella strains. No data are available for dimethyl lauramine alone, but a commercial mixture of C12-14 alkyldimethylamines has been tested and was not mutagenic in salmonella or *E. coli*. In a carcinogenicity study, when dimethyl lauramine and sodium nitrite were administered together in the drinking water, there was a significant incidence of malignant tumors of the urinary bladder and the forestomach. No neoplasms were observed with dimethyl lauramine alone. There are no carcinogenicity studies available for the other ingredients.

Dimethyl stearamine was negative in human clinical testing for dermal irritation and sensitization, although information concerning the exact dose per unit area of skin was not available for these studies.

## DISCUSSION

The available safety data are for dimethyl stearamine and dimethyl lauramine. The FDA's VCRP database indicates that dimethyl stearamine is used in non-coloring hair care products, the majority of which are hairsprays, at a concentration range of 0.04-4%. The potential adverse effects of inhaled aerosols depend on the specific chemical species, the concentration and the duration of the exposure, and their site of deposition within the respiratory system. In practice, aerosols should have at least 99% of their particle diameters in the 10 – 110 µm range and the mean particle diameter in a typical aerosol spray has been reported as ~38 µm. Particles with an aerodynamic diameter of $\leq$ 10 µm are respirable. Therefore, in the absence of inhalation toxicity data, the Panel determined that dimethyl stearamine can be used safely in hair sprays, because the product particle size is not respirable. Limited dermal exposure and no significant systemic exposure is expected to occur from the use of this ingredient in non-coloring hair care products.

The available data indicate that there is a potential for dimethyl lauramine to form nitrosamines and this property is applicable to the other tertiary aliphatic amines discussed in this safety assessment. Therefore, the Expert Panel cautions that products containing these ingredients should be formulated to avoid the formation of nitrosamines.

The CIR Expert Panel has determined that the more substantive data on dimethyl stearamine is applicable to the evaluation of additional tertiary aliphatic amines under comparable conditions of use. These include: dimethyl lauramine, dimethyl myristamine, dimethyl palmitamine, dimethyl behenamine, dimethyl cocamine, dimethyl tallowamine, dimethyl hydrogenated tallowamine and dimethyl soyamine.

## AMENDED CONCLUSION

The CIR Expert Panel concluded that dimethyl stearamine, dimethyl lauramine, dimethyl myristamine, dimethyl palmitamine, dimethyl behenamine, dimethyl cocamine, dimethyl tallowamine, dimethyl hydrogenated tallowamine and dimethyl soyamine are safe in the present practices of use and concentration as currently used in non-coloring hair care products, as described in this safety assessment.[b]

[b] Were ingredients in this group not in current use to be used in the future, the expectation is that they would be used in this product category and at concentrations comparable to others in the group.

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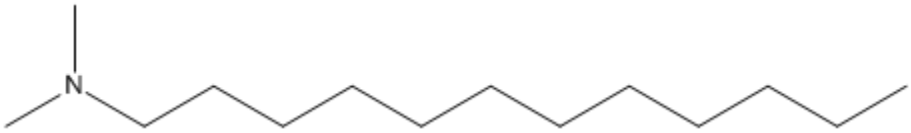
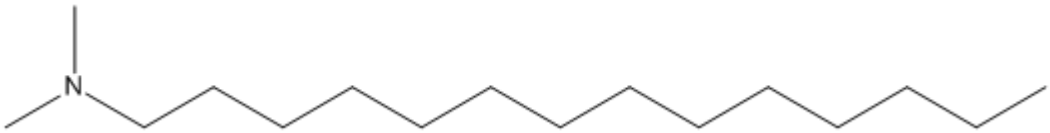
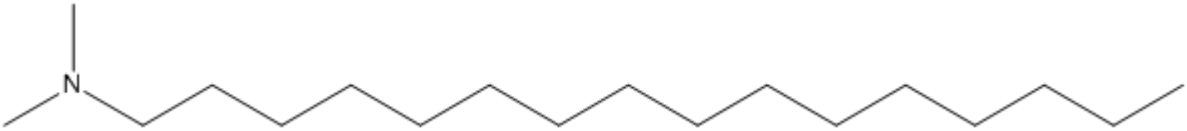
**Figure 1. Structures of dimethyl stearamine and the additional ingredients (see Table 1 for the identity of the R groups).**



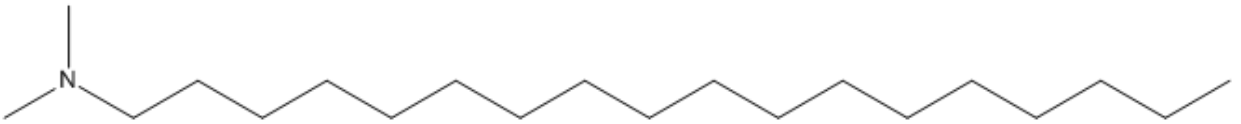
Dimethyl Lauramine



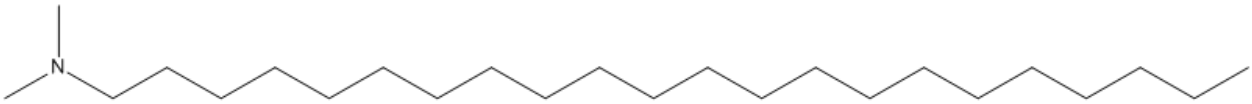
Dimethyl Myristamine



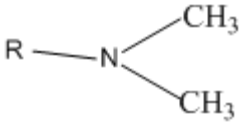
Dimethyl Palmitamine



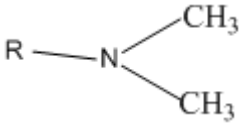
Dimethyl Stearamine



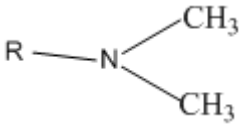
Dimthyl Behenamine



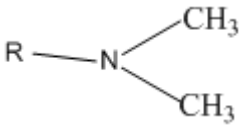
Dimethyl Cocamine



Dimethyl Tallowamine



Dimethyl Hydrogenated Tallowamine



Dimethyl Soyamine

**Table 1. The registry numbers and definitions of dimethyl stearamine and the additional ingredients.[5]**

| Ingredient | Definition |
|---|---|
| Dimethyl Stearamine (CAS No.124-28-7) | Tertiary aliphatic amine |
| Dimethyl Lauramine (CAS No. 112-18-5) | Tertiary aliphatic amine |
| Dimethyl Myristamine (CAS No. 112-75-4) | Tertiary aliphatic amine |
| Dimethyl Palmitamine (CAS No. 112-69-6) | Tertiary aliphatic amine |
| Dimethyl Behenamine (CAS No. 21542-96-1) | Tertiary aliphatic amine |
| Dimethyl Cocamine (CAS No. 61788-93-0) | A tertiary aliphatic amine where R represents the alkyl groups derived from coconut oil |
| Dimethyl Tallowamine (CAS No. 68814-69-7) | A tertiary aliphatic amine derived from Tallow Acid where R represents the alkyl groups derived from tallow. |
| Dimethyl Hydrogenated Tallowamine (CAS No. 61788-95-2) | A tertiary aliphatic amine where R represents the alkyl groups derived from hydrogenated tallow |
| Dimethyl Soyamine (CAS No. 61788-91-8) | A tertiary aliphatic amine derived from Soy Acid where R represents the alkyl groups derived from soy |

**Table 2. Technical names for dimethyl stearamine and additional ingredients.[5]**

| Ingredient Name | Other Technical Names |
|---|---|
| Dimethyl lauramine | *N*,*N*-dimethyl-1-dodecanamine |
| | dimethyldodecylamine |
| | dimethyl laurylamine |
| | lauryl dimethyl amine |
| | |
| Dimethyl myristamine | *N*,*N*-dimethyl-1-tetradecanamine |
| | dimethyl myristylamine |
| | myristyl dimethyl amine |
| | |
| Dimethyl palmitamine | *N*,*N*-dimethyl-1-hexadecanamine |
| | dimethyl palmitylamine |
| | palmityl dimethyl amine |
| | |
| Dimethyl stearamine | *N*,*N*-dimethyl-1-octadecanamine |
| | *N*,*N*-dimethyloctadecylamine |
| | dimethyl stearylamine |
| | dimantine |
| | |
| Dimethyl behenamine | *N*,*N*-dimethyl-1-docosanamine |
| | *N*,*N*-dimethyldocosylamine |
| | dimethyl behenylamine |
| | behenyl dimethyl amine |
| | |
| Dimethyl cocamine | coco dimethyl amine |
| | dimethyl coconut amine |
| | amines, coco alkyl dimethyl |
| | |
| Dimethyl tallowamine | amines, tallow alkyl dimethyl |
| | |
| Dimethyl hydrogenated tallowamine | amines, (hydrogenated tallow alkyl)dimethyl |
| | hydrogenated tallow dimethyl amine |
| | |
| Dimethyl soyamine | amines, dimethyl soy alkyl |
| | soy dimethyl amine |

**Table 3. Physical and chemical properties of dimethyl stearamine and additional ingredients.**[6,38]

| | **Dimethyl Lauramine** | **Dimethyl Myristamine** | **Dimethyl Palmitamine** | **Dimethyl Stearamine** | **Dimethyl Behenamine** |
|---|---|---|---|---|---|
| CAS No. | 112-18-5 | 112-75-4 | 112-69-6 | 124-28-7 | 21542-96-1 |
| Molecular weight | 213.41 | 241.46 | 269.51 | 297.57 | 339.64 |
| Molecular formula | $C_{14}H_{31}N$ | $C_{16}H_{35}N$ | $C_{18}H_{39}N$ | $C_{20}H_{43}N$ | $C_{24}H_{51}N$ |
| Density @ 25 °C ($g/cm^3$) | 0.7846 | - | 0.7979 | 0.8050 | - |
| Melting point (°C) | -20.3 | 43 | 12 | 22.89 | 44 |
| Boiling point @ 1 torr (°C) | 76-96 | 105-110 | 138-142 | 145-150 | 190 (@ 0.6 torr) |
| $LogK_{ow}$ | 5.44 (calc) | 6.42 (calc) | 7.41 (calc) | 8.39 (calc) | - |
| Water solubility (mg/L) | 8.58 (calc) | 0.88 (calc) | 0.089 (calc) | 0.0089 (calc) | - |
| Vapor Pressure (hPa) | 0.0159 (calc) | 0.0020 (calc) | 0.00029 (calc) | 0.00017 (calc) | - |
| | **Dimethyl Cocamine** | **Dimethyl Tallowamine** | **Dimethyl Hydrogenated Tallowamine** | **Dimethyl Soyamine** | |
| CAS No. | 61788-93-0 | 68814-69-7 | 61788-95-2 | 61788-91-8 | |
| Molecular weight | - | - | - | - | |
| Molecular formula | - | - | - | - | |
| Density @ 25 °C ($g/cm^3$) | - | - | - | - | |
| Melting point (°C) | - | - | - | - | |
| Boiling point @ 1 torr (°C) | - | - | - | - | |
| $LogK_{ow}$ | - | - | - | - | |
| Water solubility (mg/L) | - | - | - | - | |
| Vapor Pressure (hPa) | - | - | - | - | |

**Table 4. Historical and current cosmetic product uses and concentrations for dimethyl stearamine.**[18-20,39]

| Product Category | 1994 uses (total number of products in category) | 2009 uses (total number of products in category) | 2008 concentrations of use (%) |
|---|---|---|---|
| **Dimethyl Stearamine** | | | |
| **Baby products** | | | |
| Lotions, oils, powders, etc. | 1 (45) | -(132) | - |
| **Noncoloring hair care products** | | | |
| Conditioners | 6 (614) | -(1249) | 0.04 |
| Sprays/aerosol fixatives | 29 (306) | 29 (371) | 4 |
| Straighteners | 1 (61) | - (144) | - |
| Rinses | 2 (58) | - (47) | - |
| Tonics, dressings, etc. | 12 (563) | 9 (1097) | - |
| Other | 4 (376) | 2 (716) | - |
| **Total uses/ranges for Dimethyl Stearamine** | **55** | **40** | **0.04-4** |