

Admin

Priorities

EXPERT PANEL MEETING
March 6-7, 2023



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Memorandum

Date: February 10th, 2023

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

To: All Stakeholders

Re: 2024 Draft Priority List

The CIR Procedures require preparation of the 2024 Draft Priority List for public comment by June 1, 2023. However, it is advantageous for the 2024 Draft Priority List to be issued for public comment earlier (March 2023) in the process to allow more time for the acquisition of data. The draft priority list comprises nominated-for-cause ingredients and ingredients with the highest frequency of use (FOU), out of those that have yet to be reviewed by the Panel. FOU data are provided by FDA's Voluntary Cosmetic Registration Program (VCRP); this year, VCRP data were received from the FDA on February 2 (in response to a Freedom of Information Act request).

At a previous meeting, a liaison from the FDA proposed that the Panel assess the safety of Cannabidiol (CBD) and other cannabinoids as used in cosmetics. At that time, there were zero formulations reported to the VCRP containing cannabinoid ingredients; accordingly, the Panel chose to defer review at that time. However, uses are now reported for these ingredients; for example, Cannabidiol is currently reported to be used in 32 formulations and Cannabis Sativa Seed Oil is reported to be used in as many as 217 formulations (i.e., 126 for the name Cannabis Sativa (Hemp) Seed Oil, 86 under the name Cannabis Sativa Seed Oil (the INCI name), and 5 uses reported for Cannabis Sativa Oil). Thus, these ingredients are once again proposed for Panel review.

Last year CIR became aware of an in-use hair dye ingredient (1,2,4-Trihydroxybenzene) that was listed on Annex II in the EU, but not yet assessed for safety by this Panel (which was consequently added to the 2023 Priorities). Accordingly, CIR searched for other ingredients within these parameters and discovered 2 further hair dye ingredients, Basic Blue 7 (FOU = 1) and Basic Blue 9 (FOU = 4). Additionally, 2 other hair dye ingredients, Tetrabromophenol Blue (FOU = 2) and Bismuth Citrate (FOU = 1) were found with insufficient-data-to-determine-safety conclusions, by the SCCS, though not as of yet on Annex II. Consequently, these 4 ingredients are proposed herein for inclusion in the 2024 Priorities.

While this list includes only the lead ingredients, groupings of ingredients drafted by CIR Staff can be found on the following pages. The Panel is asked to consider these groupings. There are 20 reports proposed, covering 40 ingredients, on the 2024 Draft Priorities List. Once a proposal of a hair dye for assessment has been received from the PCPC Hair Color Technical Committee (HCTC), 21 new reports in total will be proposed for the 2024 docket. Reports previously prioritized and on the CIR docket at the end of 2023, as well as an extensive number of re-reviews of previous assessments, will supplement the total number of reports to be assessed in 2024.

Interested parties are encouraged to submit pertinent data to the CIR, as soon as possible, for use in the development of the Scientific Literature Reviews (SLR) for these ingredients. 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
- Toxicokinetics data, specifically dermal absorption and/or 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 botanical ingredients, the additional data needed include: species, plant 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 Draft Priorities List

Ingredient	Frequency of Use (FOU) Data Year: 2023
<i>For cause</i>	
<i>To be determined hair dye ingredient by HCTC</i>	-
Cannabidiol	32
Basic Blue 7	1
Basic Blue 9	4
Tetrabromophenol Blue	2
Bismuth Citrate	1
<i>Per FOU</i>	
Polyacrylate-13	265
Polygonum Cuspidatum Root Extract	245
Xylitylglucoside	213
Phytosphingosine	210
Sodium Hyaluronate Crosspolymer	207
Polyacrylate Crosspolymer-6	205
Trimethylpentanediyl Dibenzoate	202
Tosylamide/Epoxy Resin	189
Carnosine	184
Madecassoside	182
Propolis Extract	179
Sophora Flavescens Root Extract	179
Curcuma Longa (Turmeric) Root Extract	177
Lonicera Japonica (Japanese Honeysuckle) Flower Extract	175
Perfluorohexylethyl Triethoxysilane	172

2024 Draft Priorities Groupings for New Reports

Proposed 2024 Report – per cause

To be determined – per PCPC Hair Color Technical Committee (HCTC) FOU = __

Reported Function: Hair Colorant

Notes: Since FOU might not be a very accurate surrogate for exposure, with regard to hair dyes, the PCPC HCTC proposes one hair dye ingredient annually for CIR review. The HCTC typically submits a proposed hair dye ingredient between the 1st and 2nd meetings of the year.

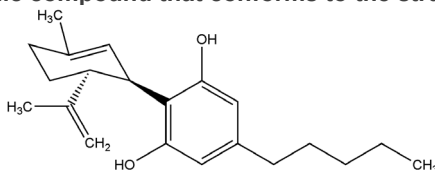
Grouping proposal: None

CBD and other cannabinoids – Previously proposed for Panel review by FDA

→Cannabidiol (CBD)

FOU = 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 (CBD) and other cannabinoids as used in cosmetics. At that time, there were zero formulations reported to the VCRP containing cannabinoid ingredients; accordingly, the Panel chose to defer review.

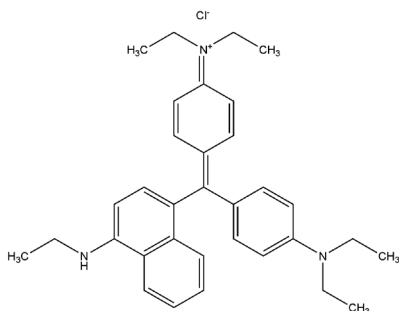
CIR draft grouping/clustering: (6 ingredients proposed with a total FOU ≤ 291) FOU

Cannabidiol	32
Cannabis Sativa Seed Oil	(reported under various names) ≤ 217
Cannabis Sativa Seed Extract	17
Cannabis Sativa Extract	10
Cannabis Sativa Flower Extract	8
Cannabis Sativa Leaf Extract	7

Basic Blue 7 – on EU Annex II – forbidden from use in cosmetics

FOU = 1

Definition: Basic Blue 7 is classed chemically as a triarylmethane color. It conforms to the structure:



Reported Function: Hair Colorant

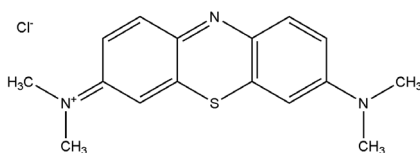
Notes: (CAS No. 2390-60-5) on EU Annex II – forbidden from use in cosmetics

Grouping proposal: None

Basic Blue 9 – on EU Annex II – forbidden from use in cosmetics

FOU = 4

Definition: Basic Blue 9 is the thiazine color that conforms to the structure:



Reported Function: Hair Colorant

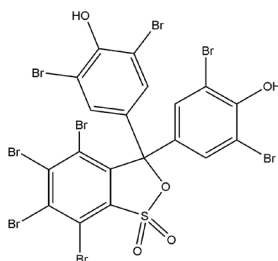
Notes: (CAS No. 61-73-4) on EU Annex II – forbidden from use in cosmetics

Grouping proposal: None

Tetrabromophenol Blue – SCCS insufficient data

FOU = 2

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



Reported Function: Hair Colorant

Notes: (CAS No. 4430-25-5) “Based on the data provided, the SCCS is of the opinion that the use of Tetrabromophenol Blue with a maximum on-head concentration of 0.2% in non-oxidative hair dye formulations does pose a risk to the health of the consumer due to the low Margin of Safety.

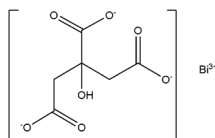
Tetrabromophenol Blue is a mixture octa-, hepta-, and hexa-bromo phenolsulfonphthaleins, and does not contain any Tetrabromo-homologue, therefore the INCI name is misleading. The criteria for meeting the specifications of other batches, similar to the present mixture should be defined. No acceptable dermal absorption study under oxidative conditions was provided. An assessment of the use of Tetrabromophenol Blue in oxidative hair dye formulations cannot be performed without an adequate dermal absorption study and stability data in an oxidative environment.” -Conclusion of the SCCS opinion at its 15th plenary meeting of 26-27 June 2012.

Grouping proposal: None

Bismuth Citrate – SCCS insufficient data

FOU = 1

Definition: Bismuth Citrate is the bismuth salt of citric acid that conforms to the structure:



Reported Function: Hair Colorant

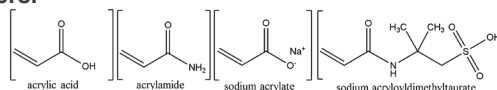
Notes: (CAS No. 813-93-4) “From the data provided by the applicant, SCCS cannot assess the safety of bismuth citrate. The following information is required to evaluate the safety of bismuth citrate. A complete and adequate physico-chemical characterisation of Bismuth citrate is needed. Skin and eye irritation studies are required at the concentration of 2% as applied for by the applicant. Clarification regarding conflicting information on the solubility of Bismuth citrate in DMSO is required before the test can be accepted as valid. The mutagenicity of bismuth citrate can presently not be assessed given the study conditions provided. A complete set of in vitro studies according to the current Notes of Guidance is required.” -Conclusion of the SCCS opinion at its 4th plenary meeting on 12 December 2013.

Grouping proposal: None

Proposed 2024 Reports – per FOU**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)

Polygonum Cuspidatum Root Extract

Polygonum Cuspidatum Extract

FOU

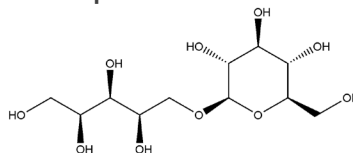
245

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Xylitylglucoside

FOU = 213

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



Reported Functions: Skin-Conditioning Agents - Humectant

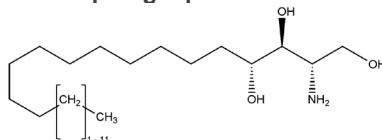
Notes: (CAS No. 1095751-96-4)

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.

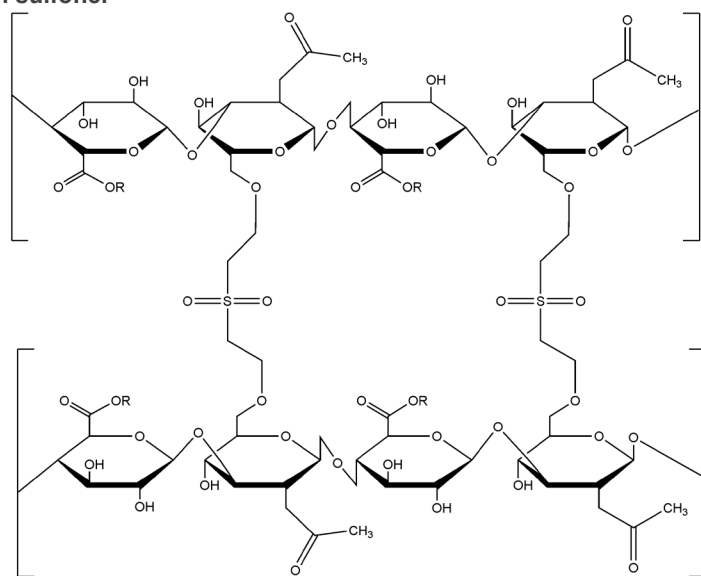
CIR draft grouping: (4 ingredients proposed with a total FOU = 233)

	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 divinyl 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 propylbisoxamine for Sodium Hyaluronate Crosspolymer-3).

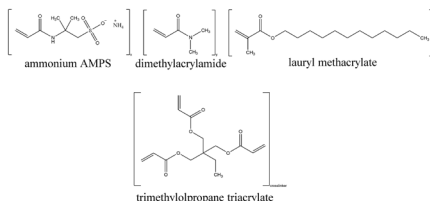
CIR draft grouping: (3 ingredients proposed with a total FOU = 210)

	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.



Reported Functions: Emulsion Stabilizers; Viscosity Increasing Agents - Aqueous

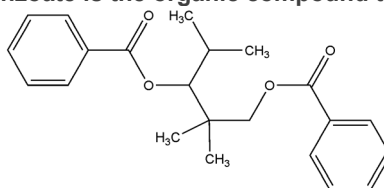
Notes:

CIR draft grouping: none

Trimethylpentanediyl Dibenzoate

FOU = 202

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



Reported Functions: Plasticizers

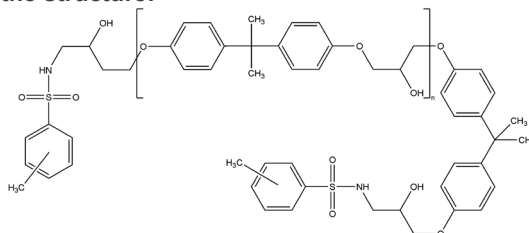
Notes: (CAS No. 68052-23-3)

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

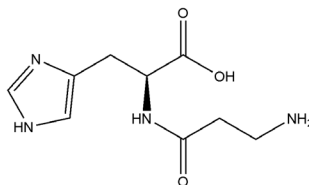
Notes: According to chemical structure, minimum molecular weight is 1012 Da.

CIR draft grouping: none

Carnosine

FOU = 184

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



Reported Functions: Skin-Conditioning Agents - Miscellaneous

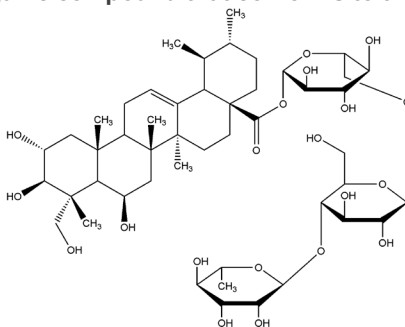
Notes: (CAS No. 305-84-0)

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 (a resinous substance found in beehives).



Reported Function: Skin-Conditioning Agents - Miscellaneous

Notes: All 3 of these ingredients are derived from the resinous substance found in beehives.

CIR draft grouping: (3 ingredients proposed with a total FOU = 227)

Propolis Extract

Propolis Wax

Propolis Cera

FOU

202

18

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)

	<u>FOU</u>
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)

CIR draft grouping: (5 ingredients proposed with a total FOU = 220)

	<u>FOU</u>
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 (Japanese Honeysuckle) Flower

FOU = 175

Extract

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))

CIR draft grouping: (2 ingredients proposed with a total FOU = 180)

Lonicera Japonica (Japanese Honeysuckle) Flower

Lonicera Japonica (Honeysuckle) Leaf Extract

FOU

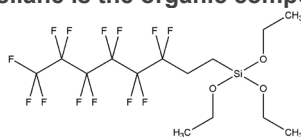
175

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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