Safety Assessment of *Salix alba* (Willow)-Derived Ingredients as Used in Cosmetics

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

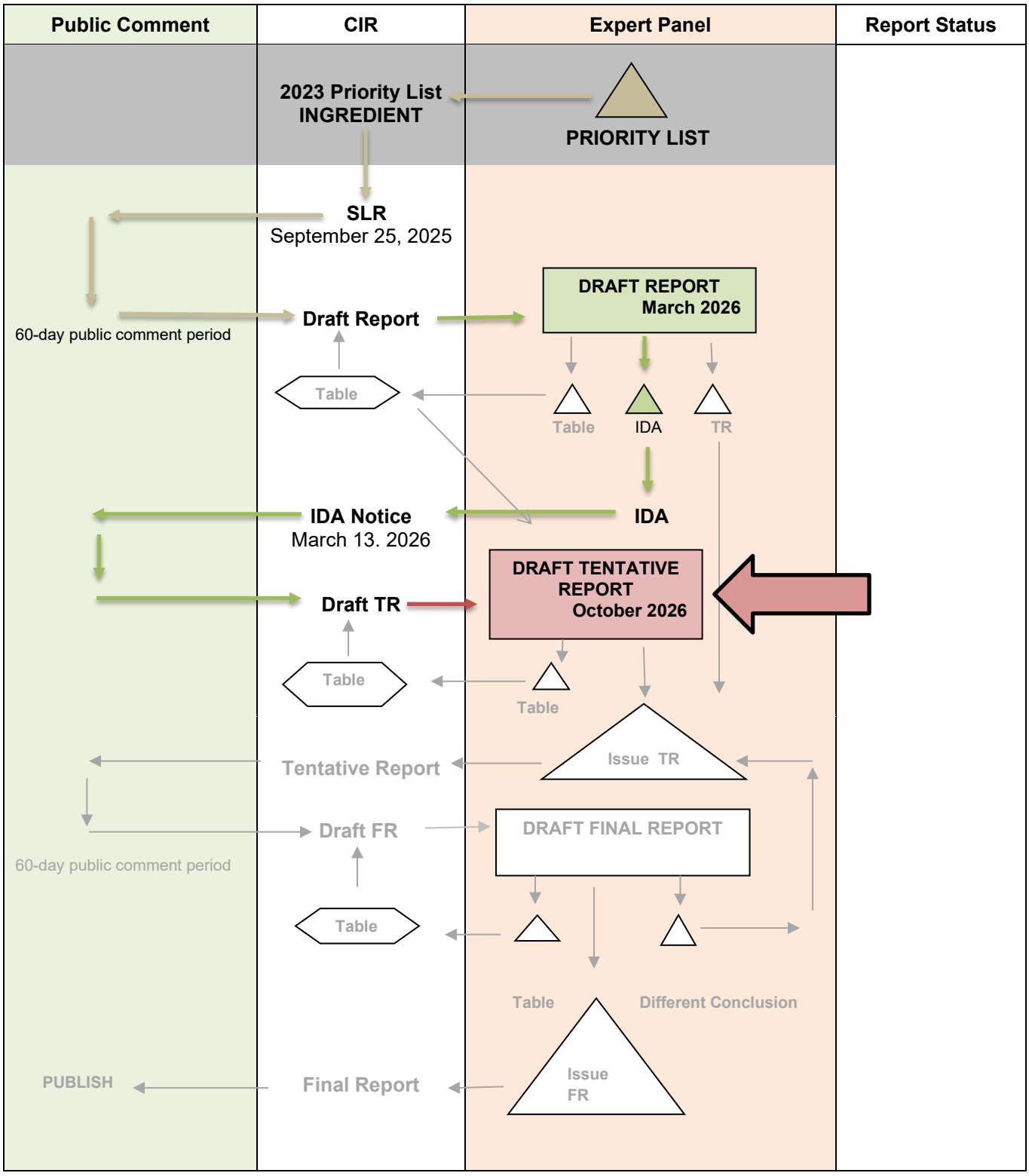
The Expert Panel for Cosmetic Ingredient Safety members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; Bruce A. Brod, M.D., M.H.C.I., F.A.A.D.; Samuel M. Cohen, M.D., Ph.D.; Curtis D. Klaassen, Ph.D.; Allan E. Rettie, Ph.D.; David Ross, Ph.D.; Paul W. Snyder, D.V.M., Ph.D.; and Susan C. Tilton, Ph.D. Previous Panel member involved in this assessment: David E. Cohen, M.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 Priya Ferguson, M.S., Associate Toxicologist/Senior Scientific Analyst/Writer, CIR.

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SAFETY ASSESSMENT FLOW CHART

INGREDIENT/FAMILY *Salix alba* (Willow)-Derived Ingredients
MEETING October 2026



COSMETIC INGREDIENT REVIEW
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Memorandum

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Priya Ferguson, M.S., Associate Toxicologist/Senior Scientific Analyst/Writer, CIR
Date: September 11, 2026
Subject: Safety Assessment of *Salix alba* (Willow)-Derived Ingredients

Enclosed is the Draft Tentative Report on the Safety Assessment of *Salix alba* (Willow)-Derived Ingredients as Used in Cosmetics. (It is identified as *report_Willow_102026* in the pdf document). At the March 2026 meeting, the Panel determined that the data were insufficient to support the safety of these cosmetic ingredients and issued an Insufficient Data Announcement (IDA) with the following data needs:

- For Salix Alba (Willow) Bark Extract:
  - Concentration of use in baby products
  - Photoallergenicity data

- For Salix Alba (Willow) Leaf Extract:
  - DART data
  - Photoallergenicity data

- For Salix Alba (Willow) Bark Powder, Salix Alba (Willow) Bark Water, Salix Alba (Willow) Extract, and Salix Alba (Willow) Flower Extract:
  - Method of manufacturing
  - Composition and impurities
  - 28-d dermal toxicity
    - If absorbed, DART and genotoxicity data may be needed
  - Dermal sensitization and irritation data at maximum use concentrations
  - Phototoxicity/photosensitization data

- For all ingredients:
  - Particle size/particle size distribution
  - Habits and practices related to airbrush use
  - Ocular irritation data at maximum use concentrations

Since the issuing of the IDA, a product specification sheet on Salix Alba (Willow) Bark Extract in glycerin and water was received (*data_Willow_102026*) and incorporated into the report in highlighted text. Also incorporated in highlighted text are changes since the last iteration of this report, including additional information characterizing the salicylate constituents and other phenolic constituents of *Salix alba* (willow) bark.

Other information included in this packet:

- comments on the March 2026 Draft Report from Council (*PCPCcomments_Willow_102026*)
- responses to comments on the Draft Report (*response-PCPCcomments_Willow_102026*)
- flow chart (*flow_ Willow_102026*)
- transcripts (*transcripts_Willow_102026*)
- report history (*history_ Willow_102026*)
- search strategy (*search_ Willow_102026)*
- data profile (*dataprofile_Willow_102026)*

A draft Abstract and Discussion have been included in this report version. The Panel should carefully consider and discuss the data (or lack thereof) and be prepared to issue a Tentative Report with a safe, safe with qualifications, insufficient data, unsafe, or split conclusion, and identify any additional items for inclusion in the Discussion.

A table is provided to indicate data insufficiencies and availability of the requested data.

Data Insufficiency	Data needs met?	Details
Salix Alba (Willow) Bark Extract		
concentration of use in baby products	no	Salix Alba (Willow) Bark Extract reports baby product use in the following categories: baby shampoos, baby lotions/oils/powders/creams, and other baby products. While no concentrations of use were reported for these particular uses, concentrations of use are available for this ingredient for some corresponding adult products (e.g., Salix Alba (Willow) Bark Extract is reported to be used at up to 0.01% in non-coloring shampoos and 1.1% and 0.53% in face and neck and body and hand products, respectively). These adult product categories may provide context for the potential concentrations of use in the corresponding baby product categories. No corresponding adult product category could be identified for the reported use in other baby products.
photoallergenicity data	no	
Salix Alba (Willow) Leaf Extract		
DART data	no	
photoallergenicity data	no	
Salix Alba (Willow) Bark Powder, Salix Alba (Willow) Bark Water, Salix Alba (Willow) Extract, and Salix Alba (Willow) Flower Extract		
method of manufacturing data	no	
composition and impurities data	no	
28-d dermal toxicity data (if absorbed, DART and genotoxicity data may be needed)	no	
dermal sensitization and irritation data at maximum use concentrations	no	
phototoxicity/photosensitization data	no	
For all ingredients		
particle size/particle size distribution data	no	
habits and practices related to airbrush use	no	
ocular irritation data at maximum use concentrations	no	

Salix alba (Willow)-Derived Ingredients History

September 2025

SLR posted

October 2025

2025 concentration of use data received

Comments on SLR from Council received

Summary HRIPT on 0.0025% Salix Alba (Willow) Bark Extract received

November 2025

Summary data received on Salix Alba (Willow) Bark Extract (method of manufacturing, composition and impurities, acute toxicity, dermal irritation, dermal sensitization)

Summary data received on Salix Alba (Willow) Leaf Extract (composition, impurities, ocular irritation, cutaneous tolerance, cutaneous sensitization, acute toxicity, mutagenicity, phototoxicity)

Studies received on Salix Alba (Willow) Bark Extract (composition, manufacturing, specifications, genotoxicity, steroidogenesis, ocular and dermal irritation, sensitization, phototoxicity)

January 2026

Concentration of use data received

March 2026

Comments received on Draft Report from Council received

Panel reviews Draft Report

Panel issues IDA with the following insufficiencies:

- For Salix Alba (Willow) Bark Extract – concentrations of use in baby products and photoallergenicity data
- For Salix Alba (Willow) Leaf Extract – DART and photoallergenicity data
- For Salix Alba (Willow) Bark Powder, Salix Alba (Willow) Water, Salix Alba (Willow) Extract, Salix Alba (Willow) Flower Extract – manufacturing data, composition and impurities data, 28-d dermal toxicity (if absorbed, DART and genotoxicity), sensitization and irritation at max use concentrations, photosensitization/phototoxicity data at maximum use concentrations
- Information on particle size and particle distribution/habits and practices related to airbrush use
- Ocular irritation at maximum use concentrations

July 2026

- Product specifications (Salix Alba (Willow) Bark Extract in glycerin and water)

October 2026

- Panel reviews Draft Tentative Report

Salix alba (Willow)-Derived Ingredients Data Profile* – October 2026 – Writer, Priya Ferguson																														
					Toxico-kinetics		Acute Tox			Repeated Dose Tox			DART		Genotox		Carci		Dermal Irritation			Dermal Sensitization				Ocular Irritation		Clinical Studies	
	Reported Use	GRAS	Method of Mfg	Constituents/ Impurities	Dermal Penetration	ADME	Dermal	Oral	Inhalation	Dermal	Oral	Inhalation	Dermal	Oral	In Vitro	In Vivo	Dermal	Oral	In Vitro	Animal	Human	In Vitro/ In Chemico	Animal	Human	Phototoxicity	In Vitro	Animal	Retrospective/ Multicenter	Case Reports
Salix Alba (Willow) Bark Extract	**X**		**X**	X				X			X			X	X	X			X	X		X	X	X	X	X			X
Salix Alba (Willow) Bark Powder	**X**			X																										
Salix Alba (Willow) Bark Water	**X**																													
Salix Alba (Willow) Extract	**X**																													
Salix Alba (Willow) Flower Extract	**X**																													
Salix Alba (Willow) Leaf Extract	**X**		**X**	X				X							X					X		X	X		X		X		

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

Salix alba (Willow)-Derived Ingredients

Ingredient	CAS #	PubMed	FDA	CompTox	ChemPort	NIOSH	NTIS	NTP	FEMA	EU	ECHA	SIDS	SCCS	AICIS	FAO	WHO	Web
Salix Alba (Willow) Bark Extract	84082-82-6	X	X								X						X
Salix Alba (Willow) Bark Powder																	
Salix Alba (Willow) Bark Water																	
Salix Alba (Willow) Extract		X															
Salix Alba (Willow) Flower Extract																	
Salix Alba (Willow) Leaf Extract	84082-82-6	X															

X= data found

Botanical and/or Fragrance Websites

Ingredient	CAS #	Dr. Duke's	Taxonomy	GRIN	Sigma-Aldrich	AHPA	AGRICOLA	IFRA	RIFM
Salix Alba (Willow) Bark Extract	84082-82-6	X	X	X					
Salix Alba (Willow) Bark Powder			X	X					
Salix Alba (Willow) Bark Water			X	X					
Salix Alba (Willow) Extract			X	X					
Salix Alba (Willow) Flower Extract			X	X					
Salix Alba (Willow) Leaf Extract	84082-82-6	X	X	X					

Search Strategy

The following search terms were searched in PubMed:

Salix alba
Salix alba leaf
Salix alba bark
Salix alba leaf extract
Salix alba bark extract
Willow leaf extract
Willow bark extract
Salix alba bark water
Willow bark water
Salix alba extract
Salix alba flower
84082-82-6
Salix alba cosmetic
Salix alba metabolism
Salix alba penetration
Salix alba dermal
Salix alba skin
Salix alba allergy
Salix alba case report
Salix alba anaphylaxis
Salix alba ocular
Salix alba clinical
Salix alba cosmetic

The following search terms were used in all links other than PubMed:

Salix alba
Willow
84082-82-6

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
- 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/

Botanical Websites

- Dr. Duke's - https://phytochem.nal.usda.gov/
- Taxonomy database - http://www.ncbi.nlm.nih.gov/taxonomy
- GRIN (U.S. National Plant Germplasm System) - https://npgsweb.ars-grin.gov/gringlobal/taxon/taxonomysimple.aspx
- Sigma Aldrich plant profiler- http://www.sigmaaldrich.com/life-science/nutrition-research/learning-center/plant-profiler.html
- American Herbal Products Association Botanical Safety Handbook (2nd Edition; 2013) - http://abc.herbalgram.org/site/DocServer/AHPABotanicalSafety_FMexcerpt.pdf?docID=4601
- National Agricultural Library NAL Catalog (AGRICOLA) https://agricola.nal.usda.gov/
- The Seasoning and Spice Association List of Culinary Herbs and Spices
- http://www.seasoningandspice.org.uk/ssa/background_culinary-herbs-spices.aspx

Fragrance Websites

- IFRA (International Fragrance Association) – https://ifrafragrance.org/
- Research Institute for Fragrance Materials (RIFM) - https://www.rifm.org/#gsc.tab=0 http://fragrancematerialsafetyresource.elsevier.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: March 6, 2026

SUBJECT: Draft Report: Safety Assessment of *Salix alba* (Willow)-Derived Ingredients as Used in Cosmetics (March 2026 meeting draft)

The Personal Care Products Council respectfully submits the following comments on the draft report, Safety Assessment of *Salix alba* (Willow)-Derived Ingredients as Used in Cosmetics.

Method of Manufacture – Since this section starts with a paragraph that indicates that it is not always known if the methods "apply to cosmetic ingredient manufacturing", the methods provided through PCPC should be identified as coming from cosmetic ingredient manufacturers.

Please correct "rotary vapor" (it should be "rotary evaporator")

Composition and Impurities - Please add the USP specifications for Salix Alba (White Willow) Bark Extract to the Composition and Impurities section.

When stating quantitative composition information, please clarify what the value represents, e.g., mg/g dried bark.

Cosmetic Use – In the Cosmetic Use section, please also state the maximum use concentration of Salix Alba (Willow) Leaf Extract reported (0.00002% in other hair preparations).

Non-Cosmetic Use – It would be helpful to state why an extract of *Salix alba* bark is used in fertilizers (salicylates are plant growth stimulators).

Genotoxicity – This section would be easier to read if the information on the leaf extract was in a

separate paragraph.

Summary – Please correct “function in skin-conditioning agents”) (“in” should be “as”)

As salicylates are important components of these ingredients, it would be helpful to mention some composition information in the Summary.

Table 5 – Please revise Table 5 to be consistent with the memo from PCPC concerning tattoo preparations (memo dated February 26, 2026).

***Salix alba* (Willow)-derived ingredients – October 2026 – Priya Ferguson**	
Comment Submitter: Personal Care Products Council **Date of Submission: March 6, 2026**	
Comment	**Response/Action**
Method of Manufacture – Since this section starts with a paragraph that indicates that it is not always known if the methods "apply to cosmetic ingredient manufacturing", the methods provided through PCPC should be identified as coming from cosmetic ingredient manufacturers.	addressed
Please correct "rotary vapor" (it should be "rotary evaporator")	addressed
Composition and Impurities - Please add the USP specifications for Salix Alba (White Willow) Bark Extract to the Composition and Impurities section	addressed
When stating quantitative composition information, please clarify what the value represents, e.g., mg/g dried bark	addressed
Cosmetic Use – In the Cosmetic Use section, please also state the maximum use concentration of Salix Alba (Willow) Leaf Extract reported (0.00002% in other hair preparations)	addressed
Non-Cosmetic Use – It would be helpful to state why an extract of Salix alba bark is used in fertilizers (salicylates are plant growth stimulators)	information not relevant to report
Genotoxicity – This section would be easier to read if the information on the leaf extract was in a 2 separate paragraphs	addressed
Summary – Please correct "function in skin-conditioning agents") ("in" should be "as")	addressed
As salicylates are important components of these ingredients, it would be helpful to mention some composition information in the Summary	this information is not typically included in the summary; ingredients are being reviewed as whole, botanical mixtures
Table 5 – Please revise Table 5 to be consistent with the memo from PCPC concerning tattoo preparations (memo dated February 26, 2026).	addressed

MARCH 2026 MEETING – FIRST REVIEW/DRAFT REPORT

Belsito Team – March 12, 2026

DR. BELSITO: Okay. So, this is a draft report on six Willow-derived ingredients. It's the first time we're looking at it. We got a good amount of data on the bark extract, less so but probably sufficient for the leaf extract, and nothing for the bark powder water extract or flower extract. Again, we'll have to have the Pyrogallol discussion with this.

And in terms of PCPC comments, I guess, the one we need to address is in terms of composition and impurities. They said, in addition to discussing heavy metal impurities, it'd be helpful to discuss salicylates, the components for which the Salix species are used in cosmetics. So, it's the salicylate content of the Willow that, I guess, is of cosmetic importance.

And they wanted either a structure for salicin or describe how it's related to salicylic acid. And Priya's comment was that, "No further details regarding potential components because this is not typically present in a CIR report." I just had a question. Is this true?

I mean, we actually mention components for this in this report. We talk about Pyrogallol. Were you specifically saying, Priya, that we should not look at specific toxicologic endpoints for the salicylates or the salicin, because we're looking at the whole product? Was that what you meant by that comment?

MS. FERGUSON: Right. Typically, we don't look at specific endpoints for parts of the plant -- or components of a botanical. And we don't usually include structures of a component of a botanical.

DR. BELSITO: Right. I agree with that.

DR. HELDRETH: Yeah, that's always our initial approach to mixtures, these botanicals, is to try to evaluate the mixtures as a whole. But once this comes to the Panel table and you find constituents of concern, then we can drill down on those if you think it needs highlighting. But we try to approach all the botanicals as whole mixtures, at least in the first go-round.

DR. BELSITO: Right.

DR. SNYDER: I had a question for the chemists. On page 20, on this Pyrogallol issue, it says that -- it's on the second paragraph where it says, "and tannin," and then, in parentheses, it says, "expressed as Pyrogallol." Can somebody explain how do tannins and Pyrogallol -- what is that -- how does --

DR. BELSITO: Well, the way I understood this is Pyrogallol is a tannin. And for all of them, like, polyphenols expressed as gallic acid, flavones as rutin, I assumed that the gallic acid was the highest concentration among the polyphenols, and that rutin was the highest among the flavones, and Pyrogallol was the highest among the tannins. But that was -- I mean, again, I'm not a chemist either.

DR. SNYDER: Because it says that the tannins were at 12 milligrams per gram, but then there's other things in -- that's not 12 milligrams per gram Pyrogallol, it's 12 milligrams per gram of tannins, plural, meaning there's -- so I'm confused by that.

DR. HELDRETH: Yeah, my understanding of it is that a lot of the tannins in plants are often called Pyrogallol tannins because, simply upon heating, they get hydrolyzed and release Pyrogallol. And so, you can kind of back-calculate, all right, this is how much tannins were in there by how much Pyrogallol is released on this heating.

So it's not really saying that there's 12 mgs per gram of Pyrogallol; it's saying that there's 12 mgs per gram Pyrogallol was released, and basically it's pointing back to how much tannin was in there.

DR. RETTIE: Yeah, total tannin.

DR. HELDRETH: Right.

DR. BELSITO: Oh, okay.

DR. SNYDER: I think that goes to our discussion to say that we noted it, but we consider it to be below the threshold of concern.

DR. BELSITO: Yeah, I mean, we don't even know if Pyrogallol is there, right? It's when it's heated, it's converted into Pyrogallol, but you don't heat your cosmetics.

DR. SNYDER: Yeah.

DR. BELSITO: Okay.

DR. KLAASSEN: But you heat -- there's a lot of tannins in tea, right? And so when you heat your tea, make hot tea, you're releasing a lot of Pyrogallol. Is that right?

DR. BELSITO: Yeah. That's why you should drink red wine instead. You don't heat that.

DR. RETTIE: Kind of goes against all the putative health benefits of especially green tea there, so not exactly sure about that, Curt, but not going to argue with you.

DR. BELSITO: Okay. I think we've dealt with the Pyrogallol situation. There's not necessarily pyrogallol present, it's used as an identifying component for tannins, since when heated they're hydrolyzed? Or what happens with heating, Bart?

DR. HELDRETH: It's hydrolyzing the tannin, which releases some Pyrogallol. I wouldn't say that this information tells us that there's no Pyrogallol present. I think that maybe you want some direction here to say, you know, the processing should -- you should take care with the processing to not release enough Pyrogallol to be a concern or something along those lines, because it's certainly possible. It's certainly possible that the ingredient as supplied, it's already been hydrolyzed, we just don't know.

DR. SNYDER: So, you're thinking safe as use, Don?

DR. BELSITO: Hold on one second; I'm getting this hydrolyzed tannins. Okay. So, I guess the issues that I had, and I suppose, in a sense, this is probably related to the salicin or salicylic concentrations; we have use in children, we have use in aerosolized products, and we have use in oral products. Oral use, use in less than three-year-old children, and aerosol use is banned in the EU. And I'm presuming that's based upon salicylate content and exposure. I have to assume.

Do we have any further details on that? Exactly how they came up with those conclusions, particularly for aerosol and oral? Because oral was a (inaudible).

MS. FERGUSON: That's for salicylic acid, not for the Willow ingredients.

DR. BELSITO: Okay. Okay, I see what you're saying. So, it would apply to these based upon the amount of salicylic acid they had, correct?

MS. FERGUSON: Right.

DR. BELSITO: Okay. On PDF Page 21, the short-term toxicity study, Priya, the dermo on the bark extract, it seems to me almost more like an irritation study than a tox study. They didn't look at anything systemic. They just report on effects on the skin. No erythema or edema were observed.

MS. FERGUSON: I can move it.

DR. BELSITO: Okay. Under the effects on pigmentation -- this is PDF Page 23 -- I would delete that entire reference because dihydroxyacetone is a stain on the stratum corneum to give you a fake tan. It has nothing to do with pigment. And all this study is showing is really that the preparation cleanses the skin. It gets rid of the dihydroxyacetone that's been incorporated into the stratum corneum. So, it's not a pigment effect at all. It's a color effect. Comments? Curt, Paul, Allan?

DR. SNYDER: None for me.

DR. BELSITO: Would you delete it?

DR. RETTIE: Where is it again, Don, exactly? Did you say 21?

DR. BELSITO: 23, Effect on Pigmentation? So, it's looking at taking skin that was essentially dyed with a dihydroxyacetone. So the dihydroxyacetone is bound into the stratum corneum, it's oxidized, and it gives this sort of brown color to the skin. There's no effect on pigmentation.

And then they're looking at eliminating that color by using the Willow bark extract in a base lotion. And it's a good cleanser, you know, it strips out some of the color, but it's not a pigment effect. It's not an effect on melanogenesis. I mean, I guess it's a pigment if you talk about pigment being a color, but it's not pigment as we think about pigmentation and melanin.

DR. RETTIE: Sounds like we could quite easily delete it then, if that's the case.

DR. BELSITO: Yeah, I would recommend, because it's not even worth a point in the Discussion.

DR. RETTIE: It's not even a straw man.

DR. BELSITO: Yeah. So, we have good sensitization data on the leaf and the bark. With phototoxicity, there's a comment that the phototoxicity was evaluated for the bark extract because it produced significant absorbance in the wavelengths of the interest, and it wasn't phototoxic in the 3T3. And also the leaf wasn't in a 3T3. But we don't know about the photo-allergenicity.

So, I thought that we needed photo-allergenicity for all of the materials, or an absorbance spectra for the components showing a molar absorption coefficient of less than or equal to a thousand, to suggest that it's not a phototoxic or photo-allergenic concern. Because salicylates clearly absorb, and some of the salicylates are photosensitizers.

DR. SNYDER: Then let's ask for it.

DR. BELSITO: Yeah. So, what I had here were insufficiencies -- well, I guess we got the information on the EU restrictions for salicylic acid. We needed photo-allergy for the bark and leaf. And although it's not OECD-approved, it is JaCVAM-approved, so I would accept a ROS assay, if it were negative, to clear the photo-allergenicity for those two.

We need manufacturing, composition and impurities on all except the bark and leaf, concentration of use for all except the bark and leaf, DART and genotox for all except the bark and leaf, and sensitization and irritation for all except the bark and leaf. So if we can get just a little bit of photo-allergy data, I thought we could go with the bark and the leaf as safe as used, but we need either a calculation of the molar extinction coefficient for the bark and the leaf, or photo-allergy data on those. So, that's where I was at.

And in the Discussion, heavy metals pesticide boilerplates, aerosol use, and the salicylate issue with the restrictions in the EU, the concern about potential salicylate toxicity, I guess, with oral and with children.

DR. SNYDER: I can agree with that.

DR. RETTIE: Yeah, I just had a small question for discussion or maybe my education. It seems that life is always getting easier with these botanicals when we have an extract of the whole plant and, hopefully, some information that helps us with safety, but we don't have that here. But we do have a flower extract, and that got me thinking, even if we had a whole plant extract, would that clear flower in this case? I guess there would always be, you know, the organs to make a flower, so probably so, but -- I'm probably digging in the weeds here. I just created a hole for myself.

DR. BELSITO: I think you're getting into the weeds. Let's address it when we have data on the whole plant.

DR. RETTIE: Yeah, yeah.

DR. BELSITO: But I think here what struck me is how different the bark and the leaf were in terms of constituents. So, I'm not comfortable reading across any of the parts of the plant at this point.

DR. RETTIE: Good old botanicals.

DR. BELSITO: So, let's save these changes and move on.

MS. FERGUSON: I have a quick question, Dr. Belsito.

DR. BELSITO: What? Go ahead, Priya.

MS. FERGUSON: For the Discussion, did you also want to mention the Pyrogallol, the heating, and having any sort of concern for that?

DR. BELSITO: Well, I mean, I guess --

DR. SNYDER: I think that raises too much attention to it now, but having understood it now better, but --

DR. BELSITO: Yeah.

DR. SNYDER: We can see what the other team thinks.

DR. BELSITO: Okay, yeah. Let me add that to discuss with the other team, the Pyrogallol. Who's reporting on this tomorrow?

DR. HELDRETH: You are.

DR. BELSITO: Okay. Edit, in Discussion, question mark, Pyrogallol. Okay. So, we'll figure that out tomorrow, Priya.

MS. FERGUSON: Thank you.

Cohen Team – March 12, 2026

DR. DAVID COHEN: This is a draft report looking at Salix Alba-derived cosmetic ingredients, which include bark extract, bark powder, bark water extract, flower extract, and leaf extract. These ingredients function primarily as skin conditioning agents, soothing agents and botanical extracts in leave on and rinse off products.

For willow bark extract, the highest reported concentration of use is approximately 1.1 percent, in face and neck leave-on products with additional reported uses up to 0.53 percent in body and hand leave-on products, and 0.4 percent in night products. There are some baby uses, although concentration of use is not reported.

We have willow leaf extract; I think we have concentration of use there but not in the other. I'm sorry, we have concentration of use on the bark extract, but not many of the others. I think we have a method of manufacturing, and composition characteristics are incomplete for most of the ingredients, limiting our ability to access equivalent plant parts for extra extraction (inaudible).

So, with that in mind, we have HRIPT and irritation for the Willow bark extract, which is largely negative at 5 percent. I'll open it up for discussion and perhaps needs for an IDA?

DR. SAM COHEN: Well, the concern I had in reading this through is that it's still listed as being present in baby products.

DR. DAVID COHEN: Yes.

DR. SAM COHEN: And it's stated up front that it's not supposed to be used in children under the age of three because of the salicylates. I don't see how we can square those round ones. If there are salicylates in there, and it seems there are, not a lot, but some, these shouldn't be used in children -- infants.

DR. DAVID COHEN: Well, the problem is, what is the definition of children here?

DR. SAM COHEN: They were saying age of three.

DR. DAVID COHEN: Well, it says baby products. It says baby products.

DR. SAM COHEN: Yeah. So, what age does the salicylate issue no longer remain? Certainly in infants it's an issue, but at what age does it no longer become an issue?

DR. TILTON: I mean, baby products would certainly be under the age of three.

DR. SAM COHEN: Yeah.

DR. DAVID COHEN: I think the dry syndrome thing is for the old kids, too, close to, you know, teenage years.

DR. TILTON: Yeah.

DR. SAM COHEN: I don't see how we can approve it for use in children.

DR. DAVID COHEN: Do we agree we have an IDA here?

DR. BERGFELD: We don't have anything on the flower.

DR. DAVID COHEN: Right. We should probably just start enumerating our data needs. Should we ask for method of manufacturing and composition data on those we don't have?

DR. TILTON: That would be method of manufacturing and impurities on the flour extract, and then, I guess, Willow extract.

DR. DAVID COHEN: Just those two right now? I'm going back and forth on that.

DR. ROSS: To add to that, you'd need Willow bark powder and Willow bark water. We don't know if we can read across from Willow bark extract to Willow bark powder, and to Willow bark water, unless we've got some constituents and method of manufacture.

DR. DAVID COHEN: I completely agree.

DR. TILTON: We usually get some description of that if not a table.

DR. ROSS: Yeah. And then, of course, the whole -- I think you mentioned, Susan, the Willow extract itself, right? We've got nothing.

DR. TILTON: Yes.

DR. DAVID COHEN: Yes, I have that. Susan gave me flower extract and Willow extract. What about irritation and sensitization on the leaf?

DR. TILTON: We also really have no data on the flower extract or the Willow extract.

DR. DAVID COHEN: You mean for sensitization?

DR. TILTON: Yes.

DR. ROSS: I think Willow leaf extract we've got --

DR. TILTON: For leaf we do.

DR. ROSS: We've got irritation and sensitization.

DR. DAVID COHEN: On?

DR. ROSS: Dermal irritation on leaf extract, 4 to 6 percent on rabbits; sensitization, guinea pig maximization test at 4 to 6 percent. We've also got ocular. So, we've got all of those with Willow leaf extract. What we don't have is DART data.

DR. DAVID COHEN: For the whole thing?

DR. ROSS: No, we've got DART data on willow bark extract, I believe. I'll just check that. Yes, we have.

DR. TILTON: Yeah. And there were no reproductive or developmental effects in parents or pups in a 28-day repeat dose.

DR. ROSS: Yeah. I mean, it raises a question of can we read across from Willow bark extract to Willow leaf extract?

DR. DAVID COHEN: How could you do that?

DR. ROSS: Well, if you look at Table 4, which is the -- you know, both of them contain the same general classes of phenolics, flavanols, and procyanidins. But I didn't see one line that was similar; every line -- and it's a big table -- was very, very different. And I checked that they were the same extracts. They're both Hydromethanolic extracts, so I'm not sure you can read across. You may get a different story tomorrow but I wasn't sure we could read across on the DART data.

DR. DAVID COHEN: Oh, read across on the DART data. I didn't know where you were going. I thought you were talking about the irritation and sensitization.

DR. ROSS: No, we're talking about DART data. There's no DART data on the Willow leaf extract, but there is on the Willow bark extract. Right? So then can you go from one to the other? I don't know. I don't think so.

DR. DAVID COHEN: All right, so what do we need DART on then?

DR. ROSS: Willow leaf extract.

DR. DAVID COHEN: We have the bark extract, but --

DR. ROSS: Yeah, you've got it on the bark extract; you need it on the leaf extract, if you cannot read across.

DR. DAVID COHEN: And what about the Willow extract?

DR. SAM COHEN: And what about flower extract?

DR. ROSS: All of the above.

DR. SAM COHEN: The only one you have it on is the bark extract.

DR. DAVID COHEN: Yeah. We need it on everything else, no, for now?

DR. ROSS: If you can't read across, correct. Yeah.

DR. DAVID COHEN: Well, I don't see how we could read across without method of manufacturing or composition.

DR. ROSS: That's exactly right, yeah.

DR. SAM COHEN: And we don't have any composition data on most of these, so you got to have that.

DR. ROSS: Yeah, that's where you start, yeah. Method of manufacture, composition, and then you can really begin to determine read across after that.

DR. SAM COHEN: I just can't imagine that there's going to be read across when you're talking about bark, versus leaf, versus flower.

DR. ROSS: I think it's going to be very difficult.

DR. SAM COHEN: Yeah, the composition is going to be totally different.

DR. ROSS: Yeah. And if you check that table, they're very different.

DR. SAM COHEN: Yeah. And that's just the leaf and the bark.

DR. DAVID COHEN: We've read across when we've had good whole-plant extracts. Where they take the whole thing, grind it up, extract it, and we have sensitization, irritation, DART data, and we just say you can read across everything. Rarely do we get that, but occasionally we have seen it, I think.

DR. SAM COHEN: We don't have it here.

DR. DAVID COHEN: We do not have it here. For irritation and sensitization, leaf extract, willow extract, all we have -- we have bark extract, right? We have leaf extract and bark extract. Is that right?

DR. ROSS: Yeah. There's some detailed composition in, I think, Table 4. I think it's Table 4. But that's it.

DR. DAVID COHEN: Wait a minute, so we have --

DR. ROSS: So, what's on your list so far, David?

DR. DAVID COHEN: We need to go through this again. Well, I have a comment about use in baby products, but it has salicylates, and it shouldn't be used in children. I have method of manufacturing, impurities and composition on those we don't have. So, we need it on the flour extract, Willow extract, Willow bark powder, and Willow bark water. Dermal irritation and sensitization on leaf extract and Willow extract?

DR. ROSS: I think you have it on leaf extract.

DR. DAVID COHEN: Yeah, I'm just going back to -- maybe when I typed it, I put in what we had versus what we didn't have. Does anyone have it open in front of them because I have a Word document in front of me, not the PDF.

MS. FIUME: So, we didn't have it for December, but we have it now. Leaf extract came in between December and now.

DR. DAVID COHEN: So, we have leaf extract.

DR. SAM COHEN: But going back to what you said earlier, David, if they just gave us the extract of the whole plant, we'd kind of solve a lot of this.

DR. ROSS: Exactly, yeah.

DR. DAVID COHEN: But I'd rather keep the IDA as broad as possible because then we could release the needs if we have a whole plant. If we don't get it, then let's get as much as we can. So what do we need on that? Let's go back.

DR. TILTON: So we would need flour and Willow extract?

DR. ROSS: Willow extract has nothing, at all, across the board. So, I'd love to say we'll get there and we could use Willow extract to clear everything, but I don't think we're going to get that. Okay. We should ask for it, but let's see what we get. But there's nothing on that data table for Willow extract.

DR. DAVID COHEN: No, I see that. Irritation. So, we have the irritation and sensitization.

DR. SAM COHEN: Basically, for the tox data, the only thing we have is on the Willow bark extract. We don't have anything else.

DR. ROSS: Now, you've got stuff on the Willow leaf extract.

DR. DAVID COHEN: We have animal stuff on the leaf extract for sensitization, right?

DR. SAM COHEN: Yeah, but not a basic toxicity or DART, or even genotox.

DR. DAVID COHEN: Yeah.

DR. ROSS: Well, you've got some acute tox.

DR. SAM COHEN: Yeah.

DR. TILTON: And there's also genotox.

DR. SAM COHEN: Yeah, there is genotox on the leaf, but not on the -- in the bark, but not on all the others.

DR. DAVID COHEN: All right, so can we continue enumerating what we need?

DR. ROSS: I think you need just about everything for everything but bark extract and leaf extract, okay?

DR. DAVID COHEN: I don't know -- because you know what's going to happen, if I say that? At the end Priya's going to say, okay, can you outline specifically what you want for the IDA? And then Wilma gets me next, or first. So, I want to make sure we outline them. I have been well-trained just in time to jump off.

DR. ROSS: You got to love botanicals, right.

DR. SAM COHEN: I think that we need some repeat-dose toxicity studies on all of them except the Willow bark extract, both either dermal and/or oral.

DR. DAVID COHEN: So we need dermal and oral tox on all but?

DR. SAM COHEN: Bark extract. Same thing on DART, the only thing we have is bark extract. And for genotox we have the bark extract and the leaf extract, but not the flower or the others. I think bark powder and bark water, I'm assuming, we'll have some read across, assuming that we get composition.

DR. DAVID COHEN: Just even the method of manufacturing would be helpful.

DR. SAM COHEN: Yeah.

DR. ROSS: I had one other issue, David, on the most commonly used one, Willow bark extract. On the ocular irritation we have some mixed data. It was used at neat in four different epi-ocular assays. They're all OECD compliant, but three of them, which were negative, as I recall, were used at 90 minutes, and one which was positive was for six hours. But that's all at neat. You could ask for epi-ocular tests at closer to the maximum concentration.

DR. DAVID COHEN: So, ocular irritation at max use?

DR. ROSS: Yeah. You know, we have data, but it's just mixed, and it's all at neat concentration.

DR. DAVID COHEN: Yeah, but you know the problem is when we have neat -- I don't know where you go when you go down from that, right? What is low from neat?

DR. ROSS: 1.1 percent.

DR. DAVID COHEN: Huh?

DR. ROSS: 1.1 percent.

DR. BERGFELD: That's where it's used, yeah.

DR. ROSS: Max concentration. But, you know, you can interpret that whichever way you want. I'm just saying it would make it very clear if you had an epi-ocular test close to maximum concentration of use. And maybe it's out there. Maybe it's not. But there was a secondary test done, an isolated chicken eye test, but again, that was inconclusive.

DR. DAVID COHEN: How fungible is that? I don't know enough about the chicken eye test to humans.

DR. ROSS: I'd rather rely on epi-ocular, OECD compliant.

DR. DAVID COHEN: Okay. So, we have a lot of data needs.

DR. BERGFELD: Interesting ingredient, though.

DR. DAVID COHEN: Yes. I'll mark that.

Full Panel – March 13, 2026

DR. BELSITO: So, this is a Draft Report on six Willow-derived ingredients and it's the first time we're looking at it. We got a good amount of data on the bark extract and the leaf extract, and absolutely no data on the bark powder, the bark water, the whole extract, and the flower extract. And we did know from composition that there were clear differences in composition between the bark and the leaf extract, so I'm not sure that we can necessarily read across to any of these plant parts.

For the bark and the leaf -- well, first of all we felt they were insufficient. I thought the insufficiencies were a little bit different. For the bark and the leaf, we have negative phototox data. We're told there's photo-absorption, which is likely because they contain salicylates. And we know salicylates are photo-absorbers. We need photo-allergenicity data for all of them, but to clear the bark and the leaf extract, in particular, which otherwise I think would be safe as used, we need photo-allergenicity.

That's going to be an issue because there's no in vitro, photo-allergy study that's OECD approved. As I mentioned before, JaCVAM has said that if a ROS assay is negative, then you can clear photo-allergy; if it's positive you can't say anything about photo-allergy. So, I would give industry the out of doing a ROS assay on the leaf and the bark extract, and if those are negative, I would be comfortable with them. Or they could do an absorbance spectra for all components and show that the molar absorption is less than or equal to a thousand which, according to Henry's Law, would clear them for photo-allergy and phototoxicity.

For the non-bark extract and non-leaf extract ingredients, essentially everything is needed. There's no data at all. So, it would be manufacturing, composition and impurities, systemic tox, so 28-day dermal absorption, if absorbed, DART, genotox studies are needed and sensitization, irritation at concentration of use and the photo.

In the report, something that I would like to point out that I think is misleading, is this effect on pigmentation. Hydroxyacetone stains the stratum corneum. It does not change melanogenesis at all; it's simply a stain on the skin. And reversing that stain just means this product is cleaning the skin of that stain. So, effect on pigmentation is a misnomer and, in fact, I would get rid of that entire study from the report. And that was it.

DR. BERGFELD: All right. Is that in the form of a motion?

DR. BELSITO: Yeah. So, for the bark and the leaf we need photo. For all of the others we need pretty much all of the data. And in the Discussion, heavy metal, pesticide boilerplate, aerosol use, the salicylate issue that the EU dealt with in terms of young children, in terms of oral mucosal exposure. We need concentration of use for all but the bark and the leaf, DART and genotox for all but the bark and the leaf, sensitization and irritation on all but the bark and the leaf.

DR. BERGFELD: David?

DR. DAVID COHEN: We listed them differently, and I was trying to align them. We have method of manufacturing, impurities, composition for most of them.

DR. BELSITO: All but the bark and the leaf.

DR. DAVID COHEN: Right. Irritation and sensitization, what do you have there?

DR. BELSITO: All but the bark and the leaf.

DR. DAVID COHEN: Good. And DART if the tox studies --

DR. BELSITO: DART and genotox for all but the bark and the leaf.

DR. DAVID COHEN: Right. How about ocular irritation?

DR. BELSITO: We didn't have that. But if you want to throw it in, it's an insufficient list.

DR. DAVID COHEN: Yeah, we had the specific data on the bark extract, which was equivocal. So, we wanted ocular irritation at max use concentration.

DR. BELSITO: I'm fine at this point.

DR. ROSS: You don't have DART on the leaf.

DR. BELSITO: What, David?

DR. ROSS: You do not have DART data, I do not think, on the leaf, so you may want to put that in. I think you said you needed DART, Don, for everything but bark and leaf. And I don't think you've got it on the leaf.

DR. BELSITO: I thought we did.

DR. DAVID COHEN: I just have we have Willow bark extract for DART.

DR. ROSS: Yeah, it's just the bark extract you've got.

DR. BELSITO: Leaf extract -- let's see. Yeah.

DR. ROSS: I think that should be added in.

DR. BERGFELD: Oh, you're asking such a big ask, yes. Go ahead.

DR. RETTIE: It's not marked in Priya's data profile.

DR. ROSS: Correct.

DR. BELSITO: Yeah, no, that's fine. I don't have a problem there.

DR. DAVID COHEN: And one other thing which troubled us a little bit, I suppose, was the salicylate constituents, some quantitative characterization of the salicylates, since these are used in baby products, and should these salicylates be present in baby products?

DR. BELSITO: Well, yeah, we discussed that, too, baby aerosol mucosal exposure. I thought that that could go in the Discussion. In the EU these products are okay for cosmetics, but then there is salicylate warnings that are sort of, I guess, put into them. I don't think we're going to get the percentage of salicylates in these. And so, I think that that's a discussion point.

DR. DAVID COHEN: Yeah, I think that makes sense, Don. Okay. I just want to make sure we're clearly addressing that.

DR. BELSITO: Right.

DR. BERGFELD: Okay. So, some things that are already talked about in the Discussion, so this is being added to it. You were putting the metals, the airbrush, and the salicylates, and now baby products in the Discussion.

DR. BELSITO: Well, the salicylate issue is babies, mucosal and aerosol.

DR. DAVID COHEN: What about percutaneous absorption?

DR. BERGFELD: Did you want that?

DR. DAVID COHEN: I mean, we have drugs that are topical salicylates that get absorbed.

DR. BELSITO: Yes, but they're pure salicylates or essentially much higher concentrations.

DR. DAVID COHEN: I don't know if that's the case. I just don't know.

DR. BELSITO: What data are you looking for, blood salicylate levels in cosmetic use?

DR. DAVID COHEN: No. We're thinking about some quantitative characterization. But, Don, I'm not suggesting that your proposal of having this in the Discussion doesn't fulfill the need; but I'm not sure I would limit that discussion to just mucous membranes and airborne. I think if you're lathering an infant with the salicylate-containing product, they'll absorb it, and it's probably not appropriate for use there.

DR. SAM COHEN: I guess the question I have is that, is it going to be allowed in children's products at all?

DR. BELSITO: Well, in the EU, you know, we need to differentiate the botanical, the Salix Alba–derived ingredients from salicylates. So, in the EU, if you look at the cosmetic regulations, they allow this product; where they're regulating are the salicylate levels, right? So, if you look at what they're saying is -- let's see, where's the EU regs here?

So, "None of the Salix alba–derived ingredients named in the report are restricted from use in any way under the rules governing EU. However, EU limits the use of salicylates in cosmetics." And their regulation for salicylic acid, other than as a preservative, are up to 3 percent rinse-off hair, 2 percent most other products, and 0.5 percent body lotions, eye shadow, mascara, eyeliner, lipstick, roll-on. "Under this annex, salicylic acid should not be used in preparations for children under the age of three," but that's the acid, not the botanical.

DR. DAVID COHEN: Yeah, I don't know what salicylates are in this botanical.

DR. BELSITO: Well, it's salicin, which is the biggest one, right?

DR. BERGFELD: It's very low concentrations.

DR. BELSITO: Pardon? Wilma, I couldn't hear you.

DR. BERGFELD: I said it's very low concentrations. And we got our use, I think in Wave 2 -- no, it's in the regular document. The highest one would be 0.01, max concentration of use in the bark.

DR. DAVID COHEN: I see on like PDF Page 9, its composition, impurities --

DR. BELSITO: So, the bark extract, Wilma, is used up to 1.1 percent in the leave-on face-and-neck preparation.

DR. BERGFELD: Well, I was looking at the use material that was sent to us, which was much lower.

DR. DAVID COHEN: On PDF Page 9, it says the bark extract --

DR. BELSITO: It's the bark extract, face and neck. Yeah, PDF Page 30, in Table 3, is 1.1 percent.

DR. DAVID COHEN: You're talking about use concentration, right?

DR. BELSITO: Yes.

DR. DAVID COHEN: But I'm just talking about there's a comment that says the cosmetic ingredient is normalized to 53 to 65 percent salicylates in a powder of that extract. That's a lot of salicylate in the powder, Don, even if you're using --

DR. BELSITO: What page are you on? You said 9?

DR. DAVID COHEN: Page 9. It's from the PCPC.

DR. ROSS: Oh, it's from the comment. Okay.

DR. DAVID COHEN: Yeah.

DR. ROSS: No, it's in the dossier somewhere and I got a bit confused by that, actually. Let me see if I can find it.

DR. BELSITO: There's a powder of an extract.

DR. DAVID COHEN: Yeah.

DR. ROSS: Yeah.

DR. BELSITO: Carol, can you comment, or someone from PCPC, about what exactly that means?

DR. EISENMANN: Not off the top of my head, no.

DR. DAVID COHEN: I don't think it's something we need to deal with immediately, now, but that's -- if there's a lot of salicylates in this, even using a low final concentration in the product, and it's applied broadly on an infant, I think we need a lot of margin.

DR. BELSITO: Well, wait a minute, no, a face-and-neck preparation is not a broad application. Let's get that straight.

DR. DAVID COHEN: We're talking about for an infant.

DR. BELSITO: I understand, but let's look at where it's used. The 1.1 is a face-and-neck preparation, right?

DR. DAVID COHEN: Okay. And let's just go --

DR. BELSITO: So that's not a broad application.

DR. DAVID COHEN: I agree with you. It's 10 percent of the body surface area.

DR. BELSITO: So, what do we have here? We have, in terms of baby products, we have essentially no reported uses.

DR. DAVID COHEN: Well, we have advanced preparation.

MS. FERGUSON: You have shampoos, lotions, oils, powders, creams and other baby products, but no concentrations of use.

DR. DAVID COHEN: Yeah, 16 baby lotions, powders --

DR. BELSITO: For which?

DR. DAVID COHEN: For bark extract. And that's the one on 9 that had very high salicylic concentrations.

DR. BELSITO: Oh, okay, hold on. I was looking at the Willow extract, so bark extract.

DR. DAVID COHEN: Bark. Bark.

DR. BELSITO: This table goes on; okay, bark extract, sorry. Yeah, okay. So, we have lotions, oils, powders, creams, we have no reported use. Shampoos, we have no reported. So, we have no reported uses; we just have our -- no reported concentrations, we just have RLD uses.

DR. DAVID COHEN: Right. We have 36 baby products, and then we have 16 baby lotions, and baby products are pretty vague. And then you have a comment that there's a lot of salicylate in this product, potentially.

And so, you know, when this comes back around, right -- I'm not suggesting I'm amending your IDA, I'm seconding your IDA. I just want us to be very cautious in a future discussion how we guide regarding the use in babies. I think this could be an important issue.

DR. ROSS: I have to admit, I got confused by that in the dossier. Now I can't find the point in the dossier where it was said. But I'm looking at the PCPC comments, and here it's on -- at least my PDF -- it's on Page 13, The Responses. "Please indicate that the cosmetic ingredient that is normalized to 53 to 65 percent salicylates is a powder of an extract."

MS. FIUME: That's in the report on Page 19, the first sentence under Salix Alba (Willow) Bark Extract.

DR. ROSS: I was really hoping you were going to tell me that. So, it's Page 19.

DR. DAVID COHEN: Yeah, it opens up Willow Bark Extract paragraph on composition and impurities. When Sam brought this up yesterday, he sounded the bell on that, and then I started looking further into it.

DR. ROSS: Yeah. No, I got it. Thank you. Thank you.

DR. BELSITO: So here it says 9.8 to 11.5 percent salicylic acid, or 18 to 22 percent salicylic acid.

DR. DAVID COHEN: Isn't that a lot?

DR. BELSITO: Well, let's assume the high number.

DR. ROSS: You're looking at 1.1 --

DR. BELSITO: When it's diluted down to the level of use in baby -- potential level of use since we have no reported use, let's assume it's the max at 1.1. You're talking about 0.242 percent.

DR. DAVID COHEN: 0.242 percent. So, that's two and a half milligrams per gram of product applied. So, on a baby you could certainly put, you know, five or ten grams of product on pretty easily; but on a whole infant, if you're smearing them down after a bath?

DR. SAM COHEN: Do we know how much salicylate is required to cause problems?

DR. BELSITO: I mean, that could be looked up. But I think what we need to do is go insufficient for concentration of use in baby products, right? It may turn out that these are used at negligible amounts.

DR. DAVID COHEN: Yeah, Don, that's totally right.

DR. BERGFELD: All right. So, Dr. Belsito, will you please present your conclusion again, and we'll go through what's going in the Discussion, including the baby product decision?

DR. BELSITO: Yeah, okay. So, I guess we're keeping everything insufficient at this point. For the bark, we need concentration of use of baby products.

DR. BERGFELD: Mm-hmm.

DR. BELSITO: For the leaf we need DART and concentration of use in baby products, if it's used. And then for all others, basically, we need everything, manufacturing, composition, impurities, absorption, if absorbed, DART, genotoxicity, sensitization, irritation at concentration of use.

DR. DAVID COHEN: Phototox.

DR. BELSITO: Phototox, photosensitization, phototox. So, yeah.

DR. SAM COHEN: One thing we talked about yesterday was, if they provided some of this data on tox for the whole plant extract, would that obviate the need to get specifics to the other parts?

DR. ROSS: Yes.

DR. DAVID COHEN: Yeah. That's in the IDA, so if we get it, it's a dream get. But I'm going to second the motion.

DR. BERGFELD: Second the motion. All right. We know what's going to go in the Discussion, if I might just reiterate that. We're going to do the metals, the airbrush, the salicylate issue, the child issue. Was there anything else that we were going to put in there?

DR. BELSITO: Not at this point.

DR. DAVID COHEN: It's too early still.

DR. BERGFELD: Okay. I just wanted to make sure that we were hitting those. All right, I'm going to call the question. All those approving of this Insufficient Data Report, please? Those who are opposed? Abstaining?

MS. FERGUSON: I have a quick question. Do you want photo-allergenicity for bark and leaf, too?

DR. BERGFELD: Correct?

DR. BELSITO: Yes.

DR. BERGFELD: Abstaining, anyone? If not approved. And you heard the answer, Priya, yes, on the phototoxs? Okay, moving on to the Polyacrylates, Dr. Cohen.

Safety Assessment of *Salix alba* (Willow)-Derived Ingredients as Used in Cosmetics

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ABBREVIATIONS

CIR	Cosmetic Ingredient Review
Council	Personal Care Products Council
CTFA	Cosmetic, Toiletry, and Fragrance Association
Dictionary	*International Cosmetic Ingredient Dictionary*
DMSO	dimethyl sulfoxide
DNA	deoxyribonucleic acid
DPRA	direct peptide reactivity assay
EC	European Commission
$EC_{1.5}$	effective concentration of a test chemical that induces a 1.5-fold increase in luciferase activity
ECHA	European Chemicals Agency
ELISA	enzyme-linked immunosorbent assay
EPA	US Environmental Protection Agency
EU	European Union
FDA	US Food and Drug Administration
GARD	genomic allergen rapid detection
GHS	Globally Harmonized System
HepG2	human hepatoma cell line
HL-60	human leukemia-60
Hprt	hypoxanthine-guanine phosphoribosyltransferase
IFRA	International Fragrance Association
IL-6	interleukin-6
I_{max}	mean maximal luciferase activity
IC_{50}	inhibitory concentration 50%
LD_{50}	median lethal dose
l.o.	leave-on
log K_{ow}	n-octanol/water partition coefficient
MoCRA	Modernization of Cosmetics Regulation Act of 2022
MTT	3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide
NA	not applicable
ND	not detected
NOAEL	no-observed-adverse-effect-level
NR	not reported
OECD	Organisation for Economic Co-operation and Development
Panel	Expert Panel for Cosmetic Ingredient Safety
RIFM	Research Institute for Fragrance Materials
RLD	Registration and Listing Data
RNA	ribonucleic acid
r.o.	rinse-off
SIRC	Statens Seruminstitut Rabbit Cornea
TG	test guideline
US	United States
USP	United States Pharmacopeia
UVA	ultraviolet A
Vis	visible light
WHO	World Health Organization
WoE	weight-of-evidence
Xprt	xanthine-guanine phosphoribosyltransferase

DRAFT ABSTRACT

The Expert Panel for Cosmetic Ingredient Safety (Panel) assessed the safety of 6 *Salix alba* (willow)-derived ingredients. Functions for this group of ingredients include hair-conditioning agent, skin-conditioning agent, absorbent, exfoliant, skin-protectant, antifungal agent, and fragrance ingredient in cosmetics. The Panel reviewed the relevant data to evaluate the safety of these ingredients. *Salix alba*-derived ingredients may contain constituents that have the potential to cause adverse effects. Because final product formulations may contain multiple botanicals, each containing the same constituent of concern, formulators are advised to be aware of these constituents and to avoid reaching levels that may be hazardous to consumers. With *Salix alba*-derived ingredients, the Panel was concerned about the potential presence of salicylates in these ingredients. Additionally, industry should continue to minimize impurities, such as heavy metals and pesticide residues, according to limits set by the US Food and Drug Administration (FDA) and the US Environmental Protection Agency (EPA). The Panel concluded that these *Salix alba*-derived ingredients are…[].

INTRODUCTION

This assessment reviews the safety of the following 6 *Salix alba*-derived ingredients as used in cosmetics formulations:

Salix Alba (Willow) Bark Extract	Salix Alba (Willow) Extract
Salix Alba (Willow) Bark Powder	Salix Alba (Willow) Flower Extract
Salix Alba (Willow) Bark Water	Salix Alba (Willow) Leaf Extract

According to the *International Cosmetic Ingredient Dictionary* (*Dictionary*), 4 of these ingredients, including Salix Alba (Willow) Bark Extract, are reported to function as skin-conditioning agents in cosmetics; other functions of these ingredients may be found in Table 1.[1] It should be noted that Salix Alba (Willow) Bark Water is reported to only function as a fragrance ingredient in cosmetics, and the Expert Panel for Cosmetic Ingredient Safety (Panel) does not typically review ingredients that function only as fragrance ingredients, because, as fragrances, the evaluation of the safety of these ingredients is the purview of the Research Institute for Fragrance Materials (RIFM). However, it appears that this ingredient is not included in their review process, and therefore, the Panel is reviewing its safety.

Salix alba (willow)-derived ingredients contain over 100 constituents, some of which have the potential to cause adverse effects. For example, salicylates, including salicylic acid have the potential to cause dermal irritation following topical exposure, and with sufficient systemic exposure, may produce salicylate toxicity.[2,3] In this assessment, the Panel is evaluating the potential toxicity of each of the *Salix alba (*willow)-derived ingredients as a whole, complex substance; toxicity from single components may not predict the potential toxicity of botanical ingredients.

Salicin, a glucose-bound form of salicylic acid, and a component of *Salix alba* (willow)-derived ingredients, has not been reviewed by the Panel. However, the Panel has previously reviewed salicylic acid and 17 salicylates in an amended report finalized in 2019.[3] In that report, the Panel concluded that salicylic acid and the 17 salicylates reviewed in that report are safe in cosmetics, in the present practices of use and concentration described in that safety assessment, when formulated to be non-irritating and non-sensitizing, which may be based on a quantitative risk assessment.

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 August 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.

The cosmetic ingredient names, according to the *Dictionary*, are written as listed above, without italics and without abbreviations. When referring to the plant from which these ingredients are derived, the standard scientific practice of using italics will be followed (i.e., *Salix alba*). Often in the published literature, the general name willow is used. If it is not known whether the substance being discussed is equivalent to the cosmetic ingredient, the test substance will be identified by the name used in the publication that is being cited (e.g., *Salix alba* (willow bark extract). However, if it is known that the substance is a cosmetic ingredient, the *Dictionary* nomenclature (e.g., Salix Alba (Willow) Bark Extract) will be used.

Furthermore, it should also be noted that the terms "willow" and "willow bark extract" may refer to several different species of willow (e.g., *Salix purpurea*, *Salix fragilis*) in the literature. For the purposes of this report, only studies explicitly using *Salix alba* - derived plant parts were included. However, a few case reports describing allergic reactions to dietary supplements containing "white willow bark" were included, since these products may in fact contain bark derived from *Salix alba*, and these case reports may assist the Panel in evaluating the potential allergenicity of *Salix alba* - derived ingredients.

Much of the data included in this safety assessment was found on the European Chemicals Agency (ECHA) website.[4] The cited information pertains to a *Salix alba* (willow) bark extract that was reported for use in a fertilizer. Please note that the ECHA website provides summaries of information generated by industry, and it is those summary data that are reported in this safety assessment when ECHA is cited.

CHEMISTRY

Definition and Plant Identification

The definitions of the ingredients included in this review are provided in Table 1. *Salix alba* is a fast-growing deciduous tree native to Europe, Asia, and North Africa, most often occurring in riparian habitats such as riverbanks, wetlands, and other moist soils.[5] These plants are capable of reaching heights up to 30 m with trunks exceeding 1 m in diameter. The leaves are narrow and lanceolate, displaying silver-grey upper surfaces and dense silky white hairs on the underside, while the bark is dark grey and deeply fissured (younger bark may be greenish-yellow).[6] The flowers of the *Salix alba* plant are produced in catkins that emerge in early spring, appearing before or with the leaves.[7] The species is dioecious, meaning male and female catkins are produced on separate trees. Male catkins are typically larger and yellowish due to exposed anthers while female catkins are smaller and greenish.

Chemical Properties

Salix Alba (Willow) Bark Extract is a white to off-white free-flowing powder with a characteristic odor.[8] The octanol/water partition coefficient (log K_{ow}) of a *Salix alba* (willow) bark extract is < 0.3.[4] Other chemical properties of this ingredient and a Salix Alba (Willow) Bark Extract in glycerin and water may be found in Table 2.

Method of Manufacture

Some of the methods below are general to the processing of *Salix alba* (willow)-derived ingredients. It is unknown if these apply to cosmetic ingredient manufacturing.

Salix Alba (Willow) Bark Extract

Data from a manufacturer state that Salix Alba (Willow) Bark Extract is prepared by extracting the bark of *Salix alba* with ethanol, followed by purification, filtration, and drying.[9] The resulting residue is then combined with 1,3-butylene glycol and filtered to obtain the final product. No synthetic reagents, preservatives, or chemical modifications are used, and residual solvent levels comply with International Fragrance Association (IFRA)/Cosmetic, Toiletry, and Fragrance Association (CTFA; now known as the Personal Care Products Council) specifications and general cosmetic ingredient quality guidelines. According to a supplier, Salix Alba (Willow) Bark Extract is processed by the grinding of plant bark and aqueous extraction at a controlled pH and temperature for a specified duration, followed by filtration, concentration, and spray drying.[10] Throughout production, batch adjustments are made as needed, with initial and final quality control testing, including microbiological sampling.

In order to prepare a *Salix alba* (willow) bark extract, plant bark was first dried and pulverized into a fine powder.[11] The powder was then extracted in a Soxhlet apparatus using ethanol as the solvent for 7 h. The solution was filtered and evaporated to obtain the bark extract.

Salix Alba (Willow) Leaf Extract

A *Salix alba* (willow) leaf extract was prepared by first collecting, rinsing, and air-drying the leaves.[12] Following drying, the leaves were pulverized via an electric grinder. Extraction was performed via cold maceration of 500 g ethyl acetate with intermittent shaking. The resulting filtrate was concentrated using a rotary evaporator. To remove chlorophyll, the extract was washed with a non-polar solvent, after which it was concentrated and stored.

Composition and Impurities

Salix species are known for their capacity to concentrate toxic heavy metals.[13] Therefore, the *Salix alba* (willow) plant and plant parts (including the bark and leaves) may contain heavy metals such as cadmium, lead, and zinc.[14]

Salix Alba (Willow) Bark Extract

A cosmetic ingredient supplier states that Salix Alba (Willow) Bark Extract is standardized to contain 53 – 65% salicylates (this ingredient is a powder of an extract).[15] According to the same supplier, the ingredient should contain 2 – 5% nitrogen and should not contain more than 20 ppm heavy metals, 10 ppm lead, 2 ppm arsenic, 1 ppm mercury, or 1 ppm cadmium.[8] According to another source, Salix Alba (Willow) Bark Extract is a mixture composed of water (68.25%), butylene glycol (29.25%), and Salix Alba (Willow) Bark Extract (2.5%).[9] For this ingredient, heavy metals and pesticide residues comply with cosmetic ingredient standards (heavy metals < 20 ppm; arsenic < 2 ppm), and no synthetic additives or preservatives are present. Salix Alba (Willow) Bark Extract should not contain certain pesticides (e.g., alachlor, dieldrin) or the allergens listed in Annex III of Commission Regulation (EU) 2023/1545 Amending Regulation (European Commission) No. 1223/2009.[16] According to another supplier, substances specified in Annex III, entries 45 – 371, of Regulation (EC) No 1223/2009 (e.g., certain fragrance allergens and other restricted cosmetic substances) are not expected to be present in Salix Alba (Willow) Bark Extract at concentrations > 0.001%.[17] Salix Alba (Willow) Bark Extract has also been reported to be a 1:5 extract (for every 1 part plant material used, 5 parts solvent is used) containing 9.8 – 11.5% or 18 – 22% salicylic acid equivalents.[18,19]

Data from the scientific literature on *Salix alba* (willow) bark report broader phytochemical compositions. In one study, the contents of salicylic derivatives, polyphenols, flavones, and tannins were measured in dried, ground bark collected from young and mature *Salix alba* trees.[20] In young bark, total salicylic derivatives (expressed as salicin equivalents), total

polyphenols (expressed as gallic acid equivalents), total flavones (expressed as rutin equivalents), and total tannins (expressed as pyrogallol equivalents) were approximately 15, 55, 4.5, and 16 mg/g bark, respectively. In mature bark, the respective values were approximately 19, 65, 3, and 16.6 mg/g bark.

The total phenolic content of a hot ethanolic extract of *Salix alba* (willow) bark was determined to be 162 mg gallic acid equivalents/g extract.[11] The amounts of salicylates, flavonoids, flavan-3-ols, and phenolic acids in a methanolic *Salix alba* (willow) bark extract have been summarized in Table 3.[21] In addition, the phenolic acid, flavanol, and procyanidin content of a hydromethanolic extract of *Salix alba* (willow) bark may be found in Table 4.[22] A chemical analysis of *Salix alba* (willow) bark reported the following structural component contents: 70.2% holocellulose, 40.3% α-cellulose, and 33.8% Klason lignin.[23]

Chemical characterization of an ethanolic *Salix alba* (willow) bark extract identified salicin, salicortin, salicoylsalicin, tremulacin, tremuloidin, salidroside, saligenin, and salicylic acid among the phenolic constituents.[24] Similarly, a World Health Organization (WHO) monograph has reported that the major biologically active constituents of *Salix alba* (willow) bark are phenolic glycosides, including salicin (approximately 1%), salicortin (up to 4%), 2'-*O*-acetylsalicortin (up to 10%), 2'-*O*-acetylsalicin (fragilin; up to 4%), and tremulacin (0.12 – 2%), as well as populin and salireposide; these compounds are collectively designated as salicylates.[25] Other significant constituents include flavonoids and tannins. The total salicin content (after hydrolysis) of *Salix alba* bark ranges from 0.5 – 1%.

Also according to WHO, *Salix alba* (willow) bark used in herbal medicines must conform to the following specifications: not more than 3% of twigs with a diameter greater than 10 mm, and not more than 2% other foreign matter, not more than 10% total residual ash following pyrolysis, not more than 3% acid-insoluble residual ash following pyrolysis, not less than 10% water-soluble extractive, and not more than 11% loss on drying.[26] The recommended maximum limit of aldrin and dieldrin is not more than 0.05 mg/kg. In addition, the product must comprise ≥ l.5% of total salicylate derivatives expressed as salicin by high-performance liquid chromatography.

The United States Pharmacopeia (USP) specifies that *Salix* species bark dry extract must contain between 90% and 110% of its labeled salicylate content, calculated as salicin on an anhydrous basis.[27] The starting plant material to extract ratio typically ranges from 5:1 to 20:1.

Salix Alba (Willow) Bark Powder

According to USP, Salix species bark powder consists of Salix species bark that has been reduced to a fine or very fine powder.[28] This powder must contain not less than 1.5% total salicylate derivates, calculated as salicin on the dried basis, and not more than 1.5% free salicin, calculated on the dried basis.

Salix Alba (Willow) Leaf Extract

Salix Alba (Willow) Leaf Extract at 4 – 6% in water is composed of 32% sugar, 29.5% mineral ashes, 3.9% proteins, and 3.1% polyphenols.[29] Specifications indicate that heavy metal impurities (including antimony, arsenic, cadmium, chromium, cobalt, mercury, nickel, lead, and vanadium) are each present at concentrations ≤ 0.5 ppm.

The total polyphenol (expressed as gallic acid), flavone (expressed as rutin), and tannin (expressed as pyrogallol) contents in young *Salix alba* (willow) leaves were determined to be 55, 8.5, and 12 mg/g leaves, respectively.[20] In mature leaves, the respective values were 70, 8, and 10 mg/g leaves. The composition of a hydromethanolic extract of *Salix alba* (willow) leaves may be found in Table 4.[22]

The major compounds present in an ethyl acetate *Salix alba* (willow) leaf extract were determined via gas chromatography-mass spectrometry analysis.[12] The detected compounds and their relative abundances (as percentages) were: heptacosan-1-ol (15.59%), tetracosanal (14.93%), n-octacosyl acetate (9.57%), cholesterol (5.11%), octacosylheptafluoro-butyrate (5.09%), octacosyl acetate (4.81%), stearyl aldehyde (4.45%), and cholest-4-en-3-one (4.08%).

USE

Cosmetic

The safety of the cosmetic ingredients addressed in this assessment is evaluated based on data received from the US FDA and the cosmetics industry on the expected use of *Salix alba* (willow)-derived ingredients 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 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.[30] 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 in 2025[31,32] and concentration of use data submitted in response to a concentration of use survey conducted by PCPC in 2025,[33] Salix Alba (Willow) Bark Extract has the highest frequency and concentration of use of the ingredients in this group. This ingredient is used in 3060 formulations at up to 1.1% (in leave-on face and neck products; Table 5). (Although all 6 ingredients have use reported in the RLD, Salix Alba (Willow) Leaf Extract is the only other ingredient with a reported concentration of use (Salix Alba (Willow) Leaf Extract is reported to be used at up to 0.00002% in other hair preparations).)

These ingredients may be incidentally ingested as they are used in products used in the mouth (e.g., Salix Alba (Willow) Bark Extract is used in mouthwashes and breath fresheners; concentration not reported). In addition, these ingredients may result in mucous membrane exposure (e.g., Salix Alba (Willow) Bark Extract is used bath soaps and body washes at 0.004%). These ingredients are also reported to be used in baby products (e.g., Salix Alba (Willow) Bark Extract is used in other baby products; concentration not reported).

Although reported uses in baby products are identified in the RLD, concentration of use data are not available for the reported categories of baby product. In cases where a baby product category is reported without an associated concentration, and 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, Salix Alba (Willow) Bark Extract has no reported concentration of use in baby shampoos; however, it is reported in shampoos (non-coloring) at a maximum concentration of 0.01%, and concentrations in baby shampoos 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

These ingredients may be incidentally inhaled as they are used in spray (e.g., Salix Alba (Willow) Bark Extract is used in hair spray; concentration not reported) and powder formulations (e.g., Salix Alba (Willow) Bark Extract is used in face powders; concentration 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 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.

Following the passage of 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.

Some products containing *Salix alba* (willow)-derived ingredients may be marketed for use with airbrush delivery systems. With the advent of MoCRA and the current product categories outlined by the FDA, 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. Some of the reported product categories for these categories listed in the RLD do require designation if airbrush application is used, and this type of application was reported (e.g., Salix Alba (Willow) Bark Extract is reported to be used in airbrush foundation formulations and in professional airbrush indoor tanning preparations (concentrations not provided)). Additionally, the Council currently surveys the cosmetic industry for maximum reported use concentrations of ingredients in products which may be used in conjunction with an airbrush delivery system; thus, this type of data may also be available, when submitted. Please note that no concentration of use data were provided indicating airbrush application. Nevertheless, 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.

None of the *Salix alba* (willow)-derived ingredients named in the report are restricted from use in any way under the rules governing cosmetic products in the European Union (EU); however, the EU limits the use of salicylates in cosmetics.[34] According to European Commission (EC) Regulation No 1223/2009, Annex III permits salicylic acid for purposes other than as a preservative at concentrations up to 3% in rinse-off hair products, up to 2% in most other products, and up to 0.5% in body lotion, eye shadow, mascara, eyeliner, lipstick, and roll-on deodorant. Under this Annex, salicylic acid should not be used in preparations for children under the age of 3, should not be used in applications that may lead to exposure of the end-user's lungs by inhalation, and should not be used in oral products. Annex V permits salicylic acid and its salts to be used as preservatives at a maximum concentration of 0.5% (as acid), also with the same restrictions regarding children under 3, oral products, and inhalation exposure; however, salicylic acid salts are permitted in shampoos for children under 3.

Non-Cosmetic

Salix alba (willow) bark has historically been used to treat various ailments such as pain, fever, inflammation, flu, and headaches; the analgesic, anti-pyretic, and anti-inflammatory properties are primarily attributed to salicin (an analogous precursor to acetylsalicylic acid) content.[11,24] Currently, *Salix alba* (willow) is used in dietary supplements (e.g., weight loss supplements), herbal treatments used for pain management, and fertilizers [13,35-37] These ingredients are also present in acne patches, wart treatments, nail fungal treatments, vitamin C serums, and various homeopathic treatments.[38,39]

According to the European Medicines Agency, willow bark supplements have several contraindications. They should be avoided by individuals with hypersensitivity to salicin, salicylates, or other non-steroidal anti-inflammatory drugs, those with active peptic ulcers, third-trimester pregnancy, glucose-6-phosphate dehydrogenase deficiency, severe liver or kidney dysfunction, coagulation disorders, and children and adolescents under 18 due to the risk of Reye's syndrome.[40] While this guidance specifically refers to willow bark derived from *Salix purpurea*, *Salix daphnoides*, and *Salix fragilis*, it is included herein, as *Salix alba* also contains salicylates and may warrant similar precautions. Similar precautions are required on labels of products containing *Salix alba* (willow) bark according to USP specifications.[6] Labels are required to state that these products should not be used in children, women who are pregnant or nursing, or by persons with known sensitivity to aspirin.

TOXICOKINETIC STUDIES

No relevant toxicokinetics studies on *Salix alba*-derived ingredients were found in the published literature, and unpublished data were not submitted. In general, toxicokinetics data are not expected to be found on botanical ingredients because each botanical ingredient is a complex mixture of constituents.

TOXICOLOGICAL STUDIES

Acute Toxicity Studies

Animal

Salix Alba (Willow) Bark Extract

No mortality or signs of toxicity were observed in mice following oral administration of Salix Alba (Willow) Bark Extract at 2000 mg/kg bw.[9] The extract was a mixture composed of water (68.25%), butylene glycol (29.25%), and Salix Alba (Willow) Bark Extract (2.5%) and was administered to 2 groups of mice (5/group; strain and sex not stated).[9]

In an acute toxicity assay performed according to Organisation for Economic Co-operation and Development (OECD) test guideline (TG) 423, a hydroalcoholic *Salix alba* (willow) bark extract (2000 mg/kg bw; 100% purity; water as vehicle) was administered by gavage to female Wistar rats (3/group).[4] The median lethal dose (LD_{50}) was determined to be > 2000 mg/kg bw.

Salix Alba (Willow) Leaf Extract

An acute oral toxicity assay was performed according to OECD TG 401 using Salix Alba (Willow) Leaf Extract (4 – 6% in water).[29] The test substance was considered to be non-toxic. No other details were provided.

Short-Term Toxicity Studies

Animal

Oral

Salix Alba (Willow) Bark Extract

A combined repeated-dose toxicity study with a reproductive/developmental toxicity test was performed in Wistar rats (12/sex/group) according to OECD TG 422.[4] Results regarding the reproductive toxicity parameters evaluated in this study can be found in the Developmental and Reproductive Toxicity section of this report. Animals were treated with 100, 300, or 1000 mg/kg bw/d of a hydroalcoholic *Salix alba (*willow) bark extract (water as vehicle; 100% purity), once a day, via gavage (controls given vehicle only). Males were treated for 28 d and females were treated for approximately 41 d. No test substance-related adverse effects were observed in this assay, and the no-observed-adverse-effect-level (NOAEL) for systemic toxicity was determined to be 1000 mg/kg bw/d.

DEVELOPMENTAL AND REPRODUCTIVE TOXICITY STUDIES

Animal

Salix Alba (Willow) Bark Extract

As stated previously, a combined repeated-dose toxicity study with a reproductive/developmental toxicity test was performed in Wistar rats (12/sex/group) according to OECD TG 422.[4] Results regarding the systemic toxicity evaluated in this study can be found in the Short-Term Toxicity Studies section of this report. Males were treated for 28 d (14 d pre-mating and 14 d during/post-mating) and females were treated for 14 d pre-mating, for up to 14 d during the mating period and through gestation, and for up to 13 d post-partum. Treatments occurred daily via gavage using a hydroalcoholic *Salix alba* (willow) bark extract (100, 300, and 1000 mg/kg bw/d; water as vehicle; controls were treated with the vehicle only). There were no differences between control- and test item-treated groups with regard to reproductive ability, mating, or gestation indices. The parental NOAEL was determined to be 1000 mg/kg bw/d. In the F1 generation, statistically significantly lower thyroid gland weights were observed in the mid- and high-dosed groups compared to control pups. However, thyroid gland weights were well within the historical range, and no effects on thyroid hormone concentration levels were observed. No developmental or endocrine changes were observed in pups. The NOAEL for reproductive effects and pup development/survival was determined to be 1000 mg/kg bw/d.

GENOTOXICITY STUDIES

Details regarding the genotoxicity studies summarized herein are found in Table 6. Salix Alba (Willow) Bark Extract (20 – 100%; up to 5000 µg/plate; in water) and hydroalcoholic *Salix alba* (willow) bark extracts (up to 5000 µg/plate; in water), yielded negative results in bacterial reverse mutation assays (performed with and without metabolic activation).[4,41-43,43] Negative results were also obtained for a hydroalcoholic *Salix alba* (willow) bark extract in an in vitro mammalian cell gene mutation test (up to 5000 µg/ml; in water) performed with and without metabolic activation. With respect to chromosomal damage, negative results were obtained for a hydroalcoholic *Salix alba* (willow) bark extract in an in vitro mammalian cell micronucleus assay (at up to 2000 µg/ml; in saline; with and without metabolic activation).[24] No genotoxicity was observed in cytokinesis block micronucleus assays performed in human peripheral blood leukocytes and HepG2 cells using *Salix alba* (willow) bark extract (up to 100 µg/ml; use of metabolic activation and vehicle not stated). With respect to deoxyribonucleic acid (DNA) strand breaks, a statistically significant elevation in DNA damage was observed in peripheral blood mononuclear cells at concentrations of 50 µg/ml and higher in a comet assay using *Salix alba* (willow) bark extract (use of metabolic activation and vehicle not stated; negative results at 5 µg/ml). However, no genotoxicity was observed in a comet assay performed in HepG2 cells using *Salix alba* (willow) bark extract (up to 100 µg/ml; use of metabolic activation and vehicle not stated). No genotoxicity was observed in either an in vivo micronucleus assay evaluating chromosomal damage or an in vivo comet assay evaluating DNA strand breaks.[44] In both assays, *Salix alba* (willow) bark extract was administered to mice via gavage at up to 2000 mg/kg bw in DMSO.

Salix Alba (Willow) Leaf Extract (4 – 6% in water) was evaluated for gene mutation in an Ames assay performed according to OECD TG 471 (no other details provided).[29] The extract was determined to be non-mutagenic.

CARCINOGENICITY STUDIES

Carcinogenicity studies on *Salix alba*-derived ingredients were found in the published literature, and unpublished data were not submitted.

ANTI-CARCINOGENICITY STUDIES

In Vitro

Salix Alba (Willow) Bark Extract

The ability of an ethanolic *Salix alba* (willow) bark extract to induce cytotoxicity in human leukemia-60 (HL-60) cells was evaluated.[11] Cells were incubated with 1, 2, 4, 6, 8, or 10 µg of the test substance for up to 24 h. The percent viability of cells after 24 h treatment with the negative control, 1, 2, 4, 6, 8, and 10 µg of extract was 98, 93, 87, 38, 50, and 16%, respectively.

OTHER RELEVANT STUDIES

Effect on Interleukin-6 (IL-6)

Salix Alba (Willow) Bark Extract

The effect of Salix Alba (Willow) Bark Extract on IL-6 levels was evaluated using cultured human dermal fibroblasts in an IL-6 enzyme-linked immunosorbent assay (ELISA).[45] Cells were treated with the test substance at concentrations of 0.01, 0.1, and 1% and incubated for 24 h. Appropriate positive and negative controls were used. IL-6 concentrations following exposure to 0.01, 0.1, and 1% of the test substance were 2860, 2600, and 1087 pg/ml, respectively. IL-6 concentrations following positive and negative control exposure were 2599 and 1423 pg/ml, respectively.

Cytotoxicity

Salix Alba (Willow) Leaf Extract

A neutral red release assay was performed on Statens Seruminstitut Rabbit Cornea (SIRC) cells using Salix Alba (Willow) Leaf Extract (4 – 6% in water).[29] The test substance was non-cytotoxic. No other details were provided.

Steroidogenesis Assay

Salix Alba (Willow) Bark Extract

An H295R steroidogenesis assay (OECD TG 456) was performed to evaluate the potential for Salix Alba (Willow) Bark Extract in DMSO to induce or inhibit the production of 17β-estradiol and testosterone in human adenocarcinoma H295R cells.[46] Cells were exposed to the test substance at multiple concentrations (0.01, 0.1, 1, 10, 100, 1000, and 10,000 µM), alongside positive, negative, and solvent controls. Hormone levels in the culture media were quantified by ELISA after 48 h of exposure. The test substance was non-cytotoxic and did not induce or inhibit 17β-estradiol or testosterone production at any test concentration, indicating no evidence of endocrine disruption via this steroidogenesis pathway.

DERMAL IRRITATION AND SENSITIZATION STUDIES

Details regarding the following dermal irritation, sensitization, and phototoxicity studies summarized below are found in Table 7. In vitro dermal irritation assays using reconstructed human epidermis showed Salix Alba (Willow) Bark Extract (tested at concentrations of 20% and 100%), as well as a hydroalcoholic *Salix alba* bark extract (tested at 100%), did not reduce tissue viability below the threshold for irritation, with mean viabilities ranging from approximately 85 to 111%.[4,47-49] No erythema or edema were observed in 2 studies where Salix Alba (Willow) Bark Extract was applied to the skin of guinea pigs (final test concentration, 0.075% aqueous; level of occlusion not stated).[9] Salix Alba (Willow) Leaf Extract (4 – 6% in water) was non-irritating in a dermal irritation assay performed according to OECD TG 404 (no details provided; likely performed in rabbits).[29] In several direct peptide reactivity assays (DRPAs), Salix Alba (Willow) Bark Extract (20 – 100% in acetonitrile) was predicted to be non-sensitizing.[47-52] KeratinoSens™ assays using 20 – 100% Salix Alba (Willow) Bark Extract (in DMSO; tested at up to 2000 µM) and Salix Alba (Willow) Leaf Extract (4 - 6% in water) yielded negative results; however, positive results were obtained in vitro sensitization assays (KeratinoSens™ and genomic allergen rapid detection (GARD) assays) using an aqueous *Salix alba* (willow) bark extract (in DMSO; tested at up to 400 µg/ml) and hydroalcoholic *Salix alba* (willow) bark extract (in DMSO; tested at up to 500 µg/ml).[4,29,53-55] Salix Alba (Willow) Bark Extract (final test concentration, 0.075%) was non-sensitizing in a guinea pig sensitization assay performed under occlusive conditions.[9] No sensitization was observed in a guinea pig maximization assay using Salix Alba (Willow) Leaf Extract (4 – 6% in water; no other details provided).[29] No irritation or sensitization was observed in HRIPTs performed in 50 subjects using 5% Salix Alba (Willow) Bark Extract and a serum containing 0.0025% Salix Alba (Willow) Bark Extract (tested neat).[56,57]

Phototoxicity

In Vitro

A 3T3 neutral red reuptake phototoxicity assay showed that 1% Salix Alba (Willow) Bark Extract in ethanol (phototoxicity was evaluated in this ingredient as it produced significant absorbance in the wavelengths of interest (290 and 700 nm)) was non-phototoxic under with 5 J/cm^2 ultraviolet A (UVA)/visible light (Vis).[58] EpiDerm™ phototoxicity assays using 0.5 – 10% Salix Alba (Willow) Bark Extract (including a 20% extract tested at final concentrations of 0.025 – 0.5%) yielded negative results (tissues irradiated with 6 J/cm^2 UVA).[59,60] Salix Alba (Willow) Leaf Extract (4 – 6% in water) was evaluated in a neutral red reuptake phototoxicity assay performed according to OECD TG 432 and was considered to be non-phototoxic.[29]

OCULAR IRRITATION STUDIES

Details regarding the ocular irritation studies summarized below are found in Table 8. Salix Alba (Willow) Bark Extract (20 – 100%) was predicted to be non-irritating in EpiOcular™ ocular irritation assays.[47-49] Conversely, a hydroalcoholic *Salix alba* (willow) bark extract (tested at 100%) was predicted to be irritating in an EpiOcular™ assay (mean cell viability was 14% (below 60% is classified as irritating)).[4] In addition, an vitro ocular irritation assay using isolated chicken eyes was performed using an undiluted hydroalcoholic *Salix alba* (willow) bark extract.[4] The test substance was not classified as a severe irritant (Globally Harmonized System (GHS) category 1) and was also not classified as a non-irritant; therefore, it was concluded that further information is required for classification. Salix Alba (Willow) Leaf Extract tested at 4 – 6% in water was a non-irritant when evaluated in an in vivo acute ocular irritation assay (likely performed in rabbits as stated in OECD TG 405).[29]

CLINICAL STUDIES

Case Reports

Salix Alba (Willow) Bark Extract

A 61-yr-old female presented with a sudden onset of shortness of breath and non-productive cough 30 min after taking a white willow bark supplement.[35] Evaluation revealed oxygen desaturation, severe hypoxemia, metabolic acidosis, bilateral

interstitial infiltrates which led to a diagnosis of acute hypoxic respiratory failure secondary to severe acute respiratory distress syndrome from reaction to white willow bark. The patient improved following treatment with steroids, antihistamines, and oxygen.

A 25-yr-old woman presented to the emergency department with anaphylaxis requiring epinephrine, antihistamines, steroids, and volume resuscitation.[61] Medication history revealed that the patient ingested 2 capsules of weight loss supplement containing white willow bark. The patient reported a history of allergy to acetylsalicylic acid. No other causes for anaphylaxis were identified.

SUMMARY

The safety of 6 *Salix alba* (willow)-derived ingredients is reviewed in this safety assessment. According to the *Dictionary*, 4 of these ingredients are reported to function as skin-conditioning agents in cosmetics; other functions are also reported.

According to 2025 RLD and concentration of use data, Salix Alba (Willow) Bark Extract has the highest frequency and concentration of use. This ingredient is reported to be used in 3060 formulations at up 1.1% in leave-on face and neck products (not spray).

No signs of toxicity were observed in an acute toxicity assay in which mice were administered Salix Alba (Willow) Bark Extract via gavage at 2000 mg/kg bw/d. An acute oral toxicity assay was performed using a hydroalcoholic *Salix alba* (willow) bark extract given to rats via gavage. The LD_{50} in this assay was determined to be > 2000 mg/kg bw. Salix Alba (Willow) Leaf Extract (4 – 6% in water) was considered to be non-toxic in an acute oral toxicity assay performed according to OECD TG 401. No erythema or edema were observed in a 2-wk dermal assay in which Salix Alba (Willow) Bark Extract (final concentration, 0.075%) was applied to the clipped skin of guinea pigs. No test substance-related systemic toxicity was observed in a combined repeated-dose and reproductive/developmental toxicity assay in which rats were given up to 1000 mg/kg bw/d of a *Salix alba* (willow) bark extract. The test substance was administered via gavage for 28 d in males (pre- and post-mating) and for 41 d in females (pre-mating, gestation, and post-partum). When reproductive and developmental toxicity parameters were evaluated in this assay, the NOAEL for reproductive effects and pup development/survival was determined to be 1000 mg/kg bw/d.

With respect to gene mutation, Salix Alba (Willow) Bark Extract (20 – 100%; up to 5000 µg/plate) and hydroalcoholic *Salix alba* (willow) bark extracts (up to 5000 µg/plate) were negative in bacterial reverse mutation assays, with and without metabolic activation, and a hydroalcoholic *Salix alba* (willow) bark extract was negative in an in vitro mammalian cell gene mutation assay (up to 5000 µg/ml). With respect to chromosomal damage, *Salix alba* (willow) bark extracts were negative in in vitro micronucleus assays at concentrations up to 2000 µg/ml, including cytokinesis-block micronucleus assays in human peripheral blood leukocytes and HepG2 cells at up to 100 µg/ml. With respect to DNA damage, *Salix alba* (willow) bark extract increased DNA strand breaks in peripheral blood mononuclear cells at ≥ 50 µg/ml, but was negative in a comet assay in HepG2 cells at up to 100 µg/ml. In vivo micronucleus and comet assays of *Salix alba* (willow) bark extract were negative at doses up to 2000 mg/kg bw. Salix Alba (Willow) Leaf Extract (4–6%) was non-mutagenic in an Ames assay.

An ethanolic *Salix alba* (willow) bark extract resulted in a decrease in cell viability of HL-60 cells in a concentration-dependent manner. Cells were incubated with 1 – 10 µg of the test substance.

The effect of Salix Alba (Willow) Bark Extract on IL-6 levels was evaluated in an IL-6 ELISA. IL-6 concentrations following exposure to 0.01, 0.1, and 1% of the test substance were 2860, 2600, and 1087 pg/ml, respectively. IL-6 concentrations following positive and negative control exposure were 2599 and 1423 pg/ml, respectively.

A neutral red release assay was performed on SIRC cells using Salix Alba (Willow) Leaf Extract (4 – 6% in water). The test substance was non-cytotoxic.

An H295R steroidogenesis assay was performed to evaluate the potential for Salix Alba (Willow) Bark Extract (up to 10,000 µM) to induce or inhibit the production of 17β-estradiol and testosterone in human adenocarcinoma H295R cells. The test substance did not inhibit or induce 17β-estradiol and testosterone production.

Salix Alba (Willow) Bark Extract was non-irritating in reconstructed human epidermis assays at 20% and 100%, and a hydroalcoholic Salix alba bark extract (tested at 100%) also did not significantly reduce tissue viability (mean viabilities approximately 85 – 111%). Salix Alba (Willow) Bark Extract (0.075%; assays performed in guinea pigs) and Salix Alba (Willow) Leaf Extract (4 – 6%; assay likely performed in rabbits) were non-irritating in dermal irritation assays. Salix Alba (Willow) Bark Extract (20 – 100%) and Salix Alba (Willow) Leaf Extract (4 – 6%) were negative in DPRA and KeratinoSens™ assays; however, positive in vitro sensitization responses were reported for aqueous and hydroalcoholic Salix alba (willow) bark extracts at up to 400 – 500 µg/ml. Salix Alba (Willow) Bark Extract (0.075%) and Salix Alba (Willow) Leaf Extract (4 – 6%) were non-sensitizing in guinea pig assays, and no irritation or sensitization was observed in HRIPTs using 5% Salix Alba (Willow) Bark Extract or a formulation containing 0.0025% Salix Alba (Willow) Bark Extract. A 3T3 neutral red reuptake phototoxicity assay showed that 1% Salix Alba (Willow) Bark Extract in ethanol was non-phototoxic. EpiDerm™ phototoxicity assays using 0.5 – 10% Salix Alba (Willow) Bark Extract (including a 20% extract tested at final

concentrations of 0.025 – 0.5%) yielded negative results. Salix Alba (Willow) Leaf Extract (4 – 6% in water) evaluated in a neutral red reuptake phototoxicity assay was considered to be non-phototoxic.

Salix Alba (Willow) Bark Extract (20 – 100%) was predicted to be non-irritating in EpiOcular™ ocular irritation assays. A hydroalcoholic *Salix alba* bark extract (tested at 100%) showed irritation potential in one in vitro assay and inconclusive results in an isolated chicken eye test, indicating that further evaluation may be needed. Salix Alba (Willow) Leaf Extract was predicted to be non-irritating in an in vivo ocular irritation assay (likely performed in albino rabbits).

A 61-yr-old woman developed acute hypoxic respiratory failure secondary to severe acute respiratory distress syndrome after ingesting a white willow bark supplement. Her condition improved with treatment that included steroids, antihistamines, and oxygen. Additionally, a published case report described a 25-yr-old patient with a known allergy to acetylsalicylic acid who presented to the emergency department with anaphylaxis following ingestion of a supplement containing white willow bark.

DRAFT DISCUSSION

[Note: This Discussion is in the draft form, and changes will be made following the Panel meeting.]

This assessment reviews the safety of 6 Salix alba (willow)-derived ingredients as used in cosmetic formulations, in accordance with the product categories and concentrations of use identified in the Use section and Use table. The Panel concluded…[TBD].

The Panel discussed the potential for salicylates to be present in these *Salix alba* (willow)-derived ingredients. Although these ingredients are not specifically restricted from use in cosmetics in the EU, the Panel noted that the EU limits the use of salicylic acid in cosmetic products, including restrictions on use in children under 3 years of age, oral products, and applications that may result in inhalation exposure. Therefore, the Panel emphasized that formulators should be aware of the salicylate content of these ingredients and avoid formulations that may result in potentially unsafe levels of salicylates, particularly in products intended for infants and young children and products that may result in inhalation or oral exposure.

The Panel also expressed concern about heavy metals, pesticide residues, and other plant species that may be present in botanical ingredients. They stressed that the cosmetics industry should continue to minimize impurities in cosmetic formulations according to limits set by the US FDA and EPA.

Use in baby products has been reported, but concentration of use data were not available for the baby product categories. When use in a baby product category is reported without an associated concentration, and an analogous adult product category with reported use concentrations is available, the adult product concentration is considered informative for exposure characterization. Accordingly, concentrations in the corresponding baby product categories are not expected to exceed those reported for the analogous adult product categories. Thus, although no concentration of use is reported for Salix Alba (Willow) Bark Extract in baby shampoos, the ingredient is reported in shampoos (non-coloring) at a maximum concentration of 0.01%, and concentrations in baby shampoos 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, an analogous adult product category could not be identified, and the adult-product bridging is not applied.

At least 1 use for the ingredients assessed in this assessment is reported in the RLD under Category 17, "other preparations." 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 such products remain unknown and the Panel's safety assessment conclusion, therefore, does not apply thereon.

The Panel discussed the issue of incidental inhalation exposure resulting from these ingredients (e.g., Salix Alba (Willow) Bark Extract is used in hair spray and face powder; concentrations not reported). Inhalation toxicity data were not available. However, the Panel noted that the majority of droplets/particles would not be respirable to any appreciable amount. Furthermore, droplets/particles deposited in the nasopharyngeal or tracheobronchial regions of the respiratory tract present no toxicological concerns based on the chemical and biological properties of these ingredients. Coupled with the small actual exposure in the breathing zone and the low concentrations at which these ingredients are used (or expected to be used) in potentially inhaled products, the available information indicates that incidental inhalation would not be a significant route of exposure that might lead to local respiratory or systemic effects. A detailed discussion and summary of the Panel's approach to evaluating incidental inhalation exposures to ingredients in cosmetic products is available at https://www.cir-safety.org/cir-findings.

The Panel's respiratory exposure resource document (***see link above)*** notes that airbrush technology presents a potential safety concern. Although frequency and/or concentration of use data are now available (and in some cases mandated) for ingredients marketed for use with airbrush delivery systems in certain product categories, no data are available for consumer habits and practices thereof, product particle size, or other relevant particle data (e.g., diameter). As a result of deficiencies in these critical data needs, the data profile is incomplete, and the safety of cosmetic ingredients applied by airbrush delivery systems cannot be determined by the Panel. Accordingly, the Panel has concluded the data are insufficient to support the safe use of cosmetic ingredients applied via an airbrush delivery system.

CONCLUSION

To be determined.

TABLES

Table 1. Definitions and reported functions[1]

Ingredient/CAS No.	Definition	Function(s)
Salix Alba (Willow) Bark Extract (84082-82-6)	Salix Alba (Willow) Bark Extract is the extract of the bark of *Salix alba*.	hair conditioning agents skin conditioning agents - occlusive
Salix Alba (Willow) Bark Powder	Salix Alba (Willow) Bark Powder is the powder obtained from the dried, ground bark of *Salix alba.*	absorbents exfoliants skin protectants
Salix Alba (Willow) Bark Water	Salix Alba (Willow) Bark Water is the aqueous solution of the steam distillate obtained from the bark of *Salix alba*.	fragrance ingredients
Salix Alba (Willow) Extract	Salix Alba (Willow) Extract is the extract of the whole plant, *Salix alba*.	antifungal agent skin-conditioning agents – emollient skin-conditioning agents – humectant
Salix Alba (Willow) Flower Extract	Salix Alba (Willow) Flower Extract is the extract of the flowers of *Salix alba.*	skin-conditioning agents – misc
Salix Alba (Willow) Leaf Extract (84082-82-6)	Salix Alba (Willow) Leaf Extract is the extract of the leaves of *Salix alba*.	skin conditioning agents - misc

Table 2. Chemical properties

Property	Value	References
Salix Alba (Willow) Bark Extract		
Physical Form	free-flowing powder	8
Color	white to off-white	8
Odor	characteristic	8
pH (3% solution in water)	4.0 – 6.0	8
Salix Alba (Willow) Bark Extract in glycerin and water		
Color	reddish-brown	17
Odor	characteristic	17
Density (g/ml @ 20ºC)	1.20 – 1.23	17
Refraction Index (20ºC)	1.44 – 1.47	17
Water Solubility	clear to slightly turbid at 10%	17
Alcohol Solubility	clear to slightly turbid at 10%	17
a *Salix alba* (willow) bark extract		
Physical Form	solid particulate/powder	4
Color	brown	4
Odor	characteristic	4
Density (g/ml @ 20ºC)	1.48	4
Vapor Pressure (Pa @ ≤ 61ºC)	< 0.001	4
Melting Point (ºC)	≥ 160	4
Water Solubility (mg/l @ 20ºC & pH = 7)	50	4
log K_{ow} (@ 25ºC)	< 0.3 (measured); - 2.2 (extrapolated)	4
Mass Median Aerodynamic Diameter (µm)	21	4

*composition of tested ingredient: > 50% glycerin, > 10 - ≤ 25% water, > 0.1 - ≤ 1% Salix Alba Bark Extract

Table 3. Composition of a methanolic Salix alba (willow) bark extract[21]

Constituent	Amount (mg/g dry weight)
Salicylates	
salicin	0.91
salicortin	0.89
total salicylate content	1.80
Flavonoids	
ampelopsin	0.07
quercetin-hexoside	0.04
other quercetin-derivatives	0.02
total flavonoids	0.13
Flavan-3-ols	
catechin	1.26
procyanidin B3	0.24
total flavan-3-ols	1.49
Phenolic Acid Derivatives	
chlorogenic acid	0.40
coumaric acid derivative	0.02
neochlorogenic acid	0.33
total phenolic acid derivatives	0.75
Other Phenolic Compounds	
syringin	0.30
triadrin	0.67
total other phenolic compounds	0.97

Table 4. Composition of hydromethanolic extracts of Salix alba (willow) bark and leaves[22]

Constituent	Bark (mg/100 g dry weight)	Leaves (mg/100 g dry weight)
Phenolic Acids		
caffeoylhexose I	57.7	2.98
caffeoylhexose II	24.7	ND
caffeoxyl hexose-deoxyhexoside I	140	ND
caffeoyl hexose-deoxyhexoside II	ND	875
1-*O*-caffeoylquinic acid	ND	117
3-*O*-caffeoylquinic acid	42	386
caffeoylhexose III	240	ND
caffeoylquinic acid dimer I	ND	60.6
caffeoylquinic acid dimer II	ND	10.1
5-*O*-caffeoylquinic acid	ND	37.9
Flavanols and Procyanidins		
(epi)catechin-(epi)gallocatechin I	131	ND
(epi)catechin-(epi)gallocatechin II	10.1	ND
(epi)catechin-(epi)gallocatechin III	59.8	ND
A-type procyanidin dimer digallate	48.7	ND
A-type procyanidin dimer I	224	ND
A-type procyanidin dimer II	22.3	241.3
A-type procyanidin dimer III	9.22	ND
B-type procyanidin trimer I	22.9	241.4
A-type procyanidin trimer I	25.9	ND
A-type procyanidin dimer IV	14.3	ND
(+)-catechin	63.8	ND
(-)-epicatechin	176	ND
epigallocatechin I	ND	320
A-type procyanidin trimer digallate	99.3	ND
A-type procyanidin trimer II	15.1	ND
B-type procyanidin trimer II	40.8	ND
B-type procyanidin trimer III	ND	124
epigallocatechin II	ND	325
B-type procyanidin tetramer I	25.5	ND
B-type procyanidin trimer IV	ND	247
B-type procyanidin tetramer II	56.1	ND
A-type procyanidin dimer V	198	ND
B-type procyanidin pentamer	ND	118
B-type procyanidin dimer I	ND	395
(epi)catechin methyl-hexoside I	68.6	ND
(epi)catechin methyl-hexoside II	56.8	ND
A-type procyanidin tetramer	33.5	ND
A-type procyanidin dimer VI	94.9	ND
A-type procyanidin trimer III	104	ND
(epi)catechin methyl-hexoside III	96.2	ND
(epi)catechin methyl-hexoside IV	28.5	ND
(epi)catechin-ethyl trimer	70.5	ND
Flavanols		
quercetin 3-*O*-rutinoside	ND	92.9
quercetin methyl-pentoside	ND	9.11
quercetin acylated-deoxylhexoside I	ND	167
quercetin acylated-deoxyhexoside II	ND	149
isorhamnetin 3-O-rutinoside	ND	460
quercetin 3-O-galactoside	ND	59.3
quercetin 3-O-glucoside	ND	98.4
quercetin-acylated-hexoside I	ND	180
quercetin-acylated-hexoside II	ND	413
quercetin 3-O-hexoside	10.5	ND
isorhamnetin-acylated-hexoside I	ND	4.65
isorhamnetin-3-galactoside	ND	146
kaempferol pentoside	6.58	ND
isorhamnetin acylated-hexoside II	ND	32.6
isorhamnetin acylated-hexoside III	ND	234
kaempferol 3-O-galactoside	12.5	ND
isorhamnetin acylated-hexoside IV	ND	28.6

ND = not detected

Table 5. Frequency and concentration of use according to likely duration and exposure and by product category[31-33]

	# of Uses RLD (2025)	Max Conc of Use % (2025)	# of Uses RLD (2025)	Max Conc of Use % (2025)	# of Uses RLD (2025)	Max Conc of Use % (2025)
	Salix Alba (Willow) Bark Extract		Salix Alba (Willow) Bark Powder		Salix Alba (Willow) Bark Water	
Totals*	**3060**	**0.00002 – 1.1**	**43**	**NR**	**31**	**NR**
summarized by likely duration and exposure**						
Duration of Use						
Leave-On	*2505*	*0.00002 – 1.1*	*NR*	*NR*	*28*	*NR*
Rinse-Off	*1375*	*0.001 – 1*	*43*	*NR*	*9*	*NR*
Diluted for (Bath) Use	*1*	*NR*	*NR*	*NR*	*NR*	*NR*
Permanent Tattoo Ink	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Unknown	*65*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type						
Baby Products	36	NR	NR	NR	NR	NR
Children's Makeup	NR	NR	NR	NR	NR	NR
Eye Area	41	NR	NR	NR	2	NR
Incidental Ingestion	28	NR	NR	NR	NR	NR
Mucous Membrane	191	0.004 – 0.005	1	NR	1	NR
Incidental Inhalation-Spray	29; 1153[a]; 1514[b]	0.025[a]; 0.00002 – 0.00003[b]	1[a]	NR	10[a]; 19[b]	NR
Incidental Inhalation-Airbrush	2	NR	NR	NR	NR	NR
Incidental Inhalation-Powder	8; 1514[b]; 16[c]	0.00002 – 0.00003[b]; 0.001 – 1.1[c]	NR	NR	19[b]	NR
Dermal Contact	3322	0.001 – 1.1	43	NR	37	NR
Deodorant (underarm)	11	NR	NR	NR	NR	NR
Hair - Non-Coloring	525	0.00002 – 0.01	NR	NR	NR	NR
Hair-Coloring	6	NR	NR	NR	NR	NR
Nail	7	NR	NR	NR	NR	NR
Tattoo Preparations	NR	NR	NR	NR	NR	NR
Other Preparations (Unknown Exposure Type)	65	NR	NR	NR	NR	NR
as reported by product category						
Baby Products						
Baby Shampoos	3	NR				
Baby Lotions/Oils/Powders/Creams	16	NR				
Other Baby Products	11 (l.o.); 6 (r.o.)	NR				
Bath Preparations (diluted for use)						
Bath Oils, Tablets, and Salts	3	NR				
Bubble Baths	4	NR				
Other Bath Preparations	3	NR				
Eye Makeup Preparations (not children's)						
Eye Shadow	1	NR				
Eye Lotion	15	NR			1	NR
Eye Makeup Remover	5	NR				
Eyelash and Eyebrow Adhesives/Glues/Sealants	1	NR				
Eyelash and Eyebrow Preparations (primers, conditioners, serums, fortifiers)	13	NR				
Eyelash Cleansers	1	NR				
Other Eye Makeup Preparations	5	NR			1	NR
Fragrance Preparations						
Perfumes	1	NR				
Other Fragrance Preparation	10	NR				

Table 5. Frequency and concentration of use according to likely duration and exposure and by product category[31-33]

	# of Uses RLD (2025)	Max Conc of Use % (2025)	# of Uses RLD (2025)	Max Conc of Use % (2025)	# of Uses RLD (2025)	Max Conc of Use % (2025)
Hair Preparations (non-coloring)						
Hair Conditioners	27 (l.o.); 78 (r.o.)	0.002 (l.o.); 0.01 (r.o.)				
Hair Sprays (aerosol fixatives)	14	NR				
Hair Straighteners	1	NR				
Rinses (non-coloring)	18	NR				
Shampoos (non-coloring)	3 (l.o.); 125 (r.o.)	0.01 (r.o.)				
Tonics, Dressings, Other Hair Grooming Aids	102	0.00003				
Wave Sets	1	NR				
Other Hair Preparations	100 (l.o.); 53 (r.o.)	0.00002 (l.o.)				
Hair Coloring Preparations						
Hair Tints	1	NR				
Hair Rinses (coloring)	1 (l.o.); 1 (r.o.)	NR				
Other Hair Coloring Preparation	2 (l.o.); 1 (r.o.)	NR				
Makeup Preparations (not eye or children's)						
Blushers and Rouges (all types)	22	NR				
Face Powders	8	NR				
Foundations	29 (traditional application); 1 (airbrush application)	0.001 (traditional application)				
Leg and Body Paints						
Lipsticks and Lip Glosses	25	NR				
Makeup Bases	7 (traditional application)	0.0063 (traditional application)				
Makeup Fixatives	4	NR				
Other Makeup Preparations	9 (traditional application)	0.0053 (traditional application)				
Manicuring Preparations						
Cuticle Softeners	1	NR				
Nail Creams and Lotions	3	NR				
Other Manicuring Preparations	3	NR				
Oral Hygiene Products						
Dentifrices	1	NR				
Mouthwashes and Breath Fresheners	1	NR				
Other Oral Products	1	NR				
Personal Cleanliness						
Bath Soaps and Body Washes	96	0.004	1	NR		
Deodorants (underarm)	11	NR				
Feminine Deodorants	1 (l.o.); 2 (r.o.)	NR				
Disposable Wipes	5	NR				
Other Personal Cleanliness Products	12 (l.o.); 37 (r.o.)	0.005			1 (r.o.)	NR
Shaving Preparations						
Aftershave Lotions	31	NR				
Beard Softeners	14	NR				
Pre-shave Lotions (all types)	1	NR				
Shaving Cream (aerosol, brushless, lather)	9	NR				
Other Shaving Preparations	13	NR				

Table 5. Frequency and concentration of use according to likely duration and exposure and by product category[31-33]

	# of Uses	Max Conc of Use	# of Uses	Max Conc of Use	# of Uses	Max Conc of Use
	RLD (2025)	% (2025)	RLD (2025)	% (2025)	RLD (2025)	% (2025)
Skin Care Preparations						
Cleansing	447	0.001 – 0.03			3	NR
Depilatories	5					
Face and Neck (excluding shaving preps)	928 (l.o.); 256 (r.o.)	0.001–1.1 (l.o.; not spray); 0.005 – 1 (r.o.; not spray)			18 (l.o.); 2 (r.o.)	NR
Body and Hand (excluding shaving preps)	157 (l.o.); 32	0.53 (l.o.; not spray)				
Foot Powders and Sprays	2	NR				
Moisturizing	500	0.002 – 0.053 (not spray)			6	NR
Night	34	0.4 (not spray)				
Paste Masks (mud packs)	77	NR	41	NR	2	NR
Skin Fresheners	138	NR			1	NR
Other Skin Care Preparations	208 (l.o.); 102 (r.o.)	0.025 (r.o)	1 (r.o.)	NR	1 (l.o.); 1 (r.o.)	NR
Suntan Preparations						
Suntan Gels, Creams, and Liquids	23	NR				
Indoor Tanning Preparations	1; 1 (professional airbrush application); 4 (professional spray application)	NR				
Other Suntan Preparations	2	NR				
Other Preparations (i.e., those that do not fit another category)	65	NR				
	Salix Alba (Willow) Extract		**Salix Alba (Willow) Flower Extract**		**Salix Alba (Willow) Leaf Extract**	
Totals*	**8**	**NR**	**34**	**NR**	**76**	**0.00002**
summarized by likely duration and exposure**						
Duration of Use						
Leave-On	*11*	*NR*	*22*	*NR*	*67*	*0.00002*
Rinse-Off	*1*	*NR*	*11*	*NR*	*17*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Permanent Tattoo Ink	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Unknown	*NR*	*NR*	*1*	*NR*	*1*	*NR*
Exposure Type						
Baby Products	NR	NR	NR	NR	NR	NR
Children's Makeup	NR	NR	NR	NR	NR	NR
Eye Area	NR	NR	NR	NR	NR	NR
Incidental Ingestion	NR	NR	5	NR	NR	NR
Mucous Membrane	NR	NR	5	NR	3	NR
Incidental Inhalation-Spray	4[a]; 7[b]	NR	9[a]; 8[b]	NR	14[a]; 35[b]	0.00002[b]
Incidental Inhalation-Airbrush	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Powder	7[b]	NR	8[b]	NR	35[b]	0.00002[b]
Dermal Contact	11	NR	28	NR	80	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	1	NR	NR	NR	4	0.00002[b]
Hair-Coloring	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR
Tattoo Preparations	NR	NR	NR	NR	NR	NR
Other Preparations (Unknown Exposure Type)	NR	NR	1	NR	1	NR

Table 5. Frequency and concentration of use according to likely duration and exposure and by product category[31-33]

	# of Uses RLD (2025)	Max Conc of Use % (2025)	# of Uses RLD (2025)	Max Conc of Use % (2025)	# of Uses RLD (2025)	Max Conc of Use % (2025)
as reported by product category						
Baby Products						
Baby Shampoos						
Baby Lotions/Oils/Powders/Creams						
Other Baby Products						
Bath Preparations (diluted for use)						
Bath Oils, Tablets, and Salts						
Bubble Baths						
Other Bath Preparations						
Eye Makeup Preparations (not children's)						
Eye Shadow						
Eye Lotion						
Eye Makeup Remover						
Eyelash and Eyebrow Adhesives/Glues/Sealants						
Eyelash and Eyebrow Preparations (primers, conditioners, serums, fortifiers)						
Eyelash Cleansers						
Other Eye Makeup Preparations						
Fragrance Preparations						
Perfumes						
Other Fragrance Preparation						
Hair Preparations (non-coloring)						
Hair Conditioners					1 (r.o.)	NR
Hair Sprays (aerosol fixatives)						
Hair Straighteners	1	NR				
Rinses (non-coloring)						
Shampoos (non-coloring)						
Tonics, Dressings, Other Hair Grooming Aids						
Wave Sets						
Other Hair Preparations					3 (l.o.)	0.00002
Hair Coloring Preparations						
Hair Tints						
Hair Rinses (coloring)						
Other Hair Coloring Preparation						
Makeup Preparations (not eye or children's)						
Blushers and Rouges (all types)						
Face Powders						
Foundations					20 (traditional application)	NR
Lipsticks and Lip Glosses			5	NR		
Makeup Bases						
Makeup Fixatives			1	NR	1	NR
Other Makeup Preparations					1 (traditional application)	NR
Manicuring Preparations						
Cuticle Softeners						
Nail Creams and Lotions						
Other Manicuring Preparations						

Table 5. Frequency and concentration of use according to likely duration and exposure and by product category[31-33]

	# of Uses RLD (2025)	Max Conc of Use % (2025)	# of Uses RLD (2025)	Max Conc of Use % (2025)	# of Uses RLD (2025)	Max Conc of Use % (2025)
Oral Hygiene Products						
Dentifrices						
Mouthwashes and Breath Fresheners						
Other Oral Products						
Personal Cleanliness						
Bath Soaps and Body Washes					3	NR
Deodorants (underarm)						
Feminine Deodorants						
Disposable Wipes						
Other Personal Cleanliness Products						
Shaving Preparations						
Aftershave Lotions			1	NR		
Beard Softeners						
Pre-shave Lotions (all types)						
Shaving Cream (aerosol, brushless, lather)						
Other Shaving Preparations						
Skin Care Preparations						
Cleansing			2	NR	9	NR
Depilatories						
Face and Neck (excluding shaving preps)	6 (l.o.)	NR	3 (l.o.); 1 (r.o.)	NR	28 (l.o.); 4 (r.o.)	NR
Body and Hand (excluding shaving preps)	1 (l.o.)	NR	1 (r.o.)	NR	4 (l.o.)	NR
Foot Powders and Sprays						
Moisturizing	4	NR	7	NR	4	NR
Night					6	NR
Paste Masks (mud packs)			7	NR		
Skin Fresheners						
Other Skin Care Preparations			5 (l.o.)	NR		
Suntan Preparations						
Suntan Gels, Creams, and Liquids						
Indoor Tanning Preparations						
Other Suntan Preparations						
Other Preparations (i.e., those that do not fit another category)			1	NR	1	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 6. Genotoxicity studies

Test Article	Vehicle	Concentration/Dose	Test System	Protocol	Results	Reference
IN VITRO						
Gene Mutation						
20% Salix Alba (Willow) Bark Extract	water	1.5, 5, 15, 50, 150, 500, 1500, and 5000 µg/plate	*Salmonella typhimurium* TA1535, TA1537, TA98, TA100 and *Escherichia coli* WP2	OECD TG 471; bacterial reverse mutation assay; performed with and without metabolic activation; appropriate positive and negative controls used	non-mutagenic; controls gave expected results	42
Salix Alba (Willow) Bark Extract	water	1.5, 5, 15, 50, 150, 500, 1500, and 5000 µg/plate	*S. typhimurium* TA1535, TA1537, TA98, TA100 and *E. coli* WP2	OECD TG 471; bacterial reverse mutation assay; performed with and without metabolic activation; appropriate positive and negative controls used	non-mutagenic; controls gave expected results	43
Salix Alba (Willow) Bark Extract	water	1.5, 5, 15, 50, 150, 500, 1500, and 5000 µg/plate	*S. typhimurium* TA1535, TA1537, TA98, TA100 and *E. coli* WP2	OECD TG 471; bacterial reverse mutation assay; performed with and without metabolic activation; appropriate positive and negative controls used	non-mutagenic; controls gave expected results	41
hydroalcoholic *Salix alba* (willow) bark extract	water	0.5, 1.58, 5, 15.81, 50, 158.1, 500, 1581, and 5000 µg/plate	*S. typhimurium* TA1535, TA1537, TA98, TA100 and *E. coli* WP2	OECD TG 471; bacterial reverse mutation assay; performed with and without metabolic activation; appropriate positive and negative controls used	non-mutagenic; controls gave expected results	4
hydroalcoholic *Salix alba* (willow) bark extract	water	62.5, 125, 250, 500, 1000, 2000, and 5000 µg/ml	Chinese hamster ovary cells	OECD TG 476; in vitro mammalian cell gene mutation test using Hprt and Xprt genes; performed with and without metabolic activation; appropriate positive and negative controls used	non-mutagenic; controls gave expected results	4
Salix Alba Willow Leaf Extract (4 – 6%)	water	NR	not stated	OECD TG 471 (Ames assay); no other details provided	non-mutagenic	29
Chromosomal Damage						
hydroalcoholic *Salix alba* (willow) bark extract	saline	without metabolic activation: 125, 250, 500, 750, 1000, 1500 and 2000 µg/ml with metabolic activation: 125, 250, 500, 1000, 1500 and 2000 µg/ml	mouse lymphoma L5178Y cells	OECD TG 487; in vitro mammalian cell micronucleus assay; performed with and without metabolic activation; appropriate positive and negative controls used	non-genotoxic; controls gave expected results	4
Salix alba (willow) bark extract	NR	5, 50, or 100 µg/ml	human peripheral blood leukocytes	cytokinesis-block micronucleus assay; 28-h exposure; use of metabolic activation not stated; micronuclei analysis performed	non-genotoxic; controls gave expected results	24
Salix alba (willow) bark extract	NR	5, 50, or 100 µg/ml	HepG2 cells	cytokinesis-block micronucleus assay; 24-h exposure; use of metabolic activation not stated; micronuclei analysis performed	non-genotoxic; controls gave expected results	24
DNA Strand Breaks						
Salix alba (willow) bark extract	NR	5, 50, or 100 µg/ml	peripheral blood mononuclear cells	comet assay; 4-h incubation; use of metabolic activation not stated; appropriate positive and negative controls used	a statistically significant elevation in DNA damage was found between the negative control and groups treated with 50 or 100 µg/ml; results were negative at 5 µg/ml	24
Salix alba (willow) bark extract	NR	5, 50, or 100 µg/ml	HepG2 cells	comet assay; 4-h incubation; use of metabolic activation not stated; appropriate positive and negative controls used	non-genotoxic; controls gave expected results	24
IN VIVO						
Chromosomal Damage						

Table 6. Genotoxicity studies

Test Article	Vehicle	Concentration/Dose	Test System	Protocol	Results	Reference
Salix alba (willow) bark extract	DMSO	500, 1000, or 2000 mg/kg bw	male Swiss albino mice (6/group)	in vivo assay; gavage administration 1/x for 7 d; appropriate positive and negative controls used; animals killed 4 h after last treatment and cells (bone marrow cells) evaluated; micronucleus assay performed on cells	non-genotoxic; controls gave expected results	44
DNA Strand Breaks						
Salix alba (willow) bark extract	DMSO	500, 1000, or 2000 mg/kg bw	male Swiss albino mice (6/group)	in vivo assay; gavage administration 1/x for 7 d; appropriate positive and negative controls used; animals killed 4 h after last treatment and cells (peripheral blood, heart and testes cells); comet assay performed on cells	non-genotoxic; controls gave expected results	44

DMSO = dimethyl sulfoxide; DNA = deoxyribonucleic acid; HepG2 = human hepatoma cell line; HPRT = hypoxanthine-guanine phosphoribosyltransferase; NR = not reported; OECD = Organisation for Economic Co-operation and Development; TG = test guideline; Xprt = xanthine-guanine phosphoribosyltransferase

Table 7. Dermal irritation, sensitization, and phototoxicity studies

Test Article	Vehicle	Concentration/ Dose	Test Population/ System	Protocol	Results	Reference
IRRITATION						
IN VITRO						
Salix Alba (Willow) Bark Extract	NR	20%; 25 mg	reconstructed human epidermis	EpiDerm™ assay; 60 min incubation; tissue viability evaluated via MTT assay; appropriate positive and negative controls used	non-irritating; mean tissue viability of approximately 85% (viability ≤ 50 indicates positive results); controls gave expected results	47
Salix Alba (Willow) Bark Extract	none	100%; 25 mg	reconstructed human epidermis	EpiDerm™ assay; 60 min incubation; tissue viability evaluated via MTT assay; appropriate positive and negative controls used	non-irritating; mean tissue viability of approximately 95% (viability ≤ 50 indicates positive results); controls gave expected results	49
Salix Alba (Willow) Bark Extract	none	100%; 25 mg	reconstructed human epidermis	EpiDerm™ assay; 60 min incubation; tissue viability evaluated via MTT assay; appropriate positive and negative controls used	non-irritating; mean tissue viability of 100% (viability ≤ 50 indicates positive results); controls gave expected results	48
a hydroalcoholic *Salix alba* (willow) bark extract (100% purity)	none	100%; 10 mg	reconstructed human epidermis (n = 3)	OECD TG 439; in vitro irritation reconstructed human epidermis assay; appropriate positive and negative controls used	non-irritating; mean tissue viability was 111.2% (viability ≤ 50 indicate positive results); controls gave expected results	4
ANIMAL						
Salix Alba (Willow) Bark Extract (mixture composed of water (68.25%), butylene glycol (29.25%), Salix Alba (Willow) Bark Extract (2.5%))	water	3% (final test concentration of Salix Alba (Willow) Bark Extract, 0.075%)	guinea pigs (n = 3; strain and sex not stated)	test substance applied topically to animals (level of occlusion not stated); animals evaluated for erythema and edema 24, 48, and 72 h after dosing	non-irritating; no erythema or edema observed	9
Salix Alba (Willow) Bark Extract (mixture composed of water (68.25%), butylene glycol (29.25%), Salix Alba (Willow) Bark Extract (2.5%))	water	3% (final test concentration of Salix Alba (Willow) Bark Extract, 0.075%)	guinea pigs (n = 5; strain and sex not stated)	test substance applied to clipped skin 5x/wk for 2 wk (level of occlusion not stated); observation prior to daily dosing and 24 h after final dosing	no erythema or edema observed	9

Table 7. Dermal irritation, sensitization, and phototoxicity studies

Test Article	Vehicle	Concentration/ Dose	Test Population/ System	Protocol	Results	Reference
Salix Alba (Willow) Leaf Extract	water	4 – 6%	not stated; however, likely 1 – 3 albino rabbits (as suggested by OECD TG 404 guidelines)	OECD TG 404; dermal irritation assay; no other details provided	non-irritating	29
SENSITIZATION						
				IN CHEMICO		
20% Salix Alba (Willow) Bark Extract	acetonitrile	5 mM for cysteine peptide assay; 25 mM for lysine peptide assay	cysteine and lysine peptides	OECD TG 442C: direct peptide reactivity assay; appropriate positive and negative controls used	not predicted to be sensitizing The mean percent depletion of cysteine and lysine was 3.13% causing minimal reactivity. The controls gave expected results	52
Salix Alba (Willow) Bark Extract	acetonitrile	5 mM for cysteine peptide assay; 25 mM for lysine peptide assay	cysteine and lysine peptides	OECD TG 442C: direct peptide reactivity assay; appropriate positive and negative controls used	not predicted to be sensitizing The mean percent depletion of cysteine and lysine was 3.22% causing minimal reactivity. The controls gave expected results	51
Salix Alba (Willow) Bark Extract	acetonitrile	5 mM for cysteine peptide assay; 25 mM for lysine peptide assay	cysteine and lysine peptides	OECD TG 442C: direct peptide reactivity assay; appropriate positive and negative controls used	not predicted to be sensitizing The mean percent depletion of cysteine and lysine was 3.08% causing minimal reactivity. The controls gave expected results	50

Table 7. Dermal irritation, sensitization, and phototoxicity studies

Test Article	Vehicle	Concentration/ Dose	Test Population/ System	Protocol	Results	Reference
			IN VITRO			
20% Salix Alba (Willow) Bark Extract	DMSO	0.98, 1.95, 3.9, 7.8, 15.6, 31.25, 62.5, 125, 250, 500, 1000, and 2000 µM	immortalized human skin keratinocytes	OECD TG 442D; KeratinoSens™ assay; appropriate positive and negative controls used	not predicted to be sensitizing The I_{max} was determined to be 0.40 and the IC_{50} was > 10,000 µM. Cell viability was lower than 70% at all relevant concentrations, indicating a negative prediction for sensitization. Positive and negative controls gave expected results.	53
Salix Alba (Willow) Bark Extract	DMSO	0.98, 1.95, 3.9, 7.8, 15.6, 31.25, 62.5, 125, 250, 500, 1000, and 2000 µM	immortalized human skin keratinocytes	OECD TG 442D; KeratinoSens™ assay; appropriate positive and negative controls used	not predicted to be sensitizing The I_{max} was determined to be 0.34 and the IC_{50} was > 10,000 µM. Cell viability was lower than 70% at all relevant concentrations, indicating a negative prediction for sensitization. Positive and negative controls gave expected results.	55
Salix Alba (Willow) Bark Extract	DMSO	0.98, 1.95, 3.9, 7.8, 15.6, 31.25, 62.5, 125, 250, 500, 1000, and 2000 µM	immortalized human skin keratinocytes	OECD TG 442D; KeratinoSens™ assay; appropriate positive and negative controls used	not predicted to be sensitizing The I_{max} was determined to be 0.33 and the IC_{50} was > 10,000 µM. Cell viability was lower than 70% at all relevant concentrations, indicating a negative prediction for sensitization. Positive and negative controls gave expected results.	54
an aqueous *Salix alba* (willow) bark extract (100% purity)	DMSO	0.2, 0.39, 0.78. 1.56, 3.1, 6.3, 13, 25, 50, 100, 200, and 400 µg/ml	immortalized human skin keratinocytes	OECD TG 442D; KeratinoSens™ assay; appropriate positive and negative controls used	predicted to be sensitizing The I_{max} was determined to be 5.51 and the $EC_{1.5}$ concentration was 152.33 µg/ml. The cell viability at the $EC_{1.5}$ concentration was higher than 70%, indicating a positive prediction for sensitization. Positive and negative controls gave expected results	4
an aqueous *Salix alba* (willow) bark extract (100% purity)	DMSO	NR	immortalized human skin keratinocytes	OECD TG 442D; KeratinoSens™ assay; appropriate positive and negative controls used	predicted to be sensitizing The I_{max} values and $EC_{1.5}$ values were determined to be 3.99/7.03 and 118.1/179.55 µg/ml, respectively. At the $EC_{1.5}$, in both repetitions, cell viability was higher than 70%. Positive and negative controls gave expected results.	4
a hydroalcoholic *Salix alba* (willow) bark extract (100% purity)	DMSO	1, 5 10, 50, 100, 200, 300,400, and 500 µg/ml	dendritic cell line	GARD assay (predicts sensitization by evaluating changes in genomic biomarker expression; positive reactions observed if test substance triggers sensitization-related pathways); 24-h incubation, cell viability measured and RNA extracted and evaluated (RNA expression profiles analyzed); appropriate positive and negative controls used	predicted to be sensitizing The mean decision value was 1.76. Values > 0 indicate positive results. Positive and negative controls gave expected results.	4
Salix Alba (Willow) Leaf Extract	water	4 – 6%	immortalized human skin keratinocytes	KeratinoSens ™ assay; no details provided	predicted to be non-sensitizing	29

Table 7. Dermal irritation, sensitization, and phototoxicity studies

Test Article	Vehicle	Concentration/ Dose	Test Population/ System	Protocol	Results	Reference
ANIMAL						
Salix Alba (Willow) Bark Extract (mixture composed of water (68.25%), butylene glycol (29.25%), Salix Alba (Willow) Bark Extract (2.5%))	Freund-type adjuvant and water	3% (final test concentration of Salix Alba (Willow) Bark Extract, 0.075%)	guinea pigs (10/group; strain and sex not stated)	guinea pig sensitization assay; intradermal injections given for first induction period, followed by a second induction using occlusive patches, and occlusive patch challenge; negative control group used; animals observed for signs of erythema and edema at 24 and 48 h after challenge patch removal; no other details provided	non-sensitizing; no erythema or edema observed	9
Salix Alba (Willow) Leaf Extract	water	4 – 6%	guinea pigs (number, sex, and strain not stated)	guinea pig maximization assay performed according to Magnusson and Kligman methods; no other details provided	non-sensitizing	29
HUMAN						
Salix Alba (Willow) Bark Extract	water	5%; 0.2 ml	50 subjects	HRIPT; 9 induction applications followed by a 10 – 14 d non-treatment period and challenge patch; reactions scored 24 and 48 h after application; open patch conditions	non-irritating and non-sensitizing	57
serum containing 0.0025% Salix Alba (Willow) Bark Extract	none	100%	50 subjects	HRIPT; no details provided	non-irritating and non-sensitizing	56
PHOTOTOXICITY						
IN VITRO						
Salix Alba (Willow) Bark Extract	ethanol	1%	Balb/c 3T3 (clone A31) mouse fibroblast cells	OECD TG 432; 3T3 neutral red reuptake phototoxicity assay; cells incubated for 60 min then irradiated or left non-irradiated with UVA/Vis, 5 J/cm^2 for 50 min; appropriate positive and negative controls used	non-phototoxic	58
20% Salix Alba (Willow) Bark Extract	NR	0.5, 1.5, 5, and 10% (final test concentrations of 0.025, 0.075, 0.25, and 0.5%)	reconstructed human epidermis	EpiDerm^{TM} model assay; test substance applied to tissues and incubated overnight; appropriate tissues were irradiated with UVA (6 J/cm^2) for 60 min; some tissues non-irradiated for use as control; appropriate positive and negative controls used	non-phototoxic	59
Salix Alba (Willow) Bark Extract	NR	0.5, 1.5, 5, and 10%	reconstructed human epidermis	EpiDerm^{TM} model assay; test substance applied to tissues and incubated overnight; appropriate tissues were irradiated with UVA (6 J/cm^2) for 60 min; some tissues non-irradiated for use as control; appropriate positive and negative controls used	non-phototoxic	60
Salix Alba (Willow) Leaf Extract	water	4 – 6%	Balb/c 3T3 (clone A31) mouse fibroblast cells	OECD TG 432; 3T3 neutral red reuptake phototoxicity assay; no other details provided	non-phototoxic	29

DMSO = dimethyl sulfoxide; $EC_{1.5}$ = effective concentration of a test chemical that induces a 1.5-fold increase in luciferase activity; GARD = genomic allergen rapid detection; HRIPT = human repeat insult patch test; I_{max} = mean maximal luciferase activity; IC_{50} = inhibitory concentration 50%; MTT = 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide; NR = not reported; OECD = Organisation for Economic Co-operation and Development; RNA = ribonucleic acid; TG = test guideline; UVA = ultraviolet A; Vis = visible light

Table 8. Ocular irritation studies

Test Article	Vehicle	Concentration/Dose	Test Population	Protocol	Results	Reference
IN VITRO						
Salix Alba (Willow) Bark Extract	none	20%; 50 mg	reconstructed human cornea-like epithelial tissue (2 replicates/group)	EpiOcular™ assay; 90 min incubation; appropriate positive and negative controls used	predicted to be non-irritating mean cell viability was approximately 90%; below 60% is classified as irritating controls gave expected results	47
Salix Alba (Willow) Bark Extract	none	100%; 50 mg	reconstructed human cornea-like epithelial tissue (2 replicates/group)	EpiOcular™ assay; 90 min incubation; appropriate positive and negative controls used	predicted to be non-irritating mean cell viability was approximately 90%; below 60% is classified as irritating controls gave expected results	48
Salix Alba (Willow) Bark Extract	none	100%; 50 mg	reconstructed human cornea-like epithelial tissue (2 replicates/group)	EpiOcular™ assay; 90 min incubation; appropriate positive and negative controls used	predicted to be non-irritating mean cell viability was approximately 95%; below 60% is classified as irritating controls gave expected results	49
hydroalcoholic *Salix alba* (willow) bark extract	none	100%; 50 mg	reconstructed human cornea-like epithelial tissue (2 replicates/group)	OECD TG 492; EpiOcular™ assay; 6-h incubation; appropriate positive and negative controls used	predicted to be an irritant mean cell viability was 14%; below 60% is classified as irritating controls gave expected results	4
hydroalcoholic *Salix alba* (willow) bark extract	none	100%; 30 mg	isolated chicken eyes (n = 3 per test substance treatment; 1 for negative control)	OECD TG 438; in vitro ocular irritation assay; parameters evaluated: mean corneal opacity, corneal swelling, fluorescein retention; 75-min incubation; appropriate positive and negative controls used	the test substance was not classified as a severe irritant (GHS category 1) and was also not classified as a non-irritant; therefore, it was concluded that further information is required for classification mean corneal opacity score: 0.5/4 corneal swelling: 0.5% (values <5% indicate minimal or no irritation) fluorescein retention score: 1.67 (falls within range indicative of severe irritation) positive and negative controls gave expected results	4
ANIMAL						
Salix Alba (Willow) Leaf Extract	water	4 – 6%	likely albino rabbits (no details provided)	OECD TG 405; no details provided; test substance applied to the conjunctival sac of one eye, second eye used as control	non-irritating	29

DPRA = direct peptide reactivity assay; GHS = Globally Harmonized System

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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: July 8, 2026

SUBJECT: Salix Alba (Willow) Bark Extract

Botanica GmBH An Evonik Company. 2025. Product specification Willow Bark Bio Extract (Salix Alba (Willow) Bark Extract in Glycerin and Water).

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Product specification

Willow Bark Bio Extract

(in Bio Glycerine/Water, not preserved (V82))

Article No.	P-00021851
Manufacturer	Botanica GmbH, Switzerland
INCI EU + CH	Glycerin, Aqua, Salix Alba Bark Extract
INCI US	Glycerin, Water, Salix Alba (Willow) Bark Extract
INCI CN	Glycerin, Water, Salix Alba (Willow) Bark Extract
Ratio	1 kg product out of ca. 0.1 kg dried material
Extraction	At room temperature with a circulating bio glycerin-water mixture
Origin	Purely natural, not animal, vegan suitable, halal suitable Origin of plant material: Batch specific
Preservation System	Without preservative, pseudo preserved, therefore avoid contamination
Shelf life	To reevaluate after 30 months
Storage Conditions	Store in closed original packaging, cool, dry, and protected from light.
Recommended Application	2 - 7 % in cosmetic formulations
Note	The plant material used are natural and not standardized. Hence, there are some variations between different harvests and origins - they do not injure the quality of the product.
Specification Date	**08.01.2025. All older specifications are no longer valid.**
Remark	Slight turbidity, sedimentation or colour changes can occur in natural products and do not injure the quality of the product. Botanica neither performs nor commissions tests on animals. The raw materials used are produced neither from nor by GMO.
VOC (CH)	Not VOC-taxed in Switzerland, as product is not listed on tariff-code positive list.
Customs tariff no.	CH: 1302.1900, EU: 1302.1970

Analysis	**Method**	**Specification**
Odour		characteristic
Color		reddish - brown
Aspect		clear – slightly turbid
Density 20°C [g/ml]	V-APP-D23	1.195 - 1.230
Refraction index 20°C	V-APP-D24	1.438 - 1.466
Solubility in Water	10%	clear - slightly turbid
Solubility in Alcohol	10%	clear - slightly turbid
Microbiology	TAMC, PhEur	<=10² cfu/g

Composition

Ingredient INCI (EU)	**CAS**	**EC**	**origin**	**%-range**
Glycerin	56-81-5	200-289-5	bio/plant	> 50%
Aqua	7732-18-5	231-791-2	min	> 10% - <= 25%
Salix Alba Bark Extract	84082-82-6	282-029-0	bio/plant	> 0.1% - <= 1%

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Defined substances, which must be indicated above defined concentrations according to EU 2009/1223, Annex III, 45 - 371 (>= 0.001 %)

Further defined substances according to EU 2009/1223, annex III, 45 - 371 are not expected at concentrations above 0.001 % in this product.

Defined substances restricted below 0.05 % by EU 2009/1223 (>= 0.001 %)

The information about the defined substances, which must be indicated above defined concentrations according to EU 2009/1223, Annex III, 45 – 371 as well as about the defined substances restricted below 0.05 % by EU 2009/1223, are based on technical literature.

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All warranty claims in respect of the conformity of our product are subject to our General Terms and Conditions of Sale and Delivery. The data listed above reflects the criteria for our internal quality tests. We do not hereby make any express or implied warranty, whether for specific properties or for fitness for any particular application or purpose. All values are valid for the product when despatched from the works. If raw materials of the customer are used, the information given will be non-binding. The Standard Test Methods can be obtained from specialized publishers.

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