Safety Assessment of Basic Yellow 87 as Used in Cosmetics

Status:	Draft Final Report for Panel Review
Release Date:	February 10, 2023
Panel Meeting Date:	March 6-7, 2023

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.; Curtis D. Klaassen, Ph.D.; Allan E. Rettie, Ph.D.; David Ross, Ph.D.; Thomas J. Slaga, 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. This safety assessment was prepared by Christina L. Burnett, MSES, Senior Scientific Analyst/Writer, CIR.

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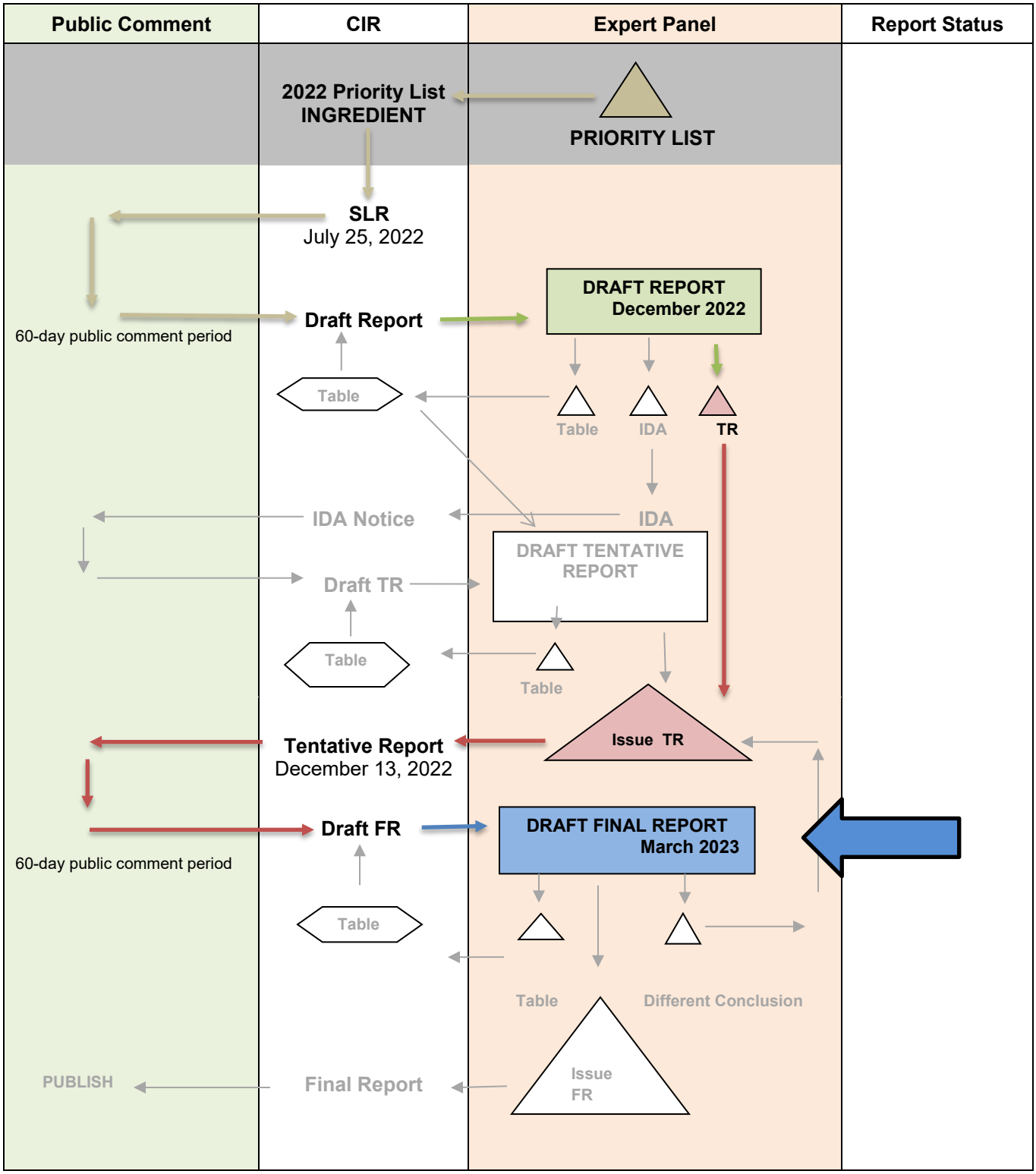
SAFETY ASSESSMENT FLOW CHART

INGREDIENT/FAMILY Basic Yellow 87

MEETING March 2023



Cosmetic Ingredient Review

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Memorandum

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Christina L. Burnett, MSES, Senior Scientific Analyst/Writer, CIR
Date: February 10, 2023
Subject: Safety Assessment of Basic Yellow 87 as Used in Cosmetics

Enclosed is the Draft Final Report of the Safety Assessment of Basic Yellow 87 as Used in Cosmetics. (It is identified as *report_BasicYellow87_032023* in the pdf document.) At the December 2022 meeting, the Panel issued a Tentative Report with the conclusion that Basic Yellow 87 is safe for use as a hair dye ingredient in the present practices of use and concentration described in the safety assessment.

Since the December meeting, CIR has received no new unpublished data. The attached Council comments on the Tentative Report have been addressed (*PCPCcomments_BasicYellow87_032023*), as noted in the check sheet immediately following the comments (*response-PCPCcomments_BasicYellow87_032023*).

As per the Panel's request at the December 2022 meeting, an updated use table format has been implemented. The frequency and concentration of use is presented both cumulatively by likely duration and exposure and individually by product category.

Additional supporting documents for this report package include a flow chart (*flow_BasicYellow87_032023*), report history (*history_BasicYellow87_032023*), a search strategy (*search_BasicYellow87_032023*), meeting transcripts (*transcripts_BasicYellow87_032023*), and a data profile (*dataprofile_BasicYellow87_032023*).

The Panel should review the Abstract, Discussion, and Conclusion, and issue a Final Report.

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: January 4, 2023

SUBJECT: Tentative Report: Safety Assessment of Basic Yellow 87 as Used in Cosmetics (release date: December 13, 2022)

The Personal Care Products Council respectfully submits the following comments on the Tentative Report, Safety Assessment of Basic Yellow 87 as Used in Cosmetics.

Dermal Penetration – Units of $\mu g/cm^2$ should be called "dose" rather than "concentration".

ADME, Animal, Dermal – What do the two values (2.56% and 2.79%) for radioactivity in the stratum corneum represent? Are these the results for the rats killed at 24 and 96 hours?

Summary – In the description of the SCCS risk assessment, please indicate that the calculation was for a hair dye containing 1% Basic Yellow 87.

Table 1 – It would be helpful to give a possible explanation for the large difference in water solubility between the values from the SCCS opinion and the ECHA dossier. The results in the SCCS opinion are for the methosulfate salt, while the results in the ECHA dossier are for the sulfate salt. The ECHA dossier also states that water solubility was at least 620 g/L. This amount dissolved in water; they did not try and dissolve more than 620 g/L.

Table 3 – For this report, Table 3 provides more information about the use of this ingredient and is the only use table necessary for this report.

Basic Yellow 87 – March 2023 – Christina Burnett	
Comment Submitter: Alexandra Kowcz, Personal Care Products Council **Date of Submission: January 4, 2023**	
Comment	**Response/Action**
Dermal Penetration – Units of μg/cm^2 should be called "dose" rather than "concentration".	Correction made.
ADME, Animal, Dermal – What do the two values (2.56% and 2.79%) for radioactivity in the stratum corneum represent? Are these the results for the rats killed at 24 and 96 h?	Data presented essentially as written in the SCCS opinion. "No further details provided" added to summary information.
Summary – In the description of the SCCS risk assessment, please indicate that the calculation was for a hair dye containing 1% Basic Yellow 87.	Detail added.
Table 1 – It would be helpful to give a possible explanation for the large difference in water solubility between the values from the SCCS opinion and the ECHA dossier. The results in the SCCS opinion are for the methosulfate salt, while the results in the ECHA dossier are for the sulfate salt. The ECHA dossier also states that water solubility was at least 620 g/l. This amount dissolved in water; they did not try and dissolve more than 620 g/l.	Table updated.
Table 3 – For this report, Table 3 provides more information about the use of this ingredient and is the only use table necessary for this report.	Table format updated per Panel's edits.

Basic Yellow 87 History

July 25, 2022– The Scientific Literature Review was issued for public comment.

August 8, 2022 – Unpublished data were received.

December 2022 - The Panel issued a Tentative Report for public comment with the conclusion that Basic Yellow 87 is safe as a hair dye ingredient in the present practices of use and concentration described in the safety assessment.

The Panel noted that Basic Yellow 87 has been reported to be used in 4 non-coloring cosmetic products (non-coloring hair conditioner, shampoo, and other hair preparations). The Federal FD&C Act mandates that color additives must be approved by the US FDA for their intended use before they are used. Basic Yellow 87 is an unapproved color additive in cosmetics products, and thereby, such uses are not permitted. Accordingly, these non-hair dye product uses are not within the purview of this Panel.

Basic Yellow 87 Data Profile* – March 2023 – 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 Yellow 87	X		X	X	X	X	X	X			X			X	X	X			X	X		X	X		X	X			

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

Basic Yellow 87

Ingredient	CAS #	PubMed	FDA	HPVIS	NIOSH	NTIS	NTP	FEMA	EU	ECHA	ECETOC	SIDS	SCCS	AICIS	FAO	WHO	Web
Basic Yellow 87	68259-00-7	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√

Search Strategy for PubMed

(((68259-00-7[EC/RN Number]) OR (Pyridinium, 1- methyl-4-[(methylphenylhydrazono)methyl]-, methyl sulfate)) OR (269-503-2[EC/RN Number])) OR (Basic Yellow 87) - 31 returns, 0 relevant

LINKS

Search Engines

- Pubmed - http://www.ncbi.nlm.nih.gov/pubmed
- Connected Papers - https://www.connectedpapers.com/

Pertinent Websites

- wINCI - http://webdictionary.personalcarecouncil.org
- 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

DECEMBER 2022 PANEL MEETING – INITIAL REVIEW/DRAFT REPORT

Belsito Team – December 5, 2022

DR. BELSITO: So, then we're moving to Basic Yellow 87. The SLR was issued for this on July 25, 2022. So, this is actually a first pass here for this, not a re-review. It's used in 40 formulations: 36 are rinse-off hair coloring products, four reported uses in non-coloring hair products. One use in an aerosol hair color spray was also reported.

Concentration of use, up to 1 percent in hair dyes and colors and up to .02 percent in coloring shampoos. And again, we're being asked to compare the tables, which we've already sort of determined we like both.

And in addition to the concentration of use survey, we got some oral, short-term tox, an in vitro dermal irritation study, guinea pig max study, in vitro ocular irritation study, Council comments, to look at. So, where are we with this?

DR. RETTIE: Yes. This is water soluble, low molecular weight 300 (inaudible). We don't have any method of manufacture, but it's a fairly simple chemistry, complement of a phenylhydrazine here with an aldehyde, both of which would be easy to get starting materials would give the hydrazone. Purity ranges all the way down to 61 percent, which I got from that that the other 30-odd percent was the methosulfate salt that was held over. So, then they measured that by iron exchange chromatography.

So, I wasn't too concerned about impurities, even though they were stated to be big ones. I wasn't all that concerned about method of manufacture. This is probably a German dye that goes back to the 1800 and synthesis is buried in Bilstein somewhere that anyone don't have access to. So, I also found it hard to find information on this thing.

DR. BELSITO: So you felt the data for composition impurities were okay?

DR. RETTIE: Could live with those, yes.

DR. BELSITO: Okay. That was one of my questions for you guys.

DR. SNYDER: You got a pretty robust 13-week study with a NOAEL of 10 milligrams per kilogram with a margin safety calculation of 184 for the 1 percent.

DR. BELSITO: Okay. And this is another thing for FDA to look into these four reported uses in non-coloring hair products. Okay. Here I said your aerosol is fine, given reported spray use.

MS. BURNETT: Right.

DR. BELSITO: For the in vitro dermal penetration, at least for an oxidative hair dye, I just have a note that it's also used in non-oxidative hair dyes. Oh, wait a minute, this substance was not tested in the presence of an oxidizing. Oh, I got that backwards. Okay. Sorry.

DR. RETTIE: Yeah, it was less than 2 percent.

DR. BELSITO: Right. And it was not used with and oxidative -- okay.

DR. RETTIE: Oxidative, less than 2 percent.

DR. BELSITO: Right. Let me delete that.

DR. RETTIE: It's also called Citrus Yellow. You cannot find hardly anything in Basic Yellow 87 until I discovered it had a synonym.

DR. KLAASSEN: It's a relatively complete document for a hair dye.

DR. RETTIE: The only other thing I had was just a minor typo, the DPRA thing that was corrected in the comments.

DR. BELSITO: Yeah, reactivity, not reactive.

DR. RETTIE: Yeah, it's still not corrected under the dermal sensitization section. It still says reactive there.

MS. BURNETT: Okay.

DR. BELSITO: Okay. So, in the discussion, we need inhalation boilerplate, negative DART and genotox, negative irritation. The sensitization boilerplate for hair dye. Safe as used as a colorant. I have a question for the group. Do we need to specify 1 percent as the SCCS did or just as used, because it's not used above 1 percent? Or wait a minute, we didn't get a concentration of use, right?

DR. SNYDER: Yeah, one percent at max.

DR. BELSITO: One percent. Okay.

DR. SNYDER: In hair dyes.

DR. BELSITO: And what do we do about the hairspray coloring? Is that considered a colorant?

MS. BURNETT: From what I estimate, it's like your Halloween hairspray. It's a non-oxidative hair dye. You just spray it on and you wash it out the next day.

DR. BELSITO: So, it is considered a hair dye.

MS. BURNETT: It's temporary, yeah. It's just like a hairspray with color in it.

DR. BELSITO: Okay. But the four non-coloring hair uses would be misbranded.

MS. BURNETT: Correct.

DR. BELSITO: If, in fact, they're not hair dyes.

MS. BURNETT: Correct.

DR. BELSITO: So, safe as used as hair dye, including the hairspray dye. And insufficient -- or misbranded for the four non-coloring hair products. Okay. Any other comments on this?

DR. SNYDER: Pretty good for hair dyes.

Cohen Team – December 5, 2022

DR. COHEN: So Basic Yellow 87. So, this is a draft report. It's the first time we're reviewing this, and the safety assessment is for one derived ingredient, which is used as a hair color. We have frequency of use. So, 40 formulations used at 1 percent in hair dyes and colors, and up to 0.02 percent in coloring shampoos. We have impurities, which seem to be quite a number. We don't have method of manufacturing.

So, I'll throw it out there. We have a negative DPRA and non-sensitizing with 1 percent intradermal challenges to guinea pigs. But I think we need to talk about the carc. issues and any other insufficiencies we may have. Anyone want to start?

DR. ROSS: I'm just pulling it up. You can start with someone else.

DR. COHEN: You want to go, Susan?

DR. TILTON: So, I noted that the EU had restricted the use in both oxidative and non-oxidative products at a max of 1 percent, indicating -- or stating that it does not pose a risk at that concentration or below. So, in terms of toxicity with low penetration in the skin, under both oxidative and non-oxidative conditions, at low dermal absorption, low acute toxicity outside of one lymphoma assay, a majority of the genotoxicity immunogenicity assays were negative.

It was non-irritating, non-sensitizing and its current use is reported to only be up to 1 percent. So, I felt that it could be safe to use, under similar conditions that the EU had reported since the current use is up to 1 percent.

DR. COHEN: Yeah. Tom, what were your thoughts on Basic Yellow 87?

DR. SLAGA: Yeah. We have a reasonable amount of data. It's not an irritant or sensitizer. There is some mutagenesis data. You know, depends if the sensitization data is acceptable to you all -- to you. I don't know, it's a possibility that we could go with safe.

DR. COHEN: And David?

DR. ROSS: Yeah. Found my notes, now. Yeah, I didn't have any dermal/oral tox concerns. The DART, there was a NOAEL there of 60 mg/kg/d, which seemed okay to me.

The genotox, as Susan mentioned, had one positive but there was quite a few negatives I believe. It wasn't irritating or sensitizing, but there was one study, David, that you mentioned I think related to purity, I think.

The ocular was a mild to moderate irritant, but I didn't see any uses around the eye. If I've got my Table of Use.

DR. COHEN: Well, it's a hair dye, so it's not supposed to be used.

DR. ROSS: And it's a coal tar product. There's a good margin of safety by the European Commission, so I was coming down as safe as used with the original conclusion.

DR. COHEN: Good. I didn't want to sort of put my finger on the balance by indicating that right out of the gate. I came to the same conclusion. It looked like this impurity issue was the same thing we spoke about with Basic Blue, right?

DR. ROSS: But this one is part of the product, isn't it? It's a part of the -- it's a counter ion for the -- let me look at the structure. I think, yeah. It's methosulfate, right?

DR. BERGFELD: I was wondering about the hair spray. There was an aerosol one. Like the color spray.

DR. COHEN: Oh, like it's pumped on.

DR. BERGFELD: Yeah, yeah. Whether that comes under hair dyes.

DR. COHEN: That's a fair -- I hadn't thought of that. So, is a typical hair dye for legal use a cream or gel?

DR. HELDRETH: I don't think there's stipulations to that. It just has to be a hair dye ingredient.

DR. COHEN: Then we should definitely put that in the discussion. Right? Because that's an atypical presentation of hair dye. Right?

DR. BERGFELD: And there's no inhalation studies, so.

DR. COHEN: So, we go as safe as used as a hair dye.

DR. BERGFELD: Yeah.

DR. COHEN: And we have in the discussion --

DR. BERGFELD: We have to talk about the hair spray. I'm trying to think if that was a semi-permanent or just a direct --

DR. HELDRETH: It's just listed as an aerosol hair color spray.

DR. BERGFELD: Oh, a spray color. I think it was just a layering agent.

DR. COHEN: That's good. Okay.

MS. BURNETT: Use both.

DR. COHEN: And just remind us, which ones we have to comment on with the tables. Go with the different tables. This one, I don't think -- you know what I mean, because I'm looking to go through the whole thing.

MS. BURNETT: This one does have both.

DR. COHEN: Yeah.

MS. BURNETT: The new and the old. In this case, because it's a hair dye, it's short and sweet.

DR. COHEN: I must say when we had reviewed it twice before it went into action, and I didn't think I was going to like them and they're starting to grow on me now.

DR. BERGFELD: What is that?

DR. COHEN: The new tables.

DR. BERGFELD: Oh, I like them.

DR. COHEN: Table 3. I know, but we weren't the warmest welcomers of these tables before.

DR. BERGFELD: No, because it didn't look like this. This is more instructive, I guess, informative.

DR. ROSS: I like the old ones.

DR. TILTON: Yeah. I like the old ones too.

DR. COHEN: Do we have --

DR. ROSS: The two newbies.

DR. COHEN: Tom, do you like the old Table 2 or the new Table 3? You should take a look at that, because we do need to feedback.

DR. SLAGA: Right now, I could go either way.

DR. BERGFELD: Good for you.

DR. TILTON: I mean, in terms of trying to interpret route of exposure, Table 2 is more straightforward.

DR. SLAGA: They both have benefits.

DR. COHEN: Yeah, but Table 2 is not hard data, it's inferential data.

DR. BERGFELD: It's the writer's interpretation.

DR. COHEN: It's an interpretation as opposed to -- its hair, right, and then you see shampoos, color sprays, and dyes. You have to read into that a little bit more. It's going to go up here and it's going to be presented a certain way. We've relied on table two as fact and it's not hard fact.

DR. ROSS: Inferentially, I think it's really use- -- it's fast because I can look at that Table 2 and get, you know, just what I said I'm looking for, you know, Table 2 for new uses. So, to me, that was great. It was a really fast way of doing this.

DR. BERGFELD: There was also discussion whether we could do both and whether the journal would accept both.

DR. ROSS: I don't think Bart's too happy about that.

DR. HELDRETH: It's fine by me. I don't know -- I would assume the journal would be fine with accepting it.

MS. BURNETT: In either case, the concern has been that, you know, we know there are like dry shampoos. So, we're putting in dry shampoo, which would go under their rinse off category but in technical use it doesn't really get completely -- it stays in your hair --

DR. HELDRETH: There's no rinsing.

MS. BURNETT: -- you brush it out, so it's still technically on you. It's being left on so there's no way to capture that. But the only problem is that we also don't know for sure unless industry, when they give us our survey back with the concentration of use, tells us this is specifically a dry shampoo, we don't know what the balance is.

DR. TILTON: Can you ask that?

MS. BURNETT: We can. I don't know if we'll get a response. And again, with the VCRP data we also will never fully know the full picture of how things are being used.

DR. HELDRETH: Right.

DR. BERGFELD: I think that we'd ask, and ask, and ask until they gave it to us.

DR. HELDRETH: We do. My understanding is the panel does ask.

DR. BERGFELD: Yeah, they know what they're selling for what reason.

MS. BURNETT: She usually does it, you know, in known applications that there could be a split. But as industry moves on and technology moves on and we know the applications change all the time, and they could be coming up with a new application as we speak. It'll take a couple years for us to catch on and then be able to ask for that data, too.

DR. BERGFELD: Well, you ask up front, what is the target use of this? As concentration, frequency, whatever you're asking them, just target use.

DR. COHEN: But that means that the questionnaire needs to be updated. Right?

DR. BERGFELD: On what we ask them through Carol. I think it goes through Carol with PCPC.

DR. COHEN: There's that form, that VCRP form, right? That voluntary --

DR. BERGFELD: No, it's not the VCRP we're asking, we're asking from PCPC.

DR. HELDRETH: Right. But that's separate from concentration.

DR. COHEN: Ah.

MS. BURNETT: We find that there's, like, an off use that usually comes through industry unless there's a lot of press or something, the instance of the airbrushes that was brought to our attention by an outside group.

DR. COHEN: Yes.

MS. BURNETT: So, and Carol ask -- when she's asking for the concentration for those things.

DR. BERGFELD: Don, can you respond? Can we ask for what the target use of what an ingredient is?

MR. BJERKE: Yeah. When it comes through the PCPC, it goes through the FDA product categories and I think there's 90 of them. And some of those include other. So, if there's a specific use that doesn't fall into one of those 90 categories, we can add that.

DR. BERGFELD: Do that and see what we get.

DR. COHEN: That's overall. That's a table disc- --

DR. BERGFELD: I mean, we have asked for like 30 years not to have Wave 2 and 3. And I can just say we still have Wave 2 and 3, but less.

DR. COHEN: Yeah. The last two waves were little splashes, they weren't tsunamis.

DR. BERGFELD: Yeah. That's what I meant.

DR. COHEN: We couldn't surf those waves, get your toes wet. Okay. So, we're okay on Basic Yellow. We'll have some specific points to discuss tomorrow and maybe we could move on.

DR. HELDRETH: Before we move on, do you have anything specific regarding the spray use and inhalation that you want in the discussion?

DR. COHEN: I thought we would talk about that tomorrow; just how do we handle that spray color?

DR. BERGFELD: Well, it depends what -- if it's an inactive spray already coupled -- it's just a dye. And it's a coating material, like, the automatic graying products that men use, it's just a coater on the outside of the cuticle.

DR. COHEN: Like a semi-perm.

DR. BERGFELD: Yeah.

MS. BURNETT: Yeah.

DR. BERGFELD: Or less.

DR. COHEN: Well, this is that though --

MS. BURNETT: I mean, we discussed this in staff and we were trying to figure out, but just it looks like regular hair spray can. They usually -- a lot of it's Halloween where you --

DR. BERGFELD: Spray on color, temporary.

MS. BURNETT: -- shake it up just like a normal hairspray. I believe it's a semipermanent.

DR. BERGFELD: There's no peroxide in it.

MS. BURNETT: I don't believe so.

DR. BERGFELD: It's just a layering agent.

MS. BURNETT: Yeah. Because it rinses off within a wash or two usually.

DR. COHEN: Yeah, it's reported as semi-permanent and oxidative hair -- okay. So, are we going to ask for further tox on that or --

DR. BERGFELD: No.

DR. COHEN: -- we're just going to comment on it?

DR. BERGFELD: In your discussion, that you assume it's a semi-permanent coloring agent, inactive.

DR. COHEN: You mean, biologically inactive. Right?

DR. BERGFELD: Yeah. Mm-hmm. It's a layering agent. It's layered onto the cuticle.

DR. COHEN: Okay. Let me just make sure I have enough for that for tomorrow. Okay.

Full Panel – December 6, 2022

DR. BELSITO: This is the first time we're looking at this. The SLR was issued in July of 2022. According to the VCRP, it's used in 40 formulations. Of these reported uses, the majority are rinse-off hair coloring products. There are four reported uses in non-coloring hair products. One use in an aerosol hair color spray was also reported. And, the concentration of use survey shows that it's one percent in hair dyes and 0.02 percent in coloring shampoos.

We looked at all of the data and felt that these were safe as used, but that the four non-coloring hair products, if in fact they're non-coloring hair products, we asked FDA to look into that. Because there seemed to be a lot of these dyes that are now getting reported as being in products other than hair dyes, they would be considered adulterated because this is not an approved colorant. But otherwise, safe as used in hair dyes, including the hair spray coloring.

DR. COHEN: Seconded.

DR. HELDRETH: Dr. Manga, from FDA, has her hand up. I think she may want to add some comment. She's in virtually.

DR. BERGFELD: Okay.

DR. MANGA: Hi, Don, and team. Good morning. Yeah, so I followed up with our team that handles the VCRP submissions. Currently how we're handling the non-hair dye products is to reach out to the person who files in VCRP and let them know that that product would be considered adulterated. And, obviously, if there's a way for us to follow up we would. Right now we don't have the resources to do that. But, we do follow up on products that are being imported.

DR. BELSITO: Okay. Thank you.

DR. BERGFELD: Thank you.

DR. BELSITO: In discussion, the inhalation boilerplate, because it is used in a spray. Point out that we have negative DART and genotoxicity data, negative irritation. Sensitization boilerplate since in one study at a high dose it was a sensitizer.

DR. BERGFELD: Are you going to also add a disclaimer regarding the other uses, in the discussion?

DR. BERGFELD: Yes, if in fact they're non-hair coloring products they would be adulterated.

DR. BERGFELD: Okay.

DR. COHEN: You went through all of our concerns. The spray, we'll put the inhalation boilerplate in. But, it was difficult for us to come to terms with it. But I think that's the only way to deal with it is that.

DR. BELSITO: Um-hmm.

DR. BERGFELD: So, do you want to repeat your conclusion then again, Don?

DR. BELSITO: Safe as used in hair dyes.

DR. BERGFELD: You want hair dyes in the conclusion.

DR. BELSITO: Yes.

DR. COHEN: Yes.

DR. BELSITO: It has to be.

DR. BERGFELD: Okay. All right, I'm going to call the question. All those in favor of this conclusion please indicate by raising your hand. Thank you, unanimous.

Safety Assessment of Basic Yellow 87 as Used in Cosmetics

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ABBREVIATIONS

ADME	absorption, distribution, metabolism, excretion
AUC	area under the curve
CIR	Cosmetic Ingredient Review
Council	Personal Care Products Council
CPSC	Consumer Product Safety Commission
DPRA	direct peptide reactivity assay
ECHA	European Chemicals Agency
FDA	Food and Drug Administration
HPLC	high performance liquid chromatography
NOAEL	no-observable-adverse-effect-level
NOEL	no-observed-effect-level
OECD	Organisation for Economic Co-operation and Development
Panel	Expert Panel for Cosmetic Ingredient Safety
REACH	Registration, Evaluation, Authorization and Restriction of Chemicals
SCCNFP	Scientific Committee on Cosmetic and Non-Food Products
SCCS	Scientific Committee on Consumer Safety
SED	systemic exposure dose
TG	test guideline
US	United States
UV-Vis	ultraviolet-visible spectroscopy
VCRP	Voluntary Cosmetic Registration Program
wINCI; *Dictionary*	web-based *International Cosmetic Ingredient Dictionary and Handbook*

ABSTRACT

The Expert Panel for Cosmetic Ingredient Safety (Panel) assessed the safety of Basic Yellow 87, which is reported to function as a hair dye in cosmetic products. The Panel reviewed the available data to determine the safety of this ingredient. The Panel concluded that Basic Yellow 87 is safe for use as a hair dye ingredient in the present practices of use and concentration described in this safety assessment.

INTRODUCTION

Basic Yellow 87 is reported to function as a hair colorant in cosmetic products, according to the web-based *International Cosmetic Ingredient Dictionary and Handbook* (wINCI; *Dictionary*).[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 exhaustive search of the world's literature. 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.

Some chemical and toxicological data on Basic Yellow 87 included in this safety assessment were obtained from robust summaries of data submitted to the European Chemicals Agency (ECHA) by companies as part of the Registration, Evaluation, Authorization and Restriction of Chemicals (REACH) chemical registration process.[2] Additionally, data were obtained from opinions produced by the European Commission's Scientific Committee on Cosmetic and Non-Food Products (SCCNFP) and Scientific Committee on Consumer Safety (SCCS).[3,4] These data summaries are available on the ECHA and European Commission's database, respectively, and when deemed appropriate, information from the summaries has been included in this report.

CHEMISTRY

Definition and Structure

Basic Yellow 87 (CAS No. 68259-00-7) is a hair colorant that conforms to the structure in Figure 1.[1] It is reported to be used in semi-permanent and, after mixing with an oxidative agent, in oxidative hair dye formulations.[3]

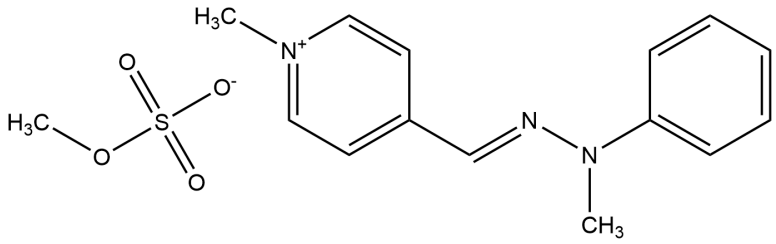

Figure 1. Basic Yellow 87

Chemical Properties

Available chemical properties of Basic Yellow 87 are provided in Table 1. Basic Yellow 87 is a yellow solid with the formula weight of 337.4 Da (methosulfate).[2,3] The log P_{ow} is -1.69 (20-25 ºC).

Method of Manufacture

No method of manufacturing data were found in the published literature, and unpublished methods were not submitted.

Composition/Impurities

The purity of Basic Yellow 87, as determined by high performance liquid chromatography (HPLC), was reported to be 61.1% - 92.6%.[3,4] Purity determined by ultraviolet-visible spectroscopy (UV-Vis) was reported to be 87.7% -92.9%.[4] Water content was reported to be $\leq$ 0.5%. Potential impurities and solvent residues may include $\leq$ 0.1% colored by-product and $\leq$ 0.1% isopropanol, respectively.[3] Salts of formulation or counter ions may include sodium chloride ($\leq$ 1.7%), methyl sulfate (up to 35.7%), and sulfate ($\leq$ 0.9%).[3,4] Heavy metal content was reported to be < 2 mg/kg (< 1 mg/kg for mercury and cadmium, each).[4]

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 this ingredient in cosmetics, and does not cover its use in airbrush delivery systems. Data are submitted by the cosmetic industry via the FDA's Voluntary Cosmetic Registration Program (VCRP) database (frequency of use) and in response to a survey conducted by the Personal Care Products Council (Council) (maximum use concentrations). The data are provided by cosmetic product categories, based on 21CFR Part 720. For most cosmetic product categories, 21CFR Part 720 does not indicate type of application and, therefore, airbrush application is not considered. Airbrush delivery systems are within the purview of the US Consumer Product Safety Commission (CPSC), while ingredients, as used in airbrush delivery systems, are within the jurisdiction of the FDA. Airbrush delivery system use for cosmetic application has not been evaluated by the CPSC, nor has the use of cosmetic ingredients in airbrush technology been evaluated by the FDA. Moreover, 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.

According to 2022 VCRP survey data, Basic Yellow 87 is used in a total of 40 formulations (Table 2).[5] Of these reported uses, the majority (35) are in rinse-off hair coloring products. Four reported uses were in non-coloring hair products. The results of the concentration of use survey provided by the Council in 2022 indicate that Basic Yellow 87 is used at up to 1% in hair dyes and colors and up to 0.02% in coloring shampoos.[6]

Basic Yellow 87 is reported to be used in color sprays and could possibly be inhaled (concentration not reported).[5,6] In practice, as stated in the Panel's respiratory exposure resource document (https://www.cir-safety.org/cir-findings), most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and tracheobronchial regions and would not be respirable (i.e., they would not enter the lungs) to any appreciable amount.

Although products containing this ingredient may be marketed for use with airbrush delivery systems, this information is not available from the VCRP or the Council survey. Without information regarding the frequency and concentrations of use of this ingredient (and without consumer habits and practices data or particle size data related to this use technology), 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. 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.

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.[7,8] Hair dye products marketed and sold in the US, though, must follow the labeling requirements established by the Food, Drug, and Cosmetic Act.

In the European Union, Basic Yellow 87 is restricted to use in oxidative and non-oxidative hair dye products at a maximum concentration of 1.0%.[9] In 2003, the SCCNFP could not make a conclusion on the safety of Basic Yellow 87 due to methodological inadequacies in in vitro mammalian cell mutation tests.[3] However, in 2011, the SCCS concluded that Basic Yellow 87 "does not pose a risk to the health of the consumer when used in non-oxidative and oxidative hair dye formulations up to a concentration of 1.0% on-head."[4]

TOXICOKINETIC STUDIES

Dermal Penetration

In Vitro

The percutaneous penetration/dermal absorption potential of a formulation containing 0.2% Basic Yellow 87 (88.6% - 92.6% pure) was studied using human female epidermis skin samples.[3] Using Franz diffusion cells, 90.2 - 109 mg/cm^2 (target dose 100 mg/cm^2) was applied to the skin surface for 30 min; the skin was then rinsed with warm water. The cells were then dismantled and a surface wipe, donor chamber rinse, filter paper support, tape strips, and the remaining skin samples were analyzed for test material content by HPLC (detection limit 2 ng/ml). The overall recovery of the applied dose was 98%. Permeation of the test material through the skin was detected in all but one of the cells treated with the formulation. The total percutaneous absorption of the test material (remaining in the skin + receptor phase) from the formulation was 0.082% of the

applied dose, approximately equal to 0.16 µg/cm^2. The SCCNFP noted that the substance was not tested in the presence of an oxidizing agent.

In another study, rat (male HanBrl: WIST (SPF)) and human (female) split-thickness skin (200 µm each) was used to determine the percutaneous absorption of [^{14}C]Basic Yellow 87 (91.6% pure).[4] The study was performed in accordance with Organisation for Economic Co-operation and Development (OECD) test guideline (TG) 428. The skin samples were mounted in flow-through diffusion cells each consisting of a donor and receptor chamber (7 membranes/species). An area of 0.64 cm^2 was exposed to 179 µg/cm^2 of the test material. The penetration through the skin membranes was determined over a 24-h period under non-occluded conditions. The receptor fluid (physiological saline; 0.9% w/v) was delivered at a flow rate of about 3 ml/h during the test period, and the perfusate was collected in 1-h intervals for the first 6 h and then at 2-h intervals for the remaining exposure period. Each skin membrane surface was rinsed 3 times with ethanol after 24 h. The skin membrane rinse fractions were combined according to the individual cells. The skin membranes were removed from the diffusion cell and stripped until the stratum corneum was removed from the skin membrane. Skin membranes remaining after stripping were digested in tissue solubilizer, the diffusion cells were washed with ethanol water (50/50 v/v), and the radioactivity was determined by liquid scintillation counting.

The total amount of the test material absorbed after 24 h, including that recovered from rat skin membrane and perfusates was 0.18% (standard deviation = 0.19%) of the applied dose. In the human skin membrane and perfusates 0.10% (standard deviation = 0.09%) was recovered. Of note, only 7 chambers were used per species, and in case of significant deviations, the conservative estimate of penetration was considered to be mean plus 2 standard deviations, i.e., 0.56% (1.0 µg/cm^2) in rats and 0.28% (0.50 µg/cm^2) in humans. It was concluded that Basic Yellow 87 penetrated at a low rate.[4,10]

In a similar percutaneous absorption study in human dermatomed skin (400 µm thickness), [^{14}C]Basic Yellow 87 (91.6% pure) was tested at 200 µg/cm^2 (nominal dose) under both oxidative and non-oxidative conditions.[4] There were 9 membranes from 4 donors for each condition tested. After 30 min exposure, the membranes were each washed and and the skin was left unoccluded for the remainder of the 24-h experimental period. Under oxidative conditions, 0.18 $\pm$ 0.9% (equivalent to 0.31 $\pm$ 0.16 µg/cm^2) of Basic Yellow 87 was systemically available (mean value) from a formulation containing a final concentration of the dye at 0.975%. Under non-oxidative conditions, 0.17 $\pm$ 0.10% (equivalent to 0.33 $\pm$ 0.19 µg/cm^2) of Basic Yellow 87 was systemically available (mean value) from a formulation containing 0.9%. The SCCS considered these experiments well performed, and thus adjusted the penetration amount by using the mean plus one standard deviative; i.e., under oxidative conditions, 0.47 µg/cm^2 (0.28%) of Basic Yellow 87 was absorbed. Under non-oxidative conditions, 0.51 µg/cm^2 (0.27%) of Basic Yellow 87 was absorbed. According to the SCCS, the latter (non-oxidative) absorption value was corrected to 0.57 µg/cm^2 to allow for the calculation of the margin of safety with 1% Basic Yellow 87. The relevant cation absorbed under oxidative and non-oxidative conditions was 0.32 µg/cm^2 and 0.38 µg/cm^2, respectively.

Absorption, Distribution, Metabolism, and Excretion (ADME)

Animal

Dermal

In an ADME study performed in accordance with OECD TG 417, 8 female Wistar rats (HanBrl:WIST (SPF) received 0.2 mg/cm^2 [^{14}C]Basic Yellow 87 (91.6% pure) dermally.[4] The concentration of radioactivity was determined in urine, feces, blood, plasma, and organs/tissues at different time points after administration. After 30 min, a skin wash and skin stripping were performed to remove any remaining test item and stratum corneum from the test site. The skin wash and skin strips were sampled to determine remaining amounts of the test material. Rats (4/timepoint) were killed at 24 h and at 96 h. Further methodology details were not provided. The results show that a very low fraction (0.3%) of the applied dose was absorbed from the skin into the systemic circulation. The concentrations of radioactivity for all blood sampling time points were below the limit of quantification. The amount of radioactivity determined in the stratum corneum was almost constant during the experimental period, accounting for 2.56% and 2.79% of the dose at 24 and 96 h, respectively (no further details provided). It was concluded that Basic Yellow 87 was poorly absorbed.

Oral

In the same ADME study described above, 9 female rats received 10 mg/kg bw [^{14}C]Basic Yellow 87 (91.6% pure) via gavage.[4] Rats (3/timepoint) were killed at 24 h, at 48 h, and at 96 h. Further methodology details were not provided. Approximately 6% of the administered test material was absorbed from the gastrointestinal tract into systemic circulation. Oral absorption was fast, with a maximum concentration in blood and plasma reached 1 h after administration and accounting of 0.143 ppm and 0.283 ppm, respectively. A two-phase decrease of concentration was then observed, with an initial half-life of 7.5 and 5.6 h in blood and plasma, respectively, and a second half-life of 48 h (blood) and 45 h (plasma). Within 96 h after exposure, almost all of the test material was removed from the blood and plasma. The area under the curve (AUC) for 0 - 24 h was 1.72 µg·h/g for blood and 2.10 µg·h/g for plasma. The test material was rapidly excreted, predominately from feces (89% after 96 h). The test material was also excreted from urine (5.3% after 96 h). Approximately 0.1% of the dose was still remaining in tissue and carcass after 96 h. The highest residue levels were found at 24 h in the liver and kidneys, but at very low amounts. The metabolite pattern in urine revealed 1 major and 10 minor metabolite fractions. The major fractions

represented more than 50% of the radioactivity in the urine or 2.5% of the dose, and was shown to contain a glucuronic acid conjugate of Basic Yellow 87 formed after hydroxylation of the phenyl moiety and its structural isomer. It was concluded that Basic Yellow 87 has low absorption after oral exposure.

In an oral bioavailability study, 15 female NMRI hybrid mice received 40 mg/kg bw Basic Yellow 87 (91.6% pure) in MilliQ water via a single gavage treatment.[4] The test material was radio-labelled and the study was performed in accordance with OECD TG 417. At 0.5, 1, 2, 4, and 24 h after treatment, 3 mice were killed, and the concentration of the test material was determined in the plasma and femur. No other tissues or endpoints were examined. Basic Yellow 87 was found to be rapidly absorbed in the gastrointestinal tract. The maximum concentration in plasma was observed 0.5 h after treatment and corresponded to 4.823 ppm equivalents/g. A two-phase decrease of the plasmatic concentration was observed with an initial half-life of 1.2 h and a second half-life of 6 h. The AUC for 0 - 24 h for plasma was 14.25 µg·h/g. The maximum concentration in the femur was observed at 0.5 h and corresponded to 1.273 ppm equivalents/g. Depletion kinetics were similar to that observed in plasma, but with a slightly slower half initial half-life of 3.3 h and a terminal half-life of 13 h. The authors assumed that the radioactivity determined in the femur was predominately located in the bone marrow, and that it correlated to the unchanged test item or its metabolites.

TOXICOLOGICAL STUDIES

Acute Toxicity Studies

Acute dermal and oral studies summarized here are described in Table 3. In an acute dermal study in rats, the LD_{50} for Basic Yellow 87 (87.7% pure) was greater than 2000 mg/kg bw.[3] In oral studies using rats, the LD_{50} in a limit study of Basic Yellow 87 (purity not reported) was between 500 and 1000 mg/kg bw in females and > 1500 mg/kg bw in males, when tested at up to 2000 mg/kg bw. [2,3] The LD_{50} was estimated to be 1000 mg/kg bw in another study where Basic Yellow 87 (purity not reported) was tested at 1000 mg/kg bw in male rats and at 500 mg/kg bw in female rats.[2]

Short-Term and Subchronic Toxicity Studies

Short-term and subchronic toxicity studies summarized here are described in Table 4. In a 2-wk gavage study, in which rats were dosed with up to 1000 mg/kg bw/d of a formulation containing 70% Basic Yellow 87, the no-observable-effect-level (NOEL) was 100 mg/kg bw/d.[11] All rats tested at 1000 mg/kg bw/d died or were killed before completion of study, and rats in the 300 mg/kg/d dose group exhibited higher absolute mean adrenal gland weights (males only), higher mean liver weights (both sexes), and epithelial cell hyperplasia and hyperkeratosis in the forestomach (males). In an oral study, rats that received up to 184 mg/kg bw Basic Yellow 87 (> 92% pure) in feed for 28-d study had decreased feed consumption, mean body weights, and body weight gains, slightly reduced total protein and globulin levels, and slightly increased albumin:globulin ratios at the highest doses tested. The no-observable-adverse-effect-level (NOAEL) for this study was 174 mg/kg bw/d and the NOEL was ~ 39 mg/kg bw/d. In a 13-wk dietary study, the NOAEL was 10 mg/kg bw/d in rats that received up to 245.2 mg/kg bw/d Basic Yellow 87 (> 92% pure).[3,4] Adverse effects included reduced feed and body weight gains (males), increase in methemoglobin levels (both sexes), and decreased white blood cell number (males) at the high dose and decreased total bilirubin levels (females) at mid and high doses.

DEVELOPMENTAL AND REPRODUCTIVE TOXICITY STUDIES

Oral

The teratogenic potential of Basic Yellow 87 (> 92% pure) was studied in mated female Wistar rats.[3] The study was performed in accordance with OECD TG 414. Groups of 22 females received 0, 20, 60, or 180 mg/kg bw of the test material in 4% carboxymethyl cellulose in twice-distilled water via gavage. The rats received the test material once daily from day 6 to day 17 of gestation. Body weights, feed consumption, mortality, and clinical signs of toxicity were recorded. On gestation day 21, all females were killed and maternal organs were examined. The uteri were weighed, and the fetuses were removed, weighed, and examine for sex and gross external abnormalities.

No maternal deaths were observed. No clinical signs were noted except for yellow feces and/or urine in the 60 and 180 mg/kg dose groups. Reduced feed consumption and weight gain were also observed at 60 and 180 mg/kg. No treatment-related changes were noted in the number of implantations, resorptions and fetuses, fetal weight, and external abnormalities, with the exception of 1 fetus with a cleft palate in the 20 mg/kg dose group, and 1 edematous fetus and a slight increase in fetal weight in the 180 mg/kg dose group. Some observed skeletal abnormalities were not considered related to the test material. Based on the results of this teratology study, the maternal and fetal NOAEL was determined to be 60 mg/kg bw/d.[3]

GENOTOXICITY STUDIES

In vitro and in vivo genotoxicity studies on Basic Yellow 87 summarized here are detailed in Table 5. Basic Yellow 87 was not mutagenic in Ames tests at up to 5000 µg/plate (87.7% and unreported purity), nor in a gene mutation test using Chinese hamster V79 cells, with and without metabolic activation, at up to 600 µg/ml (88.6% pure).[2-4] Basic Yellow 87 (91.6% pure; tested at up to 950 µg/ml) was mutagenic and/or clastogenic in a gene mutation test with mouse lymphoma cells,

with and without metabolic activation; however, a chromosomal aberration test of Basic Yellow 87 (90.5% pure; tested at up to 288 µg/ml) was negative for clastogenic and/or aneugenic activity.[3,4] In vivo testing found that Basic Yellow 87 (88.6% pure) did not induce an increased frequency of polychromatic erythrocytes or increased mean number in normochromatic erythrocytes in a mammalian erythrocyte micronucleus test when mice were given a single oral dose by gavage at up to 125 mg/kg bw.[3] No increase in unscheduled DNA synthesis was observed in hepatocytes after rats were exposed to a single dose of up to 500 mg/kg Basic Yellow 87 (88.6% pure).

CARCINOGENICITY STUDIES

No carcinogenicity studies were found in the published literature, and unpublished data were not submitted.

DERMAL IRRITATION AND SENSITIZATION STUDIES

Dermal irritation and sensitization studies on Basic Yellow 87 summarized here are detailed in Table 6. A mixture containing 0.24% Basic Yellow 87 (test concentration of 0.12% Basic Yellow 87 after dilution with another mixture) was predicted to be non-irritating in an EpiDerm™ skin model.[12] No dermal irritation was observed in rabbits tested with 0.5 g Basic Yellow 87 (87.7% pure) in 0.5 ml distilled water.[2,3] No skin reactions were observed in male and female Himalayan spotted guinea pigs that were treated for 15 d with up to 5% Basic Yellow 87 (> 92% pure).[3] Basic Yellow 87 was not peptide reactive in a direct peptide reactivity assay (DPRA; purity tested not reported), and was not sensitizing in a guinea pig maximization test with 1% intradermal induction, a 50% topical induction, and a 50% challenge (tested at > 92% pure). A formulation with 70% Basic Yellow 87 produced sensitization in 10% of animals in a guinea pig maximization test with a 1% intradermal induction, a 25% topical induction, and a 25% challenge.[13]

Phototoxicity/Photosensitization Studies

Dermal phototoxicity/photosensitization studies on Basic Yellow 87 summarized here are also detailed in Table 6. Basic Yellow 87 was not phototoxic and did not induce photosensitization in Himalayan spotted albino guinea pigs at concentrations up to 50%.[3]

OCULAR IRRITATION STUDIES

In Vitro

In vitro and animal ocular irritation studies summarized here are detailed in Table 7. In an in vitro study using isolated chicken eyes, Basic Yellow 87 (99.2% pure) was irritating when tested neat and not irritating when tested at a 5% aqueous dilution.[2] A mixture containing 0.24% Basic Yellow 87 (test concentration of 0.12% Basic Yellow 87 after dilution with another mixture) was a mild irritant in a bovine corneal opacity and permeability assay.[14] In a rabbit ocular irritation study, Basic Yellow 87 (87.7% pure) was moderately irritating.[2,3]

MARGIN OF SAFETY

The SCCS calculated the margin of safety for a product containing 1% Basic Yellow 87 (non-oxidative conditions) to be 184.[4] This calculation is based on an adjusted NOAEL (10% bioavailability due to the low oral bioavailability as shown in an ADME study) of 0.676 mg/kg bw/d from a 13-wk oral rat study (as cation) and a systemic exposure dose (SED) of 0.0037 mg/kg bw (skin area surface of 580 cm^2 x absorption through skin of 0.38 (cation) µg/cm^2 x 0.001 (unit conversion)/typical human bw of 60 kg). The margin of safety under oxidative conditions was reported to be very similar.

HAIR DYE EPIDEMIOLOGY

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 Yellow 87 is reported to be used in semi-permanent and oxidative hair dye formulations. 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

Basic Yellow 87 is reported to function as a hair colorant; specifically, it is used in semi-permanent and oxidative hair dye formulations, after mixing with an oxidative agent. According to 2022 VCRP survey data, Basic Yellow 87 is used in a total of 40 formulations. Of these reported uses, the majority (36) are in rinse-off hair coloring products. The results of the concentration of use survey provided by the Council in 2022 indicate that Basic Yellow 87 is used at up to 1% in hair dyes and colors and up to 0.02% in coloring shampoos.

In vitro percutaneous absorption studies in rat and human skin found that Basic Yellow 87 (88.6% - 92.6% pure) absorbed slowly. According to dermal and oral ADME studies in rats, Basic Yellow 87 (91.6% pure) does not readily absorb through the skin or the gastrointestinal tract. In the oral study, excretion mainly occurred in the feces. However, an oral bioavailability study in mice showed that Basic Yellow 87 (91.6% pure) rapidly absorbed in the gastrointestinal tract.

In an acute dermal study in rats, the LD_{50} for Basic Yellow 87 (87.7% pure) was greater than 2000 mg/kg bw. In oral studies using rats, the LD_{50} in a limit study of Basic Yellow 87 (purity not reported) was between 500 and 1000 mg/kg bw in females and > 1500 mg/kg bw in males when tested at up to 2000 mg/kg. The LD_{50} was estimated to be 1000 mg/kg bw in another study where Basic Yellow 87 (purity not reported) was tested at 1000 mg/kg in male rats and at 500 mg/kg in female rats.

A 2-wk gavage study, in which rats were dosed with up to 1000 mg/kg/d of a formulation containing 70% Basic Yellow 87, had a NOEL of 100 mg/kg/d. All rats tested at 1000 mg/kg/d died or were killed before completion of study and rats in the 300 mg/kg/d dose group exhibited higher absolute mean adrenal gland weights (males only), higher mean liver weights (both sexes), and epithelial cell hyperplasia and hyperkeratosis in the forestomach (males). In an oral study, rats that received up to 184 mg/kg bw Basic Yellow 87 (> 92% pure) in feed in a 28-d study had decreased feed consumption, mean body weights, and body weight gains and slightly reduced total protein and globulin levels and slightly increased albumin:globulin ratios at the highest doses tested. The NOAEL for this study was 174 mg/kg bw/d and the NOEL was ~ 39 mg/kg bw/d. In a 13-wk dietary study, the NOAEL was 10 mg/kg bw/d in rats that received up to 245 mg/kg bw/d Basic Yellow 87 (> 92% pure). Adverse effects included reduced feed and body weight gains (males), increase in methemoglobin levels (both sexes), and decreased white blood cell number (males) at high doses and decreased total bilirubin levels (females) at mid and high doses.

The maternal and fetal NOAEL for Basic Yellow 87 (> 92% pure) was determined to be 60 mg/kg bw/d in a teratogenic study in mated female rats. The dams received up to 180 mg/kg bw of the test material during days 6 - 17 of gestation. Reduced feed consumption and weight gain were observed in the mid and high dose groups and slight increase in fetal weight was observed in the high dose group.

Basic Yellow 87 was not mutagenic in Ames tests at up to 5000 µg/plate (87.7% and unreported purity), nor in a gene mutation test using Chinese hamster V79 cells, with and without metabolic activation, at up to 600 µg/ml (88.6% pure). Basic Yellow 87 (91.6% pure; tested at up to 950 µg/ml) was mutagenic and/or clastogenic in a gene mutation test with mouse lymphoma cells, with and without metabolic activation; however, a chromosomal aberration test of Basic Yellow 87 (90.5% pure; tested at up to 288 µg/ml) was negative for clastogenic and/or aneugenic activity. In vivo testing found that Basic Yellow 87 (88.6% pure) did not induce an increased frequency of polychromatic erythrocytes or increased mean number in normochromatic erythrocytes in a mammalian erythrocyte micronucleus test when mice were given a single oral dose by gavage at up to 125 mg/kg bw. No increase in unscheduled DNA synthesis was observed in hepatocytes after rats were exposed to a single dose of up to 500 mg/kg Basic Yellow 87 (88.6% pure).

A mixture containing 0.24% Basic Yellow 87 (test concentration of 0.12% Basic Yellow 87 after dilution with another mixture) was predicted to be non-irritating in an EpiDerm™ skin model. No dermal irritation was observed in rabbits tested with 0.5 g Basic Yellow 87 (87.7% pure) in 0.5 ml distilled water. No skin reactions were observed in male and female Himalayan spotted guinea pigs that were treated for 15 d with up to 5% Basic Yellow 87 (> 92% pure). Basic Yellow 87 was not peptide reactive in a DPRA (purity tested not reported), and was not sensitizing in a guinea pig maximization test with 1% intradermal induction, a 50% topical induction and a 50% challenge (tested at > 92% pure). A formulation with 70% Basic Yellow 87 produced sensitization in 10% of animals in a guinea pig maximization test with a 1% intradermal induction, a 25% topical induction, and a 25% challenge. Basic Yellow 87 was not phototoxic and did not induce photosensitization in Himalayan spotted albino guinea pigs at concentrations up to 50%.

In an in vitro study using isolated chicken eyes, Basic Yellow 87 (99.2% pure) was irritating when tested neat and not irritating when tested at a 5% aqueous dilution. A mixture containing 0.24% Basic Yellow 87 (test concentration of 0.12% Basic Yellow 87 after dilution with another mixture) was a mild irritant in a bovine corneal opacity and permeability assay. In a rabbit ocular irritation study, Basic Yellow 87 (87.7% pure) was moderately irritating.

A margin of safety for a product containing 1% Basic Yellow 87 under non-oxidative conditions was calculated to be 184. This calculation was based on an adjusted NOAEL of 0.676 mg/kg bw/d from a 13-wk oral rat study and a SED of 0.0037 mg/kg bw. The margin of safety under oxidative conditions was reported to be very similar.

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.

No carcinogenicity studies on Basic Yellow 87 were found in the published literature, and unpublished data were not submitted.

DISCUSSION

Basic Yellow 87 is reported to function as a semi-permanent and oxidative hair dye in hair coloring products. The Panel has determined that the data are sufficient to support safety of this ingredient in hair dye products, which are rinsed-off after application. The Panel noted that the available data show that Basic Yellow 87 absorbs slowly through the skin, is not genotoxic, is not toxic in developmental and reproductive studies, and has low concentrations of use. The Panel considered these findings, coupled with the short exposure time as a rinse-off product, and determined that the data are sufficient to conclude that Basic Yellow 87 is safe in the present practices and concentrations of use in hair dye formulations.

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 Food, Drug, and Cosmetic Act (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 Yellow 87 has been reported to be used in four non-coloring cosmetic product (i.e., non-coloring hair conditioner, shampoo, and other hair preparations). The Federal FD&C Act mandates that color additives must be approved by the FDA for their intended use before they are used. Basic Yellow 87 is an unapproved color additive in cosmetics products, and thereby, such use is not permitted. Furthermore, non-hair dye use is not within the purview of this Panel.

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.

The Panel discussed the issue of incidental inhalation exposure resulting from this ingredient. Basic Yellow 87 is reported to be used in an aerosol hair color spray (concentration not reported). Inhalation toxicity data were not available on this ingredient. However, the Panel noted that in aerosol products, the majority of the 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 this ingredient. Coupled with the small actual exposure in the breathing zone and the low concentrations at which the ingredient is 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, and that no data are available for consumer habits and practices thereof. As a result of deficiencies in these critical data needs, the safety of cosmetic ingredients applied by airbrush delivery systems cannot be assessed by the Panel. Therefore, the Panel has found the data insufficient to support the safe use of cosmetic ingredients applied via an airbrush delivery system.

CONCLUSION

The Expert Panel for Cosmetic Ingredient Safety concluded that Basic Yellow 87 is safe for use as a hair dye ingredient in the present practices of use and concentration described in this safety assessment.

TABLES

Table 1. Chemical properties for Basic Yellow 87

Property	Value	Reference
Physical Form	yellow solid	2,3
Formula Weight (Da)	337.4 (methosulfate)	3
Density (tapped; g/ml @ 20 °C)	0.4	2
Vapor Pressure (mmHg @ 20 °C @ 25 °C)	$< 10 \times 10^{-10}$ $< 4.1 \times 10^{-10}$	2
Melting Point (°C)	150-164, decomposition above 240	2
Water Solubility (g/l @ 20 °C)	40 (methosulfate salt) ≥ 620 (sulfate salt)	3 2
log $P_{o/w}$ (20-25 ºC)	-1.69	2,3

Table 2. Frequency[5] and concentration[6] of use (2022) according to likely duration and exposure and by product category.

	# of Uses	Max Conc of Use (%)
	Basic Yellow 87	
Totals	**40**	**0.0007-1**
summarized by likely duration and exposure*		
Duration of Use		
Leave-On	*3*	*NR*
Rinse-Off	*37*	*0.0007-1*
Diluted for (Bath) Use	*NR*	*NR*
Exposure Type*		
Eye Area	NR	NR
Incidental Ingestion	NR	NR
Incidental Inhalation-Spray	1	NR
Incidental Inhalation-Powder	NR	NR
Dermal Contact	NR	NR
Deodorant (underarm)	NR	NR
Hair - Non-Coloring	4	NR
Hair-Coloring	36	0.0007-1
Nail	NR	NR
Mucous Membrane	NR	NR
Baby Products	NR	NR
as reported by product category		
Hair Preparations (non-coloring)		
Hair Conditioner	1	NR
Shampoos (non-coloring)	1	NR
Other Hair Preparations	2	NR
Hair Coloring Preparations		
Hair Dyes/Colors (all types requiring caution statements and patch tests)	19	0.0007-1
Hair Rinses (coloring)	6	NR
Hair Shampoos (coloring)	6	0.02
Hair Color Sprays (aerosol)	1	NR
Other Hair Coloring Preparation	4	NR

*likely duration and exposure is derived based on product category (see Use Categorization https://www.cir-safety.org/cir-findings)
**Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure types may not equal the sum of total uses.
NR – not reported

Table 3. Acute toxicity studies on Basic Yellow 87

Animals	No./Group	Vehicle	Dose/Protocol	LD_{50}/Results	Reference
			DERMAL		
Crl:CD (SD)IGS BR rats	5 males and 5 females	none	2000 mg/kg (87.7% pure) in accordance with OECD TG 402; test sites (an area of approximately 10% of total surface area) were occluded for 24 h; test material moistened with water prior to application and removed with water and paper towel after treatment period; observed for signs of toxicity for 14 d	> 2000 mg/kg bw; no signs of dermal toxicity	[3]
			ORAL		
Crl:CD (SD)IGS BR rats	2 males and 2 females per group, except 5 males and 5 females in the high-dose group	water	500, 1000, 1500, or 2000 mg/kg (purity not reported) via single gavage dose (limit test)	LD_{50} between 500 and 1000 mg/kg in females and > 1500 mg/kg in males: all males survived the 500 and 1000 mg/kg doses and 1 male survived the 1500 mg/kg dose, no males survived the 2000 mg/kg dose; all females survived the 500 mg/kg dose but none survived the 1000-2000 mg/kg doses; enlarged heart observed in 1 male at 1500 mg/kg; dark-red lobes and dark areas on the lung of 1 male and 1 female at 500 mg/kg; no other visible lesions observed	[2,3]
Crl:CD (SD)IGS BR rats	5 males at 1000 mg/kg and 5 females at 500 mg/kg	water	Oral toxicity study in accordance with OECD TG 420	LD_{50} estimated as 1000 mg/kg; 2/5 males in the 1000 mg/kg died, no females died; prior to death, clinical signs in these animals included hypoactivity, ataxia, squinted eyes, liquid or mucoid feces, discolored feces, and/or discolored urine; distended stomach, ileum, duodenum, jejunum, colon, and bladder, and yellow fluid observed in 1 of the dead animals; remaining surviving males in the 1000 mg/kg and the 500 mg/kg females had similar clinical signs in addition to urine/fecal staining, crust around eyes and/or hair in the genital region; necropsy of surviving animals only showed a pale area in the liver of 1 female	[2]

Table 4. Short-term and subchronic toxicity studies of Basic Yellow 87

Test Material Dose/Concentration	Animals/Group	Study Duration	Vehicle	Protocol	Results	Reference
			ORAL			
0, 100, 300, or 1000 mg/kg/d of formulation containing 70% Basic Yellow 87	6 male and 6 female Sprague-Dawley rats per group	2-wk	water	Gavage study in accordance with OECD TG 407; animals received test material daily and were checked daily for mortality and clinical signs; feed consumption and body weight measured twice a week; hematology and blood chemistry investigation performed during week 2; all animals killed at study end and underwent necropsy; designated organs weighed and macroscopic lesions, liver, and kidneys submitted for microscopic examination	NOEL = 100 mg/kg/d; all rats in 1000 mg/kg/d dose group died or were killed prematurely after 7-15 d of treatment following numerous signs of poor clinical condition; necropsy of 1000 mg/kg/d dose group revealed all rats had dilatation/overdistension of the stomach; test material induced yellowish coloration of urine and feces in 100 and 300 mg/kg/d dose groups; ptyalism observed at all dose-levels in a dose-related manner; body weight gains and feed consumption of the 100 and 300 mg/kg/d dose groups was similar to controls, but it was markedly reduced in the 1000 mg/kg/d dose group; no significant findings in hematology for any dose group; higher urea nitrogen level and lower cholesterol level observed in males in 1000 mg/kg/d dose group; higher absolute mean adrenal gland weights observed in males in 300 mg/kg/d dose group and higher mean liver weights recorded in both sexes in the 300 mg/kg/d dose group; yellowish contents observed in urinary bladder of the males in the 300 mg/kg/d dose group; epithelial cell hyperplasia and hyperkeratosis in the forestomach observed in the 300 (males) and 1000 mg/kg/d (both sexes) dose groups	[11]
9, 38.8, or 174 mg/kg bw/d in males and 8.2, 40, or 184 mg/kg bw/d in females; purity > 92%	HanIbm: WIST rats; 5 males and 5 females per group, except 10 males and 10 females in controls and high dose groups	28-d study	feed	Study performed in accordance with OECD TG 407; controls received normal diet	NOAEL = 174 mg/kg bw/d and NOEL = ~ 39 mg/kg bw/d; yellow discoloration of feces noted in all high-dose rats, yellow urine discoloration observed in all animals that received test material; no toxicologically-significant effects on hematology, clinical biochemistry, or urinalysis observed; no abnormal findings in functional observational battery; feed intake, mean body weight, and body weight gain slightly lower in high-dose males; slightly reduced total protein and globulin level and slightly increased albumin:globulin ratios recorded in high-dose males	[3]
9.7, 48.5, or 245.2 mg/kg bw/d in males and 10.1, 48.9, or 245.0 mg/kg bw/d in females; purity > 92%	Wistar SPF-bred rats; 10 males and 10 females per group	13-wk study	feed	Study performed in accordance with OECD TG 408; control animals received normal diet	NOAEL = 10 mg/kg bw/d, corresponding to a dose of 6.76 mg/kg bw/d of the cation; no adverse effects observed in ophthalmologic or functional observational battery findings; colored feces observed in both sexes of the mid- and high-dose groups; high-dose females had increased urine pH, all tested females had decrease in uric acid levels; total bilirubin levels decreased in mid and high dose females; effects in only the high-dose group included: reduced feed and body weight gains (males), increase in methemoglobin levels (both sexes), decreased white blood cell number (males), increased platelet count (females), changes in creatinine levels, total protein amount, glucose levels, and changes in several organ/body weights and organ/brain ratios	[3,4]

Table 5. Genotoxicity studies on Basic Yellow 87

Concentration/Dose	Vehicle	Test System	Procedure	Results	Reference
IN VITRO					
33.3, 100, 333, 1000, 3300, or 5000 µg/plate following a dose range finding study of 6.67- 5000 µg/plate; purity = 87.7%	water	*Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537 and *Escherichia coli* strain WP2MvrA	Bacterial reverse mutation test in accordance with OECD TG 471; with and without S9 metabolic activation	Test material did not cause a positive increase in revertant frequencies, with or without metabolic activation	2,3
33.3, 100, 333, 1000, 2500, or 5000 µg/plate; purity not reported	twice-distilled water	*S. typhimurium* strains TA98 and TA100	Bacterial reverse mutation test in accordance with OECD TG 471; with and without metabolic activation	Test material did not induce point mutations by base pair changes or frameshifts	2
Test 1: 3, 10, 30 or 100 µg/ml without metabolic activation and 3.0, 30, 100, or 300 µg/ml with metabolic activation Test 2: 3, 10, 30, 50, 100, or 200 µg/ml without metabolic activation and 30, 50, 100, 300, 450, or 600 µg/ml with metabolic activation 88.6% pure	culture medium	Chinese hamster V79 cells	Mammalian cell gene mutation test at the HGPRT locus in accordance with OECD TG 476; with and without metabolic activation	Not mutagenic; no biologically-relevant statistically significant increase in mutant frequency observed in either test, with or without metabolic activation; SCCS noted test material had a clear cytotoxic effect (no further details provided)	3,4
Test 1: 118.8 - 950 µg/ml without metabolic activation and 59.4 - 712.5 µg/ml with metabolic activation Test 2: 200 - 600 µg/ml without metabolic activation and 30 - 120 µg/ml with metabolic activation 91.6% pure	deionized water	Mouse lymphoma L5178Y cells	Mammalian cell gene mutation test in accordance with OECD TG 476; with and without metabolic activation using rat and hamster S9-mix in Test 1 and only hamster S9-mix in Test 2	Mutagenic and/or clastogenic, with and without metabolic activation; concentration-dependent increase in mutant frequency observed, with genotoxic potency highest with metabolic activation; using hamster metabolic activation caused toxic effects at the lowest concentration in Test 2; ratio of small versus large colonies shifted towards small colonies; no further details	4
3.55 - 288 µg/ml; 90.5% pure	water	Human lymphocytes	Mammalian chromosomal aberration test in accordance with OECD TG 473; with and without metabolic activation	Negative for clastogenic and/or aneugenic activity, with and without metabolic activation; excessive cytotoxicity observed at 98.7 µg/ml in one culture, which required 200 cells to be scored from the duplicate culture – cytotoxicity was not described at higher concentrations	3
IN VIVO					
0, 12.5, 40, or 125 mg/kg bw; 88.6% pure	deionized water	Groups of 6 male and 6 female NMRI mice	Mammalian erythrocyte micronucleus test in accordance with OECD TG 474; single dose via gavage; groups of animals killed at 24, 48, or 72 h post-treatment; appropriate negative and positive controls used	Test material did not induce a statistically significant increase in the frequency of polychromatic erythrocytes; mean number of normochromatic erythrocytes not significantly increased after treatment as compared to controls	3
0, 250, or 500 mg/kg bw; 88.6% pure	not reported	Groups of 4 male Wistar HanIbm: WIST (SPF) rats	Unscheduled DNA synthesis test in accordance with OECD TG (draft) 486; single gavage dose; sampling times were 2 and 16 h post-treatment	Test material did not induce increased unscheduled DNA synthesis in hepatocytes	3

Table 6. Dermal irritation, dermal sensitization, and phototoxicity and photosensitization studies on Basic Yellow 87

Concentration/Dose	Test Population	Procedure	Results	Reference
		IRRITATION		
		IN VITRO		
Mixture containing 0.24% Basic Yellow 87; upon dilution; final test concentration of 0.12% Basic Yellow 87	reconstructed human epidermis	EpiDerm™ skin model; test material was diluted at a 1:1 ratio with another mixture prior to assessment; negative control was sterile calcium- magnesium free Dulbecco's phosphate buffered saline; the positive control was 5% sodium lauryl sulfate	Predicted to be non-irritating; mean viability = 104.3%	[12]
		ANIMAL		
0.5 g in 0.5 ml distilled water; 87.7% pure	2 male and 1 female New Zealand White rabbits	In accordance with OECD TG 404; semi-occlusive; test area = 6.25 cm^2; intact test sites for 4 h and then rinsed off; scoring of reactions at 0.5 to 1, 24, 48, and 72 h	Not irritating; primary dermal irritation index calculated to be 0.0; no evidence of corrosion; no evidence of treatment-related toxicity during treatment	[2,3]
0.5%, 1%, 3%, and 5% tested at 0.1 ml/ 7 cm^2; purity > 92%	Himalayan spotted guinea pigs; 4 males and 4 females	Study performed in accordance with OECD TG 402; 2 application sites were marked on the shaved backs of 6 treated animals; 2 animals were controls and treated with just vehicle (type not reported); a complete clock design was used so each concentration was tested 3 times on 3 different animals/sex; not occluded; treated skin flushed with water prior to each new application; skin shaved regularly and depilated on day 15 prior to final reading; skin reactions observed daily	No grading scores recorded on days 2 – 14 due to slight accumulation of test material on skin; no skin reaction was observed on final day after depilation	[3]
		SENSITIZATION		
		IN VITRO		
Not reported	lysine and cysteine peptides	DPRA; no further details provided	Not peptide reactive; no further details provided	[2]
		ANIMAL		
1% intradermal induction in physiological saline; 50% epidermal induction in twice-distilled water; challenge 50% in twice-distilled water; purity > 92%	15 female Himalayan spotted (GOHI, SPF-quality) guinea pigs	Guinea pig maximization test in accordance with OECD TG 406; 10 animals received test material, 5 were negative controls; intradermal induction (10 ml/site) included Freund's complete adjuvant followed 1 wk later with epidermal induction under occlusion, sites pre-treated with 10% sodium lauryl sulfate; 2 wk after induction, animals challenged with 50 % test material under occlusion	Not sensitizing; no reactions observed in the control or test groups during challenge	[2,3]
Formulation containing 70% Basic Yellow 87; 1% intradermal injection; 25% topical induction; challenge 25%; vehicle was sterile isotonic saline solution (0.9% sodium chloride)	Treatment group had 10 male and 10 female Dunkin-Hartley guinea pigs; control group had 5 males and 5 females	Guinea pig maximization test in accordance with OECD TG 406; intradermal induction (0.1 ml/site) included Freund's complete adjuvant followed 1 wk later with topical induction (0.5 ml) under occlusion for 48 h, sites pre-treated with 10% sodium lauryl sulfate in petrolatum; 2 wk after induction, animals challenged with 25% test material (0.5 ml) under occlusion for 24 h; animals killed at study end and cutaneous samples taken from challenge sites for histological examination	Skin coloration from test material prevented scoring for erythema, thus evaluation of skin sensitization performed by microscopic examination Histological examination revealed cutaneous reactions attributable to sensitization in 10% of animals treated with the test material.	[13]

Table 6. Dermal irritation, dermal sensitization, and phototoxicity and photosensitization studies on Basic Yellow 87

Concentration/Dose	Test Population	Procedure	Results	Reference
		PHOTOTOXICITY/PHOTOSENSITIZATION		
		ANIMAL		
0.025 ml/cm^2 dilution in concentrations of 10%, 15%, 25%, or 50% in water	15 female Himalayan spotted albino guinea pigs, 10 test and 5 control	Animals were treated with 2% dimethyl sulfoxide in ethanol to enhance skin penetration; test material applied topically and openly to 2 cm^2 areas on both flanks; 30 min after application, left flank exposed to 20 J/cm^2 UVA irradiation and right flank remained unexposed to light and served as reference; control animals exposed to UVA and vehicle; skin reactions evaluated at 24, 48, and 72 h after treatment	At 24 h, phototoxic reactions observed in 6 of the animals at 50% and 3 of the animals at 25%; positive reactions observed after 24 h in the non-radiated skin site of 1 of the animals at 50% and 2 of the animals at 25% were determined to be incidental and not related to the test material; no reactions observed at 48 or 72 h; no further details	3
0.1 ml /8 cm^2 of 50% in water	20 Himalayan spotted albino guinea pigs (sex not reported); additional 10 animals were controls	For induction, test material was applied epicutaneously to 8 cm^2 area in nuchal region that received 4 intradermal injections of Freund's complete adjuvant/ physiological saline; sites then exposed to 1.8 J/cm^2 UVB and 10 J/cm^2 UVA (5 total exposures in 2 wk); controls treated with only vehicle Challenge occurred 3 wk after beginning of induction on both flanks with test material at 10%, 15%, 25%, or 50% in water; test sites irradiated with 10 J/cm^2 UVA or left unirradiated; skin reactions evaluated at 24, 48, and 72 h post-challenge exposure	No reactions observed	3

Table 7. Ocular irritation studies on Basic Yellow 87

Concentration/Dose	Vehicle	Test Population	Procedure	Results	Reference
			IN VITRO		
99.2% pure Basic Yellow 87; 30 mg (neat) or 30 µl (5% aqueous dilution)	Not reported	Chicken eyes	Isolated chicken eye test; eyes exposed to single application for 10 s, followed by 20 ml saline rinse; corneal thickness, corneal opacity, and fluorescein retention measured; histopathology of corneas performed; negative control was saline and positive control was sodium hydroxide	Irritating when tested neat; not irritating at 5% dilution	2
Mixture containing 0.24% Basic Yellow 87; upon dilution; final concentration of 0.12% Basic Yellow 87	None	Bovine corneas	Bovine corneal opacity and permeability assay; test material was diluted at a 1:1 ratio with another mixture prior to assessment; negative control was sterile deionized water and the positive control was ethanol	Mild irritant; in vitro score = 3/3	14
			ANIMAL		
87.7% pure Basic Yellow 87; approximately 0.057 g/test eye	Neat	1 male and 2 female New Zealand White rabbits	Ocular irritation study in accordance with OECD TG 405; observations made 1, 24, 48, 72, and 96 h and 7, 14, and 21 d after instillation	Moderately irritating; no corneal effects observed; iritis (score of 1) observed 1 h after instillation in 1 animal, scores were 0 for other 2 animals and findings were reversible; redness observed in all animals from 1 to 72 h and in 1 animal for up to 21 d after instillation; chemosis and discharge noted in all animals up to 48 h after instillation	2,3

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