Safety Assessment of Sodium Hyaluronate Crosspolymers as Used in Cosmetics

Status: Draft Report for Panel Review
Release Date: September 11, 2026
Panel Meeting Date: October 5-6, 2026

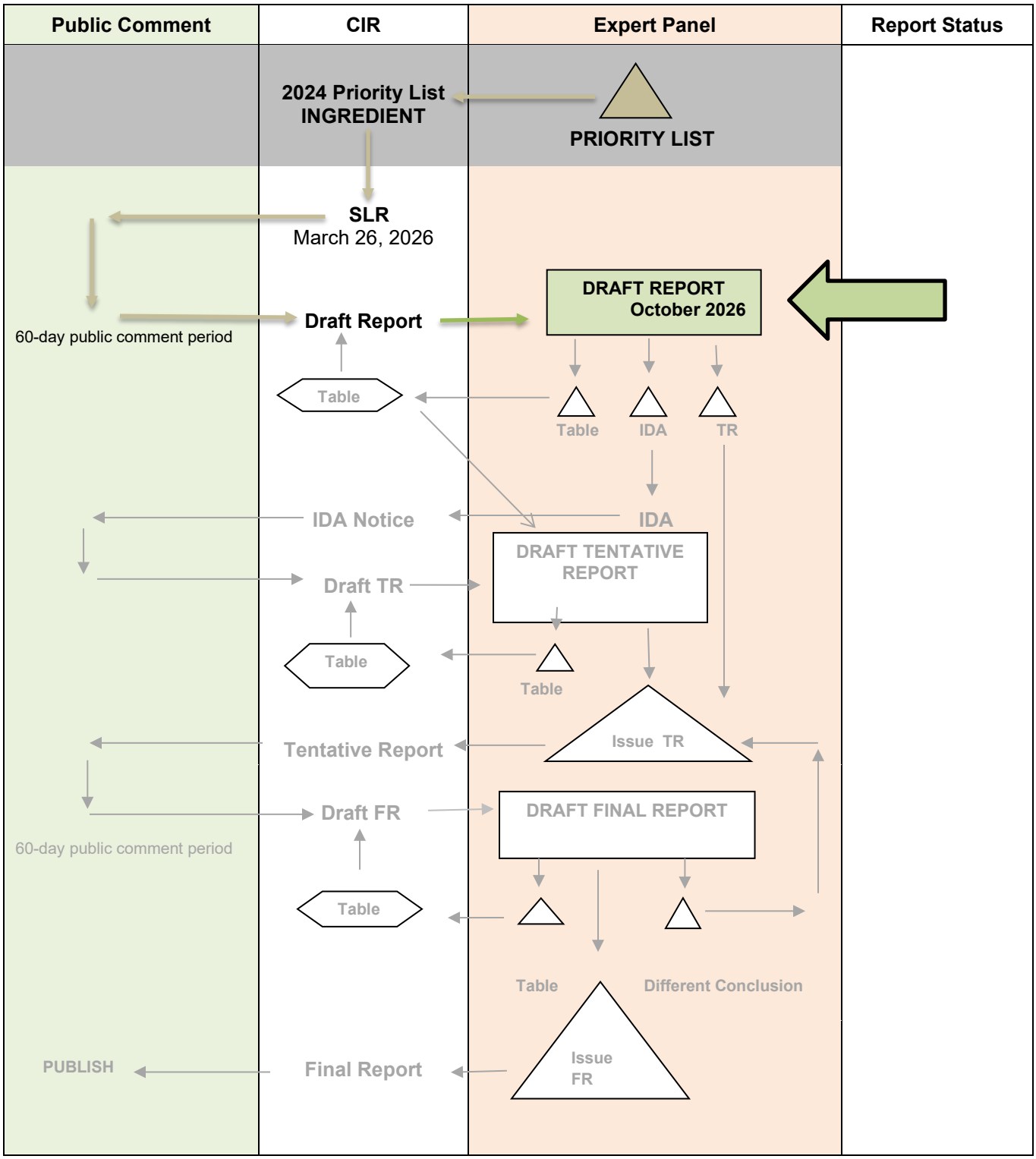
The Expert Panel for Cosmetic Ingredient Safety members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; Bruce A. Brod, M.D., M.H.C.I., F.A.A.D.; Samuel M. Cohen, M.D., Ph.D.; Curtis D. Klaassen, Ph.D.; Allan E. Rettie, Ph.D.; David Ross, Ph.D.; Paul W. Snyder, D.V.M., Ph.D.; and Susan C. Tilton, Ph.D. The Cosmetic Ingredient Review (CIR) Executive Director is Bart Heldreth, Ph.D., and the Senior Director is Monice Fiume, M.B.A. This safety assessment was prepared by Temima Nguyen, M.S., Scientific Analyst/Writer, CIR. This safety assessment was prepared by Temima Nguyen, M.S., Scientific Analyst/Writer, CIR.

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SAFETY ASSESSMENT FLOW CHART

INGREDIENT/FAMILY Sodium Hyaluronate Crosspolymers
MEETING October 2026



COSMETIC
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Memorandum

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Temima Nguyen, M.S., Scientific Analyst/Writer, CIR
Date: September 11, 2026
Subject: Safety Assessment of Sodium Hyaluronate Crosspolymers as Used in Cosmetics

Enclosed is the Draft Report on the Safety Assessment of Sodium Hyaluronate Crosspolymers as Used in Cosmetics. (It is identified as *report_ SodiumHyaluronateCrosspolymers_102026* in the pdf document). This is the first time the Panel is seeing this safety assessment on these 6 ingredients; the Scientific Literature Review (SLR) was issued by CIR on March 26, 2026.

The results of a concentration of use survey performed using MoCRA categories were submitted by industry and are included (*data1_SodiumHyaluronateCrosspolymers_102026; data2_SodiumHyaluronateCrosspolymers_102026*); concentrations of use were reported for Sodium Hyaluronate Crosspolymer, but not for any of the other 5 ingredients. (Please note that Sodium Hyaluronate Crosspolymer and Sodium Hyaluronate Crosspolymer-6 are used in baby products, but concentration of use data are not available.) Also, since the issuing of the SLR, a summary of a human repeated-insult patch test (HRIPT) on a serum containing 0.948% Sodium Hyaluronate Crosspolymer was provided (*data3_ SodiumHyaluronateCrosspolymers_102026*).

Comment on the SLR were submitted by the Council (*PCPCcomments_SodiumHyaluronateCrosspolymers_102026)*. These comments have been addressed (*response-SodiumHyaluronateCrosspolymers_102026)*.

Other items include:

- flow chart (*flow_SodiumHyaluronateCrosspolymers_102026*)
- report history (*history_SodiumHyaluronateCrosspolymers_102026*)
- search strategy (*search_SodiumHyaluronateCrosspolymers_102026*)
- data profile (*dataprofile_SodiumHyaluronateCrosspolymers_102026*)

If no further data are needed to reach a conclusion of safety, the Panel should formulate a Discussion and issue a Tentative Report. However, if additional data are required, the Panel should be prepared to identify those needs and issue an Insufficient Data Announcement.

Sodium Hyaluronate Crosspolymers History

March 26th, 2026

SLR posted.

April 24th, 2026

Comments were received from the Council on the SLR.

May 4th, 2026

A memorandum was sent indicating the results of the March 2026 PCPC concentration of use survey for Sodium Hyaluronate Crosspolymer-4, Sodium Hyaluronate Crosspolymer-6, and Sodium Hyaluronate Crosspolymer-7. No uses were reported for these three ingredients.

May 15th, 2026

A summary of a human repeat insult patch test (HRIPT) on a serum containing 0.948% Sodium Hyaluronate Crosspolymer was provided.

October 2026

Panel reviews Draft Report.

Sodium Hyaluronate Crosspolymers Data Profile* – October 2026 – Writer, Temima Nguyen																														
				Toxicokinetics			Acute Tox			Repeated Dose Tox			DART		Genotox		Carci		Dermal Irritation			Dermal Sensitization				Ocular Irritation		Clinical Studies	
	Reported Use	Method of Mfg	Impurities	log P/log K_{ow}	Dermal Penetration	ADME	Dermal	Oral	Inhalation	Dermal	Oral	Inhalation	Dermal	Oral	In Vitro	In Vivo	Dermal	Oral	In Vitro	Animal	Human	In Vitro	Animal	Human	Phototoxicity	In Vitro	Animal	Retrospective/ Multicenter	Case Reports
Sodium Hyaluronate Crosspolymer	X		X																		X			X					
Sodium Hyaluronate Crosspolymer-2																														
Sodium Hyaluronate Crosspolymer-3																														
Sodium Hyaluronate Crosspolymer-4																														
Sodium Hyaluronate Crosspolymer-6																														
Sodium Hyaluronate Crosspolymer-7																														

* "X" indicates that data were available in a category for the ingredient

Sodium Hyaluronate Crosspolymers

Ingredient	CAS #	PubMed	FDA	CompTox	ChemPort	NIOSH	NTIS	NTP	FEMA	EU	ECHA	SIDS	SCCS	AICIS	FAO	WHO	Web
Sodium Hyaluronate Crosspolymer	162975-50-0	NR	NR	NR	NR	NR	NR	NR	NR	√*	NR	NR	NR	NR	NR	NR	√
Sodium Hyaluronate Crosspolymer-2	113797-47-0	NR	NR	NR	NR	NR	NR	NR	NR	√*	NR	NR	NR	NR	NR	NR	√*
Sodium Hyaluronate Crosspolymer-3	NR	NR	NR	NR	NR	NR	NR	NR	NR	√*	NR	NR	NR	NR	NR	NR	√*
Sodium Hyaluronate Crosspolymer-4	781214-94-6	NR	NR	NR	NR	NR	NR	NR	NR	√*	NR	NR	NR	NR	NR	NR	√*
Sodium Hyaluronate Crosspolymer-6	NR	NR	NR	NR	NR	NR	NR	NR	NR	√*	NR	NR	NR	NR	NR	NR	√*
Sodium Hyaluronate Crosspolymer-7	NR	NR	NR	NR	NR	NR	NR	NR	NR	√*	NR	NR	NR	NR	NR	NR	√*

NR- not reported; √* - data is available, but is not new or relevant

Search Strategy

Pubmed

((Sodium Hyaluronate Crosspolymer) OR (113797-47-0)) OR (781214-94-6) – 1 hit / 0 useful
(crosslinked hyaluronic acid) AND (toxicity) - 255 hits / 8 useful
(Hyaluronan Crosspolymer) OR (Hyaluronic Acid Crosspolymer) – 2 hits / 0 useful
((Sodium Hyaluronate Crosspolymer) OR (crosslinked hyaluronic acid)) AND (sensitization) - 16 hits / 1 useful
(crosslinked hyaluronic acid) AND (irritation) - 20 hits / 1 useful
(crosslinked hyaluronic acid) AND (impurities) - 7 hits / 0 useful
(crosslinked hyaluronic acid) AND (inhalation) - 9 hits / 0 useful
(crosslinked hyaluronic acid) AND (carcinogenicity) - 6 hits / 0 useful
(hyaluronic acid 1,4-butanediol diglycidyl ether) - 29 hits / 2 useful

Web

Sodium Hyaluronate Crosspolymer – 2,770,000 hits / 1 useful
Sodium Hyaluronate Crosspolymer-2 – 5,470,000 hits / 0 useful
Sodium Hyaluronate Crosspolymer-3 – 5,190,000 hits / 0 useful
Sodium Hyaluronate Crosspolymer-4 – 4,760,000 hits / 0 useful
Sodium Hyaluronate Crosspolymer-7 – 3,760,000 hits / 0 useful
Sodium Hyaluronate Crosspolymer toxicity – 98,700 hits / 0 useful
Sodium Hyaluronate Crosspolymer irritation – 717,000 hits / 0 useful
crosslinked hyaluronic acid toxicity - 1,610,000 hits / 3 useful
crosslinked hyaluronic acid sensitization – 268,000 hits / 0 useful
crosslinked hyaluronic acid irritation – 230,000 hits / 0 useful
crosslinked hyaluronic acid inhalation – 375,000 hits / 1 useful
crosslinked hyaluronic acid carcinogenicity – 52,500 hits / 1 useful

LINKS

Search Engines

- Pubmed - http://www.ncbi.nlm.nih.gov/pubmed
  - appropriate qualifiers are used as necessary
  - search results are reviewed to identify relevant documents
- CompTox: https://comptox.epa.gov/dashboard/chemical/pubmed-abstract-sifter/DTXSID3039242; https://www.epa.gov/comptox-tools/downloadable-computational-toxicology-data#LM
- eChemPortal: https://www.echemportal.org/echemportal/
- DeepDyve: https://www.deepdyve.com/
- Connected Papers - https://www.connectedpapers.com/

Pertinent Websites

- wINCI - https://incipedia.personalcarecouncil.org/winci/ingredient-custom-search/
- FDA Cosmetics page - https://www.fda.gov/cosmetics
- eCFR (Code of Federal Regulations) - https://www.ecfr.gov/
- FDA search databases: https://www.fda.gov/industry/fda-basics-industry/search-databases
- Substances Added to Food (formerly, EAFUS): https://www.fda.gov/food/food-additives-petitions/substances-added-food-formerly-eafus
- GRAS listing: https://www.fda.gov/food/food-ingredients-packaging/generally-recognized-safe-gras
- SCOGS database: https://www.fda.gov/food/generally-recognized-safe-gras/gras-substances-scogs-database
- Inventory of Food Contact Substances Listed in 21 CFR: https://www.cfsanappsexternal.fda.gov/scripts/fdcc/index.cfm?set=IndirectAdditives
- Drug Approvals and Database: https://www.fda.gov/drugs/development-approval-process-drugs/drug-approvals-and-databases
- FDA Orange Book: https://www.fda.gov/drugs/drug-approvals-and-databases/approved-drug-products-therapeutic-equivalence-evaluations-orange-book
- OTC Monographs - https://dps.fda.gov/omuf; https://dps.fda.gov/omuf/monographsearch
- Inactive Ingredients Approved For Drugs: https://www.accessdata.fda.gov/scripts/cder/iig/
- FEMA (Flavor & Extract Manufacturers Association) GRAS: https://www.femaflavor.org/fema-gras
- NIOSH (National Institute for Occupational Safety and Health) - http://www.cdc.gov/niosh/
- NTIS (National Technical Information Service) - http://www.ntis.gov/
  - technical reports search page: https://ntrl.ntis.gov/NTRL/
- NTP (National Toxicology Program) - http://ntp.niehs.nih.gov/
- EUR-Lex - https://eur-lex.europa.eu/homepage.html
- Scientific Committees (SCCS, etc) opinions: https://health.ec.europa.eu/scientific-committees_en https://health.ec.europa.eu/scientific-committees/scientific-committee-consumer-safety-sccs_en
- ECHA (European Chemicals Agency – REACH dossiers) – https://echa.europa.eu/
- European Medicines Agency (EMA) - http://www.ema.europa.eu/ema/
- OECD SIDS (Organisation for Economic Co-operation and Development Screening Info Data Sets)- http://webnet.oecd.org/hpv/ui/Search.aspx
- EFSA (European Food Safety Authority) - https://www.efsa.europa.eu/en
- ECETOC (European Centre for Ecotoxicology and Toxicology of Chemicals) - http://www.ecetoc.org
- AICIS (Australian Industrial Chemicals Introduction Scheme)- https://www.industrialchemicals.gov.au/
- International Programme on Chemical Safety http://www.inchem.org/
- Office of Dietary Supplements https://ods.od.nih.gov/
- FAO (Food and Agriculture Organization of the United Nations) - http://www.fao.org/food/food-safety-quality/scientific-advice/jecfa/jecfa-additives/en/
- WHO (World Health Organization) IRIS library - https://apps.who.int/iris/
- a general Google and Google Scholar search should be performed for additional background information, to identify references that are available, and for other general information - www.google.com https://scholar.google.com/

Personal Care Products Council

Memorandum

TO: Bart Heldreth, Ph.D.
Executive Director - Cosmetic Ingredient Review

FROM: Jaap Venema, Ph.D.
EVP and Chief Scientist – Personal Care Products Council
Industry Liaison to the CIR Expert Panel

DATE: April 24, 2026

SUBJECT: Scientific Literature Review: Safety Assessment of Sodium Hyaluronate Crosspolymers as Used in Cosmetics (release date: March 26, 2026)

The Personal Care Products Council respectfully submits the following comments on the scientific literature review, Safety Assessment of Sodium Hyaluronate Crosspolymers as Used in Cosmetics.

Cytotoxicity, Sodium Hyaluronate Crosspolymer-4; Summary – The following does not make sense: "The hyaluronic acid-BDDE crosslinked hydrogel had a cell viability of 105% (control was 100%) and was slightly more cytotoxic than the control, but the difference was not statistically significant." If viability was greater than control, the tested material was not cytotoxic, rather it stimulated growth slightly.

The paper (reference 16) states: "Regarding cell viability, both hyaluronic acid gel groups outperformed the control baseline (100 ± 5%). Notably, the HA-PEGDE group exhibited significantly higher cell viability (151 ± 12%) than the HA-BDDE group (105 ± 11%) and the control baseline (Fig. 5)."

It is also not clear why the information on Sodium Hyaluronic Crosspolymer crosslinked with poly(propylene glycol) diglycidyl ether (HA-PEGDE) from reference 16 is not included in the CIR report. Although the authors may not have stated the level of ethoxylation of the PEGDE used, information on HA-PEGDE is relevant to Sodium Hyaluronic Crosspolymer-6 (crosslinked with PEG-9 diglycidyl ether).

Immunotoxicity – The meaning of the following is not clear: "The fragments treatments were degraded." It is also unlikely that: "The VYC-15L and VYC-15L fragments had moderate

inflammation." It is more likely inflammation was observed in mice treated intradermally with the fragments.

Summary – In the Summary, it would be helpful to restate the crosslinkers used for each crosspolymer, e.g., "The six sodium hyaluronic crosspolymers included in this report differ by the crosslinker used: Sodium Hyaluronate Crosspolymer (vinyl sulfone), Sodium Hyaluronate Crosspolymer-2 (diglycidyl ether), Sodium Hyaluronate Crosspolymer-3 (propylbioxyamine), Sodium Hyaluronate Crosspolymer-4 (BDDE). Sodium Hyaluronate Crosspolymer-6 (PEG-9 diglycidyl ether), Sodium Hyaluronate Crosspolymer-7 (sodium trimetaphosphate)."

Table 3 – As this table summarizes in vitro cytotoxicity studies (no studies completed in animals), the column heading "Animals/Group" should be replaced with "Cell Type".

Somewhere in this table (perhaps in the footnotes), it would be helpful to state that the polymers crosslinked with BDDE are relevant to Sodium Crosspolymer-4 which is also crosslinked with BDDE.

Sodium Hyaluronate Crosspolymers – October 2026 – Temima Nguyen	
Comment Submitter: Jaap Venema, Personal Care Products Council **Date of Submission: April 24, 2026**	
Comment	**Response/Action**
Cytotoxicity, Sodium Hyaluronate Crosspolymer-4; Summary – The following does not make sense: "The hyaluronic acid-BDDE crosslinked hydrogel had a cell viability of 105% (control was 100%) and was slightly more cytotoxic than the control, but the difference was not statistically significant." If viability was greater than control, the tested material was not cytotoxic, rather it stimulated growth slightly. The paper (reference 16) states: "Regarding cell viability, both hyaluronic acid gel groups outperformed the control baseline (100 ± 5%). Notably, the HA-PEGDE group exhibited significantly higher cell viability (151 ± 12%) than the HA-BDDE group (105 ± 11%) and the control baseline (Fig. 5)." It is also not clear why the information on Sodium Hyaluronic Crosspolymer crosslinked with poly(propylene glycol) diglycidyl ether (HA-PEGDE) from reference 16 is not included in the CIR report. Although the authors may not have stated the level of ethoxylation of the PEGDE used, information on HA-PEGDE is relevant to Sodium Hyaluronic Crosspolymer-6 (crosslinked with PEG-9 diglycidyl ether).	Addressed.
Immunotoxicity – The meaning of the following is not clear: "The fragments treatments were degraded." It is also unlikely that: "The VYC-15L and VYC-15L fragments had moderate inflammation." It is more likely inflammation was observed in mice treated intradermally with the fragments.	Addressed.
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ABBREVIATIONS

BDDE	1,4-butanediol diglycidyl ether
CCK-8	cell counting kit-8
CIR	Cosmetic Ingredient Review
Council	Personal Care Products Council
DCFH-DA	dichloro-dihydro-fluorescein diacetate
Dictionary	*International Cosmetic Ingredient Dictionary*
FDA	US Food and Drug Administration
HaCaT	human keratinocyte cell line
HAM	hyaluronic acid membrane
HCEC	human corneal epithelial cells
HDF	human dermal fibroblast cell
HRIPT	human repeated-insult patch test
L929	murine fibroblast cells
LDH	lactate dehydrogenase
l.o.	leave-on
LPS	lipopolysaccharide
MC3T3-E1	mouse pre-osteoblastic cells
MMP	mitochondrial membrane potential
MoCRA	Modernization of Cosmetics Regulation Act of 2022
MTT	3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide
NHEK	human epidermal keratinocytes
NR	not reported
Panel	Expert Panel for Cosmetic Ingredient Safety
PBS	phosphate-buffered saline
PEGDE	polyethylene glycol diglycidyl ether
RLD	Registration and Listing Data
r.o.	rinse-off
ROS	reactive oxygen species
US	United States
WoE	weight-of-evidence

INTRODUCTION

This assessment reviews the safety of the following 6 ingredients as used in cosmetic formulations:

Sodium Hyaluronate Crosspolymer	Sodium Hyaluronate Crosspolymer-4
Sodium Hyaluronate Crosspolymer-2	Sodium Hyaluronate Crosspolymer-6
Sodium Hyaluronate Crosspolymer-3	Sodium Hyaluronate Crosspolymer-7

According to the *International Cosmetic Ingredient Dictionary* (*Dictionary*), all of these ingredients are reported to function as skin conditioning agents in cosmetic products, with the exception of Sodium Hyaluronate Crosspolymer-2, which is reported to function as a humectant (Table 1).[1] The ingredients above are all sodium salts of either hyaluronic acid or a polymer of hyaluronic acid before being crosslinked.

The Expert Panel for Cosmetic Ingredient Safety (Panel) has reviewed the safety of hyaluronic acid and sodium hyaluronate. In the original review of hyaluronic acid, potassium hyaluronate, and sodium hyaluronate that was published in 2009, the Panel concluded that these ingredients are safe in the present practices of use and concentration, as described in the safety assessment.[2] In 2023, a re-review was conducted for hyaluronic acid, potassium hyaluronate, and sodium hyaluronate with the addition of hydrolyzed calcium hyaluronate, hydrolyzed hyaluronic acid, hydrolyzed sodium hyaluronate, and sodium acetylated hyaluronate.[3] The Panel concluded that these ingredients are also safe in the present practices of use and concentration, as described in the safety assessment.

Dermal absorption of polymers is typically obfuscated by both high molecular weights and crosslinking. However, residual starting materials, such as monomers, crosslinkers, and polymerization propagators and terminators, may potentially absorb. In CIR literature searches, data regarding the crosslinkers 1,4-butanediol diglycidyl ether (BDDE) and polyethylene glycol diglycidyl ether (PEGDE) were found and have been included in this assessment as these substances may be used in the synthesis of Sodium Hyaluronate Crosspolymer-4 and Sodium Hyaluronate Crosspolymer-6, respectively.

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 extensive search of the world's literature; a search was last conducted September 2026. A listing of the search engines and websites that are used and the sources that are typically explored, as well as the endpoints that the Panel typically evaluates, is provided on the Cosmetic Ingredient Review (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.

CHEMISTRY

Definition and Structure

The definitions and idealized structures of the ingredients included in this review are provided in Table 1. According to the *Dictionary*, each of these ingredients share the same polyhyaluronate salt backbone and differ only by the crosslinker (i.e., vinyl sulfone for Sodium Hyaluronate Crosspolymer; diglycidyl ether for Sodium Hyaluronate Crosspolymer-2; propylbisoxyamine for Sodium Hyaluronate Crosspolymer-3; BDDE for Sodium Hyaluronate Crosspolymer-4; PEG-9 diglycidyl ether for Sodium Hyaluronate Crosspolymer-6 (hyaluronate crosslinked with PEGDE, as seen in the literature, has a number average molecular weight of 500 Da meaning that the median number of ethylene glycol repeat units is between 8 and 9 (i.e., is between PEG-8 diglycidyl ether and PEG-9 diglycidyl ether) and is equivalent to Sodium Hyaluronate Crosspolymer-6); and sodium trimetaphosphate for Sodium Hyaluronate Crosspolymer-7).[1] Hyaluronic acid is a linear mucopolysaccharide (glycosaminoglycan) comprising disaccharide repeat units of *N*-acetyl-D-glucosamine and D-glucuronic acid; sodium hyaluronate is the sodium salt thereof and serves as the monomer for the polyhyaluronate salt backbone in these ingredients. Crosslinking of these linear polymers results in 3D networks, likely increasing molecular volume significantly.

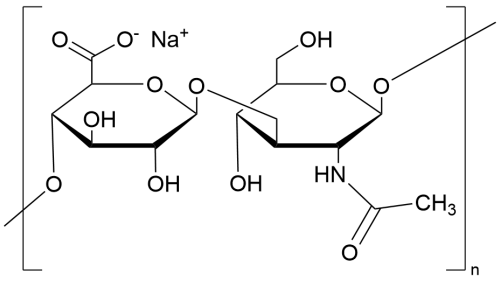


Figure 1. Sodium hyaluronate polymer backbone.[CIR Staff]

Chemical Properties

Sodium Hyaluronate Crosspolymer (CAS No. 105524-32-1) is reported to be a colorless to slightly yellow clear viscous liquid.[4] No further details were provided. Chemical properties were not found in the published literature on the other sodium hyaluronate crosspolymer ingredients, and unpublished data were not submitted.

Method of Manufacture

Methods of manufacture data, specific to the cosmetics industry, were not found in the published literature, and unpublished data were not submitted. However, manufacture of these same chemicals for use as soft-tissue fillers is documented in the published literature.[5,6]

The two crosslinkers mentioned in this report (BDDE and PEG-9 diglycidyl ether) belong to a class of chemical crosslinkers called bisepoxides.[5] Bisepoxides react with the hydroxyl groups on hyaluronic acid under strong alkaline conditions (~pH 13) to form ether linkages. During the reaction period, temperatures can reach > 40°C over a few hours. The hydroxyl groups are modified at different positions and result in a bridge between the hyaluronic acid chains, forming an elastic crosslinked hyaluronic acid hydrogel network. The hydrogel is then purified using membrane dialysis to remove the non-reacted crosslinker and low molecular weight by-products.[6] The concentration of the polymer is adjusted using an aqueous buffer and is loaded in syringes before being packed and sterilized for use.

Impurities

According to a specification, the heavy metal content of Sodium Hyaluronate Crosspolymer is not to exceed 10 ppm.[4] No further details were provided. For the purification of soft-tissue fillers comprising hyaluronate crosspolymers, dialysis is a common technique.[5]

USE

Cosmetic

The safety of the cosmetic ingredients 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 sodium hyaluronate crosspolymers in cosmetics. Registration and Listing Data (RLD) obtained from the FDA report frequency of use, and responses to a survey conducted by the Personal Care Products Council (Council) indicate maximum reported concentrations of use; it is these values that define the present practices of use and concentration that are assessed by the Panel. Since 2024, as a result of the Modernization of Cosmetics Regulation Act of 2022 (MoCRA), manufacturers and processors are required to register facilities and list their products (and ingredients therein) with the FDA (i.e., RLD). An exception is made for small businesses (average gross annual sales in the US of cosmetic products for the previous 3-yr period is less than $1,000,000, adjusted for inflation), which are exempt from MoCRA reporting for most cosmetic product categories. Eye area products, injected products, internal use products, or products that alter appearance for more than 24 h, and the facilities that manufacture these products, are not included in this exemption.[7] Another change resulting from MoCRA is the addition of tattoo preparations (permanent tattoo inks, temporary tattoo inks, and other tattoo products) to the product categories for which companies need to list their products with FDA. However, evaluating the safety of ingredients as used in tattoo preparations is not within the purview of the Panel; accordingly, such use is not included as part of the present practices of use that are assessed by the Panel.

According to RLD obtained from the FDA in 2025, Sodium Hyaluronate Crosspolymer has the most reported uses, at 5396 formulations (Table 2). [7,8] Sodium Hyaluronate Crosspolymer was the only ingredient with concentrations of use submitted in response to the survey conducted by the Council. In 2026, Sodium Hyaluronate Crosspolymer was reported to be used at up to 0.95% in traditionally applied foundations and in leave-on face and neck products.[9,10]

Some ingredients in this report are used in products that are applied near the eye, that can be incidentally ingested, and are used near mucous membranes. For example, Sodium Hyaluronate Crosspolymer has been used in eye lotions (concentrated of use not reported), lipsticks and lip glosses at up to 0.00035%, and in bath soaps and body washes at up to 0.0000007%.

For some of these ingredients, reported uses in baby products are identified in the RLD; however, concentration of use data are not available for every reported category of baby product. In cases where a baby product category is reported without an associated concentration, but an analogous adult product category with reported concentration data is available, the adult product use level may be considered informative for exposure characterization. In such cases, concentrations in the corresponding baby product category are not expected to exceed those reported for the analogous adult product category. For example, Sodium Hyaluronate Crosspolymer has no reported concentration of use in baby lotions, oils, powders, and creams but it is reported in leave-on body and hand products (not spray) at a maximum concentration of 0.002% accordingly, concentrations in baby lotions, oils, powders, and creams are not expected to exceed this value. The category “other baby products” represents a miscellaneous grouping of reported uses not assigned to specific baby product subcategories. Given its broad and non-specific nature, it does not correspond to a single analogous adult product category; therefore, the adult-product concentration bridging approach is not applied to this category.

Sodium hyaluronate crosspolymers are used in products that may be incidentally inhaled. For example, Sodium Hyaluronate Crosspolymer is used in hair sprays and face powders (concentrations of use not reported). In practice, as stated in the Panel’s respiratory exposure resource document (https://www.cir-safety.org/cir-findings), most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and tracheobronchial regions and would not be respirable (i.e., they would not enter the lungs) to any appreciable amount. Conservative estimates of inhalation

exposures to respirable particles during the use of loose powder cosmetic products are 400-fold to 1000-fold less than protective regulatory and guidance limits for inert airborne respirable particles in the workplace.

With the advent of MoCRA and the current product categories outlined therein, it is now mandatory that cosmetic products used in airbrush delivery systems be reported as such for some, but not all, product categories in the RLD. In other words, a reliable source of frequency of use data regarding the use of cosmetic ingredients in conjunction with airbrush delivery systems is now available in some instances. Additionally, the concentration of use surveys are conducted based on the same product categories as identified in the RLD. Based on RLD, some products containing Sodium Hyaluronate Crosspolymer are marketed for use with airbrush delivery systems. However, no consumer habits and practices data or particle size data are publicly available to evaluate the exposure associated with this use type, thereby preempting the ability to evaluate risk or safety. Without information regarding the consumer habits and practices data or product particle size data (or other relevant particle data, e.g., diameter) related to this use technology, the data profile is incomplete, and the Panel is not able to determine safety for use in airbrush formulations. Accordingly, the data are insufficient to evaluate the exposure resulting from cosmetics applied via airbrush delivery systems.

Also with MoCRA, the FDA created a number of new product categories including, "(17) Other preparations (i.e., those preparations that do not fit another category)" (Category 17). CIR and the Panel utilize these product categories to inform, in part, the weight-of-evidence (WoE) in exposure and risk analyses. However, citation of Category 17, alone, as the product use category is uninformative. When a product is co-categorized with both Category 17 and one or more common product use categories (e.g., eye makeup preparations), or other information in the RLD such as the product name are indicative of use type (e.g., "lip balm" is part of the product name), then those uses are accounted for and may be considered to be part of the "the present practices of use" for those products; as such, the Panel's safety conclusion may be inclusive thereon. Conversely, for instances wherein the use of an ingredient in a cosmetic product is only categorized as Category 17 and other information in the RLD is not indicative of use type, the present practices of use for these products remain unknown and the Panel's safety assessment conclusion, therefore, does not apply thereon.

The sodium hyaluronate crosspolymers named in this report are not restricted from use in any way under the rules governing cosmetic products in the European Union.[11]

Non-Cosmetic

The FDA lists hyaluronic acid, as an "absorbable (temporary) material" that is often crosslinked before being used as a dermal filler.[12] There is published literature available on hydrogels with a similar composition to Sodium Hyaluronate Crosspolymer-4 (hyaluronic acid crosslinked with BDDE) with use found in soft tissue fillers.[5] Currently, the hydrogels are also being researched for use as a vitreous substitute and for wound healing applications.[13,14]

TOXICOKINETIC STUDIES

Toxicokinetic studies were not found in the published literature, and unpublished data were not submitted.

TOXICOLOGICAL STUDIES

Acute and repeated-dose toxicity studies were not found in the published literature, and unpublished data were not submitted.

DEVELOPMENTAL AND REPRODUCTIVE TOXICITY STUDIES

Developmental and reproductive toxicity studies were not found in the published literature, and unpublished data were not submitted.

GENOTOXICITY STUDIES

Genotoxicity studies were not found in the published literature, and unpublished data were not submitted.

CARCINOGENICITY STUDIES

Carcinogenicity studies were not found in the published literature, and unpublished data were not submitted.

OTHER RELEVANT STUDIES

Cytotoxicity

The cytotoxicity studies summarized below that are relevant to Sodium Hyaluronate Crosspolymer-4 and Sodium Hyaluronate Crosspolymer-6 are described in Table 3. Studies including hyaluronic acid crosslinked with BDDE or PEGDE were included as the materials are chemically representative of Sodium Hyaluronate Crosspolymer-4 and Sodium Hyaluronate Crosspolymer-6, respectively. Data regarding the crosslinkers BDDE and PEGDE were also included because these substances may be of concern as residual starting materials depending on their concentration.

The cell viability of a primary culture of human corneal epithelial cells (HCECs) treated with a hyaluronic acid membrane (HAM) crosslinked with BDDE was assessed through cell counting kit-8 (CCK-8) analysis.[15] The HCECs were incubated with the HAM-BDDE. At 48 h, there was an increase of cell viability of 50% and the cells expressed more MK167, a cellular marker for proliferation. A hyaluronic acid hydrogel crosslinked with BDDE and a hyaluronic acid hydrogel crosslinked with PEGDE were incubated with mouse pre-osteoblastic cells (MC3T3-E1), separately, at 0.1 ml for 24 h.[16] Using CCK-8 analysis, the hyaluronic acid-BDDE crosslinked hydrogel and hyaluronic acid hydrogel crosslinked with PEGDE had a cell viability of 105% and 151%, respectively; control was 100%. In the same experiment, a lactate dehydrogenase (LDH) assay was performed and there was a slightly higher cytotoxicity for both crosslinked hyaluronic acid hydrogels, crosslinked with BDDE (3 ± 7%) and crosslinked with PEGDE (3 ± 6%), compared to the control (0 ± 8%), but the difference was not statistically significant. Multiple biphasic gel formulations were created with 5 - 15% (w/w) citric acid – hyaluronic acid content.[17] From the formulations, only the steam-sterilized biphasic gel formulation containing 6% hyaluronic acid crosslinked with BDDE and 12% citric acid-hyaluronic acid non-crosslinked was evaluated using a 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay in L929 mouse fibroblast cells for 24 h. There was no adverse effect on cell viability detected. Two crosslinkers (BDDE and PEGDE) were assessed for cytotoxicity in the human keratinocyte cell line (HaCaT) and human dermal fibroblast cell line (HDF).[18] In the MTT and LDH assays, HaCaT and HDF cells were treated with 0 – 1000 ppm of BDDE, PEGDE, or PBS (used as a control) for 24 h. Overall, when compared to the control, both cell types treated with BDDE produce lower cell viability and more LDH release than cells treated with PEGDE. Cellular integrity, reactive oxygen species (ROS) generation, and mitochondrial membrane potential (MMP) were also evaluated at 0 – 100 ppm and both crosslinkers produced effects on the cellular membrane, ROS levels and MMP at higher concentrations. However, compared to the PEGDE treated cells, the effects of BDDE treated cells were more pronounced. In a follow-up study, hyaluronic acid hydrogels were crosslinked with BDDE or PEGDE (2 g of a 20 mg/ml hydrogel in 10 ml of media).[19] Both crosslinked hydrogels were tested at low, medium, and high concentrations (25, 50, and 100%) for cytotoxicity using MTT and LDH assays as well as assessing membrane integrity, oxidative stress, and MMP. Cells treated with the hyaluronic acid hydrogel crosslinked with BDDE had a higher proportion of cell deaths, disruption of the cell membrane, higher cellular ROS levels, and greater mitochondrial membrane disruption compared to the hyaluronic acid hydrogel crosslinked with PEGDE.

Immunotoxicity

Sodium Hyaluronate Crosspolymer-4

Crosslinked hyaluronic acid products utilizing BDDE, the same crosslinker used in Sodium Hyaluronate Cross-polymer-4, were evaluated for inflammation in 6 mice with a lipopolysaccharide (LPS)-induced low-grade inflammatory phenotype.[20] LPS (5 µg/ml) was also used as a positive control at 20 µl. The mice received an acute intradermal injection of 20 µl of the vehicle control (inactivated hyaluronidase), VYC-15L (low and high molecular weight hyaluronic acid crosslinked with BDDE), VYC-15L fragments, HYC-24L+ (high molecular weight hyaluronic acid crosslinked with BDDE), or HYC-24L+ fragments. The fragments were hyaluronidase-induced degradation products. After 24 h, the mouse skin was examined microscopically. Moderate inflammation was observed in mice treated intradermally with the VYC-15L and VYC-15L fragments. HYC-24L+ and its fragments induced less inflammation, and the vehicle control produced minimal inflammation.

DERMAL IRRITATION AND SENSITIZATION STUDIES

Sensitization

Human

A human repeated-insult patch test (HRIPT) was completed in 56 subjects to test the sensitization potential of a serum containing 0.948% Sodium Hyaluronate Crosspolymer.[21] The product was applied at a dose per unit area of ~ 0.03 g/cm^2. The serum did not cause skin irritation or allergic contact dermatitis in the 56 subjects.

OCULAR IRRITATION STUDIES

Ocular irritation studies were not found in the published literature, and unpublished data were not submitted.

SUMMARY

The assessment reviews the safety of the following 6 sodium hyaluronate crosspolymer ingredients as used in cosmetic formulations: Sodium Hyaluronate Crosspolymer, Sodium Hyaluronate Crosspolymer-2, Sodium Hyaluronate Cross-polymer-3, Sodium Hyaluronate Crosspolymer-4, Sodium Hyaluronate Crosspolymer-6 and Sodium Hyaluronate Crosspolymer-7. These ingredients are reported to function in cosmetics as humectants and skin conditioning agents.

The sodium hyaluronic crosspolymers included in this report differ by the crosslinker used: Sodium Hyaluronate Crosspolymer (vinyl sulfone); Sodium Hyaluronate Crosspolymer-2 (diglycidyl ether); Sodium Hyaluronate Crosspolymer-3 (propylbioxyamine); Sodium Hyaluronate Crosspolymer-4 (BDDE); Sodium Hyaluronate Crosspolymer-6 (PEG-9 diglycidyl ether); and Sodium Hyaluronate Crosspolymer-7 (sodium trimetaphosphate). According to RLD obtained from the FDA in 2025, Sodium Hyaluronate Crosspolymer is the ingredient in this group with the most reported uses, in 5396 formulations.

Sodium Hyaluronate Crosspolymer was the only ingredient with concentrations of use submitted in response to the survey conducted by the Council. In 2026, Sodium Hyaluronate Crosspolymer was reported to be used at up to 0.95% in traditionally-applied foundations and in leave-on face and neck products.

The cell viability of a HCECs treated with a HAM crosslinked with BDDE was assessed CCK-8 analysis. The HCECs were incubated with the HAM-BDDE. At 48 h, there was an increase of cell viability of 50% and the cells expressed more MK167, a cellular marker for proliferation. A hyaluronic acid hydrogel crosslinked with BDDE and a hyaluronic acid hydrogel crosslinked with PEGDE were incubated with MC3T3-E1, separately, at 0.1 ml for 24 h. Using CCK-8 analysis, the hyaluronic acid-BDDE crosslinked hydrogel and hyaluronic acid hydrogel crosslinked with PEGDE had a cell viability of 105% and 151%, respectively (control was 100%). In the same experiment, a LDH assay was performed and there was a slightly higher cytotoxicity for both crosslinked hyaluronic acid hydrogels, crosslinked with BDDE (3 ± 7%) and crosslinked with PEGDE (3 ± 6%), compared to the control (0 ± 8%), but the difference was not statistically significant. Multiple biphasic gel formulations were created with 5 - 15% (w/w) citric acid – hyaluronic acid content. From the formulations, only the steam-sterilized biphasic gel formulation containing 6% hyaluronic acid crosslinked with BDDE and 12% citric acid-hyaluronic acid non-crosslinked was evaluated using a MTT assay in L929 mouse fibroblast cells for 24 h. There was no adverse effect on cell viability detected. Two crosslinkers (BDDE and PEGDE) were assessed for cytotoxicity in the HaCaT and HDF cells. In the MTT and LDH assays, HaCaT and HDF cells were treated with 0 – 1000 ppm of BDDE, PEGDE, or PBS (used as a control) for 24 h. Overall, when compared to the control, both cell types treated with BDDE produce lower cell viability and more LDH release than cells treated with PEGDE. Cellular integrity, ROS generation, and MMP were also evaluated at 0 – 100 ppm and both crosslinkers produced effects on the cellular membrane, ROS levels and MMP at higher concentrations. However, compared to the PEGDE treated cells, the effects of BDDE treated cells were more pronounced. In a follow-up study, hyaluronic acid hydrogels were crosslinked with BDDE or PEGDE (2 g of a 20 mg/ml hydrogel in 10 ml of media). Both crosslinked hydrogels were tested at low, medium, and high concentrations (25, 50, and 100%) for cytotoxicity using MTT and LDH assays as well as assessing membrane integrity, oxidative stress, and MMP. Cells treated with the hyaluronic acid hydrogel crosslinked with BDDE had a higher proportion of cell deaths, disruption of the cell membrane, higher cellular ROS levels, and greater mitochondrial membrane disruption compared to the hyaluronic acid hydrogel crosslinked with PEGDE.

A group of 6 mice with an LPS-induced low-grade inflammatory phenotype received an acute intradermal injection of 20 µl of the vehicle control (inactivated hyaluronidase), VYC-15L (low and high molecular weight hyaluronic acid crosslinked with BDDE), HYC-24L+ (high molecular weight hyaluronic acid crosslinked with BDDE), or the degraded fragments of the latter two formulations. Histological evaluation at 24 h concluded that the VYC-15L and fragments treatment produced the most inflammation in mice followed by HYC-24L and its fragments treatment. The vehicle control had the least inflammation observed in mice, in comparison.

An HRIPT was completed in 56 subjects to test the sensitization potential of a serum containing 0.948% Sodium Hyaluronate Crosspolymer. The serum was applied at a dose per unit area of ~ 0.03 g/cm^2 and did not cause allergic contact dermatitis or skin irritation.

DISCUSSION

To be developed.

CONCLUSION

To be determined.

TABLES

Table 1. Definitions, idealized structures, and reported functions[1CIR Staff]

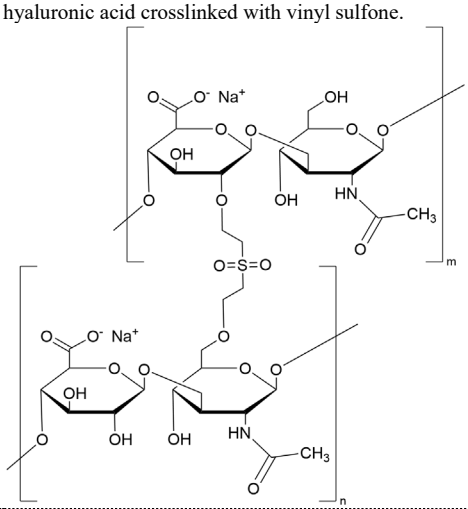
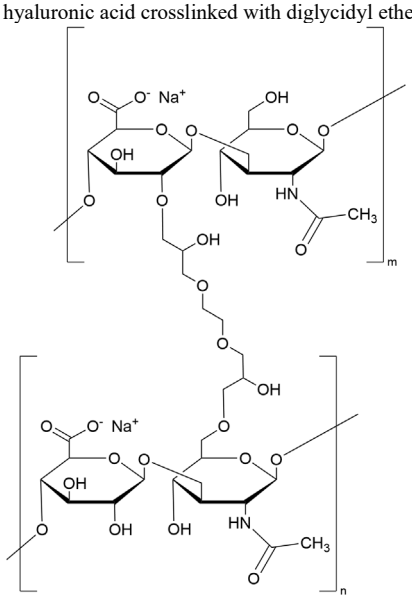
Ingredient (CAS No.)	Definition	Function(s)
Sodium Hyaluronate Crosspolymer (105524-32-1)	Sodium Hyaluronate Crosspolymer is the sodium salt of a polymer of hyaluronic acid crosslinked with vinyl sulfone. 	Skin-Conditioning Agents – Humectant Skin-Conditioning Agents – Miscellaneous
Sodium Hyaluronate Crosspolymer-2 (113797-47-0)	Sodium Hyaluronate Crosspolymer-2 is the sodium salt of a polymer of hyaluronic acid crosslinked with diglycidyl ether. 	Humectants

Table 1. Definitions, idealized structures, and reported functions[1]CIR Staff

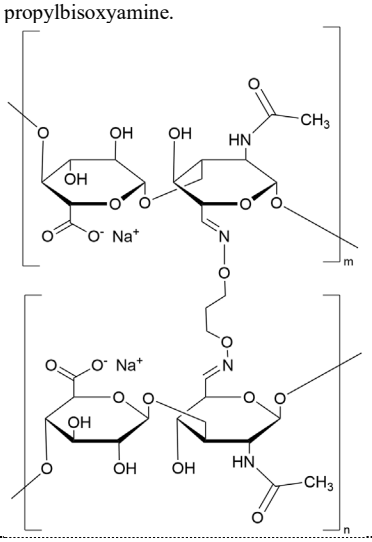
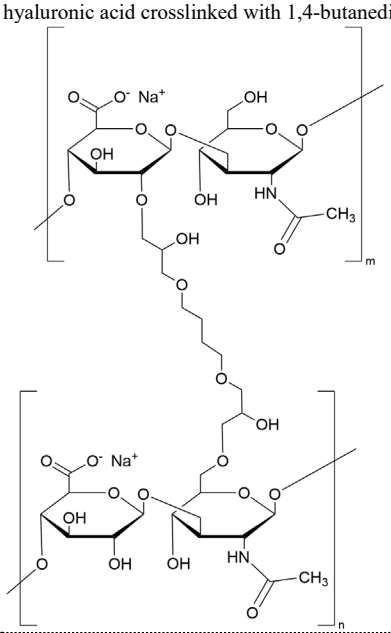
Ingredient (CAS No.)	Definition	Function(s)
Sodium Hyaluronate Crosspolymer-3	Sodium Hyaluronate Crosspolymer-3 is the sodium salt of hyaluronic acid that has been oxidized to facilitate the subsequent crosslinking by propylbisoxyamine. 	Skin-Conditioning Agents – Humectant Skin-Conditioning Agents – Miscellaneous
Sodium Hyaluronate Crosspolymer-4 (781214-94-6)	Sodium Hyaluronate Crosspolymer-4 is the sodium salt of a polymer of hyaluronic acid crosslinked with 1,4-butanediol diglycidyl ether. 	Skin-Conditioning Agents – Emollient Skin-Conditioning Agents – Humectant

Table 1. Definitions, idealized structures, and reported functions[1]CIR Staff

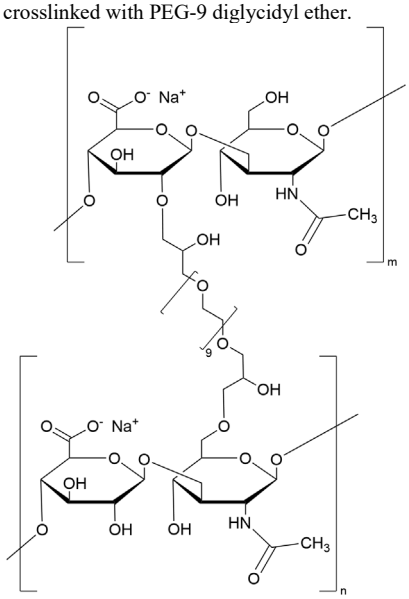
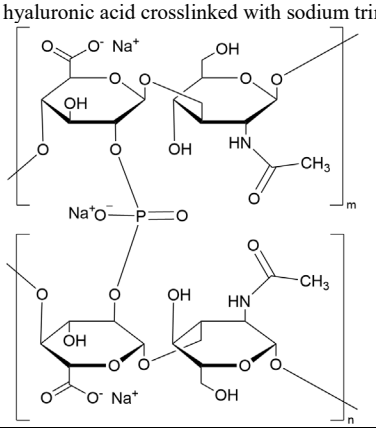
Ingredient (CAS No.)	Definition	Function(s)
Sodium Hyaluronate Crosspolymer-6	Sodium Hyaluronate Crosspolymer-6 is the polymer of sodium hyaluronate crosslinked with PEG-9 diglycidyl ether. 	Skin-Conditioning Agents – Miscellaneous
Sodium Hyaluronate Crosspolymer-7	Sodium Hyaluronate Crosspolymer-7 is the sodium salt of a polymer of hyaluronic acid crosslinked with sodium trimetaphosphate. 	Skin-Conditioning Agents – Humectant Skin-Conditioning Agents – Miscellaneous

Table 2. Frequency and concentration of use according to likely duration and exposure and by product category

	# of Uses RLD (2025)[7,8]	Max Conc of Use % (2026)[9,10]	# of Uses RLD (2025)[7,8]	Max Conc of Use % (2026)[9,10]	# of Uses RLD (2025)[7,8]	Max Conc of Use % (2026)[9,10]
	Sodium Hyaluronate Crosspolymer		Sodium Hyaluronate Crosspolymer-2		Sodium Hyaluronate Crosspolymer-3	
Totals*	**5396**	**0.0000007-0.95**	**8**	**NR**	**23**	**NR**
summarized by likely duration and exposure**						
Duration of Use						
Leave-On	*4747*	*0.00013-0.95*	*7*	*NR*	*24*	*NR*
Rinse-Off	*1446*	*0.0000007-0.47*	*1*	*NR*	*10*	*NR*
Diluted for (Bath) Use	*9*	*NR*	*NR*	*NR*	*NR*	*NR*
Unknown	*45*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type						
Baby Products	6	NR	NR	NR	NR	NR
Children's Makeup	NR	NR	NR	NR	NR	NR
Eye Area	67	NR	NR	NR	1	NR
Incidental Ingestion	234	0.00035	NR	NR	NR	NR
Mucous Membrane	351	0.0000007-0.00035	NR	NR	2	NR
Incidental Inhalation-Spray	7; 1389[a]; 2922[b]	0.0001[a]; 0.2[b]	7[b]	NR	10[a]; 15[b]	NR
Incidental Inhalation-Airbrush	1	NR	NR	NR	NR	NR
Incidental Inhalation-Powder	15; 2922[b]; 2[c]	0.2[b]; 0.00013-0.47[c]	7[b]	NR	15[b]	NR
Dermal Contact	5417	0.0000007-0.95	8	NR	33	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	200	NR	NR	NR	NR	NR
Hair-Coloring	371	0.003	NR	NR	NR	NR
Nail	4	NR	NR	NR	NR	NR
Other Preparations (Unknown Exposure Type)	45	NR	NR	NR	NR	NR
as reported by product category						
Baby Products						
Baby Shampoos						
Baby Lotions/Oils/Powders/Creams	2	NR				
Other Baby Products	1 (l.o.); 3 (r.o.)	NR				
Bath Preparations (diluted for use)						
Bath Oils, Tablets, and Salts	2	NR				
Bubble Baths	3	NR				
Other Bath Preparations	4	NR				
Eye Makeup Preparations (not children's)						
Eyebrow Pencil	4	NR				
Eye Shadow						
Eye Lotion	22	NR			1	NR
Mascara	1	NR				
Eyelash and Eyebrow Preparations (primers, conditioners, serums, fortifiers)	13	NR				
Eyelash Cleansers	4	NR				
Other Eye Makeup Preparations	23	NR				
Children's Eye Makeup Preparations						
Other Children's Eye Makeup						
Fragrance Preparations						
Perfumes	4	NR				
Other Fragrance Preparation	1	NR				
Hair Preparations (non-coloring)						
Hair Conditioners	16 (l.o); 35 (r.o.)	NR				

Table 2. Frequency and concentration of use according to likely duration and exposure and by product category

	# of Uses RLD (2025)[7,8]	Max Conc of Use % (2026)[9,10]	# of Uses RLD (2025)[7,8]	Max Conc of Use % (2026)[9,10]	# of Uses RLD (2025)[7,8]	Max Conc of Use % (2026)[9,10]
Hair Sprays (aerosol fixatives)	1 (spray)	NR				
Hair Straighteners	2	NR				
Permanent Waves	1	NR				
Rinses (non-coloring)	21	NR				
Shampoos (non-coloring)	60 (r.o.)	NR				
Tonics, Dressings, Other Hair Grooming Aids	22	NR				
Other Hair Preparations	22 (l.o); 20 (r.o.)	NR				
Hair Coloring Preparations						
Hair Dyes and Colors (all types requiring caution statements and patch tests)	368	0.003				
Hair Rinses (coloring)	2 (r.o.)	NR				
Hair Shampoos (coloring)	1 (r.o.)	NR				
Other Hair Coloring Preparation						
Makeup Preparations (not eye or children's)						
Blushers and Rouges (all types)	31	NR				
Face Powders	15	NR				
Foundations	294 (traditional)	0.95 (traditional)				
Lipsticks and Lip Glosses	234	0.00035				
Makeup Bases	38 (traditional)	NR				
Makeup Fixatives	33	NR				
Other Makeup Preparations	44 (traditional); 1 (airbrush)	0.0035 (traditional)				
Manicuring Preparations						
Cuticle Softeners	1	NR				
Nail Creams and Lotions						
Nail Polish and Enamel Removers	1	NR				
Other Manicuring Preparations	2	NR				
Personal Cleanliness						
Bath Soaps and Body Washes	60	0.0000007				
Deodorants (underarm)						
Douches					1	NR
Disposable Wipes	5	NR				
Other Personal Cleanliness Products	11 (l.o.); 32 (r.o.)	NR			1 (r.o.)	NR
Shaving Preparations						
Aftershave Lotions	1	NR				
Beard Softeners						
Pre-shave Lotions (all types)						
Shaving Cream (aerosol, brushless, lather)	2	NR				
Other Shaving Preparations						
Skin Care Preparations						
Cleansing	358	0.00035-0.47	1	NR	4	NR
Depilatories	23	NR				
Face and Neck (excluding shaving preps)	2384 (l.o.); 226 (r.o.)	not spray: 0.00013-0.95 (l.o.); 0.00013 (r.o.)	6 (l.o.)	NR	9 (l.o.)	NR
Body and Hand (excluding shaving preps)	201 (l.o); 36 (r.o.)	not spray: 0.002 (l.o.)			3 (l.o.)	NR
Foot Powders and Sprays	5	NR			1	NR
Moisturizing	850	0.0035-0.47 (not spray)			4	NR
Night	55	NR			3	NR
Paste Masks (mud packs)	130	NR			2	NR

Table 2. Frequency and concentration of use according to likely duration and exposure and by product category

	# of Uses RLD (2025)[7,8]	Max Conc of Use % (2026)[9,10]	# of Uses RLD (2025)[7,8]	Max Conc of Use % (2026)[9,10]	# of Uses RLD (2025)[7,8]	Max Conc of Use % (2026)[9,10]
Skin Fresheners	105	NR			1	NR
Other Skin Care Preparations	288 (l.o); 84 (r.o.)	0.2 (l.o); 0.0001 (r.o.)	1 (l.o.)	NR	2 (l.o); 2 (r.o.)	NR
Suntan Preparations						
Suntan Gels, Creams, and Liquids	11	NR				
Indoor Tanning Preparations	4 (traditional); 1 (spray)	NR				
Other Suntan Preparations	2	NR				
Other Preparations (i.e., those that do not fit another category)	45	NR				
	Sodium Hyaluronate Crosspolymer-4		**Sodium Hyaluronate Crosspolymer-6**		**Sodium Hyaluronate Crosspolymer-7**	
Totals*	**3**	**NR**	**715**	**NR**	**3**	**NR**
summarized by likely duration and exposure**						
Duration of Use						
Leave-On	*3*	*NR*	*677*	*NR*	*4*	*NR*
Rinse-Off	*NR*	*NR*	*237*	*NR*	*NR*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*5*	*NR*	*NR*	*NR*
Unknown	*NR*	*NR*	*18*	*NR*	*NR*	*NR*
Exposure Type						
Baby Products	NR	NR	8	NR	NR	NR
Children's Makeup	NR	NR	1	NR	NR	NR
Eye Area	NR	NR	28	NR	NR	NR
Incidental Ingestion	NR	NR	28	NR	NR	NR
Mucous Membrane	NR	NR	51	NR	NR	NR
Incidental Inhalation-Spray	3[b]	NR	7; 265[a]; 365[b]	NR	1[a]; 1[b]	NR
Incidental Inhalation-Airbrush	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Powder	3[b]	NR	2; 365[b]; 5[c]	NR	1[b]	NR
Dermal Contact	3	NR	852	NR	4	NR
Deodorant (underarm)	NR	NR	2 (not spray)	NR	NR	NR
Hair - Non-Coloring	NR	NR	28	NR	NR	NR
Hair-Coloring	NR	NR	5	NR	NR	NR
Nail	NR	NR	2	NR	NR	NR
Other Preparations (Unknown Exposure Type)	NR	NR	18	NR	NR	NR
as reported by product category						
Baby Products						
Baby Shampoos			2	NR		
Baby Lotions/Oils/Powders/Creams			5	NR		
Other Baby Products			1 (r.o.)	NR		
Bath Preparations (diluted for use)						
Bath Oils, Tablets, and Salts			2	NR		
Bubble Baths						
Other Bath Preparations			3	NR		
Eye Makeup Preparations (not children's)						
Eyebrow Pencil						
Eye Shadow			2	NR		
Eye Lotion			5	NR		
Mascara			3	NR		
Eyelash and Eyebrow Preparations (primers, conditioners, serums, fortifiers)			11	NR		
Eyelash Cleansers			1	NR		

Table 2. Frequency and concentration of use according to likely duration and exposure and by product category

	# of Uses RLD (2025)[7,8]	Max Conc of Use % (2026)[9,10]	# of Uses RLD (2025)[7,8]	Max Conc of Use % (2026)[9,10]	# of Uses RLD (2025)[7,8]	Max Conc of Use % (2026)[9,10]
Other Eye Makeup Preparations			5	NR		
Children's Eye Makeup Preparations						
Other Children's Eye Makeup			1	NR		
Fragrance Preparations						
Perfumes			3	NR		
Other Fragrance Preparation			3	NR		
Hair Preparations (non-coloring)						
Hair Conditioners			1 (l.o.)	NR		
Hair Sprays (aerosol fixatives)			1	NR		
Hair Straighteners			1	NR		
Permanent Waves						
Rinses (non-coloring)			2	NR		
Shampoos (non-coloring)			1 (l.o.); 2 (r.o.)	NR		
Tonics, Dressings, Other Hair Grooming Aids			10	NR		
Other Hair Preparations			5 (l.o.); 3 (r.o.)	NR		
Hair Coloring Preparations						
Hair Dyes and Colors (all types requiring caution statements and patch tests)			1	NR		
Hair Rinses (coloring)						
Hair Shampoos (coloring)						
Other Hair Coloring Preparation			4 (l.o.)	NR		
Makeup Preparations (not eye or children's)						
Blushers and Rouges (all types)			2	NR		
Face Powders			2	NR		
Foundations			40 (traditional)	NR	2 (traditional)	NR
Lipsticks and Lip Glosses			28	NR		
Makeup Bases			10 (traditional)	NR		
Makeup Fixatives			5	NR		
Other Makeup Preparations			3 (traditional)	NR		
Manicuring Preparations						
Cuticle Softeners			1	NR		
Nail Creams and Lotions			1	NR		
Nail Polish and Enamel Removers						
Other Manicuring Preparations						
Personal Cleanliness						
Bath Soaps and Body Washes			7	NR		
Deodorants (underarm)			2 (not spray)	NR		
Douches						
Disposable Wipes			2	NR		
Other Personal Cleanliness Products			1 (l.o.); 8 (r.o.)	NR		
Shaving Preparations						
Aftershave Lotions			1	NR		
Beard Softeners			3	NR		
Pre-shave Lotions (all types)			1	NR		
Shaving Cream (aerosol, brushless, lather)			2	NR		
Other Shaving Preparations			5	NR		
Skin Care Preparations						
Cleansing			93	NR		

Table 2. Frequency and concentration of use according to likely duration and exposure and by product category

	# of Uses RLD (2025)[7,8]	Max Conc of Use % (2026)[9,10]	# of Uses RLD (2025)[7,8]	Max Conc of Use % (2026)[9,10]	# of Uses RLD (2025)[7,8]	Max Conc of Use % (2026)[9,10]
Depilatories			2	NR		
Face and Neck (excluding shaving preps)	3 (l.o.)	NR	251 (l.o.); 47 (r.o.)	NR		
Body and Hand (excluding shaving preps)			21 (l.o.); 3 (r.o.)	NR		
Foot Powders and Sprays						
Moisturizing			120	NR	1	NR
Night			12	NR		
Paste Masks (mud packs)			13	NR		
Skin Fresheners			25	NR		
Other Skin Care Preparations			69 (l.o.); 45 (r.o.)	NR	1 (l.o.)	NR
Suntan Preparations						
Suntan Gels, Creams, and Liquids			8	NR		
Indoor Tanning Preparations			4 (traditional)	NR		
Other Suntan Preparations			2	NR		
Other Preparations (i.e., those that do not fit another category)			18	NR		

NR – not reported
l.o. – leave-on; r.o. – rinse-off
*The sum of the counts given for duration of use and by exposure type, and the sum of the frequency reported by product category, may not equal the sum of total uses because each ingredient may be used in cosmetic formulations that are reported under more than one product category.
**Likely duration and exposure are derived from survey data based on product category (see Use Categorization https://www.cir-safety.org/cir-findings)
[a] It is possible these products are sprays, but it is not specified whether the reported uses are sprays.
[b] Not specified whether a spray or a powder, but it is possible the use can be as a spray or a powder, therefore the information is captured in both categories
[c] It is possible these products are powders, but it is not specified whether the reported uses are powders.

Table 3. Cytotoxicity studies

Test Article	Vehicle	Cell Type	Dose/Concentration	Procedure	Results	Reference
RELEVANT TO SODIUM HYALURONATE CROSSPOLYMER-4 (BDDE is a crosslinker for this polymer)						
Hyaluronic acid membrane (6%) crosslinked with BDDE (0.01%)	NR	HCECs	NR	CCK-8 assay; cells were treated with the test article for 12, 24, and 48 h. Controls were untreated.	At 48 h, cells treated with the test article had a 50% increase in cell viability and expression of MK167 (cell marker for proliferation)	[15]
Hyaluronic acid hydrogel crosslinked with BDDE	NR	MC3T3-E1 cells	0.1 ml	CCK-8 assay; cells were treated with the test article for 24 h. Negative controls were untreated. Positive controls were treated with Triton X-100.	Cell viability for the cells treated with the test article was 105% compared to control which was 100%.	[16]
Hyaluronic acid hydrogel crosslinked with BDDE	NR	MC3T3-E1 cells	0.1 ml	LDH assay; cells were treated with the test article for 24 h. Negative controls were untreated. Positive controls were treated with Triton X-100.	The cells treated with the test article had a cytotoxicity of 3% ± 7%, compared to the control 0 ± 8%. The difference was not statistically significant.	[16]
Hyaluronic acid (6%) gel with citric acid (12%) and crosslinked with BDDE	NR	L929 mouse fibroblast cells	0 – 15%	Multiple biphasic gel formations were created. The MTT assay was only performed on the steam-sterilized biphasic gel formation containing 6% HA crosslinked with BDDE and 12% citric acid non-crosslinked; cells were treated with the test article for 24 h. Controls were untreated.	No adverse effect on cell viability was detected with the cells treated with the test article.	[17]
Hyaluronic acid hydrogel crosslinked with BDDE (2 g of a 20 mg/ml hydrogel in 10 ml of media)	NR	HaCaT and HDF	0, 25, 50, and 100%	MTT assay; cells were treated with the test article for 48 h. Controls were untreated.	In both cell types, cell viability decreased with the test article at 100% concentration. In comparison, the test article had significantly lower cell viability than the hyaluronic acid hydrogel crosslinked with PEGDE (2 g of a 20 mg/ml hydrogel in 10 ml of media) when treated at 100% concentration.	[19]
Hyaluronic acid hydrogel crosslinked with BDDE (2 g of a 20 mg/ml hydrogel in 10 ml of media)	NR	HaCaT and HDF	0, 25, 50, and 100%	LDH assay; cells were treated with the test article for 48 h. Controls were untreated.	HDF treated with the test article had a higher LDH release compared to cells treated with high concentrations of the hyaluronic acid hydrogel crosslinked with PEGDE (2 g of a 20 mg/ml hydrogel in 10 ml of media). For the HaCaT cells, the LDH release was similar.	[19]
Hyaluronic acid hydrogel crosslinked with BDDE (2 g of a 20 mg/ml hydrogel in 10 ml of media)	NR	NHEK and HDF	NR	Live/dead cell assay after being exposed to the test article for 7 d. No other information provided.	NHEK and HDF exposed to the test article had higher proportion of dead cells compared to cells exposed to the hyaluronic acid hydrogel crosslinked with PEGDE (2 g of a 20 mg/ml hydrogel in 10 ml of media)	[19]
Hyaluronic acid hydrogel crosslinked with BDDE (2 g of a 20 mg/ml hydrogel in 10 ml of media)	NR	HaCaT and HDF	0, 25, 50, and 100%	The cell membranes were dyed, and the integrity was assessed after being exposed to the test article.	Cells exposed to the test article (100% concentration) had slight disruption of cell membrane and morphology.	[19]

Table 3. Cytotoxicity studies

Test Article	Vehicle	Cell Type	Dose/Concentration	Procedure	Results	Reference
Hyaluronic acid hydrogel crosslinked with BDDE (2 g of a 20 mg/ml hydrogel in 10 ml of media)	NR	HaCaT and HDF	0, 25, 50, and 100%	Cellular oxidative stress was measuring using DCFH-DA assay after cells were treated with the test article for 48 h. Controls were untreated.	HaCaT cells: When exposed to the test article (100% concentration), there were higher cellular ROS levels than the control. Cells exposed to the test article had higher cellular ROS levels compared to cells exposed to the hyaluronic acid hydrogel crosslinked with PEGDE (2 g of a 20 mg/ml hydrogel in 10 ml of media) HDF cells: The test article significantly increased intracellular ROS levels at 50% and 100% concentration compared to control. Cells exposed to the test article had higher cellular ROS levels compared to cells exposed to the hyaluronic acid hydrogel crosslinked with PEGDE (2 g of a 20 mg/ml hydrogel in 10 ml of media).	[19]
Hyaluronic acid hydrogel crosslinked with BDDE (2 g of a 20 mg/ml hydrogel in 10 ml of media)	NR	HaCaT and HDF	0, 25, 50, and 100%	Mitochondrial membrane potential assay was used after cells were treated with the test article for 48 h. Controls were untreated.	HaCaT cells: Cells treated with the test article at 100% concentration had greater mitochondrial membrane disruption compared to cells exposed to the hyaluronic acid hydrogel crosslinked with PEGDE (2 g of a 20 mg/ml hydrogel in 10 ml of media). HDF cells: The test article at 50% and 100% had increased MMP and caused greater mitochondrial membrane disruption at 100% compared to the hyaluronic acid hydrogel crosslinked with PEGDE (2 g of a 20 mg/ml hydrogel in 10 ml of media).	[19]
BDDE	PBS	HaCaT and HDF	0, 5, 25, 100, 500, and 1000 ppm	MTT assay; cells were treated with the test article for 24 h. Controls were untreated.	The MTT assay indicated that, compared to the control, both cells treated with BDDE (100 – 1000 ppm) significant decrease in cell viability. Cell viability was significantly lower in the cells treated with BDDE compared to PEGDE.	[18]
BDDE	PBS	HaCaT and HDF	0, 5, 25, 100, 500, and 1000 ppm	LDH assay; cells were treated with the test article for 24 h. Controls were untreated.	In the LDH assay, compared to the control, HaCaT cells treated with BDDE (100 – 1000 ppm) and HDF cells treated with BDDE (500 – 1000 ppm) had a significantly higher LDH release. Overall, the LDH release was significantly higher in BDDE treated cells when compared to PEGDE treated cells.	[18]
BDDE	PBS	HaCaT and HDF	0, 10, 50, and 100 ppm	Cell membrane integrity was measured using dyes to stain the cell membranes after cells were treated with the test article for 24 h. Fluorescence was visualized using a fluorescence microscope after washing with PBS. Controls were untreated.	HaCaT cells: BDDE (100 ppm) induced disruption of cell membrane and shape. HDF cells: BDDE (50 and 100 ppm) induced cellular malformation	[18]

Table 3. Cytotoxicity studies

Test Article	Vehicle	Cell Type	Dose/Concentration	Procedure	Results	Reference
BDDE	PBS	HaCaT and HDF	0, 10, 50, and 100 ppm	Cellular oxidative stress was measuring using DCFH-DA assay after cells were treated with the test article for 24 h. Controls were untreated.	HaCaT cells: BDDE (50 and 100 ppm) had higher cellular ROS levels compared to the control HDF cells: BDDE (10, 50 and 100 ppm) had higher cellular ROS levels compared to the control	[18]
BDDE	PBS	HaCaT and HDF	0, 10, 50, and 100 ppm	Mitochondrial membrane potential assay was used after cells were treated with the test article for 3 h. Controls were untreated.	HaCaT cells: BDDE (50 and 100 ppm) induced mitochondrial membrane disruption with a significantly higher fluorescence ratio compared to control HDF cells: BDDE (10, 50 and 100 ppm) induced mitochondrial membrane disruption with a significantly higher fluorescence ratio compared to control	[18]
RELEVANT TO SODIUM HYALURONATE CROSSPOLYMER-6 (PEGDE is a crosslinker for this polymer)						
Hyaluronic acid hydrogel crosslinked with PEGDE	NR	MC3T3-E1 cells	0.1 ml	CCK-8 assay; cells were treated with the test article for 24 h. Negative controls were untreated. Positive controls were treated with Triton X-100.	Cell viability for the cells treated with the test article was 151% compared to control which was 100%.	[16]
Hyaluronic acid hydrogel crosslinked with PEGDE	NR	MC3T3-E1 cells	0.1 ml	LDH assay; cells were treated with the test article for 24 h. Negative controls were untreated. Positive controls were treated with Triton X-100.	The cells treated with the test article had a cytotoxicity of 3% ± 6%, compared to the control 0 ± 8%. The difference was not statistically significant.	[16]
Hyaluronic acid hydrogel crosslinked with PEGDE (2 g of a 20 mg/ml hydrogel in 10 ml of media)	NR	HaCaT and HDF	0, 25, 50, and 100%	MTT assay; cells were treated with the test article for 48 h. Controls were untreated.	In both cell types, cell viability decreased with the test article at 100% concentration. In comparison, the test article had significantly higher cell viability than the hyaluronic acid hydrogel crosslinked with BDDE (2 g of a 20 mg/ml hydrogel in 10 ml of media) when treated at 100% concentration.	[19]
Hyaluronic acid hydrogel crosslinked with PEGDE (2 g of a 20 mg/ml hydrogel in 10 ml of media)	NR	HaCaT and HDF	0, 25, 50, and 100%	LDH assay; cells were treated with the test article for 48 h. Controls were untreated.	HDF treated with the test article had a lower LDH release compared to cells treated with high concentrations of the hyaluronic acid hydrogel crosslinked with BDDE (2 g of a 20 mg/ml hydrogel in 10 ml of media). For the HaCaT cells, the LDH release was similar.	[19]
Hyaluronic acid hydrogel crosslinked with PEGDE (2 g of a 20 mg/ml hydrogel in 10 ml of media)	NR	NHEK and HDF	NR	Live/dead cell assay after being exposed to the test article for 7 d. No other information provided.	NHEK and HDF exposed to the test article had lower cytotoxicity compared to when exposed to the hyaluronic acid hydrogel crosslinked with BDDE (2 g of a 20 mg/ml hydrogel in 10 ml of media).	[19]
Hyaluronic acid hydrogel crosslinked with PEGDE (2 g of a 20 mg/ml hydrogel in 10 ml of media)	NR	HaCaT and HDF	0, 25, 50, and 100%	The cell membranes were dyed and the integrity was assessed after being exposed to the test article.	Cells exposed to the test article did not exhibit observable toxic effects in either HaCaT or HDF cells.	[19]

Table 3. Cytotoxicity studies

Test Article	Vehicle	Cell Type	Dose/Concentration	Procedure	Results	Reference
Hyaluronic acid hydrogel crosslinked with PEGDE (2 g of a 20 mg/ml hydrogel in 10 ml of media)	NR	HaCaT and HDF	0, 25, 50, and 100%	Cellular oxidative stress was measuring using DCFH-DA assay after cells were treated with the test article for 48 h. Controls were untreated.	HaCaT cells: When exposed to the test article (100% concentration), there were higher cellular ROS levels than the control. Cells exposed to the test article had lower cellular ROS levels compared to cells exposed to the hyaluronic acid hydrogel crosslinked with BDDE (2 g of a 20 mg/ml hydrogel in 10 ml of media). HDF cells: The test article significantly increased intracellular ROS levels at 50 and 100% concentration compared to control. Cells exposed to the test article had lower cellular ROS levels compared to cells exposed to the hyaluronic acid hydrogel crosslinked with BDDE (2 g of a 20 mg/ml hydrogel in 10 ml of media).	[19]
Hyaluronic acid hydrogel crosslinked with PEGDE (2 g of a 20 mg/ml hydrogel in 10 ml of media)	NR	HaCaT and HDF	0, 25, 50, and 100%	Mitochondrial membrane potential assay was used after cells were treated with the test article for 48 h. Controls were untreated.	HaCaT cells: Cells treated with the test article at 100% concentration had less mitochondrial membrane disruption compared to cells exposed to the hyaluronic acid hydrogel crosslinked with BDDE (2 g of a 20 mg/ml hydrogel in 10 ml of media). HDF cells: The test article at 100% concentration caused less mitochondrial membrane disruption compared to the hyaluronic acid hydrogel crosslinked with BDDE (2 g of a 20 mg/ml hydrogel in 10 ml of media) at 50 and 100%.	[19]
PEGDE	PBS	HaCaT and HDF	0, 5, 25, 100, 500, and 1000 ppm	MTT assay; cells were treated with the test article for 24 h. Controls were untreated.	The MTT assay indicated that, compared to the control, cells treated with PEGDE (500 – 1000 ppm) had a significant decrease in cell viability. Cell viability was significantly lower in the cells treated with BDDE compared to PEGDE.	[18]
PEGDE	PBS	HaCaT and HDF	0, 5, 25, 100, 500, and 1000 ppm	LDH assay; cells were treated with the test article for 24 h. Controls were untreated.	In the LDH assay, compared to the control, HaCaT cells treated with PEGDE (500 – 1000 ppm) and HDF cells treated with PEGDE (1000 ppm) had a significantly higher LDH release. However, the LDH release was significantly higher in BDDE treated cells compared to PEGDE treated cells.	[18]
PEGDE	PBS	HaCaT and HDF	0, 10, 50, and 100 ppm	Cell membrane integrity was measured using dyes to stain the cell membranes after cells were treated with the test article for 24 h. Fluorescence was visualized using a fluorescence microscope after washing with PBS. Controls were untreated.	HaCaT cells: PEGDE exhibited no effect on the membrane and shape. HDF cells: PEGDE (100 ppm) induced cellular malformation.	[18]
PEGDE	PBS	HaCaT and HDF	0, 10, 50, and 100 ppm	Cellular oxidative stress was measuring using DCFH-DA assay after cells were treated with the test article for 24 h. Controls were untreated.	HaCaT cells: PEGDE (100 ppm) had higher cellular ROS levels compared to the control. HDF cells: PEGDE (50 and 100 ppm) had higher cellular ROS levels compared to the control.	[18]

Table 3. Cytotoxicity studies

Test Article	Vehicle	Cell Type	Dose/Concentration	Procedure	Results	Reference
PEGDE	PBS	HaCaT and HDF	0, 10, 50, and 100 ppm	Mitochondrial membrane potential assay was used after cells were treated with the test article for 3 h. Controls were untreated.	HaCaT cells: PEGDE had no effect on MMP. HDF cells: PEGDE (10, 50 and 100 ppm) induced mitochondrial membrane disruption with a significantly higher fluorescence ratio compared to control.	[18]

BDDE – 1,4-butanediol diglycidyl ether; CCK-8 - cell counting kit-8; DCFH-DA - dichloro-dihydro-fluorescein diacetate; HaCaT – human keratinocyte cell line; HAM – hyaluronic acid membrane; HCECs – human corneal epithelial cells; HDF – human dermal fibroblast cell line; L929 cells - murine fibroblast cells; LDH - lactate dehydrogenase; MC3T3-E1 – mouse pre-osteoblastic cells; MMP - mitochondrial membrane potential; MTT - (3-(4, 5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide; NHEK – human epidermal keratinocytes; PBS – phosphate-buffered saline; PEGDE - polyethylene glycol diglycidyl ether; ROS – reactive oxygen species

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Concentration of Use by FDA Product Category[1]*

Sodium Hyaluronate Crosspolymer
Sodium Hyaluronate Crosspolymer-2
Sodium Hyaluronate Crosspolymer-3

Ingredient	Product Category	Maximum Concentration of Use
Sodium Hyaluronate Crosspolymer	Hair dyes and colors	0.003%
Sodium Hyaluronate Crosspolymer	Foundations Traditional	 0.95%
Sodium Hyaluronate Crosspolymer	Lipstick	0.00035%
Sodium Hyaluronate Crosspolymer	Other makeup preparations Traditional	 0.0035%
Sodium Hyaluronate Crosspolymer	Bath soaps and body washes	0.0000007%
Sodium Hyaluronate Crosspolymer	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.00035-0.47%
Sodium Hyaluronate Crosspolymer	Face and neck products (not spray) Leave-on Rinse-off	 0.00013-0.95% 0.00013%
Sodium Hyaluronate Crosspolymer	Body and hand products (not spray) Leave-on	 0.0011-0.002%
Sodium Hyaluronate Crosspolymer	Moisturizing products (not spray)	0.0035-0.47%
Sodium Hyaluronate Crosspolymer	Other skin care preparations Leave-on Rinse-off	 0.2% 0.0001%

*The ingredients included in the title of the table but not found in the table were included in the concentration of use survey, but no uses were reported.

Information collected in 2025
Table prepared: March 31, 2025
Updated May 15, 2026: added Foundations; face and neck product leave-on increased to 0.95%; body and hand product leave-on increased to 0.002%

[1] The new FDA cosmetic product categories under MoCRA were used for this survey.

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Personal Care Products Council

Memorandum

TO: Bart Heldreth, Ph.D.
Executive Director - Cosmetic Ingredient Review

FROM: Carol Eisenmann, Ph.D.
Personal Care Products Council (PCPC)

DATE: May 4, 2026

SUBJECT: Concentration of Use by FDA Product Category: Sodium Hyaluronate Crosspolymers-4, -6 and -7

Sodium Hyaluronate Crosspolymer-4, Sodium Hyaluronate Crosspolymer-6 and Sodium Hyaluronate Crosspolymer-7 were included in the March 2026 PCPC concentration of use survey. No uses of these three Sodium Hyaluronate Crosspolymers were reported.

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Personal Care Products Council

Memorandum

TO: Bart Heldreth, Ph.D.
Executive Director - Cosmetic Ingredient Review

FROM: Carol Eisenmann, Ph.D.
Personal Care Products Council

DATE: May 15, 2026

SUBJECT: Sodium Hyaluronate Crosspolymer

Anonymous. 2018. Summary Information: HRIPT data for a serum containing 0.948% Sodium Hyaluronate Crosspolymer.

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Summary Information

HRIPT data for a serum containing 0.948% Sodium Hyaluronate Crosspolymer

Test procedure:	Human repeated insult patch test
Date of final report:	January 24th, 2018
Test article:	Serum containing 0.948% Sodium Hyaluronate Crosspolymer
Amounts of product applied:	Approximately 0.03 g/cm^2
Test subject:	58 subjects (5 males and 53 females)
Conclusion:	Two subjects discontinued the study for personal reasons unrelated to the conduct of the study. No skin reactivity observed at any time during the course of study.

The following Dermal Score was used.

0 = No evidence of any effect
+ = Barely perceptible (Minimal, faint, uniform or spotty erythema)
1 = Mild (Pink, uniform erythema covering most of the contact site)
2 = Moderate (Pink-red erythema uniform in the entire contact site)
3 = Marked (Bright red erythema with/without petechiae or papules)
4 = Severe (Deep red erythema with/without vesiculation or weeping)

Induction Phase Summary

Test Article	Induction Scores (Number of Responses)						Evidence of Irritation
	0.5	1	2	3	4	Other	
[redacted]	0	0	0	0	0	0	No

Challenge Phase Summary

Test Article	Challenge Scores (Number of Responses)						Evidence of Sensitization
	0.5	1	2	3	4	Other	
[redacted]	0	0	0	0	0	0	No

There was no skin reactivity observed at any time during the course of the study.

Results:	Under the conditions of a repeated insult (occlusive) patch test procedure conducted in 56 subjects, test article was "Dermatologist-Tested" and was not associated with skin irritation or allergic contact dermatitis in human subjects.