

Safety Assessment of Bis-Diglyceryl Polyacyladipate-2 and Bis-Diglyceryl Polyacyladipate-1 as Used in Cosmetics

June 14, 2012

All interested persons are provided 60 days from the above date to comment on this Tentative Report and to identify additional published data that should be included or provide unpublished data which can be made public and included. Information may be submitted without identifying the source or the trade name of the cosmetic product containing the ingredient. All unpublished data submitted to CIR will be discussed in open meetings, will be available at the CIR office for review by any interested party and may be cited in a peer-reviewed scientific journal. Please submit data, comments, or requests to the CIR Director, Dr. F. Alan Andersen.

The 2012 Cosmetic Ingredient Review Expert Panel members are: Chairman, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; Ronald A. Hill, Ph.D.; Curtis D. Klaassen, Ph.D.; Daniel Liebler, Ph.D.; James G. Marks, Jr., M.D.; Ronald C. Shank, Ph.D.; Thomas J. Slaga, Ph.D.; and Paul W. Snyder, D.V.M., Ph.D. The CIR Director is F. Alan Andersen, Ph.D. This safety assessment was prepared by Monice M. Fiume, Senior Scientific Analyst/Writer.

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ABSTRACT

The CIR Expert Panel assessed the safety of bis-diglyceryl polyacryladipate-2 and bis-diglyceryl polyacryladipate-1 as used in cosmetics, finding that these ingredients are safe in cosmetic formulations in the present practices of use and concentration. Both ingredients are lanolin substitutes and are reported to function in cosmetics as skin conditioning agents – emollients. The Panel reviewed available animal and clinical data in making its determination of safety.

INTRODUCTION

This assessment reviews the safety of bis-diglyceryl polyacryladipate-2 and bis-diglyceryl polyacryladipate-1; bis-diglyceryl polyacryladipate-2 is used in over 500 cosmetic formulations. These ingredients are reported to function as skin conditioning agents - emollients. Initially in the review process, a Notice to Proceed without the Preparation of a Scientific Literature Review was issued due to the lack of published information relevant to the safety of these ingredients as used in cosmetic formulations. This assessment includes unpublished data that were submitted in response to that Notice to Proceed.

CHEMISTRY

Definitions

Bis-diglyceryl polyacryladipate-2 and bis-diglyceryl polyacryladipate-1 are mixed fatty acid esters. Bis-diglyceryl polyacryladipate-2 (CAS No. 82249-33-0) is the adipic acid diester of a mixed diglyceryl ester of caprylic, capric, stearic, isostearic and hydroxystearic acids, while bis-diglyceryl polyacryladipate-1 (CAS No. 135229-94-6;) is the adipic acid diester of a mixed diglyceryl ester of the same acids just listed, with the exception that stearic acid is not included in this diester.¹

Due to the three different isomers (alpha,alpha-, beta,beta-, and alpha,beta-) present in diglycerin, the two different connectivities (alpha- and beta-) in which diglycerin can be attached to adipic acid, and the variety of fatty acid esters (e.g., caprylate, caprate, stearate, isostearate, and hydroxystearate) to be formed with the reactive hydroxyls of bis-diglyceryl adipate, there are a multitude of structural configurations possible within each bis-diglyceryl polyacryladipate ingredient. Figure 1 depicts the structures of the mixture of chemicals present in the bis-diglyceryl polyacryladipate ingredients.

Physical and Chemical Properties

The available physical and chemical properties data are provided in Table 1.

Method of Manufacture

Both bis-diglyceryl polyacryladipate-2 and bis-diglyceryl polyacryladipate-1 are manufactured in one-pot reactions with heat, catalysts, and reduced pressure.² The raw materials used in the production of both of these esters are diglycerin, adipic acid, isostearic acid, 12-hydroxystearic acid, n-octanoic acid, and n-decanoic acid. Stearic acid is also a raw material for the production of bis-diglyceryl polyacryladipate-2.

Impurities

Acid number and hydroxyl number indicate that bis-diglyceryl polyacryladipate-2 and bis-diglyceryl polyacryladipate-1 are essentially free of starting raw materials.² A manufacturer also reports that the following parameters are checked regularly in bis-diglyceryl polyacryladipate-2, with typical findings given as: aflatoxin B1, B2, G1, and G2, <0.10 ppb each; heavy metals, i.e. As, Cd, Cr, Ni, Pb, Hg, Cu, Sn, <1 ppm each; pesticides – organochlorine, organocholorophosphorous, and pyrethroids, <0.01 ppm each class; various PCBs, <0.01 ppm each class; microbiology: pathogens absent, total viable count <10 CFU/g, and yeast/molds <10 CFU/g.

USE

Cosmetic

Bis-diglyceryl polyacryladipate-2 and bis-diglyceryl polyacryladipate-1 are suitable as lanolin substitutes,^{3,4} and are reported to function as skin conditioning agents – emollients.¹ The Food and Drug Administration (FDA) collects information from manufacturers on the use of individual ingredients in cosmetics as a function of cosmetic product category in its Voluntary Cosmetic Registration Program (VCRP). VCRP data obtained from the FDA in 2012 indicate that bis-diglyceryl polyacryladipate-2 is used in 521 cosmetic formulations and that bis-diglyceryl polyacryladipate-1 is used in 6 cosmetic formulations.⁵ Data received in response to a survey of the maximum reported use concentration by category conducted by the Personal Care Products Council (Council) report that bis-diglyceryl polyacryladipate-2 is used in leave-on products at concentrations up to 36% (reported for lipsticks) and in rinse-off products at concentrations up to 21% (reported for eye makeup remover).⁶ Bis-diglyceryl polyacryladipate-1 is used in leave-on products at concentrations up to 10% (reported for tonics, dressings, and other hair grooming aids) and in rinse-off products at a concentration of 4% (reported for eye makeup remover). Frequency and concentration of use data categorized by exposure and duration of use are provided in Table 2.

Products containing bis-diglyceryl polyacyladipate-2 may be used near the eye area and in products in which incidental ingestion may occur. Additionally, bis-diglyceryl polyacyladipate-2 is used in face powders at up to 0.8% and in “other” fragrance preparations at 2%; it is possible that this fragrance preparation is sprayed. In practice, 95% to 99% of the droplets/particles released from cosmetic sprays have aerodynamic equivalent diameters >10 μm .⁷⁻¹⁰ Therefore, most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and bronchial regions and would not be respirable (i.e., they would not enter the lungs) to any appreciable amount.^{7,9}

Both bis-diglyceryl polyacyladipate-2 and polyacyladipate-1 are listed in the European Union inventory of cosmetic ingredients.¹¹

TOXICOKINETICS

Absorption, Distribution, Metabolism, and Excretion

Published toxicokinetics data were not found and unpublished data were not provided.

TOXICOLOGICAL STUDIES

Single Dose (Acute) Toxicity

Dermal

Bis-Diglyceryl Polyacyladipate-2

Groups of 5 male and 5 female Wistar rats were dosed with a single 24-h application of 2000 mg/kg bw undiluted bis-diglyceryl polyacyladipate-2.¹² The exposure site was a shaved 5 cm x 10 cm area on the back. None of the animals died, and no signs of dermal irritation were observed. Body wt gains were normal in males but reduced in females. The dermal LD₅₀ of bis-diglyceryl polyacyladipate-2 is >2000 mg/kg bw.

Bis-Diglyceryl Polyacyladipate-1

Groups of 5 male and 5 female Sprague-Dawley rats were exposed to a single 24-h semi-occlusive application of 2000 mg/kg bw undiluted bis-diglyceryl polyacyladipate-1.¹³ The exposure site was a shaved 5 cm x 4 cm area on the back. None of the animals died, and no signs of toxicity or dermal irritation were observed. The dermal LD₅₀ of bis-diglyceryl polyacyladipate-1 is >2000 mg/kg bw.

Oral

Bis-Diglyceryl Polyacyladipate-2

Groups of 5 male and 5 female Wistar rats were dosed once by gavage with 2000 mg/kg bw bis-diglyceryl polyacyladipate-2 in corn oil.¹⁴ None of the animals died, and the oral LD₅₀ of bis-diglyceryl polyacyladipate-2 is >2000 mg/kg bw.

Bis-Diglyceryl Polyacyladipate-1

Groups of 5 male and 5 female Sprague-Dawley rats were dosed once by gavage with 5000 mg/kg bw bis-diglyceryl polyacyladipate-1 in arachis oil, with a dose volume of 10 ml/kg.¹⁵ None of the animals died, and no signs of systemic toxicity were reported. The oral LD₅₀ of bis-diglyceryl polyacyladipate-1 is >5000 mg/kg bw.

Repeated Dose Toxicity

Oral

Bis-Diglyceryl Polyacyladipate-2

Groups of 5 male and 5 female Wistar rats were dosed by gavage with 0, 180, 1800, and 4500 mg/kg bw (corresponding to 0, 0.2, 2.0, and 5.0 ml/kg bw, respectively) bis-diglyceryl polyacyladipate-2 in corn oil once daily for 28 days.¹⁶ The test volume was 10 ml/kg bw. The animals were killed at the termination of dosing, and gross and microscopic examinations were performed. The only observations made were in the high dose group males. The slight but significant reduction in total bilirubin content was not considered biologically relevant and was attributed to coincidence and an increase in prostate weight may be considered either a coincidental finding or a result of a test article-induced load reaction without histopathological manifestation. The no-observable adverse effect level (NOAEL) was 1800 mg/kg bw (2 ml/kg bw) bis-diglyceryl polyacyladipate-2.

REPRODUCTIVE AND DEVELOPMENTAL TOXICITY

Bis-Diglyceryl Polyacyladipate-2

The reproductive toxicity potential of bis-diglyceryl polyacyladipate-2 was determined in a one-generation study using groups of 24 male and 24 female Sprague-Dawley rats.¹⁷ The male animals were dosed daily by gavage with 0 or 1000 mg/kg bw bis-diglyceryl polyacyladipate-2 in corn oil from 10 wks prior to mating until the day before being killed (day 99), and the female rats were dosed by gavage with the same doses from 2 wks prior to mating until weaning and were killed day

21 following delivery. The dose volume was 10 ml/kg bw. The litters were culled on day 4, and the remaining 8 pups/litter were killed on day 21. Bis-diglyceryl polyacyladipate-2 had no effects on reproduction, fertility, or development, and no signs of general toxicity were observed.

GENOTOXICITY

In Vitro

Bis-Diglyceryl Polyacyladipate-2

The mutagenic potential of bis-diglyceryl polyacyladipate-2 was evaluated in an Ames test performed using *Salmonella typhimurium* strains TA1535, TA1537, TA1538, TA98, and TA100, with and without metabolic activation.¹⁸ The researcher stated that the test material was insoluble in all solvents specified for the Ames test, and for this reason, a spot test was performed and the product was tested directly and undiluted. Bis-diglyceryl polyacyladipate-2 was not mutagenic with or without metabolic activation. Appropriate negative and positive control results were valid.

A chromosomal aberration assay was performed using Chinese hamster lung fibroblasts (V79 cells) with and without metabolic activation for 40-400 µg/ml bis-diglyceryl polyacyladipate-2.¹⁹ Ethanol was the solvent. Bis-diglyceryl polyacyladipate-2 did not induce a significant increase in the incidence of chromosomal aberrations and was not clastogenic. Appropriate negative and positive control results were valid.

In Vivo

Bis-Diglyceryl Polyacyladipate-2

A micronucleus test was performed in mice to evaluate the genotoxic potential of bis-diglyceryl polyacyladipate-2.²⁰ Three groups of 10 NMRI mice, 5 males and 5 females per group, were given a single oral dose of 15,000 mg/kg bw in corn oil, and the groups were killed 24, 48, or 72 h after dosing. The dose volume was 30 ml/kg bw. In males, a difference in the number of polychromatic erythrocytes compared to normochromatic erythrocytes (an increase in the 48 h group and decrease in the 72 h group) was observed; this observation might be explained by an increased neoformation of polychromatic erythrocytes in male mice after administration of the test article first resulting in an increase of polychromatic erythrocytes after 48h. After 72h the number of normochromatic erythrocytes, which arise from polychromatic erythrocytes, increases, resulting in a decrease of polychromatic erythrocytes. This was not considered a genotoxic effect. Vehicle and appropriate positive control results were valid.

CARCINOGENICITY

Published carcinogenicity studies were not found and unpublished data were not provided.

IRRITATION AND SENSITIZATION

Skin Irritation

Non-Human

Bis-Diglyceryl Polyacyladipate-2

The dermal irritation potential of bis-diglyceryl polyacyladipate-2 was evaluated in an acute dermal irritation/corrosion test in 3 rabbits.²¹ A dose of 2000 mg/kg was applied neat to a shaved 8 cm x 15 cm area on the back of each animal under a semi-occlusive covering for 4 h. The test site was examined for signs of irritation at various intervals for 0.5-72 h after patch removal. No erythema or edema was observed, and bis-diglyceryl polyacyladipate-2 was non-irritating to rabbit skin after a single 4-h semi-occlusive application.

The cumulative irritation potential of 5 and 40% bis-diglyceryl polyacyladipate-2 in petrolatum was evaluated in guinea pigs, 3 per group.²² The test material was applied to a shaved area of the flank of each animal once daily for 3 consecutive days, and the test sites were scored 24 h after each application. The test volume was not stated. The cumulative irritation index was 1.2/4 with 5% and 1.3/4 with 40% bis-diglyceryl polyacyladipate-2, indicating that the test material was a weak irritant in guinea pig skin.

Human

Bis-Diglyceryl Polyacyladipate-2

The dermal irritation potential of 5% bis-diglyceryl polyacyladipate-2 in petrolatum was evaluated in 44 subjects.²² The test material was applied to the intact skin of the forearm for 24 h under an occlusive patch. The test volume was not stated. No reactions were observed after 24 h, and 5% bis-diglyceryl polyacyladipate-2 was not irritating to human skin after a single 24-h application.

Fifteen male and 35 female subjects were used to evaluate the dermal irritation potential of undiluted bis-diglyceryl polyacyladipate-2.²³ Twelve subjects were classified as atopic and seven as dermal sensitive. An occlusive patch (defined as a com-

mercial plaster) containing 2 mg/cm² of the test article was applied to the back of each subject for 48 h; the size of the application area was not specified. The test site was scored for irritation upon patch removal and 24 h later. Well-defined erythema was observed in one subject upon patch removal, but not 24 h later; the researcher determined this reaction to be toxic-irritative. It was concluded that undiluted bis-diglyceryl polyacyladipate-2 had no irritating potential in human skin.

Skin Sensitization

Non-Human

Bis-Diglyceryl Polyacyladipate-2

A guinea pig maximization test (GPMT) was used to determine the skin sensitization potential of bis-diglyceryl polyacyladipate-2.²⁴ Groups of 10 male and 10 female Pirbright white guinea pigs were used. A test concentration of 5% was used during intradermal induction. The topical induction concentration was 25% in petrolatum (w/v), and the test article was applied for 48 h under an occlusive patch to a shaved 4 cm x 6 cm area on the shoulder of each animal; the test area was pretreated with 10% sodium lauryl sulfate (SLS) 24 h prior to patching. The challenge was performed 14 days after induction, and a 24-h occlusive patch with 25% bis-diglyceryl polyacyladipate-2 in petrolatum was applied to a shaved 5 cm x 5 cm area on the flank of each animal. Vehicle controls (20 animals) were used, and 2,4-dinitrochlorobenzene was used as a positive control. Bis-diglyceryl polyacyladipate-2 did not induce any allergic response and was classified as non-sensitizing.

Bis-Diglyceryl Polyacyladipate-1

A GPMT was performed in Dunkin-Hartley guinea pigs to determine the sensitization potential of bis-diglyceryl polyacyladipate-1.²⁵ The test concentration for intradermal induction was 25% (w/v), and the topical induction was 0.2-0.3 ml undiluted test article applied with a 2 cm x 4 cm filter paper without SLS pretreatment. The challenge application was 0.1-0.2 ml undiluted test article applied with a 2 cm x 2 cm filter paper. Ten vehicle control animals were used, and the positive control was formaldehyde. Bis-diglyceryl polyacyladipate-1 did not produce any sensitization reactions.

Human

Bis-Diglyceryl Polyacyladipate-2

A human repeated insult patch test (HRIPT) of a lipstick containing 36% bis-diglyceryl polyacyladipate was initiated with 114 subjects and completed in 102 subjects.²⁶ None of the subjects discontinued testing because of test-article related effects. Approximately 0.1 ml of neat test material was applied to a 2 cm x 2 cm occlusive patch, and the patches were applied for 48-72 h three times per wk for 3 consecutive wks during the induction phase of the study. The 48-h challenge patches were applied to a treated and naive site after a 10-15 day non-treatment period. One subject had a reaction score of 2 (moderate erythema) at induction readings 4-7; there were no other reactions recorded for this subject during induction or at challenge. The lipstick containing 36% bis-diglyceryl polyacyladipate was not an irritant or a sensitizer.

Comedogenicity

Bis-Diglyceryl Polyacyladipate-2

The comedogenic potential of bis-diglyceryl polyacyladipate-2 was evaluated in rabbits.²⁷ A volume of 0.5 ml of the test article was applied neat once daily, 5 days/wk for 4 wks, to the right ears of 4 male New Zealand White (NZW) rabbits. The contralateral ears served as untreated controls. With the initial application, increasing visible hyperkeratosis extending to possible comedones (score 1/3) was observed in all four test ears. However, the scores were 0/3 for all remaining test days, and the overall comedogenic score was 0/3 for all four rabbits. It was concluded that bis-diglyceryl polyacyladipate-2 was non-comedogenic. Redness of the treated ears was observed throughout the study.

Bis-Diglyceryl Polyacyladipate-1

Three female NZW rabbits were used to evaluate the comedogenic potential of bis-diglyceryl polyacyladipate-1.²⁸ An unspecified volume of the test article was applied neat once daily, 5 days/wk for 3 wks, to the left ears of the rabbits. The right ears served as untreated controls. Gross examination reported slight transient hyperkeratosis on the control and/or treated ears of two rabbits. No hyperkeratosis or comedones were found upon microscopic examination. Bis-diglyceryl polyacyladipate-1 was non-comedogenic.

Ocular Irritation

Bis-Diglyceryl Polyacyladipate-2

The ocular irritation potential of bis-diglyceryl polyacyladipate-2 was evaluated in an acute eye irritation/corrosion test using NZW rabbits.²⁹ Undiluted test substance, 0.1 ml, was instilled into the conjunctival sac of one eye of each of three rabbits, and the contralateral eye served as a negative control. Eyes were examined for up to 72 h post-instillation. Some mild irritation of the conjunctivae was observed (a single report of a score of 2/4); all effects were reversible after 5 days. Bis-diglyceryl polyacyladipate-2 was classified as non-irritating to rabbit eyes.

SUMMARY

Bis-diglyceryl polyacyladipate-2 and bis-diglyceryl polyacyladipate-1 are mixed fatty acid esters reported to function in cosmetics as skin conditioning agents – emollients. Bis-diglyceryl polyacyladipate-1 is the adipic acid diester of a mixed diglyceryl ester of caprylic, capric, isostearic and hydroxystearic acids; bis-diglyceryl polyacyladipate-2 is a similar adipic acid diester of a mixed diglyceryl including those same acids and stearic acid. Structurally, there are a multitude of configurations possible within each bis-diglyceryl polyacyladipate ingredient.

Bis-diglyceryl polyacyladipate-2 is used in 521 cosmetic formulations; it is used in leave-on products at concentrations of up to 36% (reported for lipsticks) and in rinse-off products at concentrations up to 21% (reported for eye makeup remover). Bis-diglyceryl polyacyladipate-1 is used in 6 cosmetic formulations; it is used in leave-on products at concentrations of up to 10% (reported for tonics, dressings, and other hair grooming aids) and in rinse-off products at a concentration of 4% (reported for eye make-up remover).

Single doses of dermally applied undiluted bis-diglyceryl polyacyladipate-2 and bis-diglyceryl polyacyladipate-1 were not irritating to rabbit skin. None of the animals died during the studies, and the dermal LD₅₀ was >2000 mg/kg bis-diglyceryl polyacyladipate-2 and for bis-diglyceryl polyacyladipate-1.

Oral single-dose, repeated-dose, and reproductive studies were performed using rats. No mortality was observed following a single dose of 2000 mg/kg bis-diglyceryl polyacyladipate-2 and of 5000 mg/kg bis-diglyceryl polyacyladipate-1. In a 28-day oral toxicity study with bis-diglyceryl polyacyladipate-2, the NOAEL was 1800 mg/kg bw (2 ml/kg bw). In a one-generation reproduction study, oral administration of 1000 mg/kg bis-diglyceryl polyacyladipate-2 had no effects on reproduction, fertility, or development, and no signs of general toxicity were observed during the study.

Undiluted bis-diglyceryl polyacyladipate-2 was not mutagenic in a spot test in *S. typhimurium* with or without metabolic activation, and 40-400 µg/ml bis-diglyceryl polyacyladipate-2 was not clastogenic in a chromosomal aberration assay using Chinese hamster lung fibroblasts. Bis-diglyceryl polyacyladipate-2 was not genotoxic in a micronucleus test in which male and female NMRI mice were given a single oral dose of 15,000 mg/kg bw in corn oil and each killed 24, 48, or 72 h after dosing.

A single 24-h semi-occlusive application of 2000 mg/kg bis-diglyceryl polyacyladipate-2, applied neat, was not irritating in rabbit skin, but 5-40% bis-diglyceryl polyacyladipate-2 in petrolatum was a weak irritant in guinea pig skin in a 3-day cumulative irritation study. Bis-diglyceryl polyacyladipate-2 patched occlusively at 5% for 24 h or undiluted for 48 h was not irritating to human skin. Neither bis-diglyceryl polyacyladipate-2 nor bis-diglyceryl polyacyladipate-1 were sensitizers in the GPMT. For bis-diglyceryl polyacyladipate-2, the intradermal induction concentration was 5% with SLS pre-treatment, the topical induction concentration was 25%, and the challenge concentration was 25% with SLS pre-treatment. With bis-diglyceryl polyacyladipate-1, 25% without SLS was used for intradermal induction and undiluted test article was used for topical induction and for the challenge. A lipstick containing 36% bis-diglyceryl polyacyladipate was not an irritant or a sensitizer in a HRIPT. Neither ingredient was comedogenic in rabbit ears.

Undiluted bis-diglyceryl polyacyladipate-2 was not an ocular irritant in rabbit eyes.

DISCUSSION

Both a notice to proceed without the preparation of a scientific literature review and an insufficient data announcement were issued during the preparation of this safety assessment, suggesting an overall absence of publicly available safety test data. Unpublished data were received from industry, however, in response to the insufficient data announcement, enabling preparation of this report.

These ingredients are not acute or reproductive toxicants, they are not genotoxic, and they are not dermal irritants/sensitizers. The CIR Expert Panel recognized that data gaps remained regarding toxicokinetics and carcinogenicity data. However, bis-diglyceryl polyacyladipate-2 and bis-diglyceryl polyacyladipate-1 are used mostly in leave-on dermal applications and both ingredients are large, highly lipid-soluble compounds that are not expected to efficiently pass through the stratum corneum of the skin. As noted, even if these ingredients were to penetrate the skin, the constituent compounds do not present a toxicological concern based on the available toxicity data. While many of the available data are available only for bis-diglyceryl polyacyladipate-2, bis-diglyceryl polyacyladipate-1 was considered to be analogous from a toxicological perspective. Therefore, the Expert Panel concluded that the available data were adequate to assess the safety of both ingredients.

Because bis-diglyceryl polyacyladipate-2 is reported to be used in “other” fragrance preparations, which may be aerosolized, the Panel discussed the issue of incidental inhalation exposure. In the absence of inhalation data, the Panel noted that bis-diglyceryl polyacyladipate-2 did not produce systemic toxicity at high doses in single-dose oral and dermal studies or in a 28-day oral repeated dose study; was not a reproductive or developmental toxicant; was not genotoxic in an Ames test or in a chromosomal aberration assay with Chinese hamster lung fibroblasts; and did not cause irritation or sensitization in humans at concentrations up to 36%. Further, this ingredient is reportedly used at concentrations of ≤2% in cosmetic products that may be aerosolized. The Panel noted that 95% – 99% of droplets/particles produced in cosmetic aerosols would not be respirable to any appreciable amount. Furthermore, droplets/particles deposited in the nasopharyngeal or bronchial regions of

the respiratory tract present no toxicological concern in both cases based on the chemical and biological properties of these ingredients.

CONCLUSION

The CIR Expert Panel concluded that bis-diglyceryl polyacyladipate-2 and bis-diglyceryl polyacyladipate-1 are safe for use in cosmetic formulations in the present practices of use and concentration.

FIGURES AND TABLES

Figure 1. Chemical Structures.

The following structures represent the mixture of chemicals in bis-diglyceryl polyacyladipate ingredients.

- Wherein O-R represents the ester of caprylic, capric, **stearic**, isostearic or hydroxystearic acid, in the case of **Bis-Diglyceryl Polyacyladipate-2**
- Wherein O-R represents the ester of caprylic, capric, isostearic or hydroxystearic acid, in the case of **Bis-Diglyceryl Polyacyladipate-1**

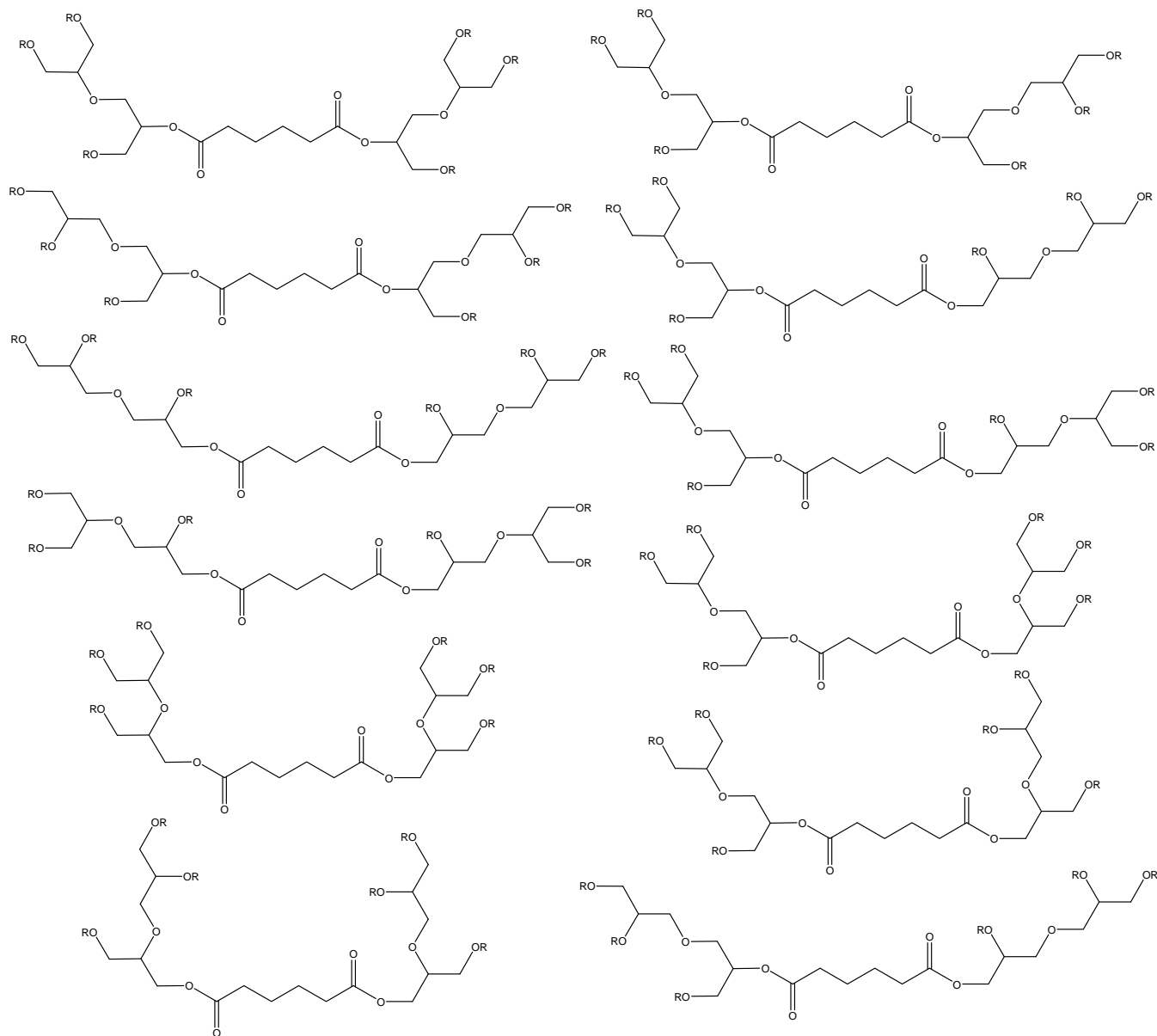
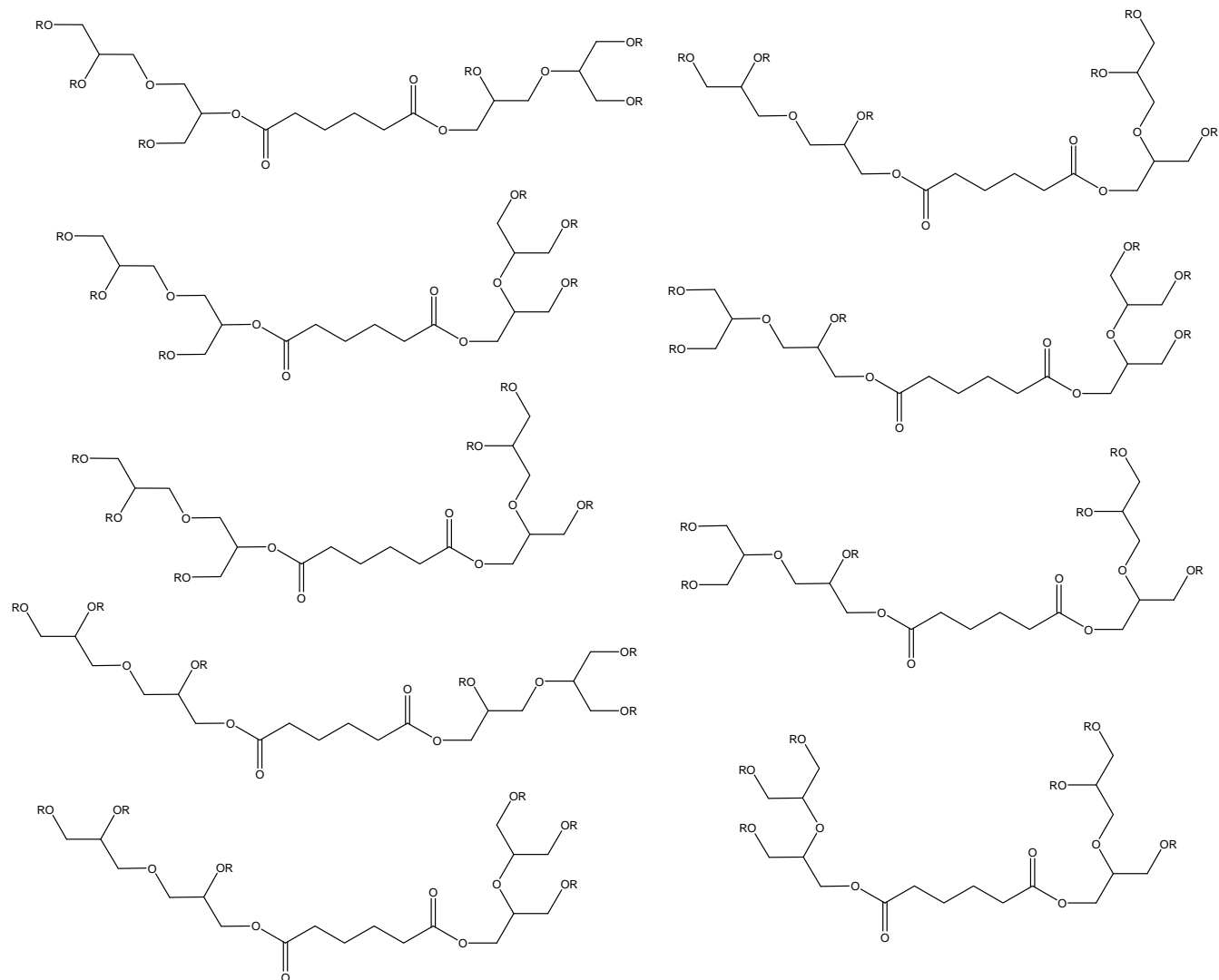


Figure 1 (continued). **Chemical Structures.**

The following structures represent the mixture of chemicals in bis-diglyceryl polyacyladipate ingredients



-Wherein the structures of caprylic, capric, stearic, isostearic, and hydroxystearic acids are:

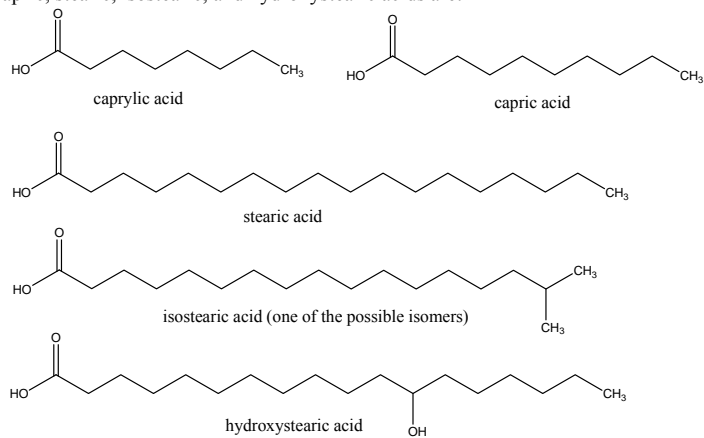


Table 1. Chemical and physical properties

Property	Description	Reference
Bis-Diglyceryl Polyacyladipate-2		
appearance	yellow, pasty, tacky, stringy substance	3
melting point	ca. 35°C	30
density	0.979 g/cm ³ (47°C)	30
water solubility	<0.001g/l (20°C)	30
solubility (other)	soluble in diethylether, hexane, benzene, and hot ethanol; miscible with fats, oils, and paraffin hydrocarbons	3
specific gravity	~0.96 g/ml (40°C)	31
log P	3.95	30
saponification value	270-290 mg KOH/g	3
acid value	max. 2 mg KOH/g	3
iodine value	max. 3 g I ₂ /100 g	3
Bis-Diglyceryl Polyacyladipate-1		
appearance	yellowish, high-viscosity fluid	4
water solubility	practically insoluble	4
solubility (other)	soluble in diethylether, and petroleum benzene miscible with fats, oils, and paraffin	4
saponification value	260-285 mg KOH/g	4
acid value	max. 3 mg KOH/g	4
iodine value	max. 5 g I ₂ /100 g	4

Table 2. Frequency and concentration of use according to duration and type of exposure

	Bis-Diglyceryl Polyacyladipate-2		Bis-Diglyceryl Polyacyladipate-1	
	<i># of Use</i> ⁵	<i>Max. Conc. of Use (%)</i> ⁶	<i># of Uses</i> ⁵	<i>Max. Conc. of Use (%)</i> ⁶
Totals*	521	0.1-36	6	0.2-10
Duration of Use				
<i>Leave-On</i>	491	0.1-36	6	0.2-10
<i>Rinse Off</i>	30	0.2-21	NR	4
<i>Diluted for (Bath) Use</i>	NR	NR	NR	NR
Exposure Type				
Eye Area	66	1-21	NR	2-7
Incidental Ingestion	256	5-36	2	NR
Incidental Inhalation - Spray	9 ^a	0.5 ^a , 2 (in a fragrance)	NR	NR
Incidental Inhalation - Powder	21	0.1-0.8	2	0.2-2
Dermal Contact	195	0.1-21	4	0.2-7
Deodorant (underarm)	NR	NR	NR	NR
Hair - Non-Coloring	25	1-15	1	10
Hair-Coloring	21	3	NR	NR
Nail	2	NR	NR	NR
Mucous Membrane	256	5-36	2	NR
Baby Products	NR	NR	NR	NR

* Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure types may not equal the sum of total uses.

^a Includes fragrance and suntan products; it is not known whether or not the reported products are sprays.

NR – none reported

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