ADMIN

Priorities

EXPERT PANEL MEETING
September 30 – October 1, 2024

Cosmetic Ingredient Review

Commitment & Credibility since 1976

Memorandum

Date: September 6th, 2024

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

To: All Stakeholders

Re: 2024/2025 Final Priority List

There are 18 reports docketed, covering 32 ingredients, on the 2024/2025 Final Priorities List. While the priority list includes only the lead ingredients, groupings of ingredients for reports can be found on the following pages. Reports previously prioritized and on the CIR docket (including Dimer Dilinoleate, *Lactobacillus* ferment ingredients, *Salix alba* (willow)-derived ingredients, HC Blue No. 1, *Pelargonium graveolens*-derived ingredients, *Houttuynia cordata*-derived ingredients, Sigesbeckia Orientalis Extract, *Centaurea cyanus* flower-derived ingredients, and Sodium Hydrosulfite), as well as an extensive number of re-reviews of previous assessments, will supplement the total number of reports/ingredients to be assessed in 2024/2025, and beyond. Rereviews to potentially be considered for reopening during 2024/2025, based on time passed since last assessment, include:

2-Nitro-*p*- & 4-Nitro-*o*-Phenylenediamine
Aloe-derived ingredients
Butylene Glycol, etc.
Capsaicin, etc.
Dimethicone Copolyol ingredients
Ethyl Methacrylate
Fossil & Synthetic Waxes (e.g., Ozokerite)
Glyceryl Monoesters
Glycyrrhetinic Acid, etc.
Maleic Acid
Methacrylic Acid
p-Methylaminophenol & Sulfate
Niacinamide & Niacin
Oryza sativa (rice)-derived ingredients
Oxyquinoline & Oxyquinoline Sulfate
PEGs Laurate
Sodium & Ammonium Lauryl Sulfate
Sodium *p*-Chloro-*m*-Cresol, etc.
Stearyl Alcohol, etc.
Tosylamide/Formaldehyde Resin
Urea
Waxes (e.g., Candelilla)

Additionally, with modernization efforts to better utilize in silico tools (e.g., DEREK), NAMs (new approach/non-animal methodologies), *Cosmetics Direct* (the US FDA mandatory reporting program to replace the now defunct voluntary program, VCRP), formalized exposure and risk assessments (when warranted), and read-across (including proposals of the Read-Across Working-Group), we believe that there is plenty of substance on the Panel's docket to extend through the end of 2025.

Accordingly, we propose no frequency-of-use (FOU)-based ingredient report additions to the Panel's docket in the coming year. However, if any interested party would like to request an ingredient review for cause (including: highlighting a potential risk/safety concern, accompanied with supporting data/ information), we would be happy to present these to the Panel for potential prioritization.

We have received data from the initial stages of *Cosmetics Direct*, with regard to mandatory cosmetic product registration, as a result of a Freedom of Information Act (FOIA) request submitted earlier this year. The data received are in a format that is "per product," and not directly amenable to culling FOU values "per ingredient," akin to those we previously obtained from the VCRP. However, CIR Staff have accomplished some initial processing of the data received to output tentative FOU values. Those tentative values are included below in the draft Final Priorities List for comparison to previous VCRP data.

Thus, interested parties are again encouraged to submit pertinent data to the CIR, as soon as possible, for use in the development of the Scientific Literature Reviews (SLR), and to participate in meetings of the Panel, for the ingredients on the 2024/2025 Final Priorities List. Although the specific data needs vary for each safety assessment, the following are typical data that the Panel reviews for each safety assessment.

- Chemistry, impurities, and method of manufacture
- Exposure and risk
- Toxicokinetics data, specifically dermal absorption and penetration
- Repeated-dose toxicity data
- Inhalation toxicity data, if the ingredient is used in a product that can be incidentally inhaled
- Reproductive/developmental toxicity data
- Genotoxicity data; if positive, carcinogenicity data may be needed
- Dermal irritation and sensitization data at maximum concentration of use

For the review of natural complex substances (NCS), including botanical or animal derived ingredients, the additional data needed include: species, organism part, extraction method, solvent, and data on component chemical characterization. It is important that these data are specific for the ingredient(s) as used in cosmetics.

2024/2025 Final Priorities List

Ingredient	Frequency of Use (FOU) - VCRP Data Year: 2023	*Tentative FOU Cosmetics Direct* Data Year: 2024
For cause		
Cannabidiol	32	112
Trimethylbenzoyl Diphenylphosphine Oxide	127	2070
Tetrabromophenol Blue	2	40
Per FOU (VCRP)		
Polyacrylate-13	**265**	**993**
Polygonum Cuspidatum Root Extract	**245**	**1094**
Xylitylglucoside	**213**	**1672**
Phytosphingosine	**210**	**2197**
Sodium Hyaluronate Crosspolymer	**207**	**2965**
Polyacrylate Crosspolymer-6	**205**	**1550**
Trimethylpentanediyl Dibenzoate	**202**	**3020**
Tosylamide/Epoxy Resin	**189**	**1580**
Carnosine	**184**	**936**
Madecassoside	**182**	**1394**
Propolis Extract	**179**	**1020**
Sophora Flavescens Root Extract	**179**	**356**
Curcuma Longa (Turmeric) Root Extract	**177**	**1896**
Lonicera Japonica (Honeysuckle) Flower Extract	**175**	**946**
Perfluorohexylethyl Triethoxysilane	**172**	**144**

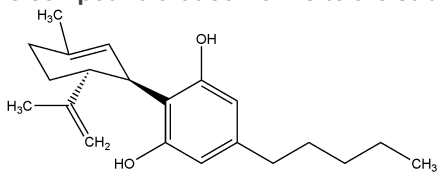
2024/2025 Final Priorities Groupings for New Reports

Planned 2024/2025 Reports – for cause

Cannabidiol – *Previously proposed for Panel review by FDA*

→Cannabidiol (aka CBD) **FOU (2023) = 32**

Definition: Cannabidiol is the organic compound that conforms to the structure:



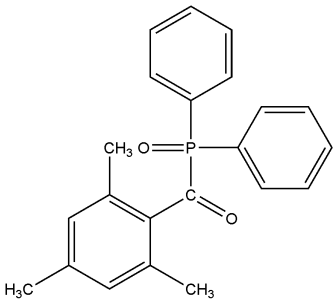
Reported **Functions**: Antiacne Agents; Antioxidants; Drug Astringents - Skin Protectant Drugs; Skin Protectants; Skin-Conditioning Agents - Miscellaneous

Notes: *(CAS No. 13956-29-1) At a previous meeting, a liaison from the FDA proposed that the Panel assess the safety of Cannabidiol. At that time, there were zero formulations reported to the VCRP containing cannabinoid ingredients; accordingly, the Panel chose to defer review.*

Grouping proposal: None

Trimethylbenzoyl Diphenylphosphine Oxide – *FDA request* **FOU (2023) = 127**

Definition: Trimethylbenzoyl Diphenylphosphine Oxide is the organic compound that conforms to the structure:



Reported **Function**: Skin Conditioning Agent

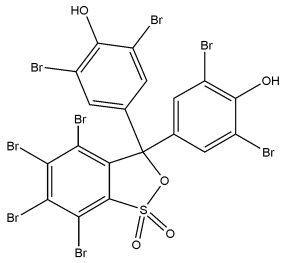
Notes: *ECHA launched a 45-d consultation for their plan for Diphenyl(2,4,6-trimethylbenzoyl)phosphine oxide (Trimethylbenzoyl Diphenylphosphine Oxide) to be added to the substances of very high concern (SVHC) list on February 17, 2023. There are new DART concerns.*

Grouping proposal: None

Tetrabromophenol Blue – SCCS insufficient data

FOU (2023) = 2

Definition: Tetrabromophenol Blue is the organic compound that conforms to the structure:



Reported **Function**: Hair Colorant

Notes: *(CAS No. 4430-25-5) There is a 2019 SCCS opinion (https://health.ec.europa.eu/system/files/2021-08/sccs_o_232_0.pdf) with a conclusion of safe when used as a hair dye in oxidative and non-oxidative hair coloring products at a final on-head concentration of up to 0.2%. Tetrabromophenol Blue has also been added to EU Annex III (entry 319) with the limitations recommended by the SCCS in 2019.*

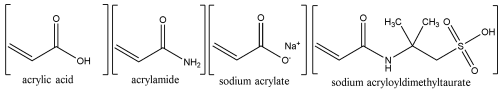
Grouping proposal: None

Planned 2024/2025 Reports – per FOU (2023)

Polyacrylate-13

FOU = 265

Definition: Polyacrylate-13 is the copolymer of acrylic acid, acrylamide, sodium acrylate, and sodium acryloyldimethyltaurate monomers.



Reported **Function**: Film Formers

Notes: *The Panel has previously assessed the safety of structurally similar ingredients in the Safety Assessment of Acryloyldimethyltaurate Polymers as Used in Cosmetics, finalized in 2017 (e.g., Acrylamide/Sodium Acryloyldimethyltaurate/Acrylic Acid Copolymer, defined as: a copolymer of acrylamide, sodium acryloyldimethyltaurate, and acrylic acid monomers), concluding that such copolymers are safe as used.*

Grouping proposal: None

Polygonum Cuspidatum Root Extract

FOU = 245

Definition: Polygonum Cuspidatum Root Extract is the extract of the roots of *Polygonum cuspidatum.* The accepted scientific name for *Polygonum cuspidatum* is *Fallopia japonica.*

Reported **Functions**: Antioxidants; Skin-Conditioning Agents – Miscellaneous

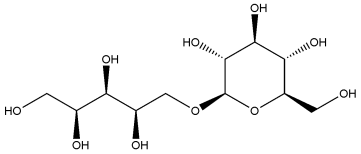
Notes: *These 2 botanical ingredients are derived from the same plant species, 1 from the root and the other from the whole plant.*

CIR draft grouping/clustering: (2 ingredients proposed with a total FOU = 245)	***FOU***
Polygonum Cuspidatum Root Extract	*245*
Polygonum Cuspidatum Extract	*-*

Xylitylglucoside

FOU = 213

Definition: Xylitylglucoside is the organic compound that conforms to the structure:



Reported **Functions**: Skin-Conditioning Agents - Humectant

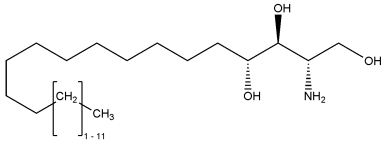
Notes: *(CAS No. 1095751-96-4)*

CIR draft grouping: None

Phytosphingosine

FOU = 210

Definition: Phytosphingosine is a synthetic sphingolipid that conforms generally to the structure:



Reported **Functions**: Hair Conditioning Agents; Skin-Conditioning Agents - Miscellaneous

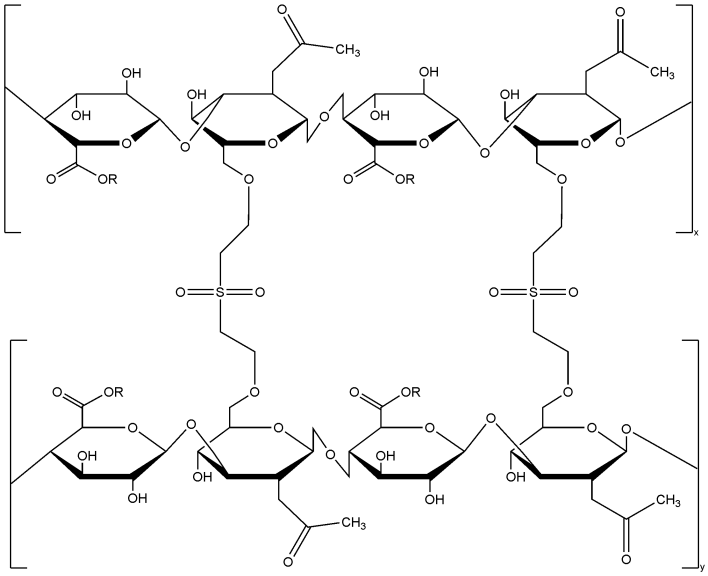
Notes: *(CAS Nos. 554-62-1; 13552-11-9) The Panel has previously assessed the safety of structurally-related ingredients in the Safety Assessment of Ceramides as Used in Cosmetics, published in IJT in 2020 (e.g., Caprooyl Phytosphingosine, defined as: the product obtained by the reaction of Caproic Acid and Phytosphingosine), concluding that such copolymers are safe as used. While Phytosphingosine contains a free amine functional group, the ceramides differ as corresponding amides.*

CIR draft grouping: (4 ingredients proposed with a total FOU = 233)	***FOU***
Phytosphingosine	*210*
Tetraacetylphytosphingosine	*17*
Acetylphytosphingosine	*4*
Phytosphingosine HCl	*2*

Sodium Hyaluronate Crosspolymer

FOU = 207

Definition: Sodium Hyaluronate Crosspolymer is the sodium salt of a polymer of Hyaluronic Acid crosslinked with *di*vinyl sulfone.



wherein R is hydrogen or sodium

Reported **Functions**: Skin-Conditioning Agents – Humectant; Skin-Conditioning Agents - Miscellaneous

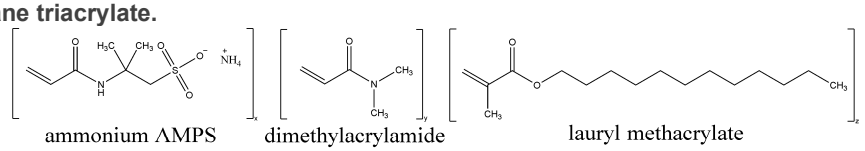
Notes: *(CAS No. 105524-32-1) These 3 ingredients share the same polyhyaluronate backbone and differ only by the crosslinker (diglycidyl ether for Sodium Hyaluronate Crosspolymer-2 and propylbisoxyamine for Sodium Hyaluronate Crosspolymer-3). (The Panel has recently addressed the safety of Sodium Hyaluronate.)*

CIR draft grouping: (3 ingredients proposed with a total FOU = 210)	***FOU***
Sodium Hyaluronate Crosspolymer	*207*
Sodium Hyaluronate Crosspolymer-2	*2*
Sodium Hyaluronate Crosspolymer-3	*1*

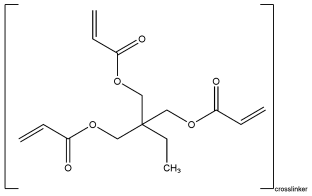
Polyacrylate Crosspolymer-6

FOU = 205

Definition: Polyacrylate Crosspolymer-6 is a copolymer of ammonium AMPS (2-acrylamido-2-methylpropane sulfonic acid), dimethylacrylamide, lauryl methacrylate, and laureth-4 methacrylate, crosslinked with trimethylolpropane triacrylate.



ammonium AMPS dimethylacrylamide lauryl methacrylate



trimethylolpropane triacrylate

***Reported* Functions**: Emulsion Stabilizers; Viscosity Increasing Agents - Aqueous

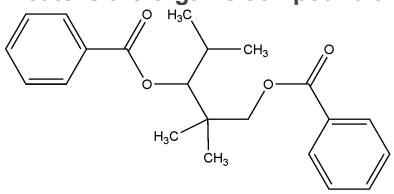
Notes:

CIR draft grouping: none

Trimethylpentanediyl Dibenzoate

FOU = 202

Definition: Trimethylpentanediyl Dibenzoate is the organic compound that conforms to the structure:



***Reported* Functions**: Plasticizers

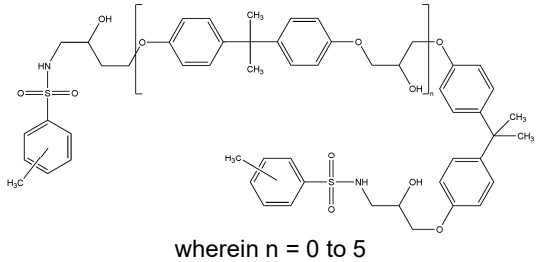
Notes: *(CAS No. 68052-23-3)*

CIR draft grouping: none

Tosylamide/Epoxy Resin

FOU = 189

Definition: Tosylamide/Epoxy Resin is the toluenesulfonamide of the condensation product of 4,4'-isopropylidenediphenol/epichlorohydrin copolymer, also known as the epoxy resin. The polymeric end-product conforms generally to the structure:



wherein n = 0 to 5

***Reported* Functions**: Dispersing Agents – Nonsurfactant; Film Formers; Plasticizers

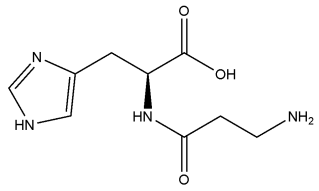
Notes: *According to chemical structure, minimum molecular weight is 1012 Da.*

CIR draft grouping: none

Carnosine

FOU = 184

Definition: Carnosine is the heterocyclic amine that conforms to the structure:



***Reported* Functions**: Skin-Conditioning Agents - Miscellaneous

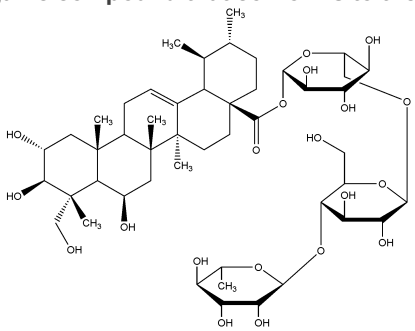
Notes: *(CAS No. 305-84-0)*

CIR draft grouping: None

Madecassoside

FOU = 182

Definition: Madecassoside is the organic compound that conforms to the structure:



***Reported* Function**: Antioxidants; Skin Protectants; Skin-Conditioning Agents - Miscellaneous

Notes: (*CAS No. 34540-22-2*)

Grouping proposal: None

Propolis Extract

FOU = 179

Definition: Propolis Extract is the extract of Propolis Wax.

***Reported* Function**: Skin-Conditioning Agents – Miscellaneous

Notes: *These 2 natural complex substance (NCS) ingredients are each derived from a resinous substance found in beehives.*

CIR draft grouping: (2 ingredients proposed with a total FOU = 205)	***FOU***
Propolis Extract	*179*
Propolis Wax	*18*
(Propolis Wax is also called "Propolis" in the VCRP data)	*7*

Sophora Flavescens Root Extract

FOU = 179

Definition: Sophora Flavescens Root Extract is the extract of the roots of *Sophora flavescens*.

Reported **Functions**: Antioxidants; Skin-Conditioning Agents – Miscellaneous

Notes: *These 3 botanical ingredients are each from the same species, Sophora flavescens, sometimes referred to as shrubby sophora. Of these 3, 2 ingredients are derived from the root, and the other is derived from the whole plant.*

CIR draft grouping: (3 ingredients proposed with a total FOU = 220)	***FOU***
Sophora Flavescens Root Extract	*179*
Sophora Flavescens Extract	*40*
Sophora Flavescens Root Powder	*1*

Curcuma Longa (Turmeric) Root Extract

FOU = 177

Definition: Curcuma Longa (Turmeric) Root Extract is the extract of the roots of *Curcuma longa*.

Reported **Functions**: Skin-Conditioning Agents - Miscellaneous

Notes: *(CAS No. 84775-52-0) The ingredients in this group are each derived from the same species.*

CIR draft grouping: (5 ingredients proposed with a total FOU = 220)	***FOU***
Curcuma Longa (Turmeric) Root Extract	*177*
Curcuma Longa (Turmeric) Root Oil	*17*
Curcuma Longa (Turmeric) Root Powder	*15*
Curcuma Longa (Turmeric) Rhizome Extract	*6*
Curcuma Longa (Turmeric) Leaf Extract	*5*

Lonicera Japonica (Honeysuckle) Flower Extract

FOU = 175

Definition: Lonicera Japonica (Honeysuckle) Flower Extract is the extract of the flowers of *Lonicera japonica.*

***Reported* Functions**: Skin-Conditioning Agents - Miscellaneous

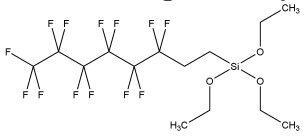
Notes: *(CAS No. 223749-79-9 (generic)) The ingredients in this group are each derived from the same species (also known as Japanese Honeysuckle).*

CIR draft grouping: (2 ingredients proposed with a total FOU = 180)	***FOU***
Lonicera Japonica (Honeysuckle) Flower Extract	*175*
Lonicera Japonica (Honeysuckle) Leaf Extract	*5*

Perfluorohexylethyl Triethoxysilane

FOU = 172

Definition: Perfluorohexylethyl Triethoxysilane is the organic compound that conforms to the structure:



***Reported* Functions**: Binders; Skin-Conditioning Agents - Miscellaneous

Notes: *(CAS No. 51851-37-7)*

Grouping proposal: None