Safety Assessment of Hexamethylene Diisocyanate (HDI) Polymers as Used in Cosmetics

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All interested persons are provided 60 days from the above date to comment on this safety assessment and to identify additional published data that should be included or provide unpublished data which can be made public and included.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 All unpublished data submitted to CIR will be discussed in open meetings, will be available at the CIR office for review by any interested party and may be cited in a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. Lillian J. Gill.

The 2016 Cosmetic Ingredient Review Expert Panel members are: Chair, 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 C. 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 Lillian J. Gill, D.P.A. This report was prepared by Lillian C. Becker, Scientific Analyst/Writer.
This is a review of the available scientific literature and unpublished data relevant to assessing the safety of 19 hexamethylene diisocyanate (HDI) polymers as used in cosmetics. The functions of HDI polymers include anticaking agents, viscosity increasing agent—aqueous, and film formers. These ingredients are copolymers, the monomers of which include HDI or other diisocyanates. The HDI monomer can cause occupational asthma and other ailments. The Cosmetic Ingredient Review (CIR) Expert Panel (Panel) reviewed available data related to these ingredients and determined that there would be no significant residual isocyanate monomers in these ingredients. Molecular weights are needed for two of these ingredients to determine if those ingredients would penetrate the skin. The Panel concluded that 17 of these ingredients are safe in cosmetics in the present practices of use and concentration and the available data are insufficient to make a determination that 2 of these ingredients are safe.

This is a review of the available scientific literature and unpublished data relevant to assessing the safety of 19 hexamethylene diisocyanate (HDI; also known as 1,6-diisocyanatoohexane) polymers, listed below, as used in cosmetics. These ingredients are copolymers, the monomers of which partially consist of HDI, or other diisocyanates. According to the International Cosmetic Ingredient Dictionary and Handbook (Dictionary), the reported functions of HDI polymers include viscosity increasing agents—aqueous, anticaking agents, and film formers (Table 1).1

- HDI/Trimethylol Hexyllactone Crosspolymer
- Bis-C16-20 Isoalkoxy TMHDI/PEG-90 Copolymer
- Bis-Hydroxyethyl Acrylate Poly(1,4-Butanediol)-9/TMHDI Copolymer
- Bis-Isostearyl 1,4-Butanediol/HDI/Hydrogenated Dimer Dilinoleyl Alcohol Copolymer
- Bis-Lauryl Cocaminopropylamine/HDI/PEG-100 Copolymer
- Bis-Methoxy PEG-10 Dimethyl MEA/HDI/Bis-PEG-10 Dimethicone Copolymer
- 1,4-Butanediol/Succinic Acid/Adipic Acid/HDI Copolymer
- Cholesterol/HDI/Pullulan Copolymer
- Decyl HDI/PEG-180 Crosspolymer
- Diethylene Glycol/DMAP Acrylamide/PEG-180/HDI Copolymer
- HDI/Di-C12-14 Alkyl Tartrate/Hydrogenated Dilinoleyl Alcohol Copolymer
- HDI/PEI-45/SMDI Crosspolymer
- HDI/PPG/Polycaprolactone Crosspolymer
- Methoxy PEG-17/Methoxy PEG-11/HDI Crosspolymer
- Methoxy PEG-17/Methoxy PEG-11/HDI Isocyanurate Trimer Crosspolymer
- PEG-240/HDI Copolymer
- Bis-Decyltetradeceth-20 Ether
- PPG-26/HDI Copolymer
- Steareth-100/PEG-136/HDI Copolymer
- Stearyl HDI/PEG-50 Copolymer

The CIR Panel has reviewed several of the constituents of these ingredients (Table 2).2-12 Polyethylene glycols (PEG), PEG-10 Dimethicone, Adipic Acid, Succinic Acid, Cholesterol, Pullulan, Glycerin, and Stearyl Alcohol were determined to be safe as used. Methoxy PEG-10, Decyltetradeceth-20, Steareth-100, and PPG-26 were determined to be safe when formulated to be non-irritating.

The ingredients in this report are copolymers, each of which is synthesized, in part, from the monomer HDI or other diisocyanate analogs. These ingredients are grouped together because their copolymers originate from these common diisocyanate monomers. Exposure to diisocyanates, such as HDI, in the work place is one of the leading causes of occupational asthma.13 Airway irritation and asthma-like symptoms, hypersensitivity pneumonitis, rhinitis, and accelerated lung deterioration have also been associated with exposure to diisocyanates. Disocyanates can also cause irritant and allergic contact dermatitis, as well as skin and conjunctival irritation. Disocyanates may act to generate haptons by reacting with and covalently bonding to endogenous proteins to induce an immune response. Hapten formation is believed to be a mechanism for recognition of an allergen by the immune system and subsequent development of allergic responses. The ingredients in this report are not diisocyanates, but are end products of a polymerization process that includes HDI, or an analog, as one of the starting materials (monomers). Accordingly, quantification of any residual diisocyanate in the final cosmetic ingredient may be paramount to determining safety.

**CHEMISTRY**

**Definition and Structure**

The definitions and approximate structures of the HDI polymers in this safety assessment are provided in Table 1. These structures are best representations based on the definitions provided in the Dictionary.1

This group is composed of copolymers, the monomers of which include some analog of HDI (Figure 1).
Figure 1. Hexamethylene Diisocyanate.

The other 3 diisocyanate monomers herein are analogs of HDI, namely trimethylhexanediisocyanate (TMHDI), saturated methylene diphenyldiisocyanate (SMDI), and the HDI trimer (Figure 2).

Figure 2. HDI analogs.

These polymers are produced by reactions of HDI with alkoxy-group-containing monomers, such as alcohols and polyethers, which also may be used as end-capping units (Figure 3).

Figure 3. Bis-C16-20 Isoalkoxy TMHDI/PEG-90 Copolymer

Some of these polymers are linear, but when tri-functional monomers (e.g., glycerin) are used as reactants, branched or cross-linked structures are probable. The degree of polymerization of these ingredients can be controlled to obtain a product having a desired functionality, such as rheology modifier. Accordingly, the molecular weights and molecular volumes of these ingredients could vary widely, unless otherwise noted in use specifications. These polymers, by virtue of their monomers, contain both hydrophilic and hydrophobic groups. The ratio of hydrophilic and hydrophobic groups may vary within one ingredient name. In the absence of ingredient-explicit specifications, estimating some of the chemical and physical properties of these ingredients is challenging. These ingredients can potentially range from liquid to solid, soluble to insoluble, or non-penetrating to penetrating into the skin. However, aside from the potential presence of a diisocyanate or end-capping agent residue, these ingredients are likely to be similar to polyurethane-type polymers.
Physical and Chemical Properties

The physical and chemical properties of each of these ingredients could vary widely depending on method of manufacture and the resulting structure and molecular weight. Available reported physical and chemical properties are presented in Table 3.

A supplier reported that HDI/Trimethylol Hexyllactone Crosspolymer was available in two grades for cosmetics (Table 4).14-16 The particle size distribution for grade 1 was reported to be: 100% <100 µm, 33.8% <10 µm, 5.5% <1 µm. The particle size distribution for grade 2 was reported to be: 100% <100 µm, 87.5% <10 µm, 7.1% <1 µm. Analysis of HDI/Trimethylol Hexyllactone Crosspolymer from a second supplier showed that the overall distribution was: 100% <100 µm, 15.1% ≤10.42 µm, and 0% <1 µm. Another source reported that the average particle size is 12-18 µm.17 A fourth source reported that the average particle size range of HDI/PPG/Polycaprolactone Crosspolymer was 12-19 µm.18

The molecular weights of these HDI polymers range from <500 Da (a small percentage of the ingredients) to 75,000 Da.19-23 For the molecular weight range of Bis-C16-20 Isoalkoxy TMHDI/PEG-90 Copolymer, 1.5% of the ingredient was reported to be <1000 Da and 1.2% was <500 Da.22 It was reported that the molecular weight of Bis-Methoxy PEG-10 Dimethyl MEA/HDI/Bis-PEG-10 Dimethicone Copolymer is >1000 Da.24 In an analysis of Bis-Lauryl Cocaminoxypropylamine/HDI/PEG-100 Copolymer, HDI/Di-C12-14 Alkyl Tartrate/Hydrogenated Dilinoleyl Alcohol Copolymer, and Steareth-100/PEG-136/HDI Copolymer, no compounds <1000 Da were detected.20,21,23,25 The molecular weight of HDI/PPG/Polyacrolactone Crosspolymer was reported to be >10,000 Da.26 The molecular weights of three batches of PEG-240/HDI Copolymer Bis-Decyltetradeceth-20 Ether were reported to range from approximately 4000-75,000 Da.19

Methoxy PEG-17/Methoxy PEG-11/HDI Isocyanurate Trimer Crosspolymer is reported to be fully crosslinked, and its MW is reported to be infinite.27 This polymer contains a 0.9% soluble fraction (in tetrahydrofuran) with a MW >1000 Da.27 HDI/C12-14 Alkyl Tartrate Hydrogenated Dilinoleyl Alcohol Copolymer, as supplied, is reported to be stable for 16 weeks in temperatures from 5-50˚C.25

Method of Manufacture

HDI/Di-C12-14 Alkyl Tartrate/Hydrogenated Dilinoleyl Alcohol Copolymer is reported to be manufactured by the condensation of an isocyanate component (HDI) and molecules containing hydroxyl groups, specifically esters of tartaric acids and alklylic diol (di-C12-14 alkyl tartrate/hydrogenated dilinoleyl alcohol).23 Polymerization is terminated by the addition of ethyl alcohol (i.e., ethyl alcohol end-caps the polymer).

HDI/Trimethylol Hexyllactone Crosspolymer is reported to be manufactured by mixing an isocyanate prepolymer (HDI/trimethylolpropane/ε-caprolactone) and a solvent for aqueous suspension polymerization at 30-100˚C for 1-6 h.17 The resulting polymer is washed with water. The product is dried at 95˚C followed by classification, sterilization, and packaging. Alkylation and endcapping agents are not used in this process.

HDI/PPG/Polyacrolactone Crosspolymer is reported to be manufactured by the same process as the HDI/Trimethylol Hexyllactone Crosspolymer, with the addition of propylene oxide/ε-glucitol in the mix for the aqueous polymerization.18

Steareth-100/PEG-136/HDI Copolymer and Bis-Lauryl Cocaminoxypropylamine/HDI/PEG-100 Copolymer are manufactured by placing pre-dried polyethylene glycol and diisocyanate together with a catalyst.28 The reaction is allowed to proceed to completion to consume the free diisocyanate. A high boiling aliphatic alcohol or surfactant molecule is used to consume the unreacted isocyanate groups at the ends of the polymer chains and thereby act as an end-capping agent.

Impurities

HDI

The residual amount of HDI in HDI/Di-C12-14 Alkyl Tartrate/Hydrogenated Dilinoleyl Alcohol Copolymer raw material was reported to be <0.5 ppm (Table 5).23 The residual diisocyanate was reported to be below the limit of detection (0.017%) for Bis-Lauryl Cocaminoxypropylamine/HDI/PEG-100 Copolymer and Steareth-100/PEG-136/HDI Copolymer; there was no free HDI detected for both of these ingredients at temperatures up to 150˚C.29 Residual HDI was <100 ppm in HDI/Trimethylol Hexyllactone Crosspolymer and HDI/PPG/Polyacrolactone Crosspolymer.17,18 No residual HDI was detected (detection limit <20 ppm) in an analysis of 3 batches of PEG-240/HDI Copolymer Bis-Decyltetradeceth-20 Ether.19

In an analysis of a skin care cream and a makeup cream that contained HDI/Trimethylol Hexyllactone Copolymer (preformulated with silica; 5% as a plastic powder), and HDI/PPG/Polyacrolactone Crosspolymer (preformulated with silica; 2.4% as a plastic powder), the amount of HDI monomer was below the limits of detection (0.4 ppm) in both of these products.30

Other Impurities

Bis-C16-20 Isoalkoxy TMHDI/PEG-90 Copolymer and Bis-Lauryl Cocaminoxypropylamine/HDI/PEG-100 Copolymer were reported to contain <1 ppm mercury, <3 ppm arsenic, and <10 ppm lead.31

In an analysis of HDI/PPG/Polyacrolactone Crosspolymer, ε-caprolactone was present at 240 ppm and ε-glucitol at 0.07 ppm, but there was no trimethylolpropane detected (detection limit <2 ppm) or propylene oxide (detection limit <1 ppm).18
In an analysis of 3 batches of HDI/Trimethylol Hexyllactone Crosspolymer, it was reported that the levels of \( \varepsilon \)-caprolactone ranged from 66 to 73ppm and trimethylolpropane from 4 to 12 ppm.\(^{17}\)

According to a product safety sheet, Methoxy PEG-17/Methoxy PEG-11/HDI Isocyanurate Trimer Crosspolymer is not expected to contain antimony, arsenic, bismuth, cadmium, chromium, copper, iron, lead, mercury, manganese, nickel, palladium, platinum, or tin; extraction experiments detected no organic materials into water.\(^{32}\) Zinc may be present as a technical impurity at <25 ppm. Dipropyl phosphate may be present at a maximum concentration of approximately 100 ppm. Zinc 2-ethylhexanoate may be present at a maximum concentration of approximately 80 ppm. At the end of the drying process, it is expected that there will be approximately 1% residual water and no volatile organic materials will persist. Butylhydroxytoluene (BHT) may be present as a technical impurity at <20 ppm. The extractable oligomer (< approximately 1000 Da) of this crosspolymer was <1%.

In an analysis of 3 batches of PEG-240/HDI Copolymer Bis-Decyltetradeceth-20 Ether, ethylene oxide (detection limit <1 ppm) and dioxane (detection limit <10 ppm) were not detected.\(^{19}\) Formaldehyde was detected at 1 and 2 ppm.

**USE**

**Cosmetic**

The safety of the cosmetic ingredients included in this safety assessment is evaluated based on the data the Panel receives from the U.S. Food and Drug Administration (FDA) and the cosmetics industry on the expected cosmetic use of ingredients. The FDA collects data from manufacturers on the use of individual ingredients in cosmetics by cosmetic product category in its Voluntary Cosmetic Registration Program (VCRP). Those received from the cosmetic industry are submitted in response to a survey conducted by the Personal Care Products Council (Council) of the maximum reported use concentrations by category.

According to the 2015 Council survey, the highest maximum concentration of use of the ingredients in this safety assessment was reported to be 31% for HDI/Trimethylol Hexyllactone Crosspolymer in foundations, a leave-on product.\(^{34,35}\)

Table 7 lists the HDI polymers with no reported uses.

Concentration of use were received for Methoxy PEG-17/Methoxy PEG-11/HDI Isocyanurate Trimer Crosspolymer, but uses were not reported in the VCRP, therefore, it should be presumed that there is at least 1 use for the reported concentration. This is also true for Bis-C16-20 Isoalkoxy TMHDI/PEG-90 Copolymer (1 use in mascara) and HDI/Di-C12-14 Alkyl Tartrate/Hydrogenated Dilinoleyl Alcohol Copolymer.

HDI/Trimethylol Hexyllactone Crosspolymer, HDI/Di-C12-14 Alkyl Tartrate/Hydrogenated Dilinoleyl Alcohol Copolymer, and Methoxy PEG-17/Methoxy PEG-11/HDI Crosspolymer were reported to be used in formulations that come in contact with mucus membranes (highest concentration reported to be 15.1% in lipsticks). HDI/Trimethylol Hexyllactone Crosspolymer, HDI/Di-C12-14 Alkyl Tartrate/Hydrogenated Dilinoleyl Alcohol Copolymer, and Methoxy PEG-17/Methoxy PEG-11/HDI Crosspolymer were reported to be used in formulations that could be incidentally ingested (highest concentration reported to be 15.1% in lipsticks). HDI/Trimethylol Hexyllactone Crosspolymer, Bis-C16-20 Isoalkoxy TMHDI/PEG-90 Copolymer, HDI/Di-C12-14 Alkyl Tartrate/Hydrogenated Dilinoleyl Alcohol Copolymer, HDI/PPG/Polycaprolactone Crosspolymer, and PEG-240/HDI Copolymer Bis-Decyltetradeceth-20 Ether were reported to be used in formulations that are applied near the eye (highest concentration reported to be 19.6% in eye shadow).

Additionally, HDI/Trimethylol Hexyllactone Crosspolymer, Diethylene Glycol/DMAP Acrylamide/PEG-180/HDI Copolymer, HDI/PPG/Polycaprolactone Crosspolymer, PEG-240/HDI Copolymer Bis-Decyltetradeceth-20 Ether, and Steareth-100/PEG-136/HDI Copolymer were reported to be used in tonics, dressings and other hair grooming aids; face and neck products; body and hand products; and indoor tanning preparations that may be sprays and could possibly be inhaled. The highest maximum reported concentration of these ingredients in a likely aerosol product is 2.5% in tonics, dressings, and neck products; body and hand products; and indoor tanning preparations that may be sprays and could possibly be inhaled. Conservative estimates of inhalation exposures to respirable particles during the use of loose powder cosmetic products are 400- to 1000-fold less than protective regulatory and guidance limits for inert airborne respirable particles in the workplace.\(^{40-42}\)

The European Union restricts the content of traces of diethylene glycol to a total of 0.1% in any cosmetic product, including the trace amount of diethylene glycol in ingredients contained in polymers, such as Diethylene Glycol/DMAP Acrylamide/PEG-180/HDI Copolymer.\(^{43}\)
TOXICOKINETICS
Absorption, Distribution, Metabolism, and Excretion

Data on toxicokinetics of HDI polymers were not found in the published literature and no unpublished data were provided.

TOXICOLOGICAL STUDIES
Single Dose (Acute) Toxicity

Dermal

Data on acute dermal toxicity of HDI polymers were not found in the published literature and no unpublished data were provided.

Oral – Non-Human

HDI/Trimethylol Hexyllactone Crosspolymer (5000 mg/kg) administered by gavage caused no clinical signs or mortalities to rats (Table 8).14,16 The oral LD$_{50}$ of Methoxy PEG-17/Methoxy PEG-11/HDI Isocyanurate Trimer Crosspolymer was reported to be >2000 mg/kg in rats.32 The oral LD$_{50}$ of PEG-240/HDI Copolymer Bis-Decyltetradecet-20 Ether was reported to be >2000->2500 mg/kg in rats.19 The oral LD$_{50}$ for Steareth-100/PEG-136/HDI Copolymer was reported to be >10,000 mg/kg in rats; clinical signs included bristled fur, diarrhea and dirty fur around the anal region due to feces.20

The acute oral LD$_{50}$ was >10,000 mg/kg in rats (n=5/sex) for a cosmetic ingredient mixture consisting of Bis-Cocaminopropylamine/HD/ PEG-100 Copolymer (concentration not specified) and butylene glycol.44

Inhalation – Non-Human

Methoxy PEG-17/Methoxy PEG-11/HDI Isocyanurate Trimer Crosspolymer

The acute inhalation LC$_{50}$ of Methoxy PEG-17/Methoxy PEG-11/HDI Isocyanurate Trimer Crosspolymer was reported to be >1.99 mg/L when administered in a dust/mist for 4 h in rats.32 The test was conducted in accordance with the Organization for Economic Cooperation and Development Test Guideline (OECD TG) 403.

Repeated Dose Toxicity

Data on dermal, oral, or inhalation repeated dose toxicity of HDI polymers were not found in the published literature and no unpublished data were provided.

REPRODUCTIVE AND DEVELOPMENTAL TOXICITY

Data on the reproductive and developmental toxicity of HDI polymers were not found in the published literature and no unpublished data were provided.

GENOTOXICITY

Methoxy PEG-17/Methoxy PEG-11/HDI Isocyanurate Trimer Crosspolymer

Methoxy PEG-17/Methoxy PEG-11/HDI Isocyanurate Trimer Crosspolymer (concentration not specified) was not mutagenic in an Ames test, with or without metabolic activation.32 No further details were provided.

PEG-240/HDI Copolymer Bis-Decyltetradecet-20 Ether

PEG-240/HDI Copolymer Bis-Decyltetradecet-20 Ether (concentration not specified) was not genotoxic when tested in accordance with OECD TG 471 (bacterial reverse-mutation test).19 No further details were provided.

Steareth-100/PEG-136/HDI Copolymer

In an Ames test conducted according to OECD TG 471, Steareth-100/PEG-136/HDI Copolymer was not mutagenic to Salmonella typhimurium (strains TA98, TA100, TA1535, and TA1537) and Escherichia coli (strain WP2uvA) at up to 5000 µg/plate.20

CARCINOGENICITY

Data on the carcinogenicity of HDI polymers were not found in the published literature and no unpublished data were provided.

IRRITATION AND SENSITIZATION

Irritation

Dermal – Non-Human

HDI/Trimethylol Hexyllactone Crosspolymer (100%), Methoxy PEG-17/Methoxy PEG-11/HDI Isocyanurate Trimer Crosspolymer (concentration not specified), and Steareth-100/PEG-136/HDI Copolymer (100%; 0.5 g; dry) were not
Dermal irritants in rabbits (Table 9). PEG-240/HDI Copolymer Bis-Decyltetradeceth-20 Ether was not a dermal irritant in guinea pigs up to 30%. 

**Dermal – Human**

**HDI/Trimethylol Hexyllactone Crosspolymer**

HDI/Trimethylol Hexyllactone Crosspolymer (100% as a dry powder) was not a dermal irritant in a human patch test (Table 9). Two foundations containing HDI/Di-C12-14 Alkyl Tartrate/ Hydrogenated Dilinoleyl Alcohol Copolymer (1.7% and 3.19%) were not irritating in human patch tests. 

**Dermal - In Vitro**

In in vitro studies, Methoxy PEG-17/Methoxy PEG-11/HDI Isocyanurate Trimer Crosspolymer (concentration not specified), PEG-240/HDI copolymer bis-decyltetradeceth-20 ether, and a mixture containing 30% Bis-C16-20 Isoalkoxy TMHDI/PEG-90 Copolymer were predicted to be non-irritating (Table 9). 

**Ocular – Non-Human – In Vivo**

In an eye irritation study of HDI/Trimethylol Hexyllactone Crosspolymer (100%), mild to moderate conjunctival redness and mild chemosis were observed in 4 of 6 rabbits 24 and 48 h after administration into the eyes (Table 4). The authors considered the particle size (at least 92.9% > 1 µm; Table 4) and the water insolubility of the tested polymer and concluded that the eye irritation observed was likely attributable to mechanical abrasion rather than to chemical irritancy. Methoxy PEG-17/Methoxy PEG-11/HDI Isocyanurate Trimer Crosspolymer (concentration not specified) was a slight ocular irritant in rabbits. PEG-240/HDI Copolymer Bis-Decyltetradeceth-20 Ether (up to 30%) was not an ocular irritant in rabbits. Steareth-100/PEG-136/HDI Copolymer (100%) was classified as a non-irritant in the eyes of rabbits. 

**Ocular – In Vitro**

PEG-240/HDI Copolymer Bis-Decyltetradeceth-20 Ether

The reported RC50 (the concentration at which 50% of the treated eggs show a positive response) for PEG-240/HDI Copolymer Bis-Decyltetradeceth-20 Ether in a chorioallantoic membrane vascular assay (CAMVA) was >100%. No further details were provided. The reported score for PEG-240/HDI Copolymer Bis-Decyltetradeceth-20 Ether in a bovine corneal opacity and permeability (BCOP) assay was calculated to be approximately 2.74. A score of 0-3 indicate an ocular non-irritant. No further details of the study were provided. 

**Sensitization**

**Non-Human**

In a Magnusson Kligman maximization test, Methoxy PEG-17/Methoxy PEG-11/HDI Isocyanurate Trimer Crosspolymer (concentration not specified) was not sensitizing in guinea pigs (Table 11). In a skin sensitization assay (species not specified), PEG-240/HDI Copolymer Bis-Decyltetradeceth-20 Ether (30%) was not a dermal sensitizer. 

**Human**

In human repeated insult patch tests (HRIPT) of 2 foundations containing HDI/Trimethylol Hexyllactone Crosspolymer (30.7% and 10%), there were no signs of dermal irritation or allergic contact dermatitis observed (Table 11). In an HRIPT of Bis-C16-20 Isoalkoxy TMHDI/PEG-90 Copolymer (30%), one subject exhibited barely perceptible erythema 48 h after the challenge. In an HRIPT of PEG-240/HDI Copolymer Bis-Decyltetradeceth-20 Ether (concentration not specified) there was no evidence of dermal irritation or allergic contact sensitization. 

**SUMMARY**

This is a review of the scientific literature and unpublished data relevant for assessing the safety of 19 HDI polymers as used in cosmetics. These ingredients consist of copolymers, the monomers of which partially are comprised of HDI, or an analog thereof. The functions of HDI polymers include viscosity increasing agents-aqueous, anticaking agents, and film formers. Exposure to diisocyanates, such as HDI, has caused occupational asthma, hypersensitivity pneumonitis, rhinitis, and accelerated lung deterioration. 

The reported ranges of molecular weights of these HDI polymers are from <500 Da (a small percentage of the ingredients) to 75,000 Da. For the molecular weight range of Bis-C16-20 Isoalkoxy TMHDI/PEG-90 Copolymer, 1.5% was reported to be <1000 Da and 1.2% was <500 Da. In an analysis of Bis-Lauryl Cocaminopropylamine/HDI/PEG-100 Copolymer, HDI/Di-C12-14 Alkyl Tartrate/Hydrogenated Dilinoleyl Alcohol Copolymer, and Steareth-100/PEG-136/HDI Copolymer, no compounds of <1000 Da were detected. The molecular weight of HDI/PPG/Polycaprolactone Crosspolymer was reported to be >10,000 Da. The molecular weights of three batches of PEG-240/HDI Copolymer Bis-Decyltetradeceth-20 Ether were reported to range from approximately 4000-75,000 Da. Methoxy PEG-17/Methoxy PEG-11/HDI Isocyanurate Trimer Crosspolymer is reported to be fully crosslinked, and its MW is reported to be infinite.
The residual amount of HDI in HDI/Di-C12-14 Alkyl Tartrate/Hydrogenated Dilinoleyl Alcohol Copolymer was reported to be <0.5 ppm. The residual diisocyanate was reported to be below the limit of detection for Bis-Lauryl Cocamidopropylamine/HDI/PEG-100 Copolymer and Steareth-100/PEG-136/HDI Copolymer. Residual HDI was <100 ppm in HDI/Trimethylol Hexyllactone Crosspolymer and HDI/PPG/Polycaprolactone Crosspolymer. In an analysis of 3 batches of PEG-240/HDI Copolymer Bis-Decyltetradeceth-20 Ether, no residual HDI was detected (detection limit <20 ppm).

In an analysis of a skin care cream and a makeup cream that contained HDI/Trimethylol Hexyllactone Copolymer and silica (5% as a plastic powder) and HDI/PPG/Polycaprolactone Crosspolymer and silica (2.4% as a plastic powder), respectively, the amount of HDI monomer was below the limits of detection in both of these products.

According to 2016 VCRP data, HDI/Trimethylol Hexyllactone Crosspolymer is used in 385 formulations, 378 of which are leave-on products and 7 of which are rinse-off products. The five other ingredients that had reported uses by the VCRP were used in 24 or fewer cosmetic formulations. The highest concentration of use was reported to be 31% for HDI/Trimethylol Hexyllactone Crosspolymer in leave-on products.

The acute oral LD₅₀ was >10,000 mg/kg in rats for a product mixture consisting of Bis-Cocamidopropylamine/HDI/PEG-100 Copolymer and butylene glycol. In an acute oral toxicity study using rats, a dose of 5000 mg/kg HDI/Trimethylol Hexyllactone Crosspolymer administered by gavage caused no clinical signs or mortalities. The oral LD₅₀ of Methoxy PEG-17/Methoxy PEG-11/HDI Isocyanurate Trimer Crosspolymer was reported to be >2000 mg/kg in rats. The acute oral LD₅₀ for PEG-240/HDI Copolymer Bis-Decyltetradeceth-20 Ether ranged from >2000–>2500 mg/kg in rats. The oral LD₅₀ for Steareth-100/PEG-136/HDI Copolymer was reported to be >10,000 mg/kg in rats.

The acute inhalation LC₅₀ of Methoxy PEG-17/Methoxy PEG-11/HDI Isocyanurate Trimer Crosspolymer was reported to be >1.99 mg/L for a 4-h exposure.

Methoxy PEG-17/Methoxy PEG-11/HDI Isocyanurate Trimer Crosspolymer, Steareth-100/PEG-136/HDI Copolymer, and PEG-240/HDI Copolymer Bis-Decyltetradeceth-20 Ether were not mutagenic in Ames tests. HDI/Trimethylol Hexyllactone Crosspolymer at 100% was not a dermal irritant on the intact or abraded skin of rabbits. Methoxy PEG-17/Methoxy PEG-11/HDI Isocyanurate Trimer Crosspolymer was reported to be dermally non-irritating in rabbits, and Steareth-100/PEG-136/HDI Copolymer at 100% was not dermally irritating to rabbits. PEG-240/HDI Copolymer Bis-Decyltetradeceth-20 Ether up to 30% was not a dermal irritant to guinea pigs in irritation assays.

Foundations containing HDI/Di-C12-14 Alkyl Tartrate/Hydrogenated Dilinoleyl Alcohol Copolymer at 1.7% and 3.19% were not irritating in human primary skin irritation tests. In a human patch test of HDI/Trimethylol Hexyllactone Crosspolymer, 2 foundations containing HDI/Trimethylol Hexyllactone Crosspolymer at 10% and 30.7%, there were no signs of dermal irritation or allergic contact dermatitis observed. In a HRIPT, PEG-240/HDI Copolymer Bis-Decyltetradeceth-20 Ether did not demonstrate any indication of dermal irritation or allergic contact sensitization.

**DISCUSSION**

The CIR Expert Panel examined the available data, which included method of manufacture and impurity data; acute oral, and inhalation toxicity; genotoxicity; dermal and ocular irritation data; and sensitization data. Three of these ingredients were not mutagenic in bacterial assays. Molecular weights for some of the ingredients were reported to range from <500 to 75,000. There were no toxicokinetic, repeated dermal toxicity, and reproductive/developmental data found in the published literature or submitted by Industry. The results of the assays for ocular and dermal irritation and dermal sensitization showed that there were no concerns that the tested ingredients would be irritating or sensitizing under the conditions of use.

The CIR Expert Panel recognizes that there are data gaps regarding use and concentration of these ingredients. However, the overall information available on the types of products in which these ingredients are used and at the concentrations provided indicate a pattern of use which was considered by the Expert Panel in assessing safety.
The Panel noted that the HDI monomer can cause occupational asthma, hypersensitivity pneumonitis, rhinitis, and accelerated lung deterioration. After examining the method of manufacture and impurity data, the Panel was comfortable that there would not be significant residual HDI (or TMHDI, SMDI, or HDI isocyanurate trimer) monomers in these ingredients. Manufacturers and formulators should continue to use good manufacturing practices (GMPs) to ensure that these monomers are not present in these ingredients and in formulation.

The Panel expressed concern regarding heavy metals that may be present in these ingredients. They stressed that the cosmetics industry should continue to use GMPs to limit these impurities in the ingredient before blending into cosmetic formulation.

These ingredients vary in size depending on the manufacturing process. Manufacturers and formulators should use GMPs to ensure that polymers with low molecular weights (<1000 Da) are not present in cosmetic products.

Unpublished data on Steareth-100/PEG-136/HDI Copolymer were submitted with the suggestion that the data be used as read across for HDI/Di-C12-14 Alkyl Tartrate/Hydrogenated Dilinoleyl Alcohol Copolymer, Bis-C16-20 Isoalkoxy TMHDI/PEG-90 Copolymer, and Bis-Lauryl Cocaminopropylamine/HDI/PEG-100 Copolymer; the Panel found the data to be appropriate for read across for these three ingredients. Inspection of the chemical structural formulas of most of the ingredients indicated that even the most minimal possible polymers would have molecular weights >1000 Da and thus would have no significant dermal absorption. For example, it was noted that the PEG monomers (PEG-17 and PEG-11) were large, and that the resulting crosspolymer, Methoxy PEG-17/Methoxy PEG-11/HDI Crosspolymer, would therefore be large enough that it would not penetrate intact skin; there is no concern about systemic exposure.

The Panel discussed the issue of incidental inhalation exposure from products that may be sprays (e.g., tonics, dressings and other hair grooming aids; face and neck products; body and hand products; indoor tanning preparations and from face powders). These ingredients are reportedly used at concentrations at up to 2.5% in products that may be sprayed and aerosolized, and at up to 12.6% in cosmetic products that may become airborne. The molecular weight of several of these ingredients was reported to be 7000 Da or greater; some ingredients had no reported molecular weight data. Limited data available from an acute inhalation study of Methoxy PEG-17/Methoxy PEG-11/HDI Isocyanurate Trimer Crosspolymer suggest little potential for respiratory effects at concentration of use. The Panel noted that droplets/particles from spray and loose-powder cosmetic products would not be respirable to any appreciable amount. Furthermore, these ingredients are not likely to cause any direct toxic effects in the upper respiratory tract, based on the properties of the HDI polymers and on data that shows that these ingredients are not irritants. Coupled with the small actual exposure in the breathing zone and the concentrations at which the ingredients are used, the available information indicates that incidental inhalation would not be a significant route of exposure that might lead to local respiratory or systemic effects. In addition, these ingredients are large macromolecules, insoluble in water, and chemically inert under physiological conditions or conditions of use, which supports the view that they are unlikely to be absorbed or cause local effects in the respiratory tract. A detailed discussion and summary of the Panel’s approach to evaluating incidental inhalation exposures to ingredients in cosmetic products is available at http://www.cir-safety.org/cir-findings.

Molecular weights were not provided for Bis-Hydroxyethyl Acrylate Poly(1,4-Butanediol)-9/TMHD Copolymer and 1,4-Butanediol/Succinic Acid/Adipic Acid/HDI Copolymer; it could not be concluded that these ingredients would not penetrate the skin. Therefore, the data needs for the other two ingredients are:

- Molecular weight distribution
- If the molecular weight is below 1000 Da, then solubility in formulation, dermal absorption, and/or 28-day dermal toxicity study
- If soluble or dermally absorbed, then systemic toxicity data including genotoxicity, carcinogenicity, and reproduction/developmental toxicity
CONCLUSION

The CIR Expert Panel concluded that the following 17 HDI polymers are safe in cosmetics in the present practices of use and concentration described in this safety assessment:

- HDI/Trimethylol Hexyllactone Crosspolymer
- Bis-C16-20 Isoalkoxy TMHDI/PEG-90 Copolymer
- Bis-Isostearyl 1,4-Butanediol/HD/Hydrogenated Dimer Dilinoleyl Alcohol Copolymer*
- Bis-Lauryl Cocaminopropylamine/HD/PEG-100 Copolymer*
- Bis-Methoxy PEG-10 Dimethyl MEA/HD/Bis-PEG-10 Dimethicone Copolymer*
- Cholesterol/HD/Pullulan Copolymer*
- Decyl HDI/PEG-180 Crosspolymer*
- Diethylene Glycol/DMAP Acrylamide/ PEG-180/HD Copolymer
- HDI/Di-C12-14 Alkyl Tartrate/Hydrogenated Dilinoleyl Alcohol Copolymer
- HDI/PEI-45/SMDI Crosspolymer*
- HDI/PPG/Polyacrylactone Crosspolymer
- Methoxy PEG-17/Methoxy PEG-11/HD Crosspolymer
- Methoxy PEG-17/Methoxy PEG-11/HD Isocyanurate Trimer Crosspolymer
- PEG-240/HD Copolymer Bis-Decyltetradeceth-20 Ether
- PPG-26/HD Copolymer*
- Steareth-100/PEG-136/HD Copolymer
- Stearyl HDI/PEG-50 Copolymer*

The available data are insufficient to make a determination that the following 2 ingredients are safe under the intended conditions of use:

- Bis-Hydroxyethyl Acrylate Poly(1,4-Butanediol)-9/TMHDI Copolymer*
- 1,4-Butanediol/Succinic Acid/Adipic Acid/HD Copolymer*

*Not reported to be in current use. Were ingredients in this group not in current use to be used in the future, the expectation is that they would be used in product categories and at concentrations comparable to others in this group.
# Table 1. Definitions, idealized structures, and functions of the HDI polymers in this safety assessment.

<table>
<thead>
<tr>
<th>Ingredient/CAS No.</th>
<th>Definition</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>HDI/Trimethylol Hexyllactone Crosspolymer</td>
<td>HDI/Trimethylol Hexyllactone Crosspolymer is a cross-linked condensation polymer formed from the reaction of hexamethylene diisocyanate (HDI) with the esterification product of trimethylolpropane with 6 to 7 moles [equivalents] of hexyllactone.</td>
<td>Anticaking agent</td>
</tr>
<tr>
<td>bis-C16-20 Isoalkoxy TMHDI/PEG-90 Copolymer</td>
<td>Bis-C16-20 Isoalkoxy TMHDI/PEG-90 Copolymer is a copolymer of trimethylhexanediisocyanate (TMHDI) and PEG-90 end-capped with a branched alcohol containing 16 to 20 carbons.</td>
<td>Viscosity increasing agent - aqueous</td>
</tr>
<tr>
<td>bis-Hydroxyethyl Acrylate Poly(1,4-Butanediol)-9/TMHDI Copolymer</td>
<td>bis-Hydroxyethyl Acrylate Poly(1,4-butanol)-9/TMHDI Copolymer is a copolymer of poly(1,4-butanol)-9 and trimethylhexanediisocyanate (TMHDI) end-capped with hydroxyethylacrylate.</td>
<td>Film former</td>
</tr>
<tr>
<td>bis-Isostearyl 1,4-Butanediol/HDI/Hydrogenated Dimer Dilinoleyl Alcohol Copolymer</td>
<td>bis-Isostearyl 1,4-Butanediol/HDI/Hydrogenated Dimer Dilinoleyl Alcohol Copolymer is a copolymer of hexamethylene diisocyanate (HDI), and hydrogenated dilinoleyl alcohol endcapped with isostearyl 1,4-butanol.</td>
<td>Viscosity increasing agent - nonaqueous</td>
</tr>
<tr>
<td>bis-Lauryl Cocaminopropylamine/HDI/PEG-100 Copolymer</td>
<td>bis-Lauryl Cocaminopropylamine/HDI/PEG-100 Copolymer is a copolymer of cocoaminopropylamine, PEG-100, and hexamethylene diisocyanate (HDI) endcapped with lauryl alcohol.</td>
<td>Viscosity increasing agent - nonaqueous</td>
</tr>
<tr>
<td>bis-Methoxy PEG-10 Dimethyl MEA/HD/bis-PEG-10 Dimethicone Copolymer</td>
<td>bis-Methoxy PEG-10 Dimethyl MEA/HD/bis-PEG-10 Dimethicone Copolymer is a copolymer of hexamethylene diisocyanate (HDI), dimethylethanolamine and bis-PEG-10 dimethicone endcapped with PEG-10 monomethyl ether.</td>
<td>Hair conditioning agent</td>
</tr>
<tr>
<td>1,4-Butanediol/Succinic Acid/Adipic Acid/HDI Copolymer 119553-67-2</td>
<td>1,4-Butanediol/Succinic Acid/Adipic Acid/HDI Copolymer is a copolymer of 1,4-butanol, succinic acid, adipic acid, and hexamethylene diisocyanate monomers.</td>
<td>Abrasive, binder, film former</td>
</tr>
<tr>
<td>Cholesterol/HD/Pullulan Copolymer</td>
<td>Cholesterol/HD/Pullulan Copolymer is a copolymer of cholesterol, hexamethylene diisocyanate, and pullulan monomers.</td>
<td>Emulsion stabilizer, humectant, viscosity increasing agent - aqueous</td>
</tr>
</tbody>
</table>
Table 1. Definitions, idealized structures, and functions of the HDI polymers in this safety assessment.

<table>
<thead>
<tr>
<th>Ingredient/CAS No.</th>
<th>Definition</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decyl HDI/PEG-180 Crosspolymer</td>
<td>Decyl HDI/PEG-180 Crosspolymer is a copolymer of hexamethylene diisocyanate (HDI), PEG-180, and decyl alcohol monomers crosslinked with glycerin.</td>
<td>Viscosity increasing agent - aqueous</td>
</tr>
<tr>
<td>Diethylene Glycol/DMAP Acrylamide/PEG-180/HDI Copolymer</td>
<td>Diethylene Glycol/DMAP Acrylamide/PEG-180/HDI Copolymer is a copolymer of diethylene glycol, dimethylaminopropyl (DMAP) acrylamide, PEG-180, and hexamethylene diisocyanate (HDI) monomers.</td>
<td>Hair conditioning agents/ skin protectants, skin-conditioning agent - miscellaneous</td>
</tr>
<tr>
<td>HDI/Di-C12-14 Alkyl Tartrate/Hydrogenated Dilinoleyl Alcohol Copolymer 1268856-56-9</td>
<td>HDI/Di-C12-14 Alkyl Tartrate/Hydrogenated Dilinoleyl Alcohol Copolymer is a copolymer of 1,6-hexamethylene diisocyanate (HDI), di-C12-14 alkyl tartrate, and hydrogenated dilinoleyl alcohol, chain-terminated by ethyl alcohol.</td>
<td>Film former</td>
</tr>
<tr>
<td>HDI/PEI-45/SMDI Crosspolymer</td>
<td>HDI/PEI-45/SMDI Crosspolymer is the crosslinked polymer formed by the reaction of PEI-45 with saturated methylene diphenyldiisocyanate (SMDI) and hexamethylene diisocyanate (HDI). [PEI is an acronym for polyethylenimine.]</td>
<td>Absorbent, dispersing agent - nonsurfactant</td>
</tr>
<tr>
<td>HDI/PPG/Polycaprolactone Crosspolymer 302791-95-3</td>
<td>HDI/PPG/Polycaprolactone Crosspolymer is a cross-linked condensation polymer of polycaprolactone, a sorbitol initiated polypropylene glycol with hexamethylene disiocyanate and trimethylolpropane.</td>
<td>Anticaking agents, bulking agent</td>
</tr>
<tr>
<td>Methoxy PEG-17/Methoxy PEG-11/HDI Crosspolymer</td>
<td>Methoxy PEG-17/Methoxy PEG-11/HDI Crosspolymer is a copolymer of methoxy PEG-17, methoxy PEG-11, and hexamethylene disiocyanate (HDI) crosslinked by water and the addition of sodium hydroxide.</td>
<td>Anticaking agent</td>
</tr>
</tbody>
</table>

[wherein R is glycerin, PEG-180, or decyl alcohol]
[wherein n is 2 or 180]
[crosslinker/crosslinking is not defined]
[wherein R is the residue of HDI and either PPG or Polycaprolactone]
[wherein R is a PEG chain or another HDI residue]
Table 1. Definitions, idealized structures, and functions of the HDI polymers in this safety assessment.

<table>
<thead>
<tr>
<th>Ingredient/CAS No.</th>
<th>Definition</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methoxy PEG-17/Methoxy PEG-11/HDI Isocyanurate Trimer Crosspolymer</td>
<td>Methoxy PEG-17/Methoxy PEG-11/HDI Isocyanurate Trimer Crosspolymer is a copolymer of methoxy PEG-17, methoxy PEG-11, and hexamethylene diisocyanate (HDI) trimer in which the free isocyanate groups are crosslinked by water to form urea linkages.</td>
<td>Anticaking agent</td>
</tr>
<tr>
<td>PEG-17/Methoxy PEG-11/HDI Isocyanurate Trimer Crosspolymer is a copolymer of methoxy PEG-17, methoxy PEG-11, and hexamethylene diisocyanate (HDI) trimer in which the free isocyanate groups are crosslinked by water to form urea linkages.</td>
<td>Viscosity increasing agent – aqueous</td>
<td></td>
</tr>
<tr>
<td>PEG-240/HDI Copolymer bis-Decyltetradeceth-20 Ether</td>
<td>PEG-240 HDI Copolymer bis-Decyltetradeceth-20 Ether is a copolymer of PEG-240, decyltetradeceth-20, and hexamethylene diisocyanate monomers.</td>
<td>Viscosity increasing agent – aqueous</td>
</tr>
<tr>
<td>PPG-26/HDI Copolymer</td>
<td>PPG-26 HDI Copolymer is a copolymer of hexamethylene diisocyanate and PPG-26 monomers.</td>
<td>Film former, plasticizer</td>
</tr>
<tr>
<td>Steareth-100/PEG-136/HDI Copolymer 103777-69-1</td>
<td>Steareth-100/PEG-136 HDI Copolymer is a copolymer of steareth-100, PEG-136, and hexamethylene diisocyanate monomers.</td>
<td>Viscosity increasing agent – aqueous</td>
</tr>
<tr>
<td>Stearyl HDI/PEG-50 Copolymer</td>
<td>Stearyl HDI/PEG-50 Copolymer is a copolymer of hexylmethylene diisocyanate, PEG-50, and stearyl alcohol monomers.</td>
<td>Film former</td>
</tr>
</tbody>
</table>

Table 2. Previous safety assessments of components/monomers of HDI polymers in this safety assessment.

<table>
<thead>
<tr>
<th>Constituent and ingredient group report</th>
<th>Conclusion</th>
<th>Maximum reported concentration of use reported for ingredients in the latest safety assessment or re-review</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polyethylene glycols (PEGs) - triethylene glycol and any PEGs ≥ 4</td>
<td>Safe for use in cosmetics in the present practices of use and concentration.</td>
<td>85%</td>
<td>2,4,6</td>
</tr>
<tr>
<td>PEG-10 dimethicone - polyoxyalkylene siloxane copolymers, alkyl-polyoxyalkylene siloxane copolymers, and related ingredients</td>
<td>Safe for use in cosmetics in the present practices of use and concentration.</td>
<td>22% hair; 15% dermal</td>
<td>2,3</td>
</tr>
<tr>
<td>Methoxy PEG-10, decyltetradeceth-20, steareth-100 - alkyl PEG ethers</td>
<td>Safe as used when formulated to be nonirritating</td>
<td>32% in a product to be diluted; 25%</td>
<td>7</td>
</tr>
<tr>
<td>Adipic acid, succinic acid - dicarboxylic acids, salts, and esters</td>
<td>Safe for use in cosmetics in the present practices of use and concentration.</td>
<td>26% in a product to be diluted; 0.4%</td>
<td>10</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>Safe as used.</td>
<td>2%</td>
<td>6,4</td>
</tr>
<tr>
<td>Pullulan - microbial polysaccharide gums</td>
<td>Safe for use in cosmetics in the present practices of use and concentration.</td>
<td>12% hair; 17% in oral hygiene; biosaccharide gum-1 6% in dermal</td>
<td>11</td>
</tr>
<tr>
<td>Glycerin</td>
<td>Safe for use in cosmetics in the present practices of use and concentration.</td>
<td>99.4%</td>
<td>6</td>
</tr>
<tr>
<td>PPG-26 - propylene glycol, tripropylene glycol, and PPGs</td>
<td>Safe as used when formulated to be nonirritating.</td>
<td>99% in product to be diluted; 73% in dermal</td>
<td>12</td>
</tr>
<tr>
<td>Stearyl alcohol with oleyl alcohol and octyl dodecanol</td>
<td>Safe as used.</td>
<td>56%</td>
<td>6,4</td>
</tr>
</tbody>
</table>

1.CIR Staff
### Table 3. Chemical and physical properties of hexamethylene diisocyanate polymers.

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HDI/Trimethylol Hexyllactone Crosspolymer</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical Form</td>
<td>Fine powder</td>
<td>14-16</td>
</tr>
<tr>
<td>Color</td>
<td>White to pale yellow</td>
<td>14-16</td>
</tr>
<tr>
<td>Molecular Weight g/mol</td>
<td>&gt;10,000</td>
<td>14-16</td>
</tr>
<tr>
<td>Density @ 20°C kg/m³ g/mL</td>
<td>1100-1250</td>
<td>14-16</td>
</tr>
<tr>
<td>Melting Point °C</td>
<td>&gt;225</td>
<td>14-16</td>
</tr>
<tr>
<td><strong>Bis-C16-20 isoalkoxy TMHDI/PEG-90 copolymer</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Color</td>
<td>Translucent</td>
<td>31, 48</td>
</tr>
<tr>
<td>Molecular Weight g/mol</td>
<td>Average &gt;7000</td>
<td>22</td>
</tr>
<tr>
<td>Density g/mL @ 25°C</td>
<td>1.03-1.08</td>
<td>22</td>
</tr>
<tr>
<td>Viscosity kg/(s m)@ 25°C</td>
<td>3-10</td>
<td>22</td>
</tr>
<tr>
<td><strong>Bis-Lauryl Cocaminopropylamine/HDIP-PEG-100 Copolymer</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Color</td>
<td>Translucent</td>
<td>31</td>
</tr>
<tr>
<td>Molecular Weight g/mol</td>
<td>&gt;10,000</td>
<td>21</td>
</tr>
<tr>
<td><strong>Bis-Methoxy PEG-10 Dimethyl MEA/BDI-BIS-PEG-10 Dimethicone Copolymer</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Molecular Weight g/mol</td>
<td>&gt;1000</td>
<td>24</td>
</tr>
<tr>
<td><strong>HDI/di-C12-14 alkyl tartrate/hydrogenated dilinoyle alcohol copolymer</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical Form</td>
<td>Viscous liquid</td>
<td>23</td>
</tr>
<tr>
<td>Color</td>
<td>Yellow</td>
<td>23</td>
</tr>
<tr>
<td>Odor</td>
<td>Characteristic</td>
<td>23</td>
</tr>
<tr>
<td>Molecular Weight g/mol</td>
<td>&gt;1000</td>
<td>23</td>
</tr>
<tr>
<td>Viscosity kg/(s m)@ 25°C</td>
<td>3-5</td>
<td>23</td>
</tr>
<tr>
<td><strong>HDI/PPG/polycaprolactone crosspolymer</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Molecular Weight g/mol</td>
<td>&gt;10,000</td>
<td>26</td>
</tr>
<tr>
<td>Density g/mL</td>
<td>0.6</td>
<td>18</td>
</tr>
<tr>
<td><strong>Methoxy PEG-17/Methoxy PEG-11/HDI Isocyanurate Trimer Crosspolymer</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical Form</td>
<td>Solid, powder, granules</td>
<td>32</td>
</tr>
<tr>
<td>Color</td>
<td>White</td>
<td></td>
</tr>
<tr>
<td>Odor</td>
<td>Odorless</td>
<td>22</td>
</tr>
<tr>
<td>Molecular Weight g/mol</td>
<td>&gt;10000</td>
<td>27</td>
</tr>
<tr>
<td>Melting Point °C</td>
<td>&gt;200</td>
<td>22</td>
</tr>
<tr>
<td><strong>PEG-240/HD1 Copolymer bis-Decyltetradeceth-20 Ether</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Molecular Weight g/mol</td>
<td>4000-75,000</td>
<td>19</td>
</tr>
<tr>
<td><strong>Steareth-100/PEG-136/HD1 copolymer</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical Form</td>
<td>Powder</td>
<td>30</td>
</tr>
<tr>
<td>Color</td>
<td>White</td>
<td>30</td>
</tr>
<tr>
<td>Molecular Weight g/mol</td>
<td>&gt;15,000</td>
<td>30</td>
</tr>
<tr>
<td>Melting Point °C</td>
<td>53-63</td>
<td>30</td>
</tr>
<tr>
<td>Water Solubility</td>
<td>Dispersible</td>
<td>30</td>
</tr>
</tbody>
</table>

### Table 4. Reported particle size distribution for 2 grades of HDI/trimethylol hexyllactone crosspolymer from 1 supplier and another sample from a second supplier.

<table>
<thead>
<tr>
<th></th>
<th>&lt;100 µm (%)</th>
<th>&lt;10 µm (%)</th>
<th>&lt;1 µm (%)</th>
<th>Median diameter (µm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1</td>
<td>100</td>
<td>33.8</td>
<td>5.5</td>
<td>12.54</td>
</tr>
<tr>
<td>Grade 2</td>
<td>100</td>
<td>87.5</td>
<td>7.1</td>
<td>6.16</td>
</tr>
<tr>
<td>Second supplier</td>
<td>100</td>
<td>15.15*</td>
<td>0</td>
<td>12.0-18.0**</td>
</tr>
</tbody>
</table>

* *≤ 10.42 µm
** Average diameter
### Table 5. Residual diisocyanate in HDI polymers.

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Residual diisocyanate</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>HDI/Di-C12-14 Alkyl Tartrate/Hydrogenated Dilinoleyl Alcohol Copolymer</td>
<td>&lt;0.5 ppm</td>
<td>23</td>
</tr>
<tr>
<td>Bis-C16-20 Isoalkoxy TMMDI/PEG-90 Copolymer</td>
<td>Below limit of detection (0.02%)</td>
<td>51</td>
</tr>
<tr>
<td>Bis-Lauryl Cocaminopropylamine/HDI/PEG-100 Copolymer</td>
<td>Below limit of detection (0.017%)</td>
<td>29</td>
</tr>
<tr>
<td>Steareth-100/PEG-136/HDI Copolymer</td>
<td>Below limit of detection (0.017%)</td>
<td>51</td>
</tr>
<tr>
<td>HDI/Trimethoxyloxy Hexyllactone Crosspolymer</td>
<td>&lt;100 ppm</td>
<td>17</td>
</tr>
<tr>
<td>HDI/PPG/Polycaprolactone Crosspolymer</td>
<td>&lt;100 ppm</td>
<td>13</td>
</tr>
<tr>
<td>PEG-240/HDI Copolymer Bis-Decyltetradeceth-20 Ether</td>
<td>Below limit of detection (20 ppm)</td>
<td>17</td>
</tr>
<tr>
<td>Steareth-100/PEG-136/HDl Copolymer</td>
<td>Below limit of detection (0.017%)</td>
<td>19</td>
</tr>
</tbody>
</table>

*Trimethylhexanediisocyanate

### Table 6. Frequency of use and concentration according to duration and exposure of HDI polymers.

<table>
<thead>
<tr>
<th>Use type</th>
<th>Uses</th>
<th>Maximum Concentration (%)</th>
<th>Uses</th>
<th>Maximum Concentration (%)</th>
<th>Uses</th>
<th>Maximum Concentration (%)</th>
<th>Uses</th>
<th>Maximum Concentration (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>HDI/Trimethoxyloxy Hexyllactone Crosspolymer</td>
<td></td>
<td>Bis-C16-20 Isoalkoxy TMMDI/PEG-90 Copolymer</td>
<td></td>
<td>Diethylene Glycol/DMAP Acrylamide/PEG-180/HDl Copolymer</td>
<td></td>
<td>HDI/Di-C12-14 Alkyl Tartrate/Hydrogenated Dilinoleyl Alcohol Copolymer</td>
</tr>
<tr>
<td>Total/range</td>
<td>385</td>
<td>0.0096-31</td>
<td>NR</td>
<td>0.6</td>
<td>6</td>
<td>NR</td>
<td>NR</td>
<td>0.026-7.6</td>
</tr>
<tr>
<td>Duration of use*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leave-on</td>
<td>378</td>
<td>0.0096-31</td>
<td>NR</td>
<td>0.6</td>
<td>1</td>
<td>NR</td>
<td>NR</td>
<td>0.026-7.6</td>
</tr>
<tr>
<td>Rinse-off</td>
<td>7</td>
<td>11.7</td>
<td>NR</td>
<td>NR</td>
<td>5</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Diluted for (bath) use</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Exposure type</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eye area</td>
<td>139</td>
<td>0.049-19.6</td>
<td>NR</td>
<td>0.6</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>1.2</td>
</tr>
<tr>
<td>Incidental ingestion</td>
<td>11</td>
<td>0.0096-15.1</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>0.026-7.6</td>
</tr>
<tr>
<td>Incidental Inhalation-sprays</td>
<td>NR</td>
<td>NR</td>
<td>33b; 39c</td>
<td>NR</td>
<td>3.0-7.6; 0.78-14.4c</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Incidental inhalation-powders</td>
<td>53; 39c</td>
<td>3-12.6; 0.78-14.4c</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Dermal contact</td>
<td>360</td>
<td>0.059-31</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>1.2</td>
</tr>
<tr>
<td>Deodorant (underarm)</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Hair-noncoloring</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>6</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Hair-coloring</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Nail</td>
<td>1</td>
<td>0.21-0.96</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Mucous Membrane</td>
<td>12</td>
<td>0.0096-15.1</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>0.026-7.6</td>
</tr>
<tr>
<td>Baby</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
</tbody>
</table>

*Trimethylhexanediisocyanate
Table 6. Frequency of use and concentration according to duration and exposure of HDI polymers. 33-35

<table>
<thead>
<tr>
<th>Use type</th>
<th>Maximum Concentration (%)</th>
<th>Uses</th>
<th>Maximum Concentration (%)</th>
<th>Uses</th>
<th>Maximum Concentration (%)</th>
<th>Uses</th>
<th>Maximum Concentration (%)</th>
<th>Uses</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HDI/PPG/Polycaprolactone</td>
<td></td>
<td>Methoxy PEG-17/ Methoxy PEG-11/ HDI Crosspolymer</td>
<td></td>
<td>Methoxy PEG-17/ Methoxy PEG-11/HDI Isocyanurate Trimer Crosspolymer</td>
<td></td>
<td>PEG-240/HDI Copolymer Bis-Decyltetradeceth-20 Ether</td>
<td></td>
</tr>
<tr>
<td>Total/range</td>
<td>24</td>
<td>2-11.8</td>
<td>3</td>
<td>NR</td>
<td>NR</td>
<td>0.025</td>
<td>4</td>
<td>1.2</td>
</tr>
<tr>
<td>Duration of use</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leave-on</td>
<td>24</td>
<td>2-11.8</td>
<td>1</td>
<td>NR</td>
<td>NR</td>
<td>0.025</td>
<td>4</td>
<td>1.2</td>
</tr>
<tr>
<td>Rinse-off</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>1</td>
<td>NR</td>
<td>0.025</td>
<td>4</td>
<td>1.2</td>
</tr>
<tr>
<td>Diluted for (bath) use</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>Exposure type</td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eye area</td>
<td>4</td>
<td>5-9.8</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>3</td>
<td>1.9-2</td>
<td></td>
</tr>
<tr>
<td>Incidental ingestion</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>Incidental inhalation-sprays</td>
<td>6; 3</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>1</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Incidental inhalation-powders</td>
<td>3; 3</td>
<td>3-11.8; 2-10.8</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>2</td>
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<tr>
<td>Dermal contact</td>
<td>22</td>
<td>2-11.8</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>0.025</td>
<td>4</td>
<td>1.2</td>
</tr>
<tr>
<td>Deodorant (underarm)</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>Hair-coloring</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>Nail</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>Mucous Membrane</td>
<td>NR</td>
<td>NR</td>
<td>3</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>Baby</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td></td>
</tr>
</tbody>
</table>

Table 7. HDI polymer ingredients that have no reported uses. 33-35

<table>
<thead>
<tr>
<th>HDI Copolymer</th>
<th>HDI Copolymer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bis-Hydroxyethyl Acrylate Poly(1,4-Butanediol)-9/TMDHI Copolymer</td>
<td>Bis-Hydroxyethyl Acrylate Poly(1,4-Butanediol)-9/TMDHI Copolymer</td>
</tr>
<tr>
<td>Bis-Lauryl Cocaminopropylamine/HDEPEG-100 Copolymer</td>
<td>Bis-Lauryl Cocaminopropylamine/HDEPEG-100 Copolymer</td>
</tr>
<tr>
<td>1,4-Butanediol/Succinic Acid/Adipic Acid/HD</td>
<td>1,4-Butanediol/Succinic Acid/Adipic Acid/HD</td>
</tr>
<tr>
<td>1 Decyl HDI/PEG-180 Crosspolymer</td>
<td>1 Decyl HDI/PEG-180 Crosspolymer</td>
</tr>
<tr>
<td>PPG-26/HD1 Copolymer</td>
<td>PPG-26/HD1 Copolymer</td>
</tr>
<tr>
<td>Bsis-Isostearyl 1,4-Butanediol/HDI/Hydrogenated Dimer Dihalogenyl Alcohol Copolymer</td>
<td>Bsis-Isostearyl 1,4-Butanediol/HDI/Hydrogenated Dimer Dihalogenyl Alcohol Copolymer</td>
</tr>
<tr>
<td>Bsis-Methoxy PEG-10 Dimethyl MEA/HDI/Bis-Peg-10 Dimethicone Copolymer</td>
<td>Bsis-Methoxy PEG-10 Dimethyl MEA/HDI/Bis-Peg-10 Dimethicone Copolymer</td>
</tr>
<tr>
<td>Cholesterol/HDI/Pullulan Copolymer</td>
<td>Cholesterol/HDI/Pullulan Copolymer</td>
</tr>
<tr>
<td>HDI/PEI-45/SMoHD Crosspolymer</td>
<td>HDI/PEI-45/SMoHD Crosspolymer</td>
</tr>
<tr>
<td>Stearyl HDPEG-50 Copolymer</td>
<td>Stearyl HDPEG-50 Copolymer</td>
</tr>
</tbody>
</table>
Table 8. Acute oral toxicity of HDI polymers in this safety assessment.

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Animal; n</th>
<th>Results; Methods</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>HDI/Trimethyl Hexyllactone Crosspolymer</td>
<td>Wistar rats (n=5/sex), 5000 mg/kg administered by intragastric feeding caused no clinical signs or mortalities</td>
<td>14-16</td>
<td></td>
</tr>
<tr>
<td>Methoxy PEG-17/Methoxy PEG-11/HDI Isocyanurate Trimer Crosspolymer</td>
<td>Rats; not specified, LD_{50}=&gt;2000 mg/kg, OECD TG 423</td>
<td>52</td>
<td></td>
</tr>
<tr>
<td>PEG-240/HDI Copolymer Bis-Decyldodecane-20 Ether</td>
<td>Rats; not specified, LD_{50}=&gt;2500 mg/kg</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>PEG-240/HDI Copolymer Bis-Decyldodecane-20 Ether</td>
<td>Rats; not specified, LD_{50}=&gt;2000 mg/kg</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>Steareth-100/PEG-136/HDI Copolymer</td>
<td>Rats; 5/sex, LD_{50}=10 000 mg/kg. No mortalities during dosing and the observation period. At 24 h post dosing, 3 rats had bristled fur, diarrhea and dirty fur around the anal region due to feces; all of which resolved at 48 h after dosing. At necropsy, 2 rats had pinhead-sized, cartilaginous elevations on the forestomach mucous membrane; all other necropsies were unremarkable.</td>
<td>20</td>
<td></td>
</tr>
</tbody>
</table>

OECD TG= Organization for Economic Cooperation and Development Test Guideline

Table 9. Dermal irritation assays of HDI polymers.

| Ingredient (concentration) | Assay                        | Results                                                              | Reference |
|----------------------------|------------------------------|                                                                     |-----------|
| HDI/Trimethylol Hexyllactone Crosspolymer (100%) | Primary irritation study in rabbits (n=6); intact and abraded skin | Slight irritation of the skin was observed in 5 of 6 rabbits. 1 rabbit showed well-defined erythema and slight edema 24 and 72 h after administration. The irritation scores were below the threshold for classifying a test substance as an irritant according to the criteria of NOHSC. | 14-16     |
| Methoxy PEG-17/Methoxy PEG-11/HDI Isocyanurate Trimer Crosspolymer (concentration not specified) | OECD TG 404 in rabbits | Non-irritating                                                       | 52        |
| PEG-240/HDI Copolymer Bis-Decyldodecane-20 Ether (3%, 10%, or 30% in a PG solution) | Single dose in guinea pigs | Not a dermal irritant                                                | 19        |
| PEG-240/HDI Copolymer Bis-Decyldodecane-20 Ether (3%, 10%, or 30% in a PG solution) | 14-Day open-application cumulative assay in guinea pigs | Not a dermal irritant                                                | 19        |
| Steareth-100/PEG-136/HDI Copolymer (100%; 0.5 g; dry) | OECD TG 404 in male rabbits (n=3) | Primary Irritation Index=0/8                                        | 20        |

Human

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Assay</th>
<th>Results</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>HDI/di-C12-14 Alkyl Tartrate/ Hydrogenated Dilinoleyl Alcohol Copolymer (1.7%) in a foundation product</td>
<td>24-h Patch test (n=21 male, 23 female)</td>
<td>No effects observed. It was noted that this study may not be predictive of effects that may occur upon exposure to this substance in moist formulations.</td>
<td>14-16</td>
</tr>
<tr>
<td>HDI/di-C12-14 Alkyl Tartrate/ Hydrogenated Dilinoleyl Alcohol Copolymer (3.19%) in a foundation product</td>
<td>Primary skin irritation test (n=20) under semi-occlusion.</td>
<td>Average irritation index was 0.0, the product was classified as non-irritating</td>
<td>23</td>
</tr>
<tr>
<td>HDI/di-C12-14 Alkyl Tartrate/ Hydrogenated Dilinoleyl Alcohol Copolymer (3.19%) in a foundation product</td>
<td>Primary skin irritation test (n=20) under semi-occlusion.</td>
<td>Average irritation index was 0.05 at the first reading and 0.00 at the second reading. The product was classified as non-irritating.</td>
<td>23</td>
</tr>
</tbody>
</table>

In Vitro

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Assay</th>
<th>Results</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mixture containing 30% Bis-C16-20 Isocetyl TMHDl/PEG-90 Copolymer (16.67%, 50%, and 100% in water; actual concentration: 5%, 15%, 30%)</td>
<td>EpiDerm™ Skin Model In Vitro Toxicity Testing System</td>
<td>The test substance is predicted to be non-irritating.</td>
<td>21</td>
</tr>
<tr>
<td>Methoxy PEG-17/Methoxy PEG-11/HDI Isocyanurate Trimer Crosspolymer (concentration not specified)</td>
<td>OECD TG 431, in vitro test for corrosion of human skin</td>
<td>Predicted to be non-irritating to the skin</td>
<td>32</td>
</tr>
<tr>
<td>Methoxy PEG-17/Methoxy PEG-11/HDI Isocyanurate Trimer Crosspolymer (concentration not specified)</td>
<td>OECD TG 439, in vitro test for skin irritation using reconstructed human epidermis</td>
<td>Predicted to be non-irritating</td>
<td>32</td>
</tr>
<tr>
<td>PEG-240/HDI Copolymer Bis-Decyldodecane-20 Ether</td>
<td>EpiDerm MTT Viability Assay ET_{50}&gt;24.0 h</td>
<td></td>
<td>19</td>
</tr>
</tbody>
</table>

ET_{50} = effective time of exposure to reduce tissue viability to 50%
NOHSC= National Occupational Health and Safety Commission of Australia
PG=propylene glycol
### Table 10. Ocular irritation studies of HDI polymers using rabbits.

<table>
<thead>
<tr>
<th>Ingredient (concentration)</th>
<th>Assay</th>
<th>Results</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>HDI/Trimethylol Hexyllactone Crosspolymer (100%)</td>
<td>Ocular irritation study (n=6)</td>
<td>Mild to moderate conjunctival redness and mild chemosis were observed in 4 of 6 rabbits 24 and 48 h after administration. 1 rabbit still showed redness 4 days after exposure, which was resolved 7 days after exposure. Mild chemosis was observed in 1 rabbit on day 1; this was resolved by day 2. The mean scores for observations 24, 48 and 72 h after exposure were 1.0 for redness and 0.1 for chemosis. It was concluded that the test substance was a slight ocular irritant but not classified as an ocular irritant according to the criteria of the NOHSC. The authors considered the particle size (at least 92.9% &gt; 1 µm; Table 4) and the water insolubility of the tested polymer and concluded that the eye irritation observed was likely attributable to mechanical abrasion rather than to chemical irritancy.</td>
<td>14-15</td>
</tr>
<tr>
<td>Methoxy PEG-17/Methoxy PEG-11/HDIIsoyanurate Trimer Crosspolymer (concentration not specified)</td>
<td>OECD TG 405</td>
<td>Slight irritant</td>
<td>32</td>
</tr>
<tr>
<td>PEG-240/HDII Copolymer Bis-Decyltetradeceth-20 Ether (3%, 10%, or 30% in PG solution)</td>
<td>Ocular irritation study</td>
<td>Not an ocular irritant</td>
<td>19</td>
</tr>
<tr>
<td>Steareth-100/PEG-136/HDICopolymer (100%; 0.1 g)</td>
<td>OECD TG 405 (n=3)</td>
<td>Classified as a non-irritant</td>
<td>20</td>
</tr>
<tr>
<td>PG=propylene glycol</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Table 11. Dermal sensitization studies of HDI polymers.

<table>
<thead>
<tr>
<th>Ingredient (concentration)</th>
<th>Assay</th>
<th>Results</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methoxy PEG-17/Methoxy PEG-11/HDIIsoyanurate Trimer Crosspolymer (concentration not specified)</td>
<td>Magnusson Kligman maximization test using guinea pigs; OECD TG 406</td>
<td>Not sensitizing</td>
<td>32</td>
</tr>
<tr>
<td>PEG-240/HDII Copolymer Bis-Decyltetradeceth-20 ether (30% in PG solution)</td>
<td>Skin sensitization assay (species not specified); challenged at 3%, 10%, and 30%.</td>
<td>Not a dermal sensitizer</td>
<td>19</td>
</tr>
<tr>
<td>HDI/Trimethylol Hexyllactone Crosspolymer in a foundation product (30.7%; 0.1-0.15 g)</td>
<td>HRIPT (n=50)</td>
<td>No signs of dermal irritation or allergic contact dermatitis observed</td>
<td>45</td>
</tr>
<tr>
<td>HDI/Trimethylol Hexyllactone Crosspolymer in a foundation product (10%; 200 µL)</td>
<td>HRIPT (n=110)</td>
<td>No signs of dermal irritation or allergic contact dermatitis observed</td>
<td>46</td>
</tr>
<tr>
<td>Bis-C16-20 Isoalkoxy TMHDI/PEG-90 Copolymer (30% active in PG/water; 0.2 g)</td>
<td>HRIPT (n=48)</td>
<td>One subject exhibited barely perceptible (0.5) erythema 48 h after the challenge.</td>
<td>22</td>
</tr>
<tr>
<td>PEG-240/HDII Copolymer Bis-Decyltetradeceth-20 Ether (concentration not specified)</td>
<td>HRIPT (n not specified)</td>
<td>No evidence of dermal irritation or allergic contact sensitization.</td>
<td>19</td>
</tr>
</tbody>
</table>

HRIPT=human repeat insult patch test
REFERENCES


