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# Safety Assessment of Hydroxyethyl Urea As Used in Cosmetics

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The 2018 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 Executive Director is Bart Heldreth, Ph.D. This safety assessment was prepared by Alice Akinsulie, Scientific Analyst/Writer.

## **ABSTRACT**

The Cosmetic Ingredient Review (CIR) Expert Panel (Panel) assessed the safety of Hydroxyethyl Urea, which is reported to function as a humectant and a hair and skin conditioning agent. The Panel reviewed the available data to determine the safety of this ingredient. The Panel concluded that Hydroxyethyl Urea is safe in cosmetics in the present practices of use and concentration described in the safety assessment when formulated to be non-irritating.

## **INTRODUCTION**

This is a review of the safety of Hydroxyethyl Urea as used in cosmetic formulations. According to the web-based *International Cosmetic Ingredient Dictionary and Handbook* (wINCI; *Dictionary*), Hydroxyethyl Urea is reported to function as a humectant and hair- and skin-conditioning agent for use in cosmetic products.<sup>1</sup>

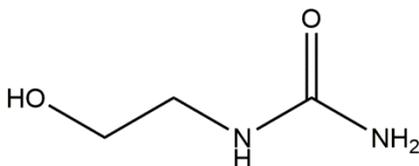
This safety assessment includes relevant published and unpublished data that are available for each endpoint that is evaluated. Published data are identified by conducting an exhaustive search of the world's literature. A listing of the search engines and websites that are used and the sources that are typically explored, as well as the endpoints that CIR typically evaluates, is provided on the CIR website (<https://www.cir-safety.org/supplementaldoc/preliminary-search-engines-and-websites>; <https://www.cir-safety.org/supplementaldoc/cir-report-format-outline>). Unpublished data are provided by the cosmetics industry, as well as by other interested parties.

Much of the data included in this safety assessment were obtained from the European Chemicals Agency (ECHA)<sup>2</sup> website and from the Australian Government Department of Health National Industrial Chemicals Notification and Assessment Scheme (NICNAS)<sup>3</sup> hazard assessments. Both of these sources provide summaries of data generated by industry, and ECHA and NICNAS, respectively, are cited as the sources of the summary data in this safety assessment as appropriate.

## **CHEMISTRY**

### **Definition and Structure**

Hydroxyethyl Urea (CAS No. 2078-71-9;1320-51-0) is the organic compound that conforms to the structure in Figure 1.<sup>1</sup> Urea is the simplest diamide of carbonic acid. Hydroxyethyl Urea is a derivative of urea, singly substituted with 2-ethanol.



**Figure 1. Hydroxyethyl Urea**

### **Physical and Chemical Properties**

Hydroxyethyl Urea is a low-molecular-weight, highly water-soluble, hygroscopic solid.<sup>3</sup> Much of the currently available toxicity data on Hydroxyethyl Urea describe a tradename aqueous mixture containing up to 60% Hydroxyethyl Urea as the test article. Additional information on the physical and chemical properties is found in Table 1.

### **Method of Manufacture**

Hydroxyethyl Urea is sold in an aqueous solution of about 50 - 60% to cosmetics finishing houses and is prepared by diluting the Hydroxyethyl Urea with water and neutralizing the excess ammonia generated with lactic acid. According to one raw material supplier, Hydroxyethyl Urea is manufactured by reacting ethanolamine with excess urea.<sup>4</sup> Specifically, 2-Hydroxyethyl Urea is made by the transamidation of urea with monoethanolamine. This is an equilibrium reaction with the product strongly favored. Ammonia and unreacted monoethanolamine are removed from the reaction by sparging with nitrogen. Lactic acid is added to neutralize any ammonia or monoethanolamine remaining in the product. The product also contains unreacted urea, which can decompose to ammonia and carbon dioxide. Carbon dioxide evolves from the product into the head space; ammonia remains in solution as ammonium lactate. Keeping the pH below 8.25 keeps more than 90% of the ammonia and ethanolamine ionized, preventing ammonolysis of Hydroxyethyl Urea.

Alternatively, Hydroxyethyl Urea could be synthesized via *N*-carbamylation of ethanolamine with potassium cyanate.<sup>5</sup>

## **Impurities**

The purity of the Hydroxyethyl Urea in the aqueous solution is likely > 90%.<sup>3</sup> The following chemicals have been reported as possible impurities of Hydroxyethyl Urea: urea (< 3.0%), ethanolamine (< 0.5%), 2-oxazolidone (< 1.0%; cyclization product), *N,N'*-bis(2-hydroxyethylurea) (< 5.0 %), diethanolamine (residue from ethanolamine) (< 0.025%).<sup>4</sup>

## **USE**

### **Cosmetic**

The safety of the cosmetic ingredient addressed in this assessment is evaluated based on data received from the US Food and Drug Administration (FDA) and the cosmetics industry on the expected use of this ingredient in cosmetics. Use frequencies of individual ingredients in cosmetics are collected from manufacturers and reported by cosmetic product category in the FDA Voluntary Cosmetic Registration Program (VCRP) database. Use concentration data are submitted by the cosmetic industry in response to a survey, conducted by the Personal Care Products Council (Council), of maximum reported use concentrations by product category.

According to 2018 VCRP data, Hydroxyethyl Urea is reported to be used in a total of 641 cosmetic formulations; 432 of those uses are in rinse-off products, and the majority of those (407) are in bath soaps and detergents (Table 2).<sup>6</sup> However, the results of the concentration of use survey conducted by the Council did not report any concentration of use data for the category of bath soaps and detergents. The survey indicated that Hydroxyethyl Urea is used at concentrations up to 20.6% in mostly leave-on products, with the greatest concentration reported for moisturizing products.<sup>7</sup>

Hydroxyethyl Urea is reported to be used in lipstick products at up to 0.009%; use in lipsticks can result in incidental ingestion.<sup>7</sup> It is also used in cosmetic sprays and could possibly be inhaled; Hydroxyethyl Urea is reported to be used at 5% in spray body and hand product formulations. In practice, 95% to 99% of the droplets/particles released from cosmetic sprays have aerodynamic equivalent diameters > 10 µm, with propellant sprays yielding a greater fraction of droplets/particles < 10 µm compared with pump sprays.<sup>8,9</sup> Therefore, most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and thoracic regions of the respiratory tract and would not be respirable (i.e., they would not enter the lungs) to any appreciable amount.<sup>10,11</sup>

Based on the data from a tradename aqueous mixture containing < 50% Hydroxyethyl Urea as the test article, Hydroxyethyl Urea is not classified as hazardous according to Australia's *Approved Criteria for Classifying Hazardous Substances*. At the proposed maximum use concentration of up to 8% in rinse-off and leave-on cosmetic products, the risk to the public associated with the use Hydroxyethyl Urea in cosmetic products is not considered to be unacceptable.<sup>3</sup> Hydroxyethyl Urea is not restricted from use in any way under the rules governing cosmetic products in the European Union.<sup>12</sup>

### **Non-Cosmetic**

Hydroxyethyl Urea has been approved for use as an indirect food additive for use only as a component of adhesives. (21 CFR 175.105)

## **TOXICOKINETIC STUDIES**

### **Dermal Penetration**

Hydroxyethyl Urea has a low molecular weight and high water solubility; therefore, dermal absorption may occur.<sup>3</sup> Based on the partition coefficient (log  $P_{ow}$  estimated to be -2.06), the rate of dermal absorption is expected to be limited.<sup>4</sup> In the gastrointestinal tract, Hydroxyethyl Urea may pass through aqueous (aq.) pores or be carried through the epithelial barrier by the passage of water.

## **TOXICOLOGICAL STUDIES**

### **Acute Toxicity Studies**

#### **Dermal**

In an acute dermal toxicity study, occlusive patches of an aq. solution containing 57.58% Hydroxyethyl Urea were applied to 5 male and 5 female Sprague-Dawley rats in accord with Organization for Economic Co-operation and Development (OECD) test guideline (TG) 402.<sup>2</sup> Thus, dermal administration of the test substance (formula) at 3473 mg/kg corresponded to a dose of 2000 mg/kg Hydroxyethyl Urea. Dermal irritation was noted at the site of test article application. Clinical observations included few feces, and dark materials were observed around the facial area. A slight body weight loss was recorded for 1 male and 1 female in the first week of observation. Because there were no deaths, the dermal LD<sub>50</sub> was reported as > 3473 mg/kg of the test material, corresponding to > 2000 mg/kg Hydroxyethyl Urea.

## Oral

Groups of 5 male and 5 female Sprague-Dawley rats were dosed by gavage with 3473 mg/kg of an aq. solution containing 57.58% Hydroxyethyl Urea; this dose corresponded to 2000 mg/kg Hydroxyethyl Urea.<sup>2,3</sup> Clinical observations included transient incidences of fecal stain, mucoid stools and dark material around the nose. The LD<sub>50</sub> of the aq. solution was > 3473 mg/kg, corresponding to > 2000 mg/kg Hydroxyethyl Urea.

## Inhalation

In an acute study performed in accord with the Office of Prevention, Pesticides and Toxic Substances (OPPTS) protocol 870.1300 (Acute Inhalation Toxicity Limit Test), the inhalation toxicity of a tradename mixture containing approximately 50% Hydroxyethyl Urea (which corresponds to > 4 mg/L of Hydroxyethyl Urea) was studied in Sprague-Dawley rats.<sup>2,3</sup> Groups of 5 male and 5 female rats were exposed nose-only for 4 hours. The test material was undiluted for groups 1 and 3 and mean aerosol mass concentrations were 0.59 mg/L for Group 1, and 0.1325 mg/L for Group 3. For Group 2, the aerosol was a 1:1 dilution of the test material with water and the mean aerosol mass concentration was 5.152 mg/L. In each instance, test concentrations were based on the non-volatile fraction (i.e., 50% for the material tested as supplied; 25% for the test material that was diluted). The mean mass median aerodynamic diameters (MMAD) and geometric standard deviation for each exposure were: 1.06  $\mu\text{m} \pm 1.80$  (Group 1); 1.63  $\mu\text{m} \pm 2.33$  (Group 2); and 1.90  $\mu\text{m} \pm 2.87$  (Group 3). There were no deaths reported during the exposure or observation period, however, animals from all groups had lungs with foci. Histopathologic evaluation of the lungs from two animals with lung foci in Group 2 showed no hemosiderophages in the lymph node of either animal. Since small foci of peracute hemorrhage in the lung are not rare in rodents, the lung foci found in animals from this study were not considered related to treatment with the test substance. With the exception of the observation of redness/red material around the nose, observations were determined not to be attributable to the test article. The LC<sub>50</sub> in rats was greater than > 5.152 mg/L/4 hours of the test material; this corresponds to > 4 mg/L Hydroxyethyl Urea.

## Short-Term Toxicity Studies

No relevant published short-term toxicity studies on Hydroxyethyl Urea were identified in a literature search for this ingredient, and no unpublished data were submitted.

## Subchronic Toxicity Studies

### Dermal

In a 90-day dermal study using semi-occlusive patches, an aqueous solution containing 57.58% of Hydroxyethyl Urea (0, 100, 330, or 1000 mg/kg bw/day) was administered to groups of 10 male and 10 female Sprague-Dawley rats (6 h/day, 7 days/wk, in deionized water).<sup>2,3</sup> Minor treatment-related dermal effects were observed during the study, including a dose-related increase in the incidence of focal/pinpoint eschar, desquamation and red pinpoint areas (a slightly higher incidence is noted in females). These were deemed to be superficial in nature. A statistically-significant increase in phosphorus (all test groups) and calcium (1000 mg/kg bw/day group) were noted in blood samples collected on day 90 in males. These findings were deemed to be possibly related to the test article, but not of biological significance; the changes in phosphorus and calcium levels were within the historical control range of the test facility. No effects on organ weights and no test article-related microscopic lesions were noted at necropsy. The no-observed-adverse-effect-level (NOAEL) was established as 1000 mg/kg bw/day, based on the absence of any toxicologically significant effects at this dose level.

## Chronic Toxicity Studies

No relevant published chronic toxicity studies on Hydroxyethyl Urea were identified in a literature search for this ingredient, and no unpublished data were submitted.

## DEVELOPMENTAL AND REPRODUCTIVE TOXICITY (DART) STUDIES

### Dermal

The potential adverse effect of Hydroxyethyl Urea on developmental and reproductive functions was tested in 4 groups of 25 female Sprague-Dawley rats.<sup>2,3</sup> An aqueous solution containing 57.58% Hydroxyethyl Urea was dermally applied using open applications of 0, 100, 330, and 1000 mg/kg bw/day in deionized water for 6 h/day on days 6 through 19 of gestation. Elizabethan collars were placed around the neck of each animal during the exposure period to minimize ingestion. None of the animals died during the study, however all females were euthanized on gestation day 20 and the neonates were examined for abnormalities. Mean feed consumption for females in the 1000 mg/kg bw/day group was statistically significantly lower than that of controls during the treatment period. However, there were no statistically significant differences in mean body weights or body weight gain between the control and test groups. No reproductive or developmental effects were observed. The NOAEL was established as 1000 mg/kg bw/day for both maternal and developmental toxicity.

## **GENOTOXICITY**

### **In Vitro**

An Ames test was conducted in accordance with OECD TG 471 using *Salmonella typhimurium* (TA1535, TA1537, TA98, TA100) and *Escherichia coli* (WP2uvrA) to evaluate the mutagenicity of an aq. solution containing 57.58% Hydroxyethyl Urea.<sup>2,3</sup> Doses of 75 - 5000 µg/plate were tested with and without metabolic activation. Dosage was adjusted for the purity of the aqueous solution containing Hydroxyethyl Urea (57.58%). In the initial toxicity mutation assay, the maximum dose tested was 5000 µg per plate; this dose was achieved using a concentration of 50 mg/mL and of the test article. All dose levels of test article, vehicle controls and positive controls were plated in triplicate. The test article was not mutagenic under the conditions of the test.

### **In Vivo**

A mammalian micronucleus test of an aq. solution containing 57.58% Hydroxyethyl Urea was performed in CrI:CD-1 (ICR) BR mice in accordance with OECD TG 474.<sup>2,3</sup> Groups of 6 male mice were dosed by gavage with 0, 500, 1000 and 2000 mg/kg bw of the test substance in deionized water, and the animals were killed 24 h after dosing. A second group of 6 males was dosed with 2000 mg/kg bw of the test substance and killed 48 h after dosing. No clinical signs of toxicity were observed at any dose level. A statistically significant increase in micronucleated polychromatic erythrocytes (PCEs) was not observed for any group. As expected, the positive control (cyclophosphamide) induced a statistically significant increase in micronucleated PCEs.

## **CARCINOGENICITY STUDIES**

No relevant published carcinogenicity studies on Hydroxyethyl Urea were identified in a literature search for this ingredient, and no unpublished data were submitted.

## **DERMAL IRRITATION AND SENSITIZATION**

### **Irritation**

#### **In Vitro**

In an EpiDerm™ study, tissue samples were exposed to 100 µL of a test material containing ≤ 50% Hydroxyethyl Urea (actual concentration not specified) for 1, 4, and 24 h.<sup>3</sup> Each treatment was conducted in duplicate. Following the treatment, a negative control (1% octoxinol; an ethoxylated alkyl phenol) was performed in duplicate for the 4 and 24 h exposure times. The ET<sub>50</sub> (the time at which the EpiDerm™ tissue viability was reduced 50% compared to control tissues) was determined to be 12.1 h. The test substance is expected to be very mildly irritating to the skin.<sup>3</sup>

#### **Animal**

The dermal irritation potential of an aq. solution containing 57.58% Hydroxyethyl Urea was evaluated using 6 male New Zealand white rabbits.<sup>2,3</sup> Occlusive patches containing 0.5 mL of the test material (at 52% and undiluted) were applied for 24 h to one intact and one abraded site (i.e. total of four test sites). The skin surface area treated per site was approximately 6.5 cm<sup>2</sup>. Slight erythema and edema were reported. Desquamation was also noted in 2/6 animals treated with 100% test substance at abraded sites. All reactions were fully reversible within 10 days. The test substance was slightly irritating to the skin.

### **Sensitization**

#### **Animal**

The dermal sensitization potential of an aq. solution containing 57.58% Hydroxyethyl Urea was evaluated in Hartley-derived albino guinea pigs.<sup>2,3</sup> Ten male and ten female guinea pigs received 0.1 ml intradermal injections of the test material at a concentration of 5% in deionized water, 5.0% test material and Freund's complete adjuvant (FCA), and FCA only. One week later, a topical induction application of 0.8 ml neat test material was applied for 48 hours. After a 2 week non-treatment period, animals were challenged with a 24 hours exposure to 0.3 ml of Hydroxyethyl Urea, applied neat; the challenge sites were pretreated with sodium lauryl sulfate. A control group of 5 male and 5 female guinea pigs were exposed to deionized water during induction and the test material at challenge. No reactions were observed; the test material was not a sensitizer. A historical study using alpha-hexylcinnamaldehyde served as the positive control.

## OCULAR IRRITATION STUDIES

### **Animal**

The potential ocular irritation of an aq. solution containing 57.58% Hydroxyethyl Urea was evaluated by instilling 0.1 ml of the test material into the conjunctival sac of one eye of 3 male and 3 female New Zealand White rabbits, in accord with OECD TG 405 (Acute Eye Irritation/Corrosion).<sup>2,3</sup> Iritis was noted in 3/6 animals at the 1 hour scoring interval, which resolved completely in all test eyes by the 48 hour scoring interval. Conjunctivitis was noted in 6/6 animals at the 1 hour scoring interval. The conjunctival irritation was resolved completely in all test eyes by study day 7. The test substance was classified as slightly irritating to the eye.

### SUMMARY

This is a review of the safety of Hydroxyethyl Urea as used in cosmetics. According to the *Dictionary*, this ingredient is reported to function in cosmetics as a humectant and a hair and skin conditioning agent. Based on 2018 VCRP data, Hydroxyethyl Urea is used in a total of 641 cosmetic formulations, the majority (407) of which are in bath soaps and detergent products. The results of the concentration of use survey conducted in 2017 by the Council did not report any concentration of use data for the category of bath soaps and detergents. The survey indicated that Hydroxyethyl Urea is used at concentrations up to 20.6% in mostly leave-on products, with the greatest concentration reported for moisturizing products.

Given the low molecular weight and high water solubility (> 699 g/L) of Hydroxyethyl Urea, dermal absorption may occur. However, dermal absorption is expected to be limited, based on the partition coefficient (log  $P_{ow}$  estimated to be -2.06).

The acute dermal and oral LD<sub>50</sub>s of an aq. solution containing 57.58% Hydroxyethyl Urea were both > 2000 mg/kg. The LC<sub>50</sub> of a mixture that contained approximately 50% Hydroxyethyl Urea was > 5.152 mg/L in male and female rats; this was calculated as corresponding to > 4 mg/l Hydroxyethyl Urea. In a 90-day dermal toxicity study with semi-occlusive patches of an aq. solution containing 57.58% Hydroxyethyl Urea in rats, the NOAEL was 1000 mg/kg bw/day.

In a dermal developmental toxicity study, open applications of an aq. solution containing 57.58% Hydroxyethyl Urea were tested on 4 groups of 25 female Sprague-Dawley rats on days 6 through 19 of gestation. A dosage level of 1000 mg/kg/day was considered to be the NOAEL for maternity and developmental toxicity. No reproductive or developmental effects were observed.

The genotoxic potential of Hydroxyethyl Urea (75 - 5000 µg/plate) was evaluated in an Ames test using *S. typhimurium* (TA1535, TA1537, TA98, TA100) and *E. coli* (WP2uvrA). Hydroxyethyl Urea was not mutagenic to bacteria under the conditions of the test. Hydroxyethyl Urea also was not genotoxic in a micronucleus study in which mice were given a single dose by gavage of up to 2000 mg/kg of an aq. solution containing 57.58% Hydroxyethyl Urea.

Based on the results of an EpiDerm™ study, tissue samples exposed to 100 µL of a test material containing ≤ 50% Hydroxyethyl Urea is expected to be mildly irritating to skin. An aq. solution containing 57.58% Hydroxyethyl Urea (tested at 52% and undiluted) was slightly irritating to rabbit skin. In a sensitization study in which guinea pigs were induced with intradermal injections of 5.0% Hydroxyethyl Urea and topical application of undiluted Hydroxyethyl Urea, and challenged with undiluted test material, no reactions were observed and the test material was not a sensitizer.

In an ocular irritation study, an aq. solution containing 57.58% Hydroxyethyl Urea was instilled into the sac of one eye of 3 male and 3 female New Zealand White rabbits. The test material was slightly irritating to rabbit eyes.

### DISCUSSION

The Panel determined that the available genotoxicity, dermal, inhalation, and reproductive/developmental toxicity data were sufficient to issue the conclusion that Hydroxyethyl Urea is safe in the present practices of use and concentration described in this report when formulated to be non-irritating. The overall favorable safety profile and low dermal toxicity mitigated concern about systemic effects from dermal penetration.

Because of the low molecular weight and high water solubility of Hydroxyethyl Urea, the Panel noted the possibility of dermal absorption. However, Hydroxyethyl Urea is absorbed dermally at a slow rate, mitigating the concern for dermal toxicity when used in rinse-off applications.

Carcinogenicity data are lacking. However, because the genotoxicity studies were negative and there are no structural alerts, the Panel was not concerned that Hydroxyethyl Urea had carcinogenic potential.

The Panel noted Hydroxyethyl Urea was slightly irritating to rabbit skin. Because the potential exists for dermal irritation with the use of products formulated using Hydroxyethyl Urea, the Panel specified that products containing Hydroxyethyl Urea must be formulated to be non-irritating.

Hydroxyethyl Urea is used in body and hand product formulations that are sprayed at a concentration of 5%, and could possibly be inhaled. Thus, the Panel discussed the issue of potential inhalation toxicity. The available inhalation data suggest little potential for respiratory effects at relevant doses. The Panel noted that in aerosol products, 95% – 99% of

droplets/particles 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 concerns based on the chemical and biological properties of these ingredients. 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. A detailed discussion and summary of the Panel's approach to evaluating incidental inhalation exposures to ingredients in cosmetic products is available at <https://www.cir-safety.org/cir-findings>.

Finally, the Panel discussed the similarity between hydroxyurea (a DNA synthesis inhibitor that acts by inhibiting ribonucleotide reductase) and Hydroxyethyl Urea. Despite the similarity in structure, Hydroxyethyl Urea lacks the key structural feature (i.e., N-OH group) required for this inhibition.

### **CONCLUSION**

The Panel concluded that Hydroxyethyl Urea is safe in cosmetics in the present practices of use and concentration described in this safety assessment when formulated to be non-irritating.

## TABLES

**Table 1.** Physical and chemical properties of Hydroxyethyl Urea

Property	Value	Reference
Physical Form	Solid	3
Color	Light yellow	3
Molecular Weight (Da)	104.11	3
Density/Specific Gravity (g/cm <sup>3</sup> @ 22.3°C)	1.36	3
Vapor pressure (mm Hg @ 25°C)	0.00021	3
Melting Point (°C)	94 - 95	13
Boiling Point (°C @ 772 mm Hg)	150 (decomposed)	3
Water Solubility (g/l @ 20°C)	699	3
Log P <sub>ow</sub>	-2.06	4
Disassociation constants (@) 25 °C)		2
pKa – 1 (N-H)	14.72 est.	
pKa – 2 (O-H)	14.83 est.	
pKa – 3 (N-H)	16.20 est.	

**Table 2.** Frequency and concentration of use according to the FDA product category

	# of Uses <sup>b</sup>	Max Conc of Use (%) <sup>c</sup>
<b>Totals*</b>	<b>641</b>	<b>0.00046 – 20.6%</b>
<b>Duration of Use</b>		
Leave-On	209	0.00046 – 20.6%
Rinse-Off	432	NR
Diluted for (Bath) Use	NR	NR
<b>Exposure Type</b>		
Eye Area	5	NR
Incidental Ingestion	2	0.009
Incidental Inhalation-Spray	13; 106 <sup>a</sup> ; 46 <sup>b</sup>	5; 0.5-2.5 <sup>a</sup>
Incidental Inhalation-Powder	13; 46 <sup>b</sup>	0.0091-5 <sup>c</sup>
Dermal Contact	622	0.00046-20.6%
Deodorant (underarm)	NR	0.00046
Hair - Non-Coloring	16	0.25-2%
Hair-Coloring	NR	NR
Nail	1	NR
Mucous Membrane	413	0.009
Baby Products	NR	NR

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

<sup>a</sup> Includes products that can be sprays, but it is not known whether the reported uses are sprays

<sup>b</sup> Not specified whether this product is a spray or a powder or neither, but it is possible it may be a spray or a powder, so this information is captured for both categories of incidental inhalation

<sup>c</sup> Includes products that can be powders, but it is not known whether the reported uses are powders

NR – no reported use

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