Safety Assessment of Basic Blue 7 as Used in Cosmetics

Status:	Draft Tentative Report for Panel Review
Release Date:	February 14, 2025
Panel Meeting Date:	March 13 - 14, 2025

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

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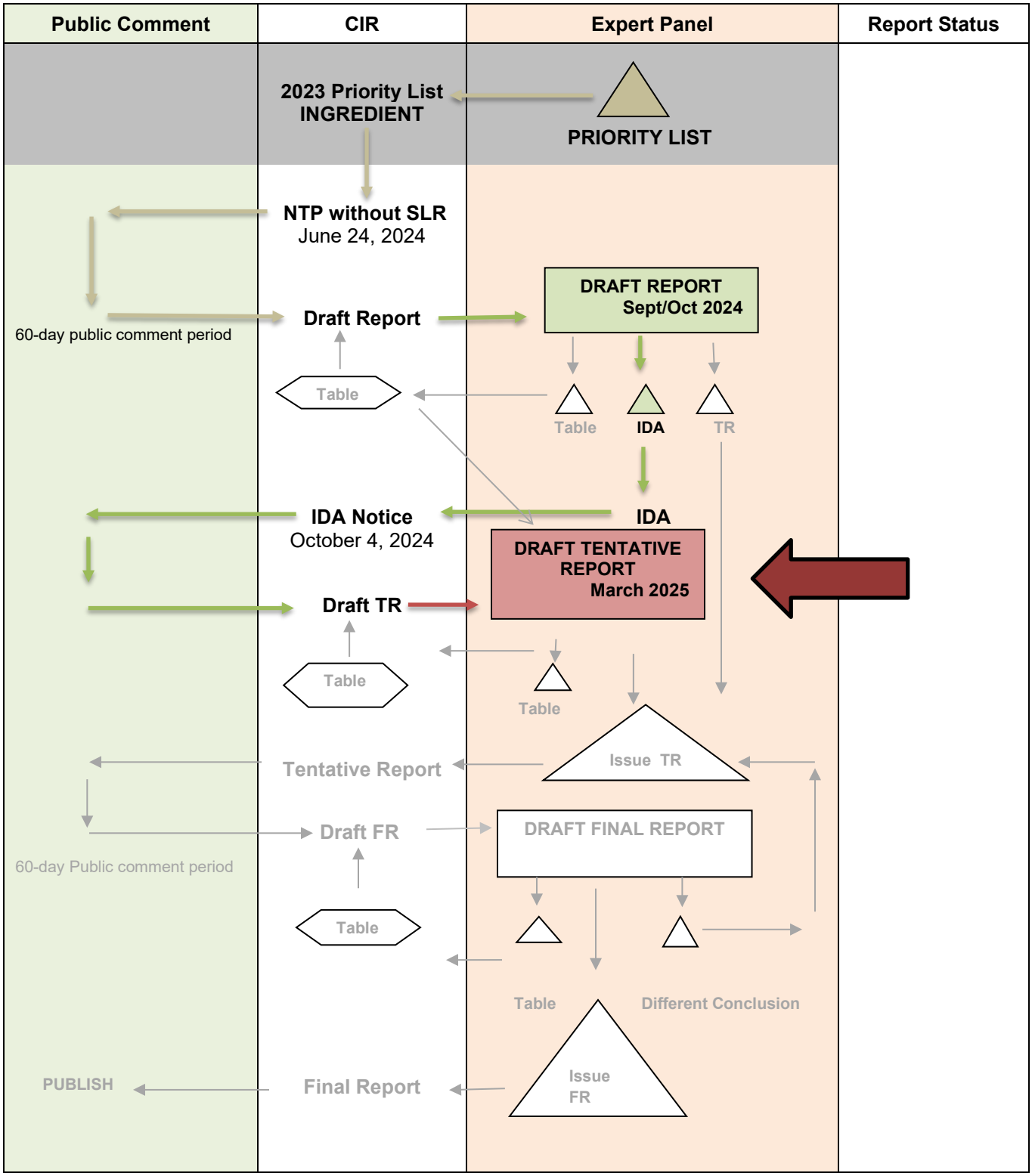
SAFETY ASSESSMENT FLOW CHART

INGREDIENT/FAMILY Basic Blue 7

MEETING March 2025



Cosmetic Ingredient Review

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Memorandum

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Christina L. Burnett, M.S., Senior Scientific Analyst/Writer, CIR
Date: February 14, 2025
Subject: Safety Assessment of Basic Blue 7 as Used in Cosmetics

Enclosed is the Draft Tentative Report on the Safety Assessment of Basic Blue 7 as Used in Cosmetics. (It is identified as *report_BasicBlue7_032025* in the pdf document). This ingredient is reported to function as a hair colorant in cosmetic formulations.

At the September 2024 meeting, the Panel issued an Insufficient Data Announcement for Basic Blue 7. The following information was requested to determine the safety of this ingredient:

- Chemical properties data
- Method of manufacturing
- Composition/impurities data
- Concentration of use
- Dermal absorption data or 28-day dermal toxicity data
    - If absorbed, additional data, including developmental and reproductive toxicity data are needed
- Genotoxicity data
- Dermal irritation and sensitization data

Since the September meeting, no new data have been received or identified in an updated literature search. The report has been updated with RLD that were received in 2024. According to those RLD, Basic Blue 7 is used in 11 formulations, which included non-coloring (1 use) and coloring hair preparations (10 uses). VCRP survey data received in 2023 reported Basic Blue 7 to be used in 1 nail polish and enamel product. No uses of this ingredient were reported in response to the concentration of use survey submitted by the Personal Care Products Council in 2023.

Comments received from the Council on the Draft Report in September 2024 have been addressed (*PCPCcomments_BasicBlue7_032025* and *response-PCPCcomments_BasicBlue7_032025*). Additional supporting documents for this report package include a flow chart (*flow_BasicBlue7_032025*), report history (*history_BasicBlue7_032025*), a search strategy (*search_BasicBlue7_032025*), meeting transcripts (*transcripts_BasicBlue7_032025*), and a data profile (*dataprofile_BasicBlue7_092024*).

The Panel should be prepared to issue a Tentative Report with a safe, safe with qualifications, insufficient, mixed, or unsafe conclusion, and Discussion items should be identified.

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

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

FROM: Alexandra Kowcz, MS, MBA
Industry Liaison to the CIR Expert Panel

DATE: September 23, 2024

SUBJECT: Draft Report: Safety Assessment of Basic Blue 7 as Used in Cosmetics (draft prepared for the Sept 30-Oct 1, 2024, CIR meeting)

The Personal Care Products Council respectfully submits the following comments on the draft report, Safety Assessment of Basic Blue 7 as Used in Cosmetics.

Cosmetic Use – It should be noted that in the United States, colors used in cosmetics other than hair dyes must be approved by the FDA. Therefore, use of Basic Blue 7 in a nail polish and enamel product is not permitted in the United States.

Although there is no other EU opinion specifically about Basic Blue 7, the 2003 SCCP opinion "Request for a Re-evaluation of Hair Dyes Listed in Annex III to Directive 76/768/EEC" does include the following questions about Basic Blue 7 "Is the bioavailability of the substance when administered by oral route, taken into account when setting the NOEL? What is the purity grade of the substance called s.b.? Does the purity imply a re-evaluation of the hair dye?"

Basic Blue 7 – March 2025 – Christina Burnett	
Comment Submitter: Alexandra Kowcz, Personal Care Products Council **Date of Submission: September 23, 2024**	
Comment	**Response/Action**
Cosmetic Use – It should be noted that in the United States, colors used in cosmetics other than hair dyes must be approved by the FDA. Therefore, use of Basic Blue 7 in a nail polish and enamel product is not permitted in the United States.	Updated use data from FDA indicate there is no longer a use reported in mail products. However, the use in non-coloring products in the new data has been noted as not permitted.
Although there is no other EU opinion specifically about Basic Blue 7, the 2003 SCCP opinion "Request for a Re-evaluation of Hair Dyes Listed in Annex III to Directive 76/768/EEC" does include the following questions about Basic Blue 7 "Is the bioavailability of the substance when administered by oral route, taken into account when setting the NOEL? What is the purity grade of the substance called s.b.? Does the purity imply a re-evaluation of the hair dye?"	Comment ignored per instruction from Dr. Heldreth.

Basic Blue 7 History

June 2024 – A Scientific Literature Review (SLR) Notice to Proceed (NTP) for Basic Blue 7 was issued.

September 2024 - The Panel issued an Insufficient Data Announcement for Basic Blue 7. The following information was requested to determine the safety of this ingredient:

- Chemical properties data
- Method of manufacturing
- Composition/impurities data
- Concentration of use
- Dermal absorption data or 28-day dermal toxicity data
    - If absorbed, additional data, including developmental and reproductive toxicity data are needed
- Genotoxicity data
- Dermal irritation and sensitization data

Basic Blue 7 Data Profile* – March 2025 – Christina Burnett																															
				Toxicokinetics			Acute Tox			Repeated Dose Tox			DART		Genotox		Carci		Dermal Irritation			Dermal Sensitization				Ocular Irritation		Clinical Studies	
	Reported Use	Method of Mfg	Impurities	log P/log K_{ow}	Dermal Penetration	ADME	Dermal	Oral	Inhalation	Dermal	Oral	Inhalation	Dermal	Oral	In Vitro	In Vivo	Dermal	Oral	In Vitro	Animal	Human	In Vitro	Animal	Human	Phototoxicity	In Vitro	Animal	Retrospective/ Multicenter	Case Reports
Basic Blue 7 (CAS No. 2390-60-5)	X	X																													

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

Basic Blue 7

Ingredient	CAS #	INCIpedia	PubMed	FDA	EU	ECHA	SCCS	SIDS	ECETOC	HPVIS	AICIS	NTIS	NTP	WHO	FAO	NIOSH	FEMA	Web
Basic Blue 7	2390-60-5	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√

Search Strategy

PubMed
((“basic blue 7”) OR (2390-60-5[EC/RN Number]) = 27 hits, most only useful for non-cosmetic use descriptions

ECHA
Dossier available as [4-[4-(diethylamino)-α-[4-(ethylamino)-1-naphthyl]benzylidene]cyclohexa-2,5-dien-1-ylidene]diethylammonium chloride, but there are no physical and chemical properties or toxicological data provided in the dossier.

EU
Annex II (entry 1328): List of substances prohibited in cosmetic products
SCCNFP Opinion 2000 (no dossier): ingredient can be safely used in hair tinting products at a maximum concentration of 0.2%.

LINKS

Search Engines

- Pubmed (- http://www.ncbi.nlm.nih.gov/pubmed)

appropriate qualifiers are used as necessary
search results are reviewed to identify relevant documents

Pertinent Websites

- wINCI - https://incipedia.personalcarecouncil.org/infobase/
- FDA databases http://www.ecfr.gov/cgi-bin/ECFR?page=browse
- FDA search databases: http://www.fda.gov/ForIndustry/FDABasicsforIndustry/ucm234631.htm;,
- Substances Added to Food (formerly, EAFUS): https://www.fda.gov/food/food-additives-petitions/substances-added-food-formerly-eafus
- GRAS listing: http://www.fda.gov/food/ingredientspackaginglabeling/gras/default.htm
- SCOGS database: http://www.fda.gov/food/ingredientspackaginglabeling/gras/scogs/ucm2006852.htm
- Indirect Food Additives: http://www.accessdata.fda.gov/scripts/fdcc/?set=IndirectAdditives
- Drug Approvals and Database: http://www.fda.gov/Drugs/InformationOnDrugs/default.htm
- FDA Orange Book: https://www.fda.gov/Drugs/InformationOnDrugs/ucm129662.htm
- (inactive ingredients approved for drugs: http://www.accessdata.fda.gov/scripts/cder/iig/
- HPVIS (EPA High-Production Volume Info Systems) - https://iaspub.epa.gov/oppthpv/public_search.html_page
- 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/
- Office of Dietary Supplements https://ods.od.nih.gov/
- FEMA (Flavor & Extract Manufacturers Association) GRAS: https://www.femaflavor.org/fema-gras
- EU CosIng database: http://ec.europa.eu/growth/tools-databases/cosing/
- ECHA (European Chemicals Agency – REACH dossiers) – http://echa.europa.eu/information-on-chemicals;jsessionid=A978100B4E4CC39C78C93A851EB3E3C7.live1
- ECETOC (European Centre for Ecotoxicology and Toxicology of Chemicals) - http://www.ecetoc.org
- 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
- SCCS (Scientific Committee for Consumer Safety) opinions: http://ec.europa.eu/health/scientific_committees/consumer_safety/opinions/index_en.htm
- AICIS (Australian Industrial Chemicals Introduction Scheme)- https://www.industrialchemicals.gov.au/
- International Programme on Chemical Safety http://www.inchem.org/
- 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) technical reports - http://www.who.int/biologicals/technical_report_series/en/
- www.google.com - a general Google search should be performed for additional background information, to identify references that are available, and for other general information

SEPTEMBER 2024 PANEL MEETING – INITIAL REVIEW/DRAFT REPORT

Belsito Team – September 30, 2024

DR. BELSITO: Next one is an interesting ingredient.

DR. SNYDER: Yeah. Basic Blue 7.

DR. BELSITO: Basic Blue 7. So, this is the first time we're reviewing the safety assessment of the ingredient. An intensive search of information of published scientific literature, online databases, and other sources provided insufficient information to generate an SLR. European regulations for the cosmetic ingredients, Basic Blue 7, is not allowed. It's categorized in Annex II.

The other data identified in the published literature were non-cosmetic uses. It's reported to be used in one nail polish and enamel product. Cosmetic Direct data were received, 29 products listed as an ingredient. None were reported in a concentration of use survey to PCPC. So, that's what we're dealing with here. It's reported to use as a hair color and in formulation, but our reported use is as nail enamel.

And I guess one question that I have is, if we get a report like this of Basic Blue 7 being used in a nail enamel, do we evaluate this, or do we evaluate a product only as defined in the dictionary? Or is this misbranded? Because the other thing, looking at this structure, is this a coal tar derivative?

DR. SNYDER: It says it is.

DR. BELSITO: It is?

DR. SNYDER: Well, we have a statement in here about coal tar.

DR. BELSITO: Well, it says that. I mean, it says that for all hair dyes. But, I mean, is this structure, is this a coal tar derivative? It looks like it's synthesized.

DR. RETTIE: It's a triarylmethane that's (inaudible). It's synthesized.

DR. BELSITO: So, is it a coal tar derivative? What is the definition of a coal tar derivative?

MS. BURNETT: A synthesized petroleum product.

DR. RETTIE: Something you can distill.

MS. FIUME: I don't remember having a hair dye that's not a coal tar derivative. But that's not to say this is something new.

DR. BELSITO: I mean, we've just assumed they are.

MS. FIUME: Right.

DR. BELSITO: But, I mean, I looked at this. And as we're getting into these more -- my basic question is -- and I've been on the Panel for how many years, and I never thought of this, you know, I mean, is this truly a coal tar derivative?

MS. FIUME: Kim, do you have any idea?

DR. NORMAN: I can't say for sure.

DR. BELSITO: What is the definition of a coal tar derivative? Because I looked at this, I go, what? This doesn't really look like a coal tar.

DR. RETTIE: Isn't a coal tar derivative something that you can distill in crude oil?

DR. BELSITO: From petroleum.

DR. RETTIE: From -- well, yeah. The crude parts. And you're not going to get this out of crude oil.

DR. ZANG: But a lot of raw materials, the chemicals, come from the petroleum sources. I don't have enough information about the synthesis, the process. Usually, if a color is made through I would say genetic engineering, made by microbials, those are like definitely not coal tar. But this one I'm not quite sure about the manufacturing process.

MS. BURNETT: This is definitely going out as IDA, so I guess we throw that question into the mix. Is this considered a coal tar hair dye, or what is this?

DR. BELSITO: Right.

MS. BURNETT: I mean, the only data I got was how it was manufactured was by this Friedel-Crafts, and Bart was like, that's not even really a great explanation.

DR. BELSITO: Okay.

MS. BURNETT: So, let me put that in there, but that's all we have.

DR. BELSITO: So, insufficient for impurities.

DR. KLAASSEN: Insufficient for almost all it.

DR. BELSITO: Concentration of use, 28-day dermal tox, and if absorbed other tox endpoint like DART, genotoxicity. And if it's not a coal tar derivative and we're looking at it as a nail enamel, sensitization and irritation.

MS. BURNETT: If it's supposed to be a coal tar hair dye ingredient, it shouldn't be used in anything other than a hair dye.

DR. BELSITO: Okay. So, then we don't have to worry about nail enamel. Nail enamel is misbranded.

MS. FIUME: Yeah. That would be like the others that we've done recently where they're misbranded.

DR. BELSITO: Right.

MS. BURNETT: Yeah. So, pretty much everything.

DR. SNYDER: Yep.

DR. RETTIE: I had a comment on the tables.

MS. BURNETT: Yeah.

DR. RETTIE: Table 1. It says it's a reddish-blue powder, and then we have density. And probably --

MS. BURNETT: It's supposed to be a (inaudible), or no?

DR. RETTIE: Currently, if it's a reddish-blue powder, you don't care about density and vapor pressure.

MS. BURNETT: Okay. So, delete those?

DR. RETTIE: You can just get rid of those, yeah.

MS. BURNETT: Okay.

DR. BELSITO: Where are you, Allan?

DR. SNYDER: Page 13, Table 1.

DR. RETTIE: Thirteen.

DR. SNYDER: Chemical property.

DR. RETTIE: Just wanted to harmonize what we're calling it.

DR. BELSITO: So, you're deleting vapor pressure?

DR. RETTIE: I was questioning whether we should delete density and vapor pressure describing it as a powder.

DR. BELSITO: Okay.

DR. RETTIE: But there's another manufacturer that sells a liquid. So, I don't know how deep you want to get into this. There's so much missing. But if you're going to leave it as reddish-blue powder, I'd get rid of density and get rid of vapor pressure.

MS. BURNETT: Or do you want to add physical properties to the IDA list?

DR. KLAASSEN: Yeah, why not. And ask them if it's a powder or a liquid.

MS. FIUME: And was method of manufacture one of the question --

MS. BURNETT: Yeah, to clarify if it's --

DR. BELSITO: So, we're adding physical properties, powder or liquid or both.

MS. FIUME: Those properties could've been in essence put into formulation.

DR. BELSITO: Right.

MS. BURNETT: Possible. And they all came from –- where did it come from -- it came from a paper that was actually describing a different use.

DR. BELSITO: Do we want additional method of manufacture because we have some method of manufacturer?

MS. BURNETT: Yeah. So, Bart wasn't exactly excited about that paper.

DR. BELSITO: Well, we can ask.

MS. BURNETT: Any clarification.

DR. BELSITO: Okay.

DR. KLAASSEN: One of the first things in organic chemistry, Friedel-Crafts reaction.

DR. BELSITO: Okay. So, method of manufacture, impurities, physical properties, use concentration, absorption, 28-day dermal, other endpoints such as DART, genotox, and nail enamel misbranded. Okay. Anything else?

DR. RETTIE: Think just technically after Friedel-Crafts, if Bart wants to leave that in we should probably put (inaudible), there's acetylation, there's alkylation. This has to be aeration because that's all we got.

MS. BURNETT: Okay.

DR. RETTIE: Wonder why he didn't like it. I'll have to ask.

MS. BURNETT: Actually, yeah, it might have been the first reference that Bart didn't care for and might have found a different one. But he still wasn't thrilled with the description.

DR. RETTIE: I'll send you the one I find.

MS. BURNETT: Okay.

Cohen Team – September 30, 2024

DR. COHEN: All right, let's go to Basic Blue.

DR. ROSS: Yeah, that one's a short read.

DR. COHEN: So, this is a draft report for Basic Blue 7, and this is reported as a hair colorant. In June 2024, the CIR issued an SLR for Basic Blue because a search didn't provide much information. It was founded under European regulation for a cosmetic ingredient. Basic Blue 7, when used as a substance in hair dye products it's categorized as Annex II and the SLR was broad sweeping in its request and no unpublished data has been received.

The 2023 VCRP survey found it to be used in a nail Polish and enamel product. No uses of this ingredient had a concentration of use. Cosmetic Direct showed 29 uses. So, indeed, David, this was a short read. Comments?

DR. ROSS: I think it's insufficient on everything.

DR. COHEN: Well, yes, so we should probably list them. Is it everything in the NTP?

DR. ROSS: I don't think it's got anything in it.

DR. TILTON: I mean, it's everything that was already listed.

DR. COHEN: In the NTP, right, the request?

DR. TILTON: Yeah.

DR. COHEN: Okay. Yeah, I thought that's all we're going to come to on that. But it does seem to be used out there. I guess, the question is where is it being used, right?

DR. EISENMANN: I did a little look at the data, and I thought it was less uses because I found when I searched for Basic Blue 7, it came up with Basic Blue 75 too, and there were a couple that didn't even -- I couldn't see the data where it was, but I did find like seven uses. So yeah, I was disappointed. I was hoping this would be zero because we didn't get any concentration of use, and I don't have a supplier that's going to be helpful.

DR. COHEN: So, you think this will probably just go through the process and graduate as use not supported?

MS. KOWCZ: Yeah. Most likely.

DR. COHEN: Okay. I don't think there's any more comments for this.

Full Panel – October 1, 2024

DR. BELSITO: Yeah. So this is the first time we're reviewing the safety assessment of this hair dye. Scientific literature-review was issued because not much is in the published literature. In fact, there's extremely little data on this ingredient. It is Annex II in Europe, which means that it should not be used in cosmetic products, probably because of lack of data. And, right now, the only reported use we have is in a nail enamel, which would be adulterated since it's a hair dye.

And we thought the data was insufficient and the following needs were method of manufacture, impurities, physical properties, use concentration, absorption -- could be a 28-day dermal or whatever -- and another endpoint, specifically DART, if absorbed, genotox. And mention in Discussion that nail enamel would be a misbranded use.

DR. COHEN: Second.

DR. BERGFELD: What did you say, David? Are you agreeing, second?

DR. COHEN: Yes, I second that.

DR. BERGFELD: Okay. Are there any other needs that would be added to this?

DR. COHEN: Don, you had sensitization and irritation in there, right?

DR. BELSITO: It's a hair dye.

DR. COHEN: Yeah. I know. I know, but sometimes we still get that data.

DR. BELSITO: We can put it in because there's a whole list of data needs. But, if we don't get it, we're not going to hold up the report, right.

DR. COHEN: No. You're absolutely right. But, you know, we do get that in many of the reports.

DR. BERGFELD: Okay. It sounds like it's been added. Anything else? All right. Call the question to go insufficient on Basic Blue 7. Unanimous again.

Safety Assessment of Basic Blue 7 as Used in Cosmetics

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ABBREVIATIONS

CIR	Cosmetic Ingredient Review
Council	Personal Care Products Council
CPSC	Consumer Product Safety Commission
Dictionary	web-based *International Cosmetic Ingredient Dictionary and Handbook* (wINCI)
FDA	Food and Drug Administration
FD&C Act	Food, Drug, and Cosmetic Act
MoCRA	Modernization of Cosmetics Regulation Act
Panel	Expert Panel for Cosmetic Ingredient Safety
PI	propidium iodide
RLD	Registration and Listing Data
SCCNFP	Scientific Committee on Cosmetic Products and Non-Food Products Intended for Consumers
US	United States
VCRP	Voluntary Cosmetic Registration Program

DRAFT ABSTRACT

The Expert Panel for Cosmetic Ingredient Safety (Panel) assessed the safety of Basic Blue 7, which is reported to function as a hair colorant in cosmetic products. The Panel reviewed the available data to determine the safety of this ingredient. The Panel concluded that [to be determined].

INTRODUCTION

This assessment reviews the safety of Basic Blue 7 as used in cosmetic formulations. According to the web-based *International Cosmetic Ingredient Dictionary and Handbook* (*Dictionary*), this ingredient is reported to function as a hair colorant in cosmetic products.[1]

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 January 2025. A listing of the search engines and websites that are used and the sources that are typically explored, as well as the endpoints that the Panel typically evaluates, is provided on the Cosmetic Ingredient Review (CIR) website (https://www.cir-safety.org/supplementaldoc/preliminary-search-engines-and-websites; https://www.cir-safety.org/supplementaldoc/cir-report-format-outline). Unpublished data are provided by the cosmetics industry, as well as by other interested parties.

CHEMISTRY

Definition and Structure

Basic Blue 7 (CAS No. 2390-60-5) is classed chemically as a triarylmethane color.[1] It conforms to the structure in Figure 1.

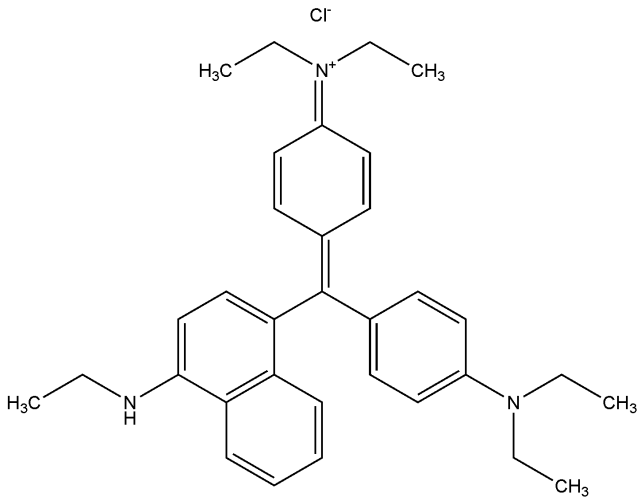

Figure 1. Basic Blue 7

Chemical Properties

Chemical properties for Basic Blue 7 are summarized in Table 1. Basic Blue 7 is a reddish-blue powder with a formula weight of 514.14 g/mol, and an estimated log K_{ow} of 4.06.[2-4]

Method of Manufacture

Triarylmethane dyes such as Basic Blue 7 may be manufactured via a multitude of synthetic methodologies; although, Friedel-Crafts is historically the most common method.[5] However, no method of manufacturing data specific to how cosmetic raw material manufacturers produce this ingredient were found in the published literature, and unpublished data were not submitted.

Impurities

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

USE

Cosmetic

The safety of the cosmetic ingredient addressed in this assessment is evaluated based on data received from the US Food and Drug Administration (FDA) and the cosmetics industry on the expected use of Basic Blue 7 in cosmetics. Data included herein were obtained from the FDA and in response to a survey of maximum use concentrations conducted by the Personal Care Products Council (Council), and it is these values that define the present practices of use and

concentration. Frequencies of use obtained from the FDA include data from the Voluntary Cosmetic Registration Program (VCRP) database as well as Registration and Listing Data (RLD). As a result of the Modernization of Cosmetics Regulation Act (MoCRA) of 2022, the VCRP was terminated in 2023 and, as of 2024, manufacturers and processors have been mandated to register and list their products (and ingredients therein) with the FDA (i.e., RLD). An exception is made for small businesses, which are exempt from MoCRA reporting for most cosmetic product categories. However, to utilize the exemption, the small business must not sell eye area products, injected products, internal use products, or products that alter appearance for more than 24 h.[6] Please note, at this time, it is not appropriate to contrast data from the VCRP and RLD to determine a trend in frequency of use because there are numerous differences in the ways the data for the VCRP and the RLD were collected and processed, and because reporting frequency of use is now mandatory (as opposed to the past practice of voluntary reporting). Although the VCRP program is now defunct, trends in frequency of use from the RLD alone are not yet possible in that a baseline is currently not available.

According to RLD that CIR received in 2024, Basic Blue 7 is used in 11 formulations, which include non-coloring (1 use) and coloring hair preparations (10 uses; Table 2).[7] VCRP survey data received in 2023 reported Basic Blue 7 to be used in 1 nail polish and enamel product.[8] No uses of this ingredient were reported in response to the concentration of use survey submitted by the Personal Care Products Council in 2023.[9]

Some products containing Basic Blue 7 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. None of the reported product categories for this ingredient as listed in the RLD include a designation using airbrush application, so it is possible that this ingredient is used with airbrush delivery systems, but not reported as such. 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.

This ingredient is considered a coal tar hair dye for which regulations require caution statements and instructions regarding patch tests in order to be exempt from certain adulteration and color additive provisions of the US Federal Food, Drug, and Cosmetic Act (FD&C Act). In order to be exempt, the following caution statement must be displayed on all coal tar hair dye products:

> Caution - this product contains ingredients which may cause skin irritation on certain individuals and a preliminary test according to accompanying directions should be made. This product must not be used for dyeing the eyelashes or eyebrows; to do so may cause blindness.

However, as of 2024, Basic Blue 7 is reported to be used in non-coloring hair preparations. Basic Blue 7 is exempt from certain adulteration and color additive provisions of the FD&C Act ***only*** when it is used as a coal tar hair dye ingredient. The FD&C Act mandates that color additives must be approved by FDA for their intended use before they are used. Basic Blue 7 is not an approved color additive in non-hair dye cosmetic products, and thereby, use in non-coloring hair products is not permitted.

Product labels shall also bear patch test instructions for determining whether the product causes skin irritation. However, whether or not patch testing prior to use is appropriate is not universally agreed upon. The Panel recommends that an open patch test be applied and evaluated by the beautician and/or consumer for sensitization 48 h after application of the test material and prior to the use of a hair dye formulation. Conversely, a report in Europe suggests that self-testing has severe limitations, and may even cause morbidity in consumers.[10,11] Hair dye products marketed and sold in the US, though, must follow the labeling requirements established by the FD&C Act.

Under European regulations for cosmetic ingredients, Basic Blue 7, when used as a substance in hair dye products, is **c**ategorized in Annex II, the list of substances prohibited in cosmetic products in Europe**.**[12] Historically, in 2000, the Scientific Committee on Cosmetic Products and Non-Food Products Intended for Consumers (SCCNFP) concluded that Basic Blue 7 can be used safely in hair tinting products at a maximum concentration of 0.2%.[13] It further stated that it could not be excluded that Basic Blue 7 is a contact allergen. No data accompanied the 2000 dossier and an update to this dossier could not be found.

Non-Cosmetic

Basic Blue 7 is commonly used to dye anionic substrates (e.g. wool, silk, cotton, leather, nylon, and acrylics).[2,14] It is also reported to be used as a stain in molecular biology and in stamping and flexographic printing inks.[2] Research has been

performed on its use in polymer films and optoelectronic applications.[2,14] The use of Basic Blue 7 as a photodynamic therapy for cancer treatment has also been studied.[15-19]

TOXICOKINETIC STUDIES

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

TOXICOLOGICAL STUDIES

Acute Toxicity Studies

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

Short-Term, Subchronic, and Chronic Toxicity Studies

Short-term, subchronic, and chronic toxicity studies were not found in the published literature, and unpublished data were not submitted.

DEVELOPMENTAL AND REPRODUCTIVE TOXICITY STUDIES

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

GENOTOXICITY STUDIES

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

CARCINOGENICITY STUDIES

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

OTHER RELEVANT STUDIES

Cytotoxicity

Photodynamic induced cytotoxicity by Basic Blue 7 in 95% ethanol was studied using 2 human leukemic cell lines, K-52 and TF-1.[16] The cells were incubated with 1 x 10^{-8} to 1 x 10^{-6} M of the test material and irradiated with different doses of white light (530 - 650 nm). Cell survival was assessed by propidium iodide (PI) staining using flow cytometry analysis. A concentration of 5 x 10^{-8} M was found to kill 75% of cells, and a concentration of 1 x 10^{-7} M induced more than 99% of cell killing.

In a similar study, the photodynamic effect of Basic Blue 7 in 95% ethanol and photoirradiation was studied on normal peripheral blood mononuclear cells.[16] The cells were preincubated with 1 x 10^{-9} to 1 x 10^{-7} M of the test material followed by photoirradiation (550 - 650 nm for 0, 30, 60, or 120 min) and overnight culture. PI assay in flow cytometry was used to evaluate the cells. The highest percentage of dead cells were observed in the monocyte population. Lymphocytes had a lower sensitivity to the Basic Blue 7 photodynamic action than the monocytes (12% vs 80% of PI-positive cells). Further investigation evaluated the effects of Basic Blue 7 on phototreatment of lymphocyte function using a mitogen-induced proliferation assay. A decrease of mitogen response was observed. Leukemic cells from acute myeloid leukemia and B-cell precursor leukemia exhibited sensitivity to the photodynamic effects of Basic Blue 7.

DERMAL IRRITATION AND SENSITIZATION STUDIES

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

OCULAR IRRITATION STUDIES

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

EPIDEMIOLOGICAL STUDIES

Hair dyes may be broadly grouped into oxidative (permanent) and direct (temporary or semi-permanent) dyes. The oxidative dyes consist of precursors mixed with developers to produce color, while direct hair dyes consist of preformed colors. Basic Blue 7 is reported to be used as a direct dye. While the safety of individual hair dye ingredients is not addressed in epidemiology studies that seek to determine links, if any, between hair dye use and disease, such studies do provide broad information. The Panel determined that the available hair dye epidemiology data do not provide sufficient evidence for a causal relationship between personal hair dye use and cancer. A detailed summary of the available hair dye epidemiology data is available at https://www.cir-safety.org/cir-findings.

SUMMARY

According to RLD that CIR received in 2024, Basic Blue 7 is used in 11 formulations, which include non-coloring (1 use) and coloring hair preparations (10 uses). VCRP survey data received in 2023 reported Basic Blue 7 to be used in 1 nail polish and enamel product. No uses of this ingredient were reported in response to the concentration of use survey submitted by the Personal Care Products Council in 2023.

With regard to the reported use in non-coloring hair preparations, the US Federal FD&C Act mandates that color additives must be approved by FDA for their intended use before they are used. Basic Blue 7 is not an approved color additive in non-hair dye cosmetic products, and thereby, use in non-coloring hair products is not permitted. Under European regulations for cosmetic ingredients, Basic Blue 7, when used as a substance in hair dye products, is **c**ategorized in Annex II, the list of substances prohibited in cosmetic products in Europe**.**

The Panel determined that the available hair dye epidemiology data do not provide sufficient evidence for a causal relationship between personal hair dye use and cancer.

Impurities data, toxicokinetics studies, acute and repeated-dose toxicity studies, developmental and reproductive toxicity studies, genotoxicity studies, carcinogenicity studies, dermal irritation and sensitization studies, and ocular irritation studies on Basic Blue 7 were not found in a literature search, and unpublished data were not submitted.

DRAFT DISCUSSION

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

This assessment reviews the safety of Basic Blue 7 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 **[**to be determined].

The Panel recognizes that hair dyes containing this ingredient, as coal tar hair dye products, are exempt from certain adulteration and color additive provisions of the Federal FD&C Act, when the label bears a caution statement and patch test instructions for determining whether the product causes skin irritation. The Panel expects that following this procedure will identify prospective individuals who would have an irritation/sensitization reaction and allow them to avoid significant exposures. The Panel considered concerns that such self-testing might induce sensitization, but agreed that there was not a sufficient basis for changing this advice to consumers at this time.

The Panel noted that Basic Blue 7 has been reported in non-coloring hair preparations. However, this ingredient is exempt from certain adulteration and color additive provisions of the FD&C Act ***only*** when it is used as a coal tar hair dye ingredient. Accordingly, because Basic Blue 7 is not an approved color additive in cosmetic products, use in non-coloring hair preparations is not permitted.

In considering hair dye epidemiology data, the Panel concluded that the available epidemiology studies are insufficient to scientifically support a causal relationship between hair dye use and cancer or other toxicological endpoints, based on lack of strength of the associations and inconsistency of findings. Use of direct hair dyes, while not the focus in all investigations, appears to have little evidence of any association with adverse events as reported in epidemiology studies.

As stated in the Use section, products containing this ingredient may be marketed for use with airbrush delivery systems. While it may be known in some (but not all) instances whether or not there is use in airbrush applications, information regarding the consumer habits and practices data, product particle size data, and/or other relevant particle data (e.g., diameter) related to this use technology are absent, and thus the data are insufficient to evaluate the exposure resulting from cosmetics applied via airbrush delivery systems.

CONCLUSION

To be determined…

TABLES

Table 1. Chemical properties

Property	Value	Reference
Physical Form	Reddish-blue powder Blue liquid (solvated)	2 3
Formula Weight (g/mol)	514.14	2
Density (g/ml @ 20 ºC)	1.05 - 1.2 (solvated)	3
Melting Point (ºC)	333.89 (MPBPVP v 1.43 estimated)	4
Boiling Point (ºC)	759.65 (MPBPVP v 1. 43 estimated)	4
Viscosity (kg/(m x s)@ 25 ºC)	< 0.1 (solvated)	3
Water Solubility	Slightly soluble in cold water; soluble in hot water, easily soluble in ethanol	20
log K_{ow}	4.06 (KOWWIN v 1.68 estimated)	4

Table 2. Frequency (RLD/VCRP) and concentration of use of Basic Blue 7 according to likely duration and exposure and by product category

	# of Uses		Max Conc of Use
	RLD (2024)[7]	VCRP (2023)[8]	% (2023)[9]
Totals*	**11**	**1**	**NR**
summarized by likely duration and exposure**			
Duration of Use			
Leave-On	***	*1*	*NR*
Rinse-Off	***	*NR*	*NR*
Diluted for (Bath) Use	***	*NR*	*NR*
Exposure Type			
Eye Area	***	NR	NR
Incidental Ingestion	***	NR	NR
Incidental Inhalation-Spray	***	NR	NR
Incidental Inhalation-Powder	***	NR	NR
Dermal Contact	***	NR	NR
Deodorant (underarm)	***	NR	NR
Hair - Non-Coloring	***	NR	NR
Hair-Coloring	***	NR	NR
Nail	***	1	NR
Mucous Membrane	***	NR	NR
Baby Products	***	NR	NR
as reported by product category			
Hair Preparations (non-coloring)	*1*		
Tonics, Dressings, and Other Hair Grooming Aids	1	NR	NR
Other Hair Preparations	1	NR	NR
Hair Coloring Preparations	*10*		
Hair Dyes and Colors (all types requiring caution statements and patch tests)	9	NR	NR
Hair Tints	1	NR	NR
Manicuring Preparations			
Nail Polishes and Enamels	NR	1	NR

NR – not reported

*The total FOU provided for RLD refers to the ingredient count supplied by FDA, and is not a summation of the number of uses per category because each product may be categorized under multiple ***product*** categories. For data supplied via the VCRP or by the Council survey, the sum of all exposure types may not equal the sum of total uses because each ingredient may be used in cosmetics with multiple ***exposure*** types.

**Likely duration and exposure are derived from VCRP and survey data based on product category (see Use Categorization https://www.cir-safety.org/cir-findings)

***In the RLD, each ingredient may be reported under several product categories, making a summation of RLD misleading in comparison to VCRP data. Accordingly, RLD are presented below by product category (as supplied by FDA), but are not summarized by likely duration and exposure.

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