Safety Assessment of Inorganic Hydroxides as Used in Cosmetics

Status: Draft Report for Panel Review
Release Date: August 28, 2015
Panel Meeting Date: September 21-22, 2015

The 2015 Cosmetic Ingredient Review Expert Panel members are: Chairman, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; Ronald A. Hill, Ph.D.; Curtis D. Klaassen, Ph.D.; Daniel 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, DPA. This safety assessment was prepared by Christina L. Burnett, Scientific Analyst/Writer and Bart Heldreth, Ph.D., Chemist CIR.

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Memorandum

To: CIR Expert Panel Members and Liaisons
From: Christina L. Burnett, Senior Scientific Writer/Analyst
Date: August 28, 2015
Subject: Draft Report of the Safety Assessment on Inorganic Hydroxides

Enclosed is the Draft Report of the Safety Assessment of Inorganic Hydroxides as Used in Cosmetics. (It is identified as *inooh092015rep* in the pdf document).

In June 2015, CIR issued the Scientific Literature Review (SLR) for inorganic hydroxide ingredients. These hydroxides are all alkaline salts and are reported to function as pH adjusters in cosmetics. Data requested with the issuance of the SLR included types and concentrations of impurities and/or general composition of inorganic hydroxides that are used in cosmetics, as well as any additional toxicological data that would help the Panel assess the safety of the use of these ingredients in cosmetics.

Concentration of use data and a material safety data sheet were provided by the Personal Care Products Council (Council), and, since the June announcement, the Council has provided comments on the SLR, which have been considered. The data have been incorporated into the report, and both the data and the comments can be found in this report package (*inooh092015data1 - inooh092015 data3* and *inooh092015pcpc*, respectively).

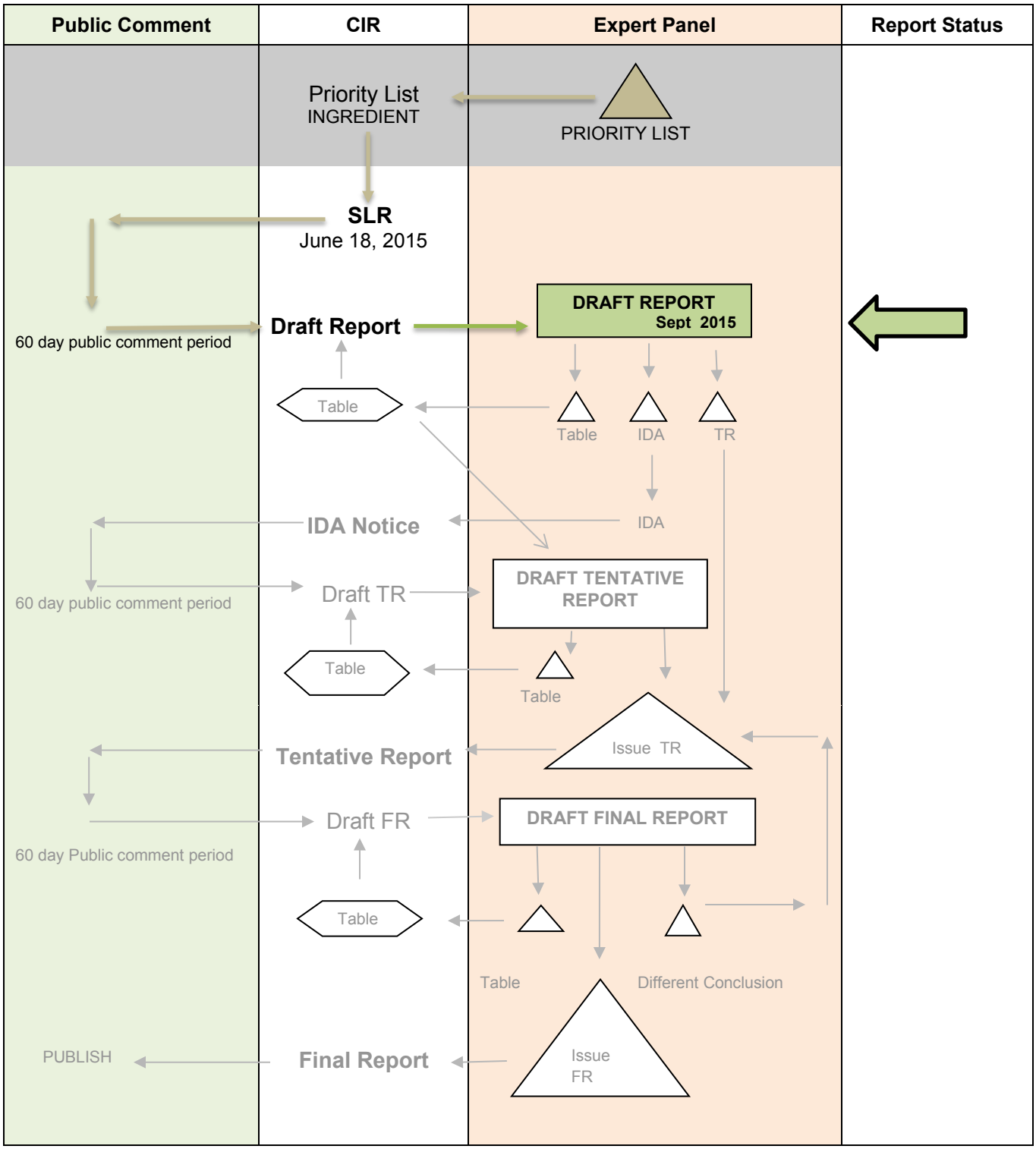
According to the FDA's VCRP data provided in 2015, sodium hydroxide has the most reported uses in cosmetic products, with a total of 5147; about half of the uses are in leave-on skin care products. Potassium hydroxide has the second greatest number of overall uses reported, with a total of 1074; the majority of the uses also are in leave-on skin care products. The results of the Council's concentration of use survey indicate that calcium hydroxide has the highest reported maximum concentration of use; it is used at up to 13.2% in rinse-off shaving preparations. However, it is only used up to 0.5% in leave-on products (deodorants). Sodium hydroxide is used at up to 10% in an "other" skin care preparation, which may or may not be a leave-on product. The next highest concentration of use for sodium hydroxide in a leave-on product is 6.9% in a face or neck product. Potassium hydroxide is used up to 7% in a leave-on body and hand product.

If no further data are needed, the Panel should issue a Tentative Report. If data are needed, an Insufficient Data Announcement should be issued, and the data needs listed.

SAFETY ASSESSMENT FLOW CHART

INGREDIENT/FAMILY Inorganic Hydroxides

MEETING Sept 2015



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Inorganic Hydroxides History

June 205 – Scientific Literature Reviews announced for Inorganic Hydroxides.

Inorganic Hydroxides Data Profile – September 2015 – Writers: Christina Burnett and Bart Heldreth															
	In-Use	**Physical/Chemical Properties**	**Method of Manufacturing**	**Composition/Impurities**	**Tocikokinetics**	**Acute Toxicity**	**Repeated Dose Toxicity**	**Repro. /Develop. Toxicity**	**Genotoxicity**	**Carcinogenicity**	**Irritation/Sensitization – Non-Human**	**Irritation/Sensitization - Human**	**Ocular/Mucosal**	**Phototoxicity**	**Case Studies**
Calcium Hydroxide	X	X	X	X		X			X		X		X		
Magnesium Hydroxide	X	X	X	X		X		X	X		X		X		
Potassium Hydroxide	X	X	X	X		X			X		X		X		
Sodium Hydroxide	X	X	X	X		X			X		X	X	X		

X indicates that data were available in the category for that ingredient.

Search Strategy for Inorganic Hydroxides (Performed by Christina Burnett)

November 2014-May 2015: SCIFINDER search for 4 inorganic hydroxide ingredients, including available CAS numbers::

- Initial search for "adverse effect, including toxicity" yielded:
  - 855 references for sodium hydroxide
    - Limits for "dermal" yielded 30 results, 20 relevant
    - Limits for "irritation" yielded 147 results, 107 relevant
    - Limits for "sensitization yielded 58 results, 31 relevant
  - 144 references for potassium hydroxide
    - Limits for "dermal" yielded 13 results, 7 relevant
    - Limits for "irritation" yielded 42 results, 36 relevant
    - Limits for "sensitization yielded 21 results, 16 relevant
  - 194 references for magnesium hydroxide
    - Limits for "dermal" yielded 2 results, 0 relevant
    - Limits for "irritation" yielded 8 results, 0 relevant
    - Limits for "sensitization" yielded 5 results, 0 relevant
  - 600 references for calcium hydroxide
    - Limits for "dermal" yielded 8 results, 1 relevant
    - Limits for "irritation" yielded 21 results, 4 relevant
    - Limits for "sensitization" yielded 35 results, 1 relevant

Search Terms	TOXLINE Hits (excluding PUBMED, English only)	PUBMED Hits	ECHA Hits
calcium hydroxide OR 1305-62-0	513	6201 dermal = 9 irritation = 23 sensitization = 7	yes
magnesium hydroxide OR 1309-42-8	361	1820 dermal = 5 irritation = 1 sensitization = 3	yes
potassium hydroxide OR 1310-58-3	514	1995 dermal = 6 irritation = 8 sensitization = 1	yes
sodium hydroxide OR 1310-73-2	2158	8568 dermal = 22 irritation = 59 sensitization = 11	yes

Total references ordered or downloaded: 67

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Distributed for comment only -- do not cite or quote

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INTRODUCTION

This report addresses the safety of the inorganic hydroxides calcium hydroxide (also known as calcium hydrate or slaked lime), magnesium hydroxide, potassium hydroxide (potassium hydrate or potash), and sodium hydroxide (sodium hydrate, lye, or caustic soda). These ingredients are all alkaline salts and are reported to function as pH adjusters in cosmetics.[1] Sodium hydroxide has been reacted with fats to form soap for millennia.

The inorganic hydroxides in this report, with the exception of magnesium hydroxide, are well known caustic agents that can cause severe burns and corrosion with acute exposures. Sodium hydroxide is commonly used as a positive control in efficacy studies of skin protective creams and in other studies of irritant contact dermatitis.[2]

Some chemical and toxicological data on the inorganic hydroxides included in this safety assessment were obtained from robust summaries of data submitted to the European Chemical Agency (ECHA) by companies as part of the REACH chemical registration process. These data summaries are available on the ECHA website.[3-6]

CHEMISTRY

Definition

Inorganic hydroxides are alkaline salts formed by treating oxides with water or via decomposing salts by adding other soluble hydroxides to a solution thereof (e.g., adding sodium hydroxide to magnesium sulfate will produce magnesium hydroxide). The formation of an inorganic hydroxide, such as specifically lime or calcium hydroxide, by reaction of an oxide with water is a known as slaking.[7] The resulting highly water soluble ingredients only vary structurally by the metal cation. These variations result in different degrees of alkalinity across these four ingredients, ranging in pK_b values from 0.2 to 4.0. Used primarily as pH adjusters (to increase the pH of an otherwise acidic formulation), the caustic nature of these ingredients is unlikely to be observable in typical, final cosmetic formulations.

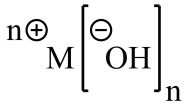


Figure 1. Inorganic Hydroxides (wherein "M" is group I or II metal)

The definitions, structures, and functions of the inorganic hydroxides included in this report are provided in Table 1.

Chemical and Physical Properties

The inorganic hydroxides are all highly water soluble, white solids with specific gravities around 2. Physical and chemical properties of the inorganic hydroxides in this report are provided in Table 2.

Method of Manufacturing

Calcium Hydroxide

Calcium hydroxide may be formed by the hydration of lime or treating an aqueous solution of a calcium salt with alkali.[8]

Magnesium Hydroxide

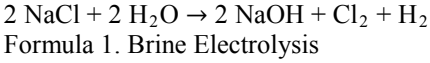
Magnesium hydroxide may be formed by reacting magnesium chloride or sulfate and sodium hydroxide.[8] Most commercial-grade magnesium hydroxide is obtained from seawater or brine using lime or dolomitic lime.[7]

Potassium Hydroxide

Potassium hydroxide may be produced by treating oxides with water, known as brine electrolysis.[7,8]

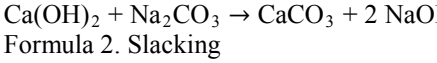
Sodium Hydroxide

Sodium hydroxide is formed by brine electrolysis.[7]



Formula 1. Brine Electrolysis

Sodium hydroxide may also be formed by reacting lime with soda ash.[7]



Formula 2. Slacking

Impurities

The *U.S. Pharmacopeia* and *Food Chemicals Codex* list specifications for the acceptable levels of impurities for the inorganic hydroxides listed in this report.[9,10] These specifications are provided in Table 3.

USE

Cosmetic

The safety of the cosmetic ingredients included in this safety assessment is evaluated on the basis of the expected use in cosmetics. The Cosmetic Ingredient Review (CIR) Expert Panel (Panel) utilizes data received from the Food and Drug Administration (FDA) and the cosmetics industry in determining the expected cosmetic use. The data received from the FDA are those it collects from manufacturers on the use of individual ingredients in cosmetics by cosmetic product category in its Voluntary Cosmetic Registration Program (VCRP), and those from the cosmetic industry are submitted in response to a survey of the maximum reported use concentrations by category conducted by the Personal Care Products Council (Council).

According to the 2015 VCRP data, sodium hydroxide has the most reported uses of the ingredients listed in this safety assessment in cosmetic products, with a total of 5147; about half of the uses are in leave-on skin care products. (Table 4).[11] Potassium hydroxide has the second greatest number of overall uses reported, with a total of 1074; the majority of the uses also are in leave-on skin care products. The results of the concentration of use survey conducted in 2014 by the Council indicate calcium hydroxide has the highest reported maximum concentration of use; it is used at up to 13.2% in rinse-off shaving preparations.[12] However, it is only used up to 0.5% in leave-on products (deodorants). Sodium hydroxide is used at up to 10% in an "other" skin care preparation, which may or may not be a leave-on product. The next highest concentration of use for sodium hydroxide in a leave-on product is 6.9% in a face or neck product. Potassium hydroxide is used up to 7% in a leave-on body and hand product.

Some of these ingredients may be used in products that can be incidentally ingested or come into contact with mucous membranes. For example, sodium hydroxide is used in lipstick (at least one use at up to 0.26%) and in bath soaps and detergents (860 uses at up to 12.9%). Additionally, some of these ingredients were reported to be used in hair sprays and body and hand sprays and could possibly be inhaled. For example, potassium hydroxide was reported to be used in hair sprays at a maximum concentration of 0.69%. 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 below 10 μm compared with pump sprays.[13-16] Therefore, most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and bronchial regions and would not be respirable (i.e., they would not enter the lungs) to any appreciable amount.[14,15]

Europe's Scientific Committee on Consumer Safety (SCCS) opined that potassium hydroxide is safe for use as a callosity softener/remover with a concentration of up to 1.5%.[17] A proposed change to the European Commission's regulation under Annex III List of Substances Which Cosmetic Products Must Not Contain Except Subject to the Restrictions Laid Down has been sent to the World Trade Organization (WTO) for consideration. Currently, sodium hydroxide, potassium hydroxide, and calcium hydroxide are listed on Annex III with the restrictions listed here.[18] The uses of sodium hydroxide and potassium hydroxide may not exceed 5% in nail cuticle solvents; 2% for general use and 4.5% in professional use of hair; must have a pH below 12.7 when used as a pH adjuster in depilatories; and must have pH below 11 in other uses. The use of calcium hydroxide may not exceed 7% in hair straighteners containing calcium hydroxide and a guanidine salt, must have a pH below 12.7 when used as a pH adjuster in depilatories, and must have a pH below 11 in all other uses.

Magnesium hydroxide is not restricted from use in any way under the rules governing cosmetic products in the European Union.[18]

Non-Cosmetic

The inorganic hydroxides in this report are generally recognized as safe (GRAS) as direct food substances based upon following current good manufacturing practice conditions of use (21CFR§184). Additionally, they are GRAS as feed additives for animals (21CFR§582). The FDA has also reviewed calcium hydroxide and magnesium hydroxide for use as an active ingredient in over-the-counter (OTC) drugs. Based on evidence currently available, there are inadequate data to establish general recognition of the safety and effectiveness of this ingredient in certain drug products (21CFR §310).

Calcium hydroxide is used in mortar, plaster, cement and other building and paving materials.[8] It is also used in lubricants, drilling fluids, pesticides, fireproofing coatings, water paints, as egg preservative, in the manufacture of paper pulp, in rubber vulcanization in water treatment, as an absorbent for carbon dioxide, and in dehairing hides. Therapeutically, it is used as an astringent.

Magnesium hydroxide may be used therapeutically as an antacid, cathartic, or laxative.[8] It is an approved OTC active ingredient (21 CFR§ 331.11).

Non-cosmetic uses of potassium hydroxide include mordant for wood, mercerizing cotton, absorbing carbon dioxide, removing paint and varnish, electroplating, photoengraving and lithography, printing inks, debudding calves' horns and dissolving scales and hair in skin scrapings.[8]

Sodium hydroxide is a well-known strong base and is extremely corrosive. Sodium hydroxide solutions are used to neutralize acids and make sodium salts (for example, in petroleum refining to remove sulfuric and organic acids); to treat

cellulose during viscose rayon and cellophane production; to reclaim rubber; in plastics manufacturing; and in dehorning calves.[7,8]

TOXICOKINETICS

No relevant published toxicokinetics studies on inorganic hydroxides were identified in a literature search for these ingredients and no unpublished data were submitted: these types of data are not expected as the constituents of inorganic hydroxides (the metal ion and hydroxide ion) are normal physiological constituents at low concentrations. Data on the kinetics of the metal ions of these ingredients are abundant in the published literature, but these data are not useful in assessing the safety of these ingredients as they are used in cosmetics.

TOXICOLOGICAL STUDIES

Acute Toxicity

Animal acute dose toxicity studies are presented in Table 5.[3-6,19-22] In oral toxicity studies, calcium hydroxide had an LD_{50} > 7300 mg/kg bodyweight in rats and mice and magnesium hydroxide had an LD_{50} > 2000 mg/kg bodyweight in rats. An LD_{50} of 1230 mg/kg bodyweight was observed in rats that received potassium hydroxide at doses that increased in log fashion by factor of 2 starting at 0.1 mg/ml solution. Other oral studies of potassium hydroxide in rats have LD_{50} results of 333 to 388 mg/kg bodyweight. Oral studies of sodium hydroxide led to extensive gastric damages in the animal tested. In dermal toxicity studies, calcium hydroxide had an LD_{50} >2.5 g/kg bodyweight in rabbits, and mice treated with 50% sodium hydroxide had better survival rates with the test compound was washed off within an hour of application. In inhalation studies in rats, the LC_{50}s for magnesium hydroxide and sodium hydroxide were > 2.1 mg/l and > 0.75 mg/l, respectively.

Repeated Dose Toxicity

No relevant published repeated dose toxicity studies on inorganic hydroxides were identified in a literature search for these ingredients and no unpublished data were submitted.

REPRODUCTIVE AND DEVELOPMENTAL TOXICITY

Magnesium Hydroxide

The reproductive effects of magnesium hydroxide (pH = 10) were studied in rats that received the test material via gavage.[5] Groups of 10 male and 10 female Wistar rats received 0, 110, 330, or 1000 mg/kg bw/day magnesium hydroxide in water daily. Males were exposed for 29 days (i.e. 2 weeks prior to mating, during mating, and up until treatment end) and females were exposed for 41-45 days (i.e.2 weeks prior to mating, during mating, during post-coitum, and during at least 4 days of lactation). No treatment-related effects were observed on clinical signs, body weight or weight gain, feed consumption, or hematology. In parental males, lower total protein levels (330 and 1000 mg/kg dose groups), lower albumin levels (1000 mg/kg dose group), and lower calcium levels (330 and 1000 mg/kg dose groups) in the blood and lower sodium and potassium excretion (1000 mg/kg dose group) and higher calcium concentration in urine (1000 mg/kg dose group) were observed; however, these changes only just exceeded or remained within normal ranges and there were no corresponding histopathological changes. No toxicologically relevant changes from the test material were observed in parental organ weights or in gross pathology. There were no treatment related effects on reproduction development. The no observed adverse effect level (NOAEL) for parental systemic effects, parental reproductive effects, and offspring effects in this one generation rat study of magnesium hydroxide is 1000 mg/kg bw/day.

GENOTOXICITY

Genotoxicity studies are presented in Table 6.[3-6,23] Calcium hydroxide, magnesium hydroxide, and sodium hydroxide were not genotoxic in several different in vitro assays. Potassium hydroxide was not genotoxic in one Ames test, but results were ambiguous in another Ames test and a chromosome aberration test. Sodium hydroxide was not genotoxic in an in vivo mouse oocyte aneuploidy induction study at up to 0.015M. Genotoxic effects due to high non-physiological pH that may yield false-positive results

IRRITATION AND SENSITIZATION

Dermal Irritation

Sodium hydroxide is a corrosive material that can produce immediate coagulative necrosis resulting in considerable tissue damage with ulceration and sloughing.[24] Toxicity is a function of pH, with greater toxicity associated with increasing pH values. High concentrations can cause deep burns and readily denatures keratin. Following exposure, the chemical must be removed quickly and completely in order to avoid further damage to the skin or possible systemic injury.

A representative sampling of dermal irritation studies are presented in Table 7.[2-6,25-34] Magnesium hydroxide was not irritating or corrosive in in vitro tests (concentrations not reported); however, potassium hydroxide and sodium hydroxide were corrosive at concentrations as low as 1%. Calcium hydroxide was generally irritating but not corrosive in dermal rabbit studies (concentrations not reported). Potassium hydroxide was irritating and/or corrosive in rabbit (at 2% or greater) and guinea pig (at 10%) studies. Sodium hydroxide was irritating/corrosive in a concentration dependent manner in rat, rabbit,

and pig studies. In humans, sodium hydroxide was irritating at concentrations as low as 0.5%. Because of the large number of studies the include sodium hydroxide as a positive control, only a sampling has been presented in this safety assessment.

Ocular Irritation

Caustic chemicals like sodium hydroxide can rapidly penetrate ocular tissues.[24] Toxicity is a function of pH, with greater toxicity associated with increasing pH values. The concentration of the solution and duration of contact with the eye are important determinants of the eventual clinical outcome.

A representative sampling of ocular irritation studies are presented in Table 8.[3-6,34-38] Calcium hydroxide was predicted to be irritating in hen's egg test-chorioallantoic membrane (HET-CAM) in vitro tests while magnesium hydroxide was predicted not to be irritating in a bovine corneal opacity and permeability (BCOP) in vitro test. In rabbit studies, calcium hydroxide was severely irritating at a concentration as low as 10% and pH of 9. Potassium hydroxide and sodium hydroxide were severely irritating and/or corrosive in a concentration-dependent manner. Magnesium hydroxide was not irritating in a rabbit study.

Dermal Sensitization

Dermal sensitization studies are summarized in Table 9.[4-6] Potassium hydroxide (0.1%) was not sensitizing in a guinea pig study while magnesium hydroxide in propylene glycol was sensitizing in a local lymph node assay (LLNA) when tested at up to 50%. In a human repeat insult patch test (HRIPT), sodium hydroxide was not sensitizing when induced at up to 1.0% and challenged at 0.125%, but irritation was observed.

CASE REPORT

No relevant case reports were discovered in the published literature regarding exposure to inorganic hydroxides in cosmetic products; however numerous cases of accidental occupational or industrial exposures were reported. [3,4,6,39]

SUMMARY

The inorganic hydroxides, calcium hydroxide, magnesium hydroxide, potassium hydroxide, and sodium hydroxide, are all alkaline salts and function most commonly as pH adjusters in cosmetics. Inorganic hydroxides, with the exception of magnesium hydroxide, are well known caustic agents that can cause severe burns and corrosion in acute exposures. Sodium hydroxide is commonly used as a positive control in efficacy studies of skin protective creams and in other studies of irritant contact dermatitis.

According to the 2015 VCRP data, sodium hydroxide has the most reported uses of the ingredients listed in this safety assessment in cosmetic products, with a total of 5147; about half of the uses are in leave-on skin care products. Potassium hydroxide has the second greatest number of overall uses reported, with a total of 1074; the majority of the uses also are in leave-on skin care products. The results of the concentration of use survey conducted in 2014 by the Council indicate calcium hydroxide has the highest reported maximum concentration of use; it is used at up to 13.2% in rinse-off shaving preparations. However, it is only used up to 0.5% in leave-on products (deodorants). Sodium hydroxide is used at up to 10% in an "other" skin care preparation, which may or may not be a leave-on product. The next highest concentration of use for a leave-on product for sodium hydroxide is 6.9% in a face or neck product.

The inorganic hydroxides in this report are GRAS as direct food substances and as feed additives for animals. The FDA has also reviewed calcium hydroxide and magnesium hydroxide for use as an active ingredient in over-the-counter drugs. Inorganic hydroxides have numerous non-cosmetic uses.

In oral toxicity studies, calcium hydroxide had an LD_{50} > 7300 mg/kg bodyweight in rats and mice and magnesium hydroxide had an LD_{50} > 2000 mg/kg bodyweight in rats. An LD_{50} of 1230 mg/kg bodyweight was observed in rats that received potassium hydroxide at doses that increased in log fashion by a factor of 2 starting at 0.1 mg/ml solution. Other oral studies of potassium hydroxide in rats have LD_{50} results of 333 to 388 mg/kg bodyweight. Oral studies of sodium hydroxide led to extensive gastric damages in the animal tested. In dermal toxicity studies, calcium hydroxide had an LD_{50} >2.5 g/kg bodyweight in rabbits, and mice treated with 50% sodium hydroxide had better survival rates when the test compound was washed off within an hour of application. In inhalation studies in rats, the LC_{50}s for magnesium hydroxide and sodium hydroxide were > 2.1 mg/l and > 750 µg/l, respectively.

The NOAEL for parental and offspring effects following oral exposure to magnesium hydroxide (pH = 10) was 1000 mg/kg bw/day. No treatment-related effects were observed on clinical signs, body weight or weight gain, feed consumption, or hematology. No toxicologically relevant changes from the test material were observed in parental organ weights or in gross pathology. There were no treatment related effects on reproduction development.

Calcium hydroxide, magnesium hydroxide, and sodium hydroxide were not genotoxic in several different in vitro assays. Potassium hydroxide was not genotoxic in one Ames test, but results were ambiguous in another Ames test and a chromosome aberration test. Sodium hydroxide was not genotoxic in in vivo mice studies at up to 0.015M.

Magnesium hydroxide was not irritating or corrosive in in vitro tests; however, potassium hydroxide and sodium hydroxide were corrosive at concentrations as low as 5%. Calcium hydroxide was irritating but not corrosive in dermal rabbit studies. Potassium hydroxide was irritating and/or corrosive in rabbit and guinea pig studies at concentrations of 2% or greater. Sodium hydroxide was irritating and/or corrosive in a concentration dependent manner in rat, rabbit, and pig

studies. In humans, sodium hydroxide was irritating at concentrations as low as 0.5%. Because of the large number of studies that include sodium hydroxide as a positive control, only a sampling has been presented in this safety assessment.

Calcium hydroxide was irritating in HET-CAM in vitro tests while magnesium hydroxide was not irritating in a bovine corneal opacity and permeability BCOP in vitro test. In rabbit studies, calcium hydroxide was severely irritating at a concentration of 10% and pH of 9. Potassium hydroxide and sodium hydroxide were severely irritating and/or corrosive in a concentration-dependent manner. Magnesium hydroxide was not irritating in a rabbit study.

Potassium hydroxide (0.1%) was not sensitizing in a guinea pig study while magnesium hydroxide in propylene glycol was sensitizing in an LLNA when tested at up to 50%. In an HRIPT, sodium hydroxide was not sensitizing when induced at up to 1.0% and challenged at 0.125%, but irritation was observed.

No relevant case reports were discovered in the published literature regarding exposure to inorganic hydroxides in cosmetic products; however numerous cases of accidental occupational or industrial exposures were reported.

DISCUSSION

To be determined…

CONCLUSION

To be determined…

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TABLES

Table 1. Definitions, structures, and functions of the ingredients in this safety assessment.[1]

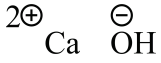
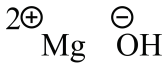
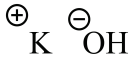
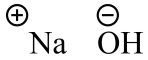
Ingredient/CAS No.	Definition & Structure	Function
Calcium Hydroxide 1305-62-0	Calcium Hydroxide is the inorganic base that conforms to the formula 	pH adjuster
Magnesium Hydroxide 1309-42-8	Magnesium Hydroxide is an inorganic base that conforms to the formula 	absorbent; pH adjuster
Potassium Hydroxide 1310-58-3	Potassium Hydroxide is the inorganic base that conforms to the formula 	pH adjuster
Sodium Hydroxide 1310-73-2	Sodium Hydroxide is the inorganic base that conforms to the formula 	denaturant; pH adjuster

Table 2. Physical and chemical properties of inorganic hydroxides

Property	Value	Reference
Calcium Hydroxide		
Physical form	crystals or soft, odorless granules or powder with a slight bitter or alkaline taste	8
Molecular weight (g/mol)	74.09	8
pK_b	2.4	8
Specific gravity	2.08-2.34	8
Solubility at 25 °C, g/l	1.59	10
Magnesium Hydroxide		
Physical form	bulky white, amorphous powder	8
Molecular weight (g/mol)	58.32	8
Melting point (°C)	350 (decomposes)	40
pK_b	4.0	8
Specific gravity	2.36	40
Solubility at 25 °C, g/l	0.0117	7
Potassium Hydroxide		
Physical form	White or slightly yellow lumps, rods, pellets	8
Molecular weight (g/mol)	56.11	8
Melting point (°C)	360	8
Boiling point (°C)	1327	17
pK_b	0.5	8
Specific gravity	2.044	40
Solubility at 25 °C g/l	1100	17
Sodium Hydroxide		
Physical Form	Brittle, white, translucent crystalline solid	7
Molecular Weight (g/mol)	39.998	7
Melting point (°C)	318	7
Boiling point °C at 760 mm Hg	1388	7
pK_b	0.2	8
Specific gravity at 20 °C	2.13	7
Solubility at 25 °C g/l	1000	10

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Table 3. Impurities acceptance criteria by the *US Pharmacopeia* and *Food Chemicals Codex* [9,10]

Calcium Hydroxide	
Acid-insoluble substances	NMT 0.5%
Arsenic (for 1 g sample)	NMT 3 mg/kg
Carbonate (for 2 g sample)	NMT a slight effervescence observed
Fluoride (for 1 g sample)	NMT 0.005%
Heavy metals (for 2 g sample)	NMT 20 µg/g
Lead (for 1 g sample)	NMT 2 mg/kg
Magnesium and alkali salts (for 500 mg sample)	NMT 4.8%
Magnesium Hydroxide	
Calcium Oxide (for 500 mg sample)	NMT 1%
Carbonate (for 0.1g sample)	NMT a slight effervescence observed
Lead	NMT 2 mg/kg
Heavy metals (for 1 g sample)	NMT 20 µg/g
Potassium Hydroxide	
Carbonate (as K_2CO_3)	NMT 3.5%
Lead (for 1 g sample)	NMT 2 mg/kg
Mercury (for 10 g sample)	NMT 0.1 mg/kg
Sodium Hydroxide	
Arsenic (for 1 g sample)	NMT 3 mg/kg
Carbonate (as Na_2CO_3)	NMT 3.0%
Lead (for 1 g sample)	NMT 2 mg/kg
Mercury (for 10 g sample)	NMT 0.1 mg/kg

NMT = no more than

Table 4. Frequency and concentration of use according to duration and type of exposure for inorganic hydroxide.[11,12]

	# of Uses	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*
	Calcium Hydroxide		**Magnesium Hydroxide**	
Totals†	**99**	**0.1-13.2**	**14**	**1.1-1.6**
Duration of Use				
Leave-On	18	0.11-0.5	4	NR
Rinse Off	81	0.1-13.2	8	1.1-1.6
Diluted for (Bath) Use	NR	NR	2	NR
Exposure Type				
Eye Area	NR	NR	NR	NR
Incidental Ingestion	NR	NR	NR	NR
Incidental Inhalation -Sprays	spray: NR possible: 2[a]; 1[b]	spray: NR possible: 0.18[a]	NR	NR
Incidental Inhalation - Powders	powder: NR possible: 1[b]	NR	powder: 1	NR
Dermal Contact	71	0.1-13.2	7	1.1
Deodorant (underarm)	NR	spray: NR possible: NR not spray: 0.5	NR	NR
Hair - Non-Coloring	28	0.18-6	NR	NR
Hair-Coloring	NR	NR	7	1.6
Nail	NR	NR	NR	NR
Mucous Membrane	NR	NR	2	1.1
Baby Products	NR	NR	NR	NR

	Potassium Hydroxide		**Sodium Hydroxide**	
Totals†	**1074**	**0.0000049-10**	**5147**	**0.0000083-12.9**
Duration of Use				
Leave-On	681	0.0000049-7	2802	0.0000083-10
Rinse Off	387	0.00048-10	2267	0.00002-12.9
Diluted for (Bath) Use	6	0.3-6.4	78	0.00002-0.28
Exposure Type				
Eye Area	61	0.000049-0.5	191	0.0000083-0.86
Incidental Ingestion	4	0.00049-0.005	36	0.00083-0.26
Incidental Inhalation -Sprays	spray: 9 possible: 252[a]; 240[b]	spray: 0.00049-0.69 possible: 0.0045-0.77[a]; 0.3-10[b]	spray: 13 possible: 1284[a]; 745[b]	spray: 0.000025-0.35 possible: 0.0025-0.93[a]; 0.09-2[b]
Incidental Inhalation - Powders	powder: NR possible: 240[b]; 3[c]	powder: 0.0000049 possible: 0.3-10[b]	powder: 2 possible: 745[b]; 16[c]	powder: 0.0000083-0.25 possible: 0.09-2[b]
Dermal Contact	995	0.0000049-10	4310	0.0000083-12.9
Deodorant (underarm)	spray: NR possible: 3[a]	NR	spray: NR: possible: 129[a]	spray: 0.4 possible: NR not spray: 0.01-1.1
Hair - Non-Coloring	60	0.005-0.77	444	0.00002-3
Hair-Coloring	1	0.31	329	0.001-1.7
Nail	10	0.02-1.7	8	0.13-1
Mucous Membrane	102	0.00049-6.4	1253	0.00002-12.9
Baby Products	3	0.19-0.21	47	0.13-0.16

NR = Not reported.

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

[a.] It is possible these products may be sprays, but it is not specified whether the reported uses are sprays.

[b.] Not specified whether a powder or a spray, so this information is captured for both categories of incidental inhalation.

[c.] It is possible these products may be powders, but it is not specified whether the reported uses are powders.

Table 5. Acute toxicity studies

Ingredient	Concentration/Dose	Study Protocol	Results	Reference
		Oral		
calcium hydroxide	details not provided	oral study in mice and rats (no further details provided)	$LD_{50} \geq 7300$ mg/kg bodyweight	[3]
magnesium hydroxide in water	2000 mg/kg	oral gavage (10 ml/kg dose volume) in 3 female Wistar rats	$LD_{50} > 2000$ mg/kg bodyweight	[5]
magnesium hydroxide	details not provided	oral study in rats (no further details provided)	$LD_{50} = 8500$ mg/kg	[41]
potassium hydroxide	details not provided	oral gavage in male Sprague Dawley rats 14 day conventional test (10 animals/dose) or 1 week up-and-down test (1 animal/dose)	$LD_{50} = 333$ mg/kg bodyweight in conventional method, $LD_{50} = 388$ mg/kg bodyweight in up-and-down test	[19]
potassium hydroxide in water	0.1 mg/ml solution with doses increased in log fashion by factor of 2	oral gavage in 5 male/dose Carwoth-Wistar rats	$LD_{50} = 1230$ mg/kg bodyweight	[42]
potassium hydroxide	details not provided	oral gavage in 9 male/dose Charles River albino rats	$LD_{50} = 365$ mg/kg bodyweight	[43]
sodium hydroxide	0.2 N	oral study in rats (no further details provided)	Extensive damage to gastric mucosa observed	[44]
sodium hydroxide	8.3%	oral study in cats (no further details provided)	Superficial layer of squamous mucosa was destroyed; submucosal and transmural thrombosis observed in the blood vessels	[45]
sodium hydroxide	7 ml of 0.5 N	oral gavage in 26 Wistar rats (no further details provided)	Entire gastric mucosa fell off; intestinal metaplasia in 18/26 rats	[46]
sodium hydroxide in water	0.4%, 0.5%, or 0.62% corresponding to 20, 25, or 31 mg/kg bodyweight	oral study in male rats (no further details provided)	Increasing concentrations resulted in increasing gastric injury; erosion scores were 10%, 65%, and 70% for 0.4%, 0.5%, and 0.62% NaOH, respectively	[20]
		Dermal		
calcium hydroxide	2.5 g/kg bodyweight	dermal exposure to 5 male and 5 female New Zealand White rabbits; patches semi-occluded; test area 100 cm^2; test site rinsed with water after 24 h	$LD_{50} > 2.5$ g/kg bodyweight	[3]
sodium hydroxide in water	50%	Dermal exposure in groups of 27 54A/He and C57 black mice, test sites were irrigated immediately, or after 30 min, 1 h, 2 h, or not at all (no further details provided)	Mortality rate of the mice was 0%, 20%, 40%, 80%, and 71% when application sites were irrigated immediately, after 30 min, after 1 h, after 2 h, or not at all	[21]
		Inhalation		
magnesium hydroxide	2.1 mg/l	4-h whole-body inhalation of aerosol in groups of 5 male and female Wistar rats	$LC_{50} > 2.1$ mg/l	[5]
sodium hydroxide	0.75 mg/l	whole body exposure of aerosol for 2 h in 24 male Wistar rats, microscopic examinations performed on cross sections of nose, larynx, trachea with esophagus, and lungs at 1 h and 24 h post-exposure	No mortalities during test; acute laryngitis observed in 11 animals after 1 h and after 24 h; average severity of lesions was 1.58 (very slight) at 1 h and 1.25 (very slight) at 24 h	[22]

Table 6. Genotoxicity studies

Ingredient	Concentration/Dose	Study Protocol	Results	Reference
		In Vitro		
calcium hydroxide	0.3 to 3750 µg/plate	Ames test in *Salmonella typhimurium* strains TA 98, TA100, TA 1535, and TA 1537 and *Escherichia coli* strain WP2 uvr A, with and without metabolic activation	-not mutagenic	[3]
calcium hydroxide in glycerol	30, 100, or 300 mM	-chromosome aberration study, with and without metabolic activation, in human dental pulp cells -test material was incubated with cells in one of 3 scenarios: 30 h continuous treatment with colcemid added 3 h before harvest; 3 h treatment with 27 h recovery and colcemid added 3 h before harvest; or 2 h treatment with a 28 h recovery and colcemid added 3 h before harvest (metabolic activation scenario)	-not genotoxic	[23]
magnesium hydroxide in dimethyl sulfoxide (DMSO)	100 to 5000 µg/plate	Ames test in *S. typhimurium* strains TA 98, TA 100, TA 1535, and TA 1537 and *E. coli* strain WP2 uvr A, with and without metabolic activation	-not mutagenic	[5]
magnesium hydroxide in DMSO	1, 3, 10, or 33 µg/ml	mouse lymphoma L5178Y/TK mutation test, with and without metabolic activation	-not mutagenic -test material precipitated at concentrations greater than 33 µg/ml	[5]
magnesium hydroxide in DMSO	3, 10, or 33 µg/ml	chromosome aberration test in human lymphocytes, with and without metabolic activation	-not clastogenic -test material precipitated at concentrations greater than 33 µg/ml	[5]
potassium hydroxide in distilled water	0.01, 0.05, 0.1, 0.5, or 1 mg/plate	Ames test in *S. typhimurium* strains TA 97 and TA 102, with and without metabolic activation	not genotoxic	[6]
potassium hydroxide in distilled water	0.00945% to 0.019%	Ames test in *E. coli* strains B/Sd-4/3,4 and B/Sd-4/1,3,4,5 without metabolic activation	-ambiguous results (no further details)	[47]
potassium hydroxide	0, 4, 8, 12, 16, or 20 mM	Chinese hamster ovary (CHO) chromosome aberration test, with and without metabolic activation	-ambiguous results: positive with metabolic activation at 12 mM and pH 10.4 but negative without metabolic activation -genotoxic effects due to high non-physiolocial pH that may yield false-positive results	[48]
sodium hydroxide	details not provided	Ames test in *S. typhimurium* strains TA 98, TA 100, TA 1535, TA 1537, TA 1538 (no further details provided)	not genotoxic	[49]
sodium hydroxide	0, 4, 8, or 16 mM with corresponding pH values of 7.4, 9.1, 9.7, or 10.6, respectively	CHO-K1 cell chromosomal aberration test, with and without metabolic activation	not clastogenic	[48]
sodium hydroxide	details not provided	Unscheduled DNA synthesis assay in E. coli strains WP2, WP67, CM871 (no further details provided)	not genotoxic	[49]
sodium hydroxide	details not provided	Unscheduled DNA synthesis assay in E. coli strains WP2, WP2uvrA,WP67, CM611, WP100, W3110polA+, p3478pola-, with and without metabolic activation (no further details provided)	not genotoxic	[50]
		In Vivo		
sodium hydroxide (as a control substance)	10 mg/kg of 15 mM	Chromosome aberration bone marrow micronucleus assay in 5 male and 5 female CD- mice via a single intraperitoneal dose	-no significant increase of nuclei was observed	[51]
sodium hydroxide (as a control substance)	0.3-0.4 ml of 0.01 M	Aneuploidy induction study in female Swiss mice oocytes; mice injected intraperitoneally and chromosome spreads were made 12 h after injection (no further details provided)	-no non-disjunction observed	[52]

Table 7. Dermal irritation studies

Ingredient	Concentration/	Study Protocol	Results	Reference
		In Vitro		
magnesium hydroxide	details not provided	Human three dimensional epidermal model using 10 mg test material moistened with 25 µl purified water	Not irritating	[5]
magnesium hydroxide	details not provided	Human three dimensional epidermal model using 25 mg test material moistened with 25 µl purified water	Not corrosive	[5]
potassium hydroxide	10%	Epiderm and Skin^{2}ZS1301 in vitro models (validation study)	Corrosive	[53]
potassium hydroxide	5% and 10%	In vitro skin corrosion – transcutaneous electrical resistance test (TER) (validation study)	Corrosive at both concentrations tested	[54]
potassium hydroxide	5% and 10%	Skin^{2}ZK1350 in vitro model (validation study)	Corrosive at 10%, non-corrosive at 5%	[54]
potassium hydroxide	5%	Leiden human reconstructed epidermal in vitro model (validation study)	Corrosive and irritant	[55]
potassium hydroxide	5% and 10%	In vitro membrane barrier test method (validation study)	Corrosive at both concentrations tested	[54]
potassium hydroxide	5%	SkinEthic in vitro model	Irritant	[56]
potassium hydroxide	5% and 10%	Episkin model (validation study)	Corrosive at both concentrations tested	[54]
potassium hydroxide	10%	SkinEthic reconstituted human epidermal model (validation study)	Corrosive	[57]
sodium hydroxide in water	4.9%	Skin^{2}ZK1350 in vitro model	Corrosive	[58]
sodium hydroxide in water	16% and 24%	-irritation study in Yorkshire weanling pigs skin flaps -test area was 5 cm^2 area on the lower abdominal skin -dose volume = 200 µl	Severe necrosis of all epidermal cell layers and dermis, with some lesions extending into the subcutaneous layers. A decrease in glucose utilization and changes in vascular resistance were observed	[59]
sodium hydroxide	1%	-in vitro study using human breast or abdominal tissues -test material (150 µl) applied to the epidermis of at least 6 skin discs for 24 h before rinsing with water -transcutaneous electrical resistance (TER) was measured	Corrosive effects observed (TER was below 11.0 kohms/disc at 7.7)	[26]
		Non-Human In Vivo		
calcium hydroxide	details not provided	-irritation study in 3 Himalayan rabbits -treated skin was cleaned with soap and water immediately after exposure -0.5 g test material applied to shaved skin for 4 h -sites graded immediately and at 1, 24, 48, and 72 h and on days 7 and 4 post-exposure	Irritating but not corrosive	[3]
calcium hydroxide	details not provided	-Draize irritation study in 3 New Zealand White rabbits -0.5 g test material applied to shaved skin and semi-occluded for 4 h -sites graded at 1, 24, 48, and 72 h post-patch removal	Not irritating	[3]
calcium hydroxide	details not provided	-5 male and 5 female New Zealand White rabbits -2500 mg/kg applied via semi-occluded patches on shaved skin for 24 h -treated skin was rinsed with water 24 h after application	Irritating; redness followed by scabbing, was observed at the test site following rinsing	[3]

Table 7. Dermal irritation studies

Ingredient	Concentration/	Study Protocol	Results	Reference
potassium hydroxide	1% and 2%	-Draize irritation study in 6 rabbits -occlusive 1 in^2 patches on clipped skin -0.5 ml applied for 4 h	Not corrosive at 1%, corrosive at 2%	[33]
potassium hydroxide	10%	-irritation study in 6 Hartley guinea pigs -0.5 ml test material on intact and abraded skin for 4 h, patches occluded -sites graded after 4, 24, and 48 h	Corrosive	[60]
potassium hydroxide	5% and 10%	-6 rabbits exposed to 0.2 ml test material in 19 mm diameter Hill Top chamber for 1 or 4 h or 0.5 ml on Webril gauze patches for 4 h -patches occluded -sites graded 30 min, 24, 48, and 72 h after patch removal	Severe irritation at both concentrations tested	[61]
potassium hydroxide	10%	-irritation study in 6 rabbits -0.5 ml test material applied under occlusive patches on abraded and intact skin for 4 h -sites observed after 4, 24, and 48 h	Corrosive	[60]
potassium hydroxide	5%	-modified Draize study in 6 albino rabbits -0.1 ml test material applied to area of 20 mm^2 for 24 h under occlusive patches on abraded and intact skin	Mild irritant on intact skin, extreme irritant on abraded skin	[43]
sodium hydroxide	details not provided	-stepwise screening test for skin irritation in mice (no further details provided)	-minimum concentration for skin irritation was 5% (50 mg/kg) -minimum intradermal test response was 0.25% to 0.3% (1.25-1.5 mg/kg)	[34]
sodium hydroxide	8%	-test material was applied for 1 min with 2 cm diameter filter paper to the abdomens of 20 SD rats -test area was washed with 500 ml distilled water at 1, 10, or 30 min post-exposure -test sites examined at 1-min intervals for up to 90 min	-subcutaneous tissue pH did not recover to pre-experiment values by the 90^{th} min -tissue pH value did not exceed 8.0 (at 1 min) -no difference in effects were observed when washing was at 10 or 30 min	[62]
sodium hydroxide	0.36% and 5%	-test material (0.5 ml) was applied for 4 h to 4 New Zealand White rabbits -semi-occluded patches on clipped dorso-lumbar skin -test sites washed after patch removal -test sites examined 1, 24, 48, 72, and 144 h after patches were removed	-test material was corrosive at 5% when tested in 1 rabbit, scores of 4 for erythema were recorded up to 168 h post-patch removal, edema scores of 1 were recorded at 24 and 48 h -no irritation was observed in 3 rabbits at 0.36%	[4]
sodium hydroxide	4.9% by weight	Irritation study in 3 Vienna White rabbits (1 male, 2 females); patches were occlusive and applied to shaved skin (one intact and one abraded site) for 24 h; sites observed for reactions at 24 and 72 h post-application with last check after 8 days	Moderately irritating with a primary irritation index (PII) score of 5.6; mild necrosis was observed after 24 h and parchment-like/leather-like necrosis was observed after 72 h that was observed after 8 days	[4]
sodium hydroxide	1% w/v aq. solution	Irritation study in 6 New Zealand White rabbits; patches were 2.5 cm^2 and the shaved sites were occluded for 2 h; sites observed for reactions at 1, 24, 48, 72 h and 7 days	Slight skin irritant; very slight erythema in 2 animals at 1 h, well-defined reaction observed in 1 animal and same very slight irritation in 2 other animals at 24 h; very slight irritation observed in 3 animals at 48 and 72 h that persisted in 1 animal until day 7	[4]

Table 7. Dermal irritation studies

Ingredient	Concentration/	Study Protocol	Results	Reference
sodium hydroxide	0.95% by weight	Irritation study in 3 female Vienna White rabbits; patches were occlusive and applied to shaved skin (one intact and one abraded site); sites observed for reactions at 24 and 72 h post-application with last check after 8 days	Mildly irritating with a PII score of 2.7; fully reversible erythema in 2 rabbits with spot-like necrosis observed at 72 h for 2 animals	[4]
sodium hydroxide	5% aqueous	Irritation study in 6 New Zealand White rabbits exposed for 2 h to 0.5 ml test material; test site was 2.5 cm^2, shaved and occluded; sites were scored at 24, 48, and 72 h and on day 7	Skin irritant; Slight dermal irritation observed in 3 animals 1 h post-patch removal; 1 rabbit had caustic burn with "in depth" skin damage and small dermal hemorrhages; 2 rabbits had small dermal hemorrhages with some slight tissue necrosis; similar reaction observed at 24, 48, and 72 h and on day 7; one patch had poor skin contact during the 2 h patching	[4]
sodium hydroxide in water	8%, 16% or 24%	-irritation study in 4 Yorkshire weanling pigs -200 µl on a 5 cm^2 area on the lower abdominal skin for 30 min	-highly irritating at 8% and 16%, corrosive at 24% -gross blisters developed within 15 min of application -8% and 16% produced severe necrosis in all epidermal layers -24% produced numerous and severe blisters with necrosis extending into the subcutaneous tissue	[59]
		Human		
sodium hydroxide	0.5% in aq. solution	-test material (50 µl) used as a positive control and irritation inducer in an efficacy study of skin protective creams in 20 human subjects -test material applied on 18 mm diameter area on 5/13 test sites	-yielded expected irritation as a positive control	[2]
sodium hydroxide	0.5%	Patch test in 30 subjects with 0.2 ml of the test substance on a 25 mm Plain Hill Top Chamber containing a Webril pad for 15 and 30 min, 1, 2, 3, and 4 h.	Irritating to the skin, maximum exposure time was limited to 1 h due to strong level of response	[26]
sodium hydroxide	2% in distilled water	Closed patch test in 12 mm diameter Finn chambers of experimental irritants in 16 subjects; patch was removed after 1h	Visual median score after 24 h and 96 h was 1 out 3 (weak positive reaction), respectively	[27]

Table 7. Dermal irritation studies

Ingredient	Concentration/	Study Protocol	Results	Reference
sodium hydroxide	up to 5% aq.	-patch test in healthy male volunteers of 7 known irritants to determine the optimum concentration to produce mild to moderate reactions in ~75% of individuals tested; -test substance (30 µl/cm^2) applied to the volar area of the forearm with 8 mm Finn chambers; -patches removed after 48 h and reactions assessed 1 h later.	-0% of the subjects had a positive reaction at 1%, 29% of the subjects had a positive reaction at 2%, and 100% of the subjects had a positive reaction at 4%; -at 2%, 4 subjects had +/- reactions; -at 3%, 2 subjects had +/- reactions, 1 subject had 1+ reaction, and 4 subjects had 2+ reaction; -at 5%, 2 subjects had 3+ reaction and 1 subject had 4+ reaction; -the severity of irritant reactions to sodium hydroxide rose sharply with increasing concentration, with considerable pain in some volunteers, that led to removing the patches before 48 h.	[29]
sodium hydroxide	0.5% dissolved in water	-test material was used as a positive control and irritation inducer in an efficacy study of perflurorpolyethers as protective preparations; -7 male and 3 female subjects; -irritant application of 0.05 ml occurred 30 min after pretreatment with protective preparation in 12 mm diameter Finn chambers; -chambers removed after 30 min of exposure and the skin was rubbed dry; -subjects were treated over a 12-day period.	-sodium hydroxide yielded expected irritation as a positive control	[30]
sodium hydroxide	0.5% dissolved in water	-test material was used as a positive control and irritation inducer in an efficacy study of perflurorpolyethers as protective preparations; -7 male and 13 female subjects; -irritant application of 0.05 ml occurred 30 min after pretreatment with protective preparation in 12 mm diameter Finn chambers; -chambers removed after 30 min of exposure and the skin dried; -subjects were treated over a 12-day period.	-sodium hydroxide induced significant irritant reaction from day 1 until the end of the first week, and to a smaller extent from end of week1 to the end of week 2, as indicated by visual score values, transepidermal water loss (TEWL), and chromametry of the control sites.	[25]
sodium hydroxide	2% in sterile water, pH 13.7	-closed patch test of different irritants in 16 volunteers (10 female, 6 male) on both arms using 12 mm diameter Finn chambers; -skin damage was evaluated visually and by polysulfide rubber replica; -sodium hydroxide patch was removed at the most 1 h post-application; -visual assessments of the test sites were performed 24, 48, and 96 h post-application; -skin surface imprints with polysulfide rubber were made.	-at 24 h, reactions were observed in 12 subjects with 3 being scored a 3; -at 48 h, reactions were observed in 9 subjects with 5 being scored a 3; -at 96 h, reactions were observed in 11 subjects with 4 being scored a 3; -in 31% of the imprints, skin damage was observed	[28]

Table 7. Dermal irritation studies

Ingredient	Concentration/	Study Protocol	Results	Reference
sodium hydroxide	1 g/v% in distilled water, pH 12.7	-test of barrier function of the skin following exposure to low concentrations of known irritants; -allergic patch testing in 42 subjects with miscellaneous diseases; -test sites were on unaffected skin of the volar forearm; -test substance (100 µl) was applied for 48 h by 12 mm Finn chambers; -24 h post-exposure, the skin water vapor loss was measured.	-sodium hydroxide was observed to increase skin water vapor loss when compared to unexposed skin ($3.6\ g/m^2\ h \pm 2.0$, $p < 0.05$).	[32]
sodium hydroxide	0.5 mol/l	-19 subjects received two 30 min exposures/day with a 3-h interval for 4 days -50 µl test material via occlusive (Finn Chambers or Scanpor 12 mm diameter discs) and non-occlusive patches -test sites were rinsed with 10 ml of tap water and dried after the 30 min applications	-highly irritating -application of test material was discontinued after the 3rd day because of the severity of the reactions -increased in TEWL values observed at day 3 -visual scores showed highly significant irritation	[31]

Table 8. Ocular irritation studies

Ingredient	Concentration	Study Protocol	Results	Reference
		Non-Human – In Vitro		
calcium hydroxide	50 mg, no further details provided	-HET-CAM in vitro test	-irritating	[3]
calcium hydroxide	250 mg, no further details provided	-HET-CAM in vitro test	-irritating	[3]
magnesium hydroxide in physiological saline	details not provided	-BCOP in vitro test	-not irritating -irritancy score was 501 after 240 min of treatment	[5]
		Non-Human – In Vivo		
calcium hydroxide	150g/l	-acute eye irritation/corrosion study in 3 male New Zealand White rabbits -0.1 ml instilled into the conjunctival sac of one eye, eye was not rinsed -observations made at 1, 24, 48, and 72 h after treatment up to 21 days	-irritating	[3]
calcium hydroxide	10%, pH 9	-acute eye irritation/corrosion study in 1 male New Zealand White rabbit -100 mg instilled into the conjunctival sac -eyes examine after 1 h	-irritating -very severe reactions were observed 1 h after exposure, with pronounced chemosis, necrotized appearance of the conjunctiva, whitish watering and total opacity of the cornea, showing nacreous appearance -iris became totally obscured -test was discontinued after treatment with 1 rabbit for humanitarian reasons.	[3]
calcium hydroxide	0.01, 0.03, or 0.10 g, no further details provided	-acute eye irritation/corrosion study in New Zealand White rabbits -9 rabbits received low dose, 6 rabbits each received medium and high doses -test material applied directly to the cornea of one eye of each rabbit -observations made a 1, 3, 7, 14, and 21 days after treatment	-irritating -study halted at 14 days for the medium and high dose groups due to severe eye irritation -expected return to normalcy in the eye of the low dose group was greater than 21 days.	[35]
magnesium hydroxide	details not provided	-acute eye irritation/corrosion study in 3 male New Zealand White rabbits -rabbits received an average instillation of 57.3 mg (dose volume 0.1 ml) of the test substance in the conjunctival sac of one eye, eye was not rinsed -observations made at 1, 24, 48, and 72 h after instillation	-not irritating -slight dulling of normal luster and/or epithelial damage in 2 rabbits resolved within 24 or 48 h -iridial irritation grade 1 observed in all rabbits resolved within 24h -irritation of the conjunctivae consisting of redness, chemosis, and discharge in all rabbits resolved within 72 h	[5]
potassium hydroxide in water	0.1%, 0.5%, 1%, 5%	- acute eye irritation/corrosion study in 10 albino rabbit eye -0.1 ml instilled for 5 min or 24 h, with observations performed at 1, 24, 48, and 72 h and 7 days -eyes rinsed following exposure	-highly corrosive at 5% for 5 min (1 rabbit) -irritant at1% for 5 min (3 rabbits) -marginal irritant at 0.5% for 24 h (3 rabbits) -no ocular reactions at 0.1% for 24 h (3 rabbits)	[43]
sodium hydroxide in water	1.0% or 2.0%	- acute eye irritation/corrosion study in 6 New Zealand White rabbits -0.1 ml instilled into lower conjunctival sac -observations made a 4, 24, 48, 72, and 96 h	-2% caused moderate corneal injury (score = 2.0 out of 4); severe conjunctival irritation was observed between 4 and 96 h -lesser effects were observed with the 1% solution (no further details provided)	[36]

Table 8. Ocular irritation studies

Ingredient	Concentration	Study Protocol	Results	Reference
sodium hydroxide in water	0.5% or 10%	- acute eye irritation/corrosion study in New Zealand White rabbits -3 groups of 3 rabbits for 0.5%; 4 groups of 3 rabbits for 10% -0.5% groups received 0.01, 0.03, or 0.1 ml -10% groups received 0.003, 0.01, 0.05 ml, or 0.1 ml -observations made at 1 h and 1, 2, 3, 4, 7, 14, and 21 days -eyes were not washed	-slight eye irritant at 0.5%, corrosive at 10% -at 0.5%, no corneal effects at 0.01-0.1 ml; grade 1 iridial effects observed in 2/3 animals that cleared by day 1 at 0.1ml -at 10%, irreversible effects on the eye at 0.05 and 0.1 ml	[4]
sodium hydroxide	details not provided	-eye irritation study in rats (no details provided)	-eye irritation observed at a concentration of 1.25%	[34]
sodium hydroxide in distilled water	0.004% (0.001 M) , 0.04% (0.01 M), 0.2% (0.05 M), 0.4% (0.1M), 1.2% (0.3 M)	- acute eye irritation/corrosion study in a minimum of 7 Stauffland albino rabbits -0.1 ml instilled into the lower conjunctival sac -observations made 1, 2, 3, 4, 7 days, then every 3-4 days up to 21 days post-treatment	-non-irritating at 0.004%-0.2% -mild irritation at 0.4% -corrosive at 1.2%	[37]
sodium hydroxide in water	0.1%, 0.3%, 1.0%, or 3.0% corresponding to pH values of 12.3, 12.8, 13.1, or 13.5	- acute eye irritation/corrosion study in New Zealand albino rabbits -2 groups of 6 rabbits; eyes were washed 30 sec after exposure for 2 min with 300 ml tap water and eyes were unwashed after exposure in the second -0.1 ml instilled into conjunctival sac -observations made 1 h and 1, 2, 3, and 7 days post-treatment	-conjunctivitis observed at 1.0% and 3.0% that lasted through day 7 -duration of corneal opacities produced by 1.0% reduced as a result of washing test eyes 30 s after instillation	[38]

Table 9. Sensitization studies

Ingredient	Concentration	Study Protocol	Results	Reference
		Non-Human		
potassium hydroxide in water	0.1%	Intracutaneous repeat insult test in 5 male albino guinea pigs	not sensitizing	[43]
magnesium hydroxide in propylene glycol	0%, 10%, 25%, or 50%	Local lymph node assay (LLNA) in groups of 5 female CBA/J mice	-sensitizing -SI values for 10%, 25%, and 50% were 2.0, 3.6, and 5.9, respectively -EC_3 value calculated to be 19.4% -very slight erythema was observed in all animals treated at 50%	[5]
		Human		
sodium hydroxide	induction 0.63% to 1.0%; challenge 0.125%	modified HRIPT in 15 male subjects	-not sensitizing -irritation response well correlated with the concentration of the irritant	[63]

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2015 FDA VCRP Raw Data		
AMMONIUM HYDROXIDE	03B - Eyeliner	18
AMMONIUM HYDROXIDE	03F - Mascara	17
AMMONIUM HYDROXIDE	03G - Other Eye Makeup Preparations	3
AMMONIUM HYDROXIDE	05A - Hair Conditioner	7
AMMONIUM HYDROXIDE	05C - Hair Straighteners	7
AMMONIUM HYDROXIDE	05D - Permanent Waves	28
AMMONIUM HYDROXIDE	05F - Shampoos (non-coloring)	11
AMMONIUM HYDROXIDE	05G - Tonics, Dressings, and Other Hair Grooming Aids	2
AMMONIUM HYDROXIDE	05I - Other Hair Preparations	3
AMMONIUM HYDROXIDE	06A - Hair Dyes and Colors (all types requiring caution statements and patch tests)	899
AMMONIUM HYDROXIDE	06B - Hair Tints	1
AMMONIUM HYDROXIDE	06F - Hair Lighteners with Color	5
AMMONIUM HYDROXIDE	06G - Hair Bleaches	8
AMMONIUM HYDROXIDE	06H - Other Hair Coloring Preparation	17
AMMONIUM HYDROXIDE	07C - Foundations	1
AMMONIUM HYDROXIDE	07I - Other Makeup Preparations	1
AMMONIUM HYDROXIDE	08E - Nail Polish and Enamel	1
AMMONIUM HYDROXIDE	08G - Other Manicuring Preparations	1
AMMONIUM HYDROXIDE	12A - Cleansing	15
AMMONIUM HYDROXIDE	12B - Depilatories	1
AMMONIUM HYDROXIDE	12C - Face and Neck (exc shave)	33
AMMONIUM HYDROXIDE	12D - Body and Hand (exc shave)	10
AMMONIUM HYDROXIDE	12F - Moisturizing	10
AMMONIUM HYDROXIDE	12G - Night	13
AMMONIUM HYDROXIDE	12H - Paste Masks (mud packs)	1
AMMONIUM HYDROXIDE	12I - Skin Fresheners	3
AMMONIUM HYDROXIDE	12J - Other Skin Care Preps	13
AMMONIUM HYDROXIDE	13A - Suntan Gels, Creams, and Liquids	1
CALCIUM HYDROXIDE	05C - Hair Straighteners	27
CALCIUM HYDROXIDE	05G - Tonics, Dressings, and Other Hair Grooming Aids	1
CALCIUM HYDROXIDE	07C - Foundations	13
CALCIUM HYDROXIDE	11B - Beard Softeners	1
CALCIUM HYDROXIDE	11G - Other Shaving Preparation Products	6
CALCIUM HYDROXIDE	12A - Cleansing	6
CALCIUM HYDROXIDE	12B - Depilatories	42
CALCIUM HYDROXIDE	12D - Body and Hand (exc shave)	1
CALCIUM HYDROXIDE	12I - Skin Fresheners	1
CALCIUM HYDROXIDE	12J - Other Skin Care Preps	1
MAGNESIUM HYDROXIDE	02A - Bath Oils, Tablets, and Salts	2
MAGNESIUM HYDROXIDE	06A - Hair Dyes and Colors (all types requiring caution statements and patch tests)	1

MAGNESIUM HYDROXIDE	06G - Hair Bleaches	6
MAGNESIUM HYDROXIDE	07B - Face Powders	1
MAGNESIUM HYDROXIDE	07C - Foundations	2
MAGNESIUM HYDROXIDE	12H - Paste Masks (mud packs)	1
MAGNESIUM HYDROXIDE	12J - Other Skin Care Preps	1
POTASSIUM HYDROXIDE	01B - Baby Lotions, Oils, Powders, and Creams	3
POTASSIUM HYDROXIDE	02B - Bubble Baths	3
POTASSIUM HYDROXIDE	02D - Other Bath Preparations	3
POTASSIUM HYDROXIDE	03B - Eyeliner	1
POTASSIUM HYDROXIDE	03C - Eye Shadow	5
POTASSIUM HYDROXIDE	03D - Eye Lotion	34
POTASSIUM HYDROXIDE	03E - Eye Makeup Remover	4
POTASSIUM HYDROXIDE	03F - Mascara	4
POTASSIUM HYDROXIDE	03G - Other Eye Makeup Preparations	13
POTASSIUM HYDROXIDE	04E - Other Fragrance Preparation	2
POTASSIUM HYDROXIDE	05A - Hair Conditioner	10
POTASSIUM HYDROXIDE	05B - Hair Spray (aerosol fixatives)	7
POTASSIUM HYDROXIDE	05F - Shampoos (non-coloring)	18
POTASSIUM HYDROXIDE	05G - Tonics, Dressings, and Other Hair Grooming Aids	5
POTASSIUM HYDROXIDE	05H - Wave Sets	7
POTASSIUM HYDROXIDE	05I - Other Hair Preparations	13
POTASSIUM HYDROXIDE	06H - Other Hair Coloring Preparation	1
POTASSIUM HYDROXIDE	07C - Foundations	1
POTASSIUM HYDROXIDE	07D - Leg and Body Paints	2
POTASSIUM HYDROXIDE	07E - Lipstick	2
POTASSIUM HYDROXIDE	07F - Makeup Bases	4
POTASSIUM HYDROXIDE	07I - Other Makeup Preparations	3
POTASSIUM HYDROXIDE	08B - Cuticle Softeners	7
POTASSIUM HYDROXIDE	08G - Other Manicuring Preparations	3
POTASSIUM HYDROXIDE	09A - Dentifrices	1
POTASSIUM HYDROXIDE	09C - Other Oral Hygiene Products	1
POTASSIUM HYDROXIDE	10A - Bath Soaps and Detergents	51
POTASSIUM HYDROXIDE	10B - Deodorants (underarm)	3
POTASSIUM HYDROXIDE	10E - Other Personal Cleanliness Products	41
POTASSIUM HYDROXIDE	11A - Aftershave Lotion	11
POTASSIUM HYDROXIDE	11D - Preshave Lotions (all types)	1
POTASSIUM HYDROXIDE	11E - Shaving Cream	43
POTASSIUM HYDROXIDE	11F - Shaving Soap	1
POTASSIUM HYDROXIDE	11G - Other Shaving Preparation Products	2
POTASSIUM HYDROXIDE	12A - Cleansing	168
POTASSIUM HYDROXIDE	12B - Depilatories	20
POTASSIUM HYDROXIDE	12C - Face and Neck (exc shave)	111
POTASSIUM HYDROXIDE	12D - Body and Hand (exc shave)	129
POTASSIUM HYDROXIDE	12F - Moisturizing	214
POTASSIUM HYDROXIDE	12G - Night	23
POTASSIUM HYDROXIDE	12H - Paste Masks (mud packs)	19
POTASSIUM HYDROXIDE	12I - Skin Fresheners	7

POTASSIUM HYDROXIDE	12J - Other Skin Care Preps	71
POTASSIUM HYDROXIDE	13A - Suntan Gels, Creams, and Liquids	2
POTASSIUM HYDROXIDE	13B - Indoor Tanning Preparations	1
SODIUM HYDROXIDE	01A - Baby Shampoos	6
SODIUM HYDROXIDE	01B - Baby Lotions, Oils, Powders, and Creams	16
SODIUM HYDROXIDE	01C - Other Baby Products	25
SODIUM HYDROXIDE	02A - Bath Oils, Tablets, and Salts	1
SODIUM HYDROXIDE	02B - Bubble Baths	64
SODIUM HYDROXIDE	02D - Other Bath Preparations	13
SODIUM HYDROXIDE	03A - Eyebrow Pencil	1
SODIUM HYDROXIDE	03B - Eyeliner	14
SODIUM HYDROXIDE	03C - Eye Shadow	2
SODIUM HYDROXIDE	03D - Eye Lotion	80
SODIUM HYDROXIDE	03E - Eye Makeup Remover	16
SODIUM HYDROXIDE	03F - Mascara	18
SODIUM HYDROXIDE	03G - Other Eye Makeup Preparations	60
SODIUM HYDROXIDE	04A - Cologne and Toilet waters	3
SODIUM HYDROXIDE	04B - Perfumes	4
SODIUM HYDROXIDE	04E - Other Fragrance Preparation	4
SODIUM HYDROXIDE	05A - Hair Conditioner	83
SODIUM HYDROXIDE	05B - Hair Spray (aerosol fixatives)	2
SODIUM HYDROXIDE	05C - Hair Straighteners	31
SODIUM HYDROXIDE	05D - Permanent Waves	1
SODIUM HYDROXIDE	05E - Rinses (non-coloring)	2
SODIUM HYDROXIDE	05F - Shampoos (non-coloring)	224
SODIUM HYDROXIDE	05G - Tonics, Dressings, and Other Hair Grooming Aids	55
SODIUM HYDROXIDE	05H - Wave Sets	4
SODIUM HYDROXIDE	05I - Other Hair Preparations	36
SODIUM HYDROXIDE	06A - Hair Dyes and Colors (all types requiring caution statements and patch tests)	320
SODIUM HYDROXIDE	06D - Hair Shampoos (coloring)	3
SODIUM HYDROXIDE	06H - Other Hair Coloring Preparation	6
SODIUM HYDROXIDE	07A - Blushers (all types)	1
SODIUM HYDROXIDE	07B - Face Powders	2
SODIUM HYDROXIDE	07C - Foundations	9
SODIUM HYDROXIDE	07D - Leg and Body Paints	3
SODIUM HYDROXIDE	07F - Makeup Bases	12
SODIUM HYDROXIDE	07H - Makeup Fixatives	1
SODIUM HYDROXIDE	07I - Other Makeup Preparations	26
SODIUM HYDROXIDE	08B - Cuticle Softeners	8
SODIUM HYDROXIDE	09A - Dentifrices	3
SODIUM HYDROXIDE	09C - Other Oral Hygiene Products	33
SODIUM HYDROXIDE	10A - Bath Soaps and Detergents	860
SODIUM HYDROXIDE	10B - Deodorants (underarm)	129
SODIUM HYDROXIDE	10C - Douches	2
SODIUM HYDROXIDE	10E - Other Personal Cleanliness Products	277
SODIUM HYDROXIDE	11A - Aftershave Lotion	112

SODIUM HYDROXIDE	11D - Preshave Lotions (all types)	2
SODIUM HYDROXIDE	11E - Shaving Cream	28
SODIUM HYDROXIDE	11F - Shaving Soap	1
SODIUM HYDROXIDE	11G - Other Shaving Preparation Products	14
SODIUM HYDROXIDE	12A - Cleansing	296
SODIUM HYDROXIDE	12B - Depilatories	16
SODIUM HYDROXIDE	12C - Face and Neck (exc shave)	365
SODIUM HYDROXIDE	12D - Body and Hand (exc shave)	378
SODIUM HYDROXIDE	12E - Foot Powders and Sprays	2
SODIUM HYDROXIDE	12F - Moisturizing	1078
SODIUM HYDROXIDE	12G - Night	101
SODIUM HYDROXIDE	12H - Paste Masks (mud packs)	39
SODIUM HYDROXIDE	12I - Skin Fresheners	14
SODIUM HYDROXIDE	12J - Other Skin Care Preps	205
SODIUM HYDROXIDE	13A - Suntan Gels, Creams, and Liquids	8
SODIUM HYDROXIDE	13B - Indoor Tanning Preparations	15
SODIUM HYDROXIDE	13C - Other Suntan Preparations	13

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Personal Care Products Council
Committed to Safety, Quality & Innovation

TO: Lillian Gill, D.P.A.
Director - COSMETIC INGREDIENT REVIEW (CIR)

FROM: Halyna Breslawec, Ph.D.
Industry Liaison to the CIR Expert Panel

DATE: April 18, 2014

SUBJECT: Concentration of Use Information for Sodium Hydroxide and other Hydroxides

Concentration of Use by FDA Product Category

Sodium Hydroxide
Potassium Hydroxide
Ammonium Hydroxide
Calcium Hydroxide
Lithium Hydroxide
Magnesium Hydroxide

Ingredient	Product Category	Maximum Concentration of Use
Sodium Hydroxide	Baby Shampoos	0.16%
Sodium Hydroxide	Baby lotions, oils and creams not powder	 0.13%
Sodium Hydroxide	Other baby products	0.16% (rinse-off)
Sodium Hydroxide	Bath oils, tablets and salts	0.00002%
Sodium Hydroxide	Bubble baths	0.087-0.12%
Sodium Hydroxide	Other bath preparations	0.28%
Sodium Hydroxide	Eyebrow pencils	0.000083-0.48%
Sodium Hydroxide	Eyeliners	0.0000083-0.1%
Sodium Hydroxide	Eye shadow	0.000083-0.4%
Sodium Hydroxide	Eye lotion	0.018-0.86%
Sodium Hydroxide	Eye makeup remover	0.01%
Sodium Hydroxide	Mascaras	0.0000083-0.28%
Sodium Hydroxide	Other eye makeup preparations	0.02-0.3%
Sodium Hydroxide	Perfumes	0.0001-0.00083%
Sodium Hydroxide	Other fragrance preparations	0.21-0.35% (0.35% is a rinse-off product)
Sodium Hydroxide	Hair conditioners	0.00002-0.9%
Sodium Hydroxide	Hair sprays aerosol pump spray	 0.16-0.19% 0.00005-0.3%
Sodium Hydroxide	Hair straighteners	2.4-3%
Sodium Hydroxide	Permanent waves	0.64%
Sodium Hydroxide	Rinses (noncoloring)	0.09%
Sodium Hydroxide	Shampoos (noncoloring)	0.0001-1.6%
Sodium Hydroxide	Tonics, dressings and other hair grooming aids	0.03-0.93%
Sodium Hydroxide	Other hair preparations (noncoloring)	0.25-0.29%
Sodium Hydroxide	Hair dyes and colors	0.32-1.7%
Sodium Hydroxide	Hair shampoos (coloring)	0.001-0.06%
Sodium Hydroxide	Hair color sprays	0.003%
Sodium Hydroxide	Hair bleaches	0.04-0.31%
Sodium Hydroxide	Other hair coloring preparations	0.06-0.21%
Sodium Hydroxide	Face powders	0.0000083-0.25%
Sodium Hydroxide	Foundations	0.00083-0.53%
Sodium Hydroxide	Leg and body paints	0.03%
Sodium Hydroxide	Lipstick	0.00083-0.26%
Sodium Hydroxide	Makeup bases	0.00065-0.2%
Sodium Hydroxide	Rouges	0.042%
Sodium Hydroxide	Makeup fixatives	0.4-0.6%

Sodium Hydroxide	Other makeup preparations	0.03%
Sodium Hydroxide	Basecoats and undercoats	0.13%
Sodium Hydroxide	Cuticle softeners	1%
Sodium Hydroxide	Nail polish and enamel	0.17%
Sodium Hydroxide	Other manicuring preparations	0.3% (rinse-off)
Sodium Hydroxide	Bath soaps and detergents	0.04-12.9%
Sodium Hydroxide	Deodorants (underarm) not spray pump spray	 0.01-1.1% 0.4%
Sodium Hydroxide	Feminine hygiene deodorants	0.13%
Sodium Hydroxide	Other personal cleanliness products	0.06-0.41%
Sodium Hydroxide	Aftershave lotions	0.046-0.43%
Sodium Hydroxide	Preshave lotions	0.23%
Sodium Hydroxide	Shaving cream	0.00081-1.1%
Sodium Hydroxide	Other shaving preparations	0.25% (rinse-off)
Sodium Hydroxide	Skin cleansing	0.13-8.5%
Sodium Hydroxide	Depilatories	0.5-3%
Sodium Hydroxide	Face and neck products not spray spray	 0.051-6.9% 0.05%
Sodium Hydroxide	Body and hand products not spray spray	 0.037-2% 0.000025-0.057%
Sodium Hydroxide	Foot products	0.09-2%
Sodium Hydroxide	Moisturizing products not spray spray	 0.00017-1.4% 0.015%
Sodium Hydroxide	Night products not spray	 0.063-3.2%
Sodium Hydroxide	Paste masks and mud packs	0.25-1.2%
Sodium Hydroxide	Skin fresheners	0.0025-0.43%
Sodium Hydroxide	Other skin care preparations	0.13-10%
Sodium Hydroxide	Suntan products not spray aerosol	 0.14-0.3% 0.025%
Sodium Hydroxide	Indoor tanning preparations	0.009-0.25%
Sodium Hydroxide	Other suntan preparations	0.012-0.38%
Potassium Hydroxide	Baby lotions, oils and creams not powders	 0.21%
Potassium Hydroxide	Other baby products	0.19% (leave-on)
Potassium Hydroxide	Bubble baths	2.3%
Potassium Hydroxide	Other bath preparations	0.3-6.4%
Potassium Hydroxide	Eyebrow pencils	0.000049-0.5%
Potassium Hydroxide	Eyeliners	0.077%
Potassium Hydroxide	Eye shadow	0.000049-0.045%
Potassium Hydroxide	Eye lotions	0.28-0.36%

Potassium Hydroxide	Eye makeup removers	0.077%
Potassium Hydroxide	Mascara	0.008-0.5%
Potassium Hydroxide	Colognes and toilet waters	0.18%
Potassium Hydroxide	Perfumes	0.00049%
Potassium Hydroxide	Other fragrance preparations	0.15% (rinse-off)
Potassium Hydroxide	Hair conditioners	0.023-0.45%
Potassium Hydroxide	Hair sprays aerosol pump spray	 0.36-0.69% 0.02-0.41%
Potassium Hydroxide	Rinses (noncoloring)	0.005%
Potassium Hydroxide	Shampoos (noncoloring)	0.02-0.43%
Potassium Hydroxide	Tonics, dressings and other hair grooming aids	0.01-0.77%
Potassium Hydroxide	Other hair preparations (noncoloring)	0.18%
Potassium Hydroxide	Hair dyes and colors	0.31%
Potassium Hydroxide	Blushers (all types)	0.0005%
Potassium Hydroxide	Face powders	0.0000049%
Potassium Hydroxide	Foundations	0.063-0.12%
Potassium Hydroxide	Lipstick	0.00049-0.005%
Potassium Hydroxide	Makeup bases	0.038-0.38%
Potassium Hydroxide	Other makeup preparations	0.13%
Potassium Hydroxide	Cuticle softeners	1-1.7%
Potassium Hydroxide	Nail creams and lotions	0.02-0.38%
Potassium Hydroxide	Other manicuring preparations	0.1% (rinse-off)
Potassium Hydroxide	Bath soaps and detergents	3.9-5.1%
Potassium Hydroxide	Feminine hygiene deodorants	0.3%
Potassium Hydroxide	Other personal cleanliness products	0.15%
Potassium Hydroxide	Aftershave lotions	0.12-0.23%
Potassium Hydroxide	Shaving cream	0.00048-7.2%
Potassium Hydroxide	Other shaving preparations	0.32%
Potassium Hydroxide	Skin cleansing	0.2-7.2%
Potassium Hydroxide	Depilatories	0.25-4.9%
Potassium Hydroxide	Face and neck products not spray	 0.015-5.1%
Potassium Hydroxide	Body and hand products not spray	 0.15-7%
Potassium Hydroxide	Foot products	0.3% 10% (rinse-off)
Potassium Hydroxide	Moisturizing products not spray	 0.021-0.53%
Potassium Hydroxide	Night products not spray	 0.53-0.57%
Potassium Hydroxide	Paste masks and mud packs	0.079-0.5%
Potassium Hydroxide	Skin fresheners	0.75%
Potassium Hydroxide	Other skin care preparations	0.08-2.9%
Potassium Hydroxide	Suntan products	

	not spray	0.15%
Potassium Hydroxide	Indoor tanning products	0.0045%
Ammonium Hydroxide	Eyebrow pencils	0.58%
Ammonium Hydroxide	Eyeliners	0.0036-2.3%
Ammonium Hydroxide	Eye lotion	0.57%
Ammonium Hydroxide	Mascara	0.032-0.9%
Ammonium Hydroxide	Other eye makeup preparations	0.0041-0.05%
Ammonium Hydroxide	Other fragrance preparations	0.56% (leave-on)
Ammonium Hydroxide	Hair conditioners	0.34%
Ammonium Hydroxide	Hair sprays aerosol pump spray	 0.01% 0.15%
Ammonium Hydroxide	Hair straighteners	1-2.9%
Ammonium Hydroxide	Permanent waves	6.1%
Ammonium Hydroxide	Shampoos (noncoloring)	1.32%
Ammonium Hydroxide	Tonics, dressings and other hair grooming aids	0.23-1.5%
Ammonium Hydroxide	Other hair preparations (noncoloring)	0.34% (rinse-off)
Ammonium Hydroxide	Hair dyes and colors	2.5-10.4%
Ammonium Hydroxide	Hair lighteners with color	4.1%
Ammonium Hydroxide	Hair bleaches	3.5%
Ammonium Hydroxide	Foundations	0.0000082-0.6%
Ammonium Hydroxide	Cuticle softeners	0.07%
Ammonium Hydroxide	Other manicuring preparations	0.0021% (leave-on)
Ammonium Hydroxide	Aftershave lotions	0.57%
Ammonium Hydroxide	Shaving cream	0.28%
Ammonium Hydroxide	Skin cleansing	0.3%
Ammonium Hydroxide	Face and neck products not spray	 0.0021-1.5%
Ammonium Hydroxide	Body and hand products not spray	 1.5%
Ammonium Hydroxide	Foot products	0.63%
Ammonium Hydroxide	Moisturizing products not spray	 0.000056%
Ammonium Hydroxide	Night products not spray	 0.56%
Ammonium Hydroxide	Paste masks and mud packs	1.7%
Ammonium Hydroxide	Skin fresheners	0.3%
Ammonium Hydroxide	Other skin care preparations	1-1.5%
Ammonium Hydroxide	Suntan products not spray	 0.00038%
Calcium Hydroxide	Hair straighteners	5.1-6%
Calcium Hydroxide	Permanent waves	5.5%
Calcium Hydroxide	Tonics, dressings and other hair grooming aids	0.18%
Calcium Hydroxide	Foundations	0.11%

Calcium Hydroxide	Deodorants not spray	 0.5%
Calcium Hydroxide	Other shaving preparations	13.2%
Calcium Hydroxide	Skin cleansing	0.1%
Calcium Hydroxide	Depilatories	3.6-7.5%
Lithium Hydroxide	Hair straighteners	1.5-3%
Magnesium Hydroxide	Hair bleaches	1.6%
Magnesium Hydroxide	Bath soaps and detergents	1.1%

Information collected in 2014
Table prepared April 17, 2014

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Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

TO: Lillian Gill, D.P.A.
Director - COSMETIC INGREDIENT REVIEW (CIR)

FROM: Beth A. Lange, Ph.D.
Industry Liaison to the CIR Expert Panel

DATE: August 5, 2015

SUBJECT: Safety Data Sheet: Magnesium Hydroxide

Dr. Paul Lohmann. 2015. Safety data sheet: Magnesium Hydroxide.

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Dr. Paul Lohmann®

Safety data sheet
according to 1907/2006/EC, Article 31

Printing date 18.05.2015 *Revision: 25.03.2014*

SECTION 1: Identification of the substance/mixture and of the company/undertaking

· **1.1 Product identifier**

· **Trade name: magnesium hydroxide**

· **Article number:** C35
· **CAS Number:**
1309-42-8
· **EC number:**
215-170-3
· **1.2 Relevant identified uses of the substance or mixture and uses advised against**
No further relevant information available.
· **Application of the substance / the mixture**
Pharma Active ingredients
Food additive

· **1.3 Details of the supplier of the safety data sheet**
· **Manufacturer/Supplier:**
Dr. Paul Lohmann GmbH KG
Hauptstraße 2
D-31860 Emmerthal
GERMANY
MSDS@lohmann-chemikalien.de

· **Further information obtainable from:** Product safety department
· **1.4 Emergency telephone number:** During normal opening times: +49 5155 63-0

SECTION 2: Hazards identification

· **2.1 Classification of the substance or mixture**
· **Classification according to Regulation (EC) No 1272/2008**
The substance is not classified according to the CLP regulation.

· **Classification according to Directive 67/548/EEC or Directive 1999/45/EC** Not applicable.
· **Information concerning particular hazards for human and environment:** Not applicable.

· **2.2 Label elements**
· **Labelling according to Regulation (EC) No 1272/2008** Void
· **Hazard pictograms** Void
· **Signal word** Void
· **Hazard statements** Void
· **2.3 Other hazards**
· **Results of PBT and vPvB assessment**
· **PBT:** Not applicable.
· **vPvB:** Not applicable.

SECTION 3: Composition/information on ingredients

· **3.1 Chemical characterisation: Substances**
· **CAS No. Description**
1309-42-8 magnesium hydroxide
· **Identification number(s)**
· **EC number:** 215-170-3

SECTION 4: First aid measures

· **4.1 Description of first aid measures**
· **General information:** No special measures required.
· **After inhalation:** Supply fresh air; consult doctor in case of complaints.
· **After skin contact:** Generally the product does not irritate the skin.

(Contd. on page 2)

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Printing date 18.05.2015 *Revision: 25.03.2014*

Trade name: magnesium hydroxide

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· **After eye contact:**
Rinse opened eye for several minutes under running water. If symptoms persist, consult a doctor.
· **After swallowing:** Seek medical treatment.
· **4.2 Most important symptoms and effects, both acute and delayed** No further relevant information available.
· **4.3 Indication of any immediate medical attention and special treatment needed**
No further relevant information available.

SECTION 5: Firefighting measures

· **5.1 Extinguishing media**
· **Suitable extinguishing agents:** Use fire extinguishing methods suitable to surrounding conditions.
· **5.2 Special hazards arising from the substance or mixture** No further relevant information available.
· **5.3 Advice for firefighters**
· **Protective equipment:** No special measures required.

SECTION 6: Accidental release measures

· **6.1 Personal precautions, protective equipment and emergency procedures** Not required.
· **6.2 Environmental precautions:** Do not allow to enter sewers/ surface or ground water.
· **6.3 Methods and material for containment and cleaning up:** Pick up mechanically.
· **6.4 Reference to other sections** No dangerous substances are released.

SECTION 7: Handling and storage

· **7.1 Precautions for safe handling** Thorough dedusting.
· **Information about fire - and explosion protection:** The product is not flammable.

· **7.2 Conditions for safe storage, including any incompatibilities**
· **Storage:**
· **Requirements to be met by storerooms and receptacles:** No special requirements.
· **Information about storage in one common storage facility:** Not required.
· **Further information about storage conditions:** None.
· **7.3 Specific end use(s)** No further relevant information available.

SECTION 8: Exposure controls/personal protection

· **Additional information about design of technical facilities:** No further data; see item 7.

· **8.1 Control parameters**
· **Ingredients with limit values that require monitoring at the workplace:** Not required.
· **Additional information:** The lists valid during the making were used as basis.

· **8.2 Exposure controls**
· **Personal protective equipment:**
· **General protective and hygienic measures:**
The usual precautionary measures are to be adhered to when handling chemicals.
· **Respiratory protection:** Not required.
· **Protection of hands:**
The glove material has to be impermeable and resistant to the product/ the substance/ the preparation.
Due to missing tests no recommendation to the glove material can be given for the product/ the preparation/ the chemical mixture.
Selection of the glove material on consideration of the penetration times, rates of diffusion and the degradation
· **Material of gloves**
The selection of the suitable gloves does not only depend on the material, but also on further marks of quality and varies from manufacturer to manufacturer.

(Contd. on page 3)

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(Contd. of page 2)

· **Penetration time of glove material**
The exact break through time has to be found out by the manufacturer of the protective gloves and has to be observed.
· **Eye protection:** Safety glasses
· **Body protection:** Protective work clothing

SECTION 9: Physical and chemical properties

· **9.1 Information on basic physical and chemical properties**	
· **General Information**	
· **Appearance:**	
Form:	Powder
Colour:	Whitish
· **Odour:**	Characteristic
· **pH-value (50 g/l) at 20 °C:**	10,5
· **Change in condition**	
Melting point/Melting range:	Undetermined.
Boiling point/Boiling range:	Undetermined.
· **Flash point:**	Not applicable.
· **Flammability (solid, gaseous):**	Product is not flammable.
· **Danger of explosion:**	Product does not present an explosion hazard.
· **Density at 20 °C:**	2,4 g/cm³
· **Solubility in / Miscibility with water:**	Insoluble.
· **9.2 Other information**	No further relevant information available.

SECTION 10: Stability and reactivity

· **10.1 Reactivity**
· **10.2 Chemical stability**
· **Thermal decomposition / conditions to be avoided:** To avoid thermal decomposition do not overheat.
· **10.3 Possibility of hazardous reactions** Reacts with acids.
· **10.4 Conditions to avoid** No further relevant information available.
· **10.5 Incompatible materials:** No further relevant information available.
· **10.6 Hazardous decomposition products:** No dangerous decomposition products known.

SECTION 11: Toxicological information

· **11.1 Information on toxicological effects**
· **Acute toxicity:**

· **LD/LC50 values relevant for classification:**		
Oral	LD50	8500 mg/kg (rat)

· **Primary irritant effect:**
· **on the skin:** No irritant effect.
· **on the eye:** No irritating effect.
· **Sensitisation:** No sensitising effects known.
· **Additional toxicological information:**
When used and handled according to specifications, the product does not have any harmful effects to our experience and the information provided to us.

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(Contd. of page 3)

The substance is not subject to classification according to the latest version of the EU lists.

SECTION 12: Ecological information

· **12.1 Toxicity**
· **Aquatic toxicity:** No further relevant information available.
· **12.2 Persistence and degradability** No further relevant information available.
· **12.3 Bioaccumulative potential** No further relevant information available.
· **12.4 Mobility in soil** No further relevant information available.
· **Additional ecological information:**
· **General notes:**
Water hazard class 1 (German Regulation) (Self-assessment): slightly hazardous for water
Do not allow undiluted product or large quantities of it to reach ground water, water course or sewage system.
· **12.5 Results of PBT and vPvB assessment**
· **PBT:** Not applicable.
· **vPvB:** Not applicable.
· **12.6 Other adverse effects** No further relevant information available.

SECTION 13: Disposal considerations

· **13.1 Waste treatment methods**
· **Recommendation** Smaller quantities can be disposed of with household waste.

· **Uncleaned packaging:**
· **Recommendation:** Disposal must be made according to official regulations.

SECTION 14: Transport information

· **14.1 UN-Number** · **ADR, ADN, IMDG, IATA**	Void
· **14.2 UN proper shipping name** · **ADR, ADN, IMDG, IATA**	Void
· **14.3 Transport hazard class(es)** · **ADR, ADN, IMDG, IATA** · **Class**	Void
· **14.4 Packing group** · **ADR, IMDG, IATA**	Void
· **14.5 Environmental hazards:** · **Marine pollutant:**	No
· **14.6 Special precautions for user**	Not applicable.
· **14.7 Transport in bulk according to Annex II of MARPOL73/78 and the IBC Code**	Not applicable.
· **Transport/Additional information:**	Not dangerous according to the above specifications.
· **UN "Model Regulation":**	-

SECTION 15: Regulatory information

· **15.1 Safety, health and environmental regulations/legislation specific for the substance or mixture**
No further relevant information available.

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Trade name: magnesium hydroxide

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· **15.2 Chemical safety assessment:** Not applicable.

SECTION 16: Other information

This information is based on our present knowledge. However, this shall not constitute a guarantee for any specific product features and shall not establish a legally valid contractual relationship.

· **Department issuing MSDS:** Product safety department
· **Contact:**
· **Abbreviations and acronyms:**
RID: Règlement international concernant le transport des marchandises dangereuses par chemin de fer (Regulations Concerning the International Transport of Dangerous Goods by Rail)
ICAO: International Civil Aviation Organisation
ADR: Accord européen sur le transport des marchandises dangereuses par Route (European Agreement concerning the International Carriage of Dangerous Goods by Road)
IMDG: International Maritime Code for Dangerous Goods
IATA: International Air Transport Association
GHS: Globally Harmonised System of Classification and Labelling of Chemicals
EINECS: European Inventory of Existing Commercial Chemical Substances
CAS: Chemical Abstracts Service (division of the American Chemical Society)
LC50: Lethal concentration, 50 percent
LD50: Lethal dose, 50 percent

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Personal Care Products Council
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Memorandum

TO: Lillian Gill, D.P.A.
Director - COSMETIC INGREDIENT REVIEW (CIR)

FROM: Beth A. Lange, Ph.D.
Industry Liaison to the CIR Expert Panel

DATE: July 21, 2015

SUBJECT: Comments on the Scientific Literature Review: Safety Assessment of Inorganic Hydroxides as Used in Cosmetics

Key Issues

The use of Sodium Hydroxide in soap making should be discussed somewhere in this report. The highest use concentrations reported are in soap. In this application, Sodium Hydroxide reacts with fats to form soap. Perhaps, the FDA's definition of soap versus cosmetics should also be mentioned in this report.

The SIARs on Sodium Hydroxide at http://www.chem.unep.ch/irptc/sids/OECDSIDS/NAHYDROX.pdf and Potassium Hydroxide at http://www.chem.unep.ch/irptc/sids/OECDSIDS/POTASSIUMHYD.pdf provide useful summaries of the toxicity concerns for this compound.

Cosmetic Use, Summary - It is misleading to state that Sodium Hydroxide and Potassium Hydroxide are used at 10% in leave-on products. It is not known for sure if the other skin care product in the Council survey reported to contain 10% Sodium Hydroxide is actually a leave-on product. The only product category with 10% concentration for Potassium Hydroxide is foot care products and the company reporting this product clearly indicated that it was a rinse-off product as noted in the table provided by the Council.

The March 2014 SCCS opinion on Potassium Hydroxide as a callous softener/remover should be mentioned in the cosmetic use section. Please note that the proposed change to Annex III based on this opinion has been sent to the World Trade Organization (WTO). The WTO comment period ends August 16, 2015.

The Data Needs section requests information on "cosmetic-grade inorganic hydroxides". Use of the term "cosmetic-grade" is not appropriate as there is no organization setting purity standards for cosmetic ingredients.

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The USP (Calcium Hydroxide, Magnesium Hydroxide) and Food Chemical Codex (Calcium Hydroxide, Potassium Hydroxide, Sodium Hydroxide, Magnesium Hydroxide) specifications should be mentioned in the CIR report.

Additional Considerations

Cosmetic Use - Please delete the word "survey" associated with 2015 VCRP data. The VCRP data was received from FDA in 2015. It was not a survey that was completed in 2015.

Toxicokinetics, Summary - The sentence under the toxicokinetics section and the mention of toxicokinetics in the Summary suggests developing kinetic data on these ingredients may be possible (or useful). At low concentrations, these ingredients would dissociate at physiological pH. Although there is much information on the normal kinetics of the ions, it would not be useful for assessing the safety of these ingredients as they are used in cosmetics.

Genotoxicity - Information on the effects of pH on genotoxicity potential would also be helpful. For example, it would be helpful if the statement in Table 5, "genotoxic effects due to high non-physiological pH that may yield false-positive results" was also included in the text of the genotoxicity section. What types of cells were examined in the *in vivo* mouse studies?

Dermal Irritation - In the dermal irritation section, it would also be helpful to state that dermal irritation is a function of pH (or state this once in a general irritation section). What concentrations of Magnesium Hydroxide were not irritating or corrosive? What concentrations of Calcium Hydroxide were irritating in rabbit studies?

Summary - The case report at the end of the Summary should not be presented in the Summary if it is not presented elsewhere in the report. It is not correct to state that there is no repeated dose toxicity study. Although presented in the Reproductive and Developmental Toxicity section, the oral study of Magnesium Hydroxide in which rats were treated by gavage (males 29 days, females 41-45 days) should also be considered a repeated dose study.

Table 3 - For this report, it would be helpful to know how many products containing Sodium Hydroxide reported to the VCRP were soaps and detergents.

The foot product containing 10% Potassium Hydroxide is a rinse-off product. This needs be corrected in Table 3.

Table 5 - Please include the cell types that were examined in the *in vivo* studies.

Table 6 - As human cells were used in some of the in vitro studies, the heading should be changed from "Non-Human *In Vitro*" to "*In Vitro*".

Table 8 - Did the authors of the LLNA discuss whether or not the Magnesium Hydroxide was irritating?