Amended Safety Assessment of Basic Blue 99 as Used in Cosmetics

Status:	Tentative Amended Report for Public Comment
Last Panel Review:	June 15-16, 2026
Release Date:	July 1, 2026

*All interested persons are provided 60 days from the above release date (i.e., by **August 30, 2026**) to comment on this safety assessment, and to identify additional published data that should be included or provide unpublished data which can be made public and included. Information may be submitted without identifying the source or the trade name of the cosmetic product containing the ingredient. All unpublished data submitted to CIR will be discussed in open meetings, will be available for review by any interested party and may be cited in a peer-reviewed scientific journal. Please submit data, comments, or requests to the CIR Executive Director, Dr. Bart Heldreth.*

The Expert Panel for Cosmetic Ingredient Safety members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; Bruce A. Brod, M.D., M.H.C.I., F.A.A.D.; Samuel M. Cohen, M.D., Ph.D.; Curtis D. Klaassen, Ph.D.; Allan E. Rettie, Ph.D.; David Ross, Ph.D.; Paul W. Snyder, D.V.M., Ph.D.; and Susan C. Tilton, Ph.D. Previous Panel members involved in this assessment: David E. Cohen, M.D., and Thomas J. Slaga, 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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ABBREVIATIONS

3D	three-dimensional
CIR	Cosmetic Ingredient Review
Council	Personal Care Products Council
CPSC	Consumer Product Safety Commission
Dictionary	*International Cosmetic Ingredient Dictionary*
DMSO	dimethyl sulfoxide
EC	European Commission
EHE	equivalent human epidermis
EU	European Commission
FDA	Food and Drug Administration
FD&C Act	Food, Drug, and Cosmetic Act
LD_{50}	median lethal dose
LLNA	local lymph node assay
MoCRA	Modernization of Cosmetics Regulation Act of 2022
MTT	3-[4,5-dimethylthiazol-2-yl]-2,5 diphenyl tetrazolium bromide
NOAEL	no-observed-adverse-effect level
NOEL	no-observed-effect-level
OECD	Organisation for Economic Co-operation and Development
Panel	Expert Panel for Cosmetic Ingredient Safety
RLD	Registration and Listing Data
SCCS	Scientific Committee on Consumer Safety
TUNEL	terminal deoxynucleotidyl transferase dUTP nick-end labeling
TG	test guideline
US	United States

ABSTRACT

The Expert Panel for Cosmetic Ingredient Safety (Panel) reassessed the safety Basic Blue 99, which is reported to function as a hair dye in cosmetic products. The Panel reviewed the relevant data to determine the safety of this ingredient. Accordingly, the Panel issued an amended report with a revised conclusion stating that the available data are insufficient to make a determination of safety for Basic Blue 99 under the intended conditions of use as a hair dye ingredient.

INTRODUCTION

According to the *International Cosmetic Ingredient Dictionary* (*Dictionary*), Basic Blue 99 is reported to function in cosmetics as a hair colorant and a hair conditioning agent.[1] Basic Blue 99 was previously reviewed by the Expert Panel for Cosmetic Ingredient Safety (Panel) in a safety assessment that was published in 2007.[2] At that time, the Panel concluded that Basic Blue 99 "is safe as a hair dye ingredient in the present practices of use and concentration." In accordance with its Procedures, the Panel evaluates the conclusions of previously-issued reports approximately every 15 years, and it has been at least 15 years since this assessment has been issued. In December 2022, the Panel determined that this safety assessment should be re-opened for re-evaluation due to concerns regarding the variability of the composition of the ingredient.

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 May 2026. A listing of the search engines and websites that are used and the sources that are typically explored, as well as the endpoints that the Panel typically evaluates, is provided on the Cosmetic Ingredient Review (CIR) website (https://www.cir-safety.org/supplementaldoc/preliminary-search-engines-and-websites; https://www.cir-safety.org/supplementaldoc/cir-report-format-outline). Unpublished data are provided by the cosmetics industry, as well as by other interested parties.

Excerpts from the 2007 report on Basic Blue 99 are disseminated throughout the text of this re-review document, as appropriate, and are identified by *italicized text.* (This information is not included in the tables or the Summary section).

Some chemical and toxicological data on Basic Blue 99 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.[3] Additionally, data were obtained from opinions produced by the Scientific Committee on Consumer Safety (SCCS) of the European Commission (EC).[4,5] These data summaries are available on the databases for ECHA and the EC, respectively, and when deemed appropriate, information from the summaries has been included in this report.

CHEMISTRY

Definition and Structure

According to the *Dictionary*, Basic Blue 99 (CAS No. 68123-13-7) is the naphthoquinoneimine color that conforms to structure in Figure 1.[1]

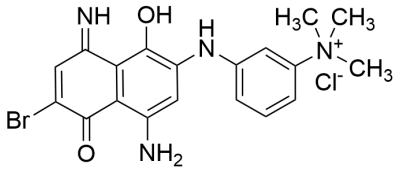


Figure 1. Basic Blue 99, according to *Dictionary* monograph.

However, according to cosmetic ingredient manufacturer's submissions provided to the EU SCCS in the 2026 opinion, Basic Blue 99 also comprises 4 other major constituents, including a regio isomer of the naphthoquinoneimine in Figure 1 and three different dibrominated analogues, Figure 2.[4]

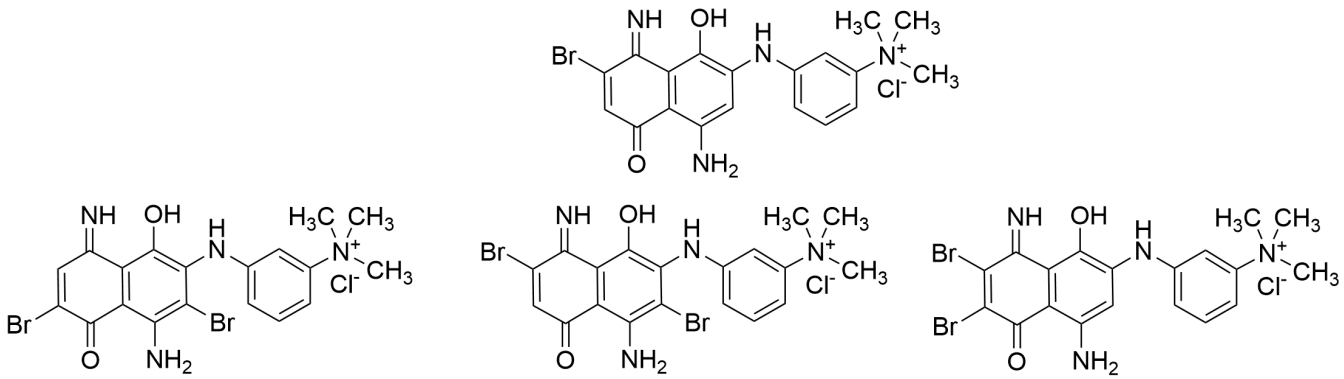


Figure 2. Additional major constituents Basic Blue 99

According to manufacturer submissions, the 2 mono-brominated analogues comprise more than 50% of this ingredient, while the 3 dibrominated analogues variably comprise approximately another 30%. This ingredient is a non-oxidative, temporary to semi-permanent, direct-dye hair colorant. Thus, unlike oxidative hair dyes, no oxidation or coupling is needed before use.

Chemical Properties

Chemical properties for Basic Blue 99 and its major constituents are summarized in Table 1. As described generally, Basic Blue 99 is a blue-black fine powder with a density of 2.19 g/ml and water solubility of 10 - 100 g/l at 20ºC.[3,4] Basic Blue 99 is reported to be soluble in ethanol and dimethyl sulfoxide (DMSO). The formula weights for the main and major constituents are 451.8 or 530.7 as chloride and 416.3 or 495.2 as cation.[4] The log P_{ow} values were estimated to be 1.12 for the main constituent and 1.12, 1.51, or 2.01 for the major constituents.

Method of Manufacture

Method of manufacturing data were not found in the published literature, and unpublished data were not submitted.

Composition and Impurities

According to a supplier, Basic Blue 99 must be at least 63% pure Basic Blue 99 in the color mixture and have no more than 100 ppm of iron.[2] *Another supplier of Basic Blue 99 has a specification of 60.7% dye content, 25.7% sugar content, 11.8% inorganic salts, and 1.8 % volatile matter/water crystallization. The majority of the additional contents of hair dye are understood as being part of the color and not undesirable chemical impurities.*

In the 2026 SCCS opinion, manufacturer submissions indicate that 4 batches of Basic Blue 99 were comprised of 13.3 - 31.2% identified impurities and 1.4 - 2.4% unidentified impurities.[4] Known constituents had the same molecular backbones and the following substituents: 8-amino-5-hydroxy-4-iminonaphthalen-1(4H)-one; 5-amino-8-hydroxynaphthalene-1,4-dione; 5-hydroxy-4-imionaphthalen-1(4H)-one; 3-amino-*N*,*N*,*N*-trimethylanilinium; bromide, chloride, and methyl. Additionally, trace heavy metals and anions for 4 batches of Basic Blue 99 were determined (Table 2). Ethylene glycol content was 71 - 7200 ppm.

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 99 in cosmetics. Registration and Listing Data (RLD) obtained from the FDA report frequency of use, and responses to a survey conducted by the Personal Care Products Council (Council) indicate maximum reported concentrations of use; it is these values that define the present practices of use and concentration that are assessed by the Panel. Since 2024, as a result of the Modernization of Cosmetics Regulation Act of 2022 (MoCRA), manufacturers and processors are required to register facilities and list their products (and ingredients therein) with the FDA (i.e., RLD). An exception is made for small businesses (average gross annual sales in the US of cosmetic products for the previous 3-yr period is less than $1,000,000, adjusted for inflation), which are exempt from MoCRA reporting for most cosmetic product categories. Eye area products, injected products, internal use products, or products that alter appearance for more than 24 h, and the facilities that manufacture these products, are not included in this exemption.[6] Another change resulting from MoCRA is the addition of tattoo preparations (permanent tattoo inks, temporary tattoo inks, and other tattoo products) to the product categories for which companies need to list their products with FDA. However, evaluating the safety of ingredients as used in tattoo preparations is not within the purview of the Panel; accordingly, such use is not included as part of the present practices of use that are assessed by the Panel.

According to RLD obtained from the FDA in 2025, Basic Blue 99 is reported in 856 formulations, with the majority of the uses reported in hair coloring preparations (246 in hair dyes and colors, 121 in hair tints, and 226 hair rinses; Table 3).[7,8] RLD also indicate that Basic Blue 99 is used in non-coloring hair preparations (78 formulations) and 1 use in a rinse-off personal cleanliness product. The results of the concentration of use survey conducted by the Council in 2025 indicate Basic Blue 99 is used at up to 0.88% in hair dyes and colors.[9]

Following the passage of MoCRA, the FDA created a number of new product categories including, “(17) Other preparations (i.e., those preparations that do not fit another category)” (Category 17). CIR and the Panel utilize these product categories to inform, in part, the WoE in exposure and risk analyses. However, citation of Category 17, alone, as the product use category is uninformative. When a product is co-categorized with both Category 17 and one or more common product use categories (e.g., eye makeup preparations), or other information in the RLD such as the product name are indicative of use type (e.g., “lip balm” is part of the product name), then those uses are accounted for and may be considered to be part of the “the present practices of use” for those products; as such, the Panel’s safety conclusion may be inclusive thereon. Conversely, for instances wherein the use of an ingredient in a cosmetic product is only categorized as Category 17 and other information in the RLD is not indicative of use type, the present practices of use for these products remain unknown and the Panel’s safety assessment conclusion, therefore, does not apply thereon.

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.

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.

However, according to the RLD, Basic Blue 99 has been reported to be used in non-coloring hair preparations and a personal cleanliness product. Basic Blue 99 is exempt from certain adulteration and color additive provisions of the FD&C Act only when used as coal tar hair dye ingredients. With regard to the reported use in non-coloring hair preparations and personal cleanliness products, the FD&C Act mandates that color additives must be approved by FDA for their intended use before they are used. Basic Blue 99 is not approved as a color additive in non-hair dye cosmetic products, and thereby, use in non-coloring hair preparations and personal cleanliness products is not permitted.

Basic Blue 99 is reported to be used in hair color sprays (concentration not reported) and could possibly be inhaled. 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).

It is possible that some products containing Basic Blue 99 may be marketed for use with airbrush delivery systems. With the advent of MoCRA and the current product categories outlined therein, 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 indicating airbrush application, so it is possible that this ingredient is used with airbrush delivery systems, but not reported as such. Additionally, concentration of use surveys are conducted based on product categories as stated in the RLD, but airbrush use was not reported in response to the survey. No consumer habits and practices data or particle size data are publicly available to evaluate the exposure associated with airbrush technology, 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. If this ingredient was to be used in airbrush formulations, the data are insufficient to evaluate the exposure resulting from cosmetics applied in such a manner.

In the European Union (EU), the 2026 opinion by the SCCS stated that the committee does not consider the use of Basic Blue 99 safe for use as an ingredient in non-oxidative hair dye formulations when used at 1% because the collective evidence indicates a potential for genotoxicity.[4] Additionally, the SCCS regards Basic Blue 99 as a skin sensitizer. The SCCS noted throughout its opinion that many of the studies provided were not representative of the material specifications outlined in the current submission.

TOXICOKINETIC STUDIES

Skin Penetration/Dermal Absorption

In rat studies of aqueous solutions of [^{14}C] labeled Basic Blue 99 (up to 1%) to assess skin penetration potential, most of the test material was recovered in rinse water, patches, or in the treated area of the skin.[2] Levels of this radiolabel were low in the urine and feces. It was determined there was very low percutaneous absorption of Basic Blue 99 in rats. In human volunteers treated topically (to hair) with a hair setting solution containing [^{14}C] labeled Basic Blue 99 (40% aqueous solution containing 0.1% of other dyes), levels of this radiolabel in the urine were less than 0.1% of the applied dose.

The percutaneous absorption of Basic Blue 99 (43.4% pure) in aqueous solution and a formulated cream material was determined using dermatomed pig skin samples (400 µm thick) mounted in glass diffusion cells.[4] Basic Blue 99 was tested at 1.09% w/w in both the aqueous solution and formulation. The aqueous solution was applied at 10 µl/cm^2 and the formulated solution was applied at 10 mg/cm^2, corresponding to109 µg/cm^2 of the test substance. The receptor fluid was 25% ethanol in physiologic saline solution. The test was performed in accordance with Organisation for Economic Co-operation and Development (OECD) test guideline (TG) 428. The penetration of Basic Blue 99 through the skin was below the limit of quantitation (0.004 µg/cm^2/h over 48 h = 0.2 µg/cm^2 or 0.18% of dose penetrated at 48 h) for both the aqueous solution and the formulation. The mean recovery was between 74 and 78% for the aqueous solution and between 75 and 79% for the formulation. The majority of the applied Basic Blue 99 was washed from the surface of the skin at 30 min (aqueous solution = mean 64.6%; formulation material = mean 70.5%). A further 4.37% and 3.28% of the dose from the respective test items

were removed from the surface during the terminal wash at 48 h. No Basic Blue 99 was recovered from the tape strips, representing stratum corneum (total < 3.25% of dose) for both the aqueous solution and formulation. Small amounts (mean 3.12% (standard deviation 3.68) aqueous solution and 0.549% (standard deviation 0.264) formulation) were recovered from the remaining epidermis/dermis. The manufacturer's submissions recommended using the percutaneous penetration values of 11.62 μg/cm^2 to the SCCS for the aqueous solution of Basic Blue 99 and 1.37 μg/cm^2 for the formulation with Basic Blue 99. However, the SCCS did not consider this study adequate as it was performed using a batch of material with 43.4% purity, but calculations were based on 100% purity. The SCCS also found limitations with testing materials (e.g., high ethanol content of the receptor fluid) and methods used.

Absorption, Distribution, Metabolism, and Excretion

Aqueous solutions of [^{14}C] labeled Basic Blue 99 were poorly absorbed when administered orally and intraperitoneally in rats.[2] *Most of the radiolabel was recovered in the feces within the first 24 h. The radiolabel was also recovered at lower quantities in the urine, and was barely detectable in expired air, blood, and carcass, when measured.*

TOXICOLOGICAL STUDIES

Acute Toxicity Studies

In acute oral toxicity studies, the median lethal dose (LD_{50}) values of Basic Blue 99 were 2700 mg/kg bw in mice and between 1000 mg/kg bw and greater than 2000 mg/kg bw in rats.[2]

Additional acute toxicity studies were not found in the updated literature search, and unpublished data were not submitted.

Subchronic Toxicity Studies

In a subchronic study, mice (10 per dose group) that received Basic Blue 99 at up to 500 mg/kg bw/d in the diet for 90 d did not give any indications of cumulative toxicity.[2] *No deaths occurred. Discoloration of organs involved in the elimination of Basic Blue 99 from the animals was noted. A 90-d oral toxicity study of rats (10 animals per sex per dose group) that received up to 360 mg/kg bw Basic Blue 99 via gavage also found no indications of cumulative toxicity. The no-observable-effect-level (NOEL) was between 180 to 360 mg/kg bw/d (range due to an increase in the dose after 8 wk).*

In a 90-d oral toxicity study, groups of 10 male and 10 female SPF bred Wistar rats received 0, 10, 60, or 240 mg/kg bw/d Basic Blue 99 (62.8% pure) in water via gavage (10 mg/kg daily).[4] An additional 5 rats per sex were treated at the same doses for a 4-wk recovery period after the initial 13-wk treatment period concluded. Rats were checked daily for mortality and clinical signs of toxicity. The rats were also checked for body weight gains and feed consumption. Ophthalmology examination, hematological and clinical chemistry studies, and urinalysis were also conducted. Rats were killed for necropsy and histopathological study at the end of treatment and recovery periods.

No deaths occurred during the treatment period. Daily and weekly clinical observations were restricted to stained blue urine and feces associated with the blue color of the test material. No relevant changes were noted with grip strength or motor activity. Body weights and feed consumption were unaffected. There were no ophthalmological findings. Minimal to slight changes to red blood cell parameters, granulocytes, and large unstained cells were noted. Additionally, minimal to slightly lower concentrations of glucose, urea, and creatinine were noted, but determined to be not relevant. A minimal disturbance to the electrolyte (or water) balance in 60 and 240 mg/kg bw/d animals was substantiated by higher sodium, calcium, and chloride concentrations. In females, there was only a minimal, reversible, increase of the chloride concentration. A change in phosphate concentration was noted in 60 and 240 mg/kg bw/d animals (males increased, female decreased) with a poor dose relationship. This finding, which persisted to the end of the recovery period in high-dose males, was considered of equivocal toxicological relevance. At necropsy, the absolute and relative mean organ weights were not affected, and macroscopic changes were restricted to bluish discoloration in the stomach in 60 and 240 mg/kg/d males and 240 mg/kg/d females. At the end of the recovery period, an accentuated lobular pattern was noted in all 240 mg/kg/d males. Microscopically, there were no changes of toxicological relevance to the morphology of tissue and organs. The no-observed-effect level (NOEL) for Basic Blue 99 in this study could not be established. The no-observed-adverse-effect level (NOAEL) was determined to be 60 mg/kg bw/d for males and females, but due to the material being only 62.8% pure, the NOAEL value was re-calculated to be 37 mg/kg bw/d.[4]

DEVELOPMENTAL AND REPRODUCTIVE TOXICITY STUDIES

Basic Blue 99 (50 mg/kg/d) administered by gavage did not cause embryotoxic or teratogenic effects in 29 rats.[2] *No mortalities were observed in the dams that had been treated on days 6 through 15 of gestation and no cumulative toxicity was observed.*

The developmental toxicity potential of Basic Blue 99 (62.8% pure) was assessed in groups of 25 female SPF-bred Han Wistar rats treated on gestation days 6 - 20 in a study performed in accordance with OECD TG 414.[4] The rats received 0, 60, 200, or 500 mg/kg bw/d of the test material dissolved in distill water via gavage. Maternal clinical signs of toxicity, feed consumption, and body weight gain were monitored. Dams were killed on gestation day 21. The number of corpora lutea, live and dead fetuses, implantations, and resorptions were recorded. Uterus and fetal weights were also recorded, as were any external abnormalities Half of the fetuses were examined for soft-tissue abnormalities and half for skeletal abnormalities.

One non-treatment-related maternal death was observed in a rat in the 500 mg/kg bw/d group on day 11. Black feces, due to the content of the test material, were observed in all animals of the 200 and 500 mg/kg bw/d dose groups starting on day 7. No treatment-related effects were noted in body weight gains and feed consumption. No adverse effects were observed in the relevant reproduction parameters. At necropsy, all treated animals had a bluish discoloration of the organs. The sex ratio of fetuses was near 50/50. Statistically significant increases in mean body weights were calculated in the high dose group male and female fetuses. No adverse effects were observed in external and visceral examinations, and no skeletal or cartilage abnormalities were observed. A statistically significant decrease in incidences of non-ossified talus and non-ossified cervical vertebral body were observed in the 500 mg/kg bw/d in both individual and litter basis. The NOAEL for embryo/fetal toxicity was 200 mg/kg bw/d (due to the purity of the test substance, the NOAEL value was re-calculated to 125.8 mg/kg bw/d) and the NOEL for embryo/fetal toxicity was 60 mg/kg bw/d. No teratological or embryo lethal effects were observed at up to 500 mg/kg bw.[4]

GENOTOXICITY STUDIES

Some genotoxicity assays are no longer considered appropriate as standard methods for evaluating genotoxic potential under current OECD guidance. (See https://www.cir-safety.org/cir-findings for details.) Although these assays may be reported in the published literature, unpublished reports, or data submissions, the results from these assays are of limited interpretability and therefore the studies are not summarized herein.[2,4]

Basic Blue 99 (tested at up to 2500 µg/plate) was mutagenic with and without metabolic activation in the Ames test using Salmonella typhimurium, producing both reverse and frameshift mutations.[2] *However, Basic Blue 99 did not induce mutations using Escherichia coli at up to 100 µg/ml. Basic Blue 99 was not genotoxic in one chromosome aberration test in Chinese hamster V79 cells when tested in dimethyl sulfoxide (DMSO) at up to 10 µg/ml without metabolic activation and at up to 250 µg/ml with metabolic activation; however, this ingredient was considered to be clastogenic with or without metabolic activation in another chromosome aberration test in the same cell system using a deionized water vehicle and at doses up to 1.5 µg/ml without metabolic activation and up to 45.0 µg/ml with metabolic activation. Basic Blue 99 was not genotoxic in micronucleus assays using mouse bone marrow cells (at up to 1500 mg/kg bw).*

Additional genotoxicity data are summarized in Table 4. In in vitro gene mutation studies, Basic Blue 99 (62.8% pure for one study and tested as received in another study) was mutagenic with and without metabolic activation in Ames tests with *S. typhimurium* cells when tested at up to 5000 µg/plate.[4] Basic Blue 99 (62.8% pure; tested at up to 40 µg/ml with and without metabolic activation at up to 24 h exposure) was not mutagenic in a gene mutation assay at the *tk* locus of L5178Y mouse lymphoma cells by the study authors, but the SCCS noted equivocal mutagenic effects. No mutagenicity was observed to Basic Blue 99 (69.5% pure; tested at up to 30 µg/ml with metabolic activation and 11 µg/ml without metabolic activation) in gene mutation assay at the hprt locus of L5178Y mouse lymphoma cells. In studies of chromosomal damage, Basic Blue 99 (62.8% pure) induced a clear increase in the number of micronuclei when tested at up to 300 µg/ml with metabolic activation and up to 50 µg/ml without metabolic activation in a micronucleus assay using V79 cells. Chromosomal damage was not observed in an in vivo micronucleus induction test in mice at up to 5 mg/kg bw Basic Blue 99 (62.8% pure) via intraperitoneal injection.

CARCINOGENICITY STUDIES

Carcinogenicity studies were not included in the original report and were not found in the updated literature search, and unpublished data were not submitted.

DERMAL IRRITATION AND SENSITIZATION

Irritation

Undiluted Basic Blue 99 (0.5 g/in^2) produced no observable reactions in one 24-h dermal irritation study with 6 rabbits, but was considered mildly irritating in another study with 6 rabbits.[2] *The primary irritation index in the second study was calculated to be 0.2.*

In Vitro

In an evaluation of an equivalent human epidermis (EHE) three-dimensional (3D) model that utilized immortalized keratinocytes (HaCaT cells), the potential toxic effects induced by Basic Blue 99 (> 63% pure) were studied and compared to those observed in monolayer cultured cells.[12] Comet assay results indicated Basic Blue 99 (up to 35 µg/ml) did not induce DNA damage in the monolayer cell culture nor in the 3D cell culture. To measure cell viability, the 3-[4,5-dimethylthiazol-2-yl]-2,5 diphenyl tetrazolium bromide (MTT) assay (Basic Blue 99 tested at up to 50 µg/ml) and the terminal deoxynucleotidyl transferase dUTP nick-end labeling (TUNEL) assay (Basic Blue 99 tested at up to 500 µg/ml) were performed in monolayer culture and in the EHE model, respectively. Basic Blue 99 had more pronounced necrotic death in monolayer cultures, while apoptosis was observed in a 3D environment. Based on the data generated from the EHE 3D model, the authors stated a decrease in the keratinocytes viability was expected after human dermal exposure to Basic Blue 99, which could result in dermal irritation. However, it should be noted this study was published before the OECD TG 439 on reconstructed human epidermis 3D models was finalized. The study does not meet the OECD TG requirements as the

viability measurement was performed within the incorrect timeframe with inadequate cell incubation time and the wrong assay was used to measure cell viability.

Animal

The potential for dermal irritation by Basic Blue 99 (50.2% pure) was studied in 1 male and 2 female New Zealand White rabbits in accordance with OECD TG 404.[4] The undiluted test material was applied (0.5 g) under semi-occlusion to the intact left flank of each animal for 4 h. Scoring for skin reactions was performed 1, 24, 48, and 72 h after removal of the dressing, as well as 7, 10, and 14 d later. The mean erythema/eschar score and the mean edema score was 0 for all 3 animals. No signs of irritation were observed; however, slight blue staining was observed in all animals from the 1 h reading to 14 d after treatment. No corrosive effects were noted and no clinical signs were observed. Basic Blue 99 was considered to be not irritating to rabbit skin.

Sensitization

No delayed contact hypersensitivity was observed in a guinea pig maximization test (n = 10) of aqueous Basic Blue 99 induced at 75 % and challenged at 25%.[2] *In a local lymph node assay (LLNA) using groups of 4 mice, Basic Blue 99 was not considered sensitizing when tested at up to 25% in twice-distilled water; however, in another study using groups of 5 mice, Basic Blue 99 may induce sensitization when tested at up to 2.0% in DMSO. The results of the latter assay had responses statistically significantly greater than the vehicle control, but no test/control ratios were greater than 3. A positive response was also observed in the 0.25% group, but the difference was not statistically significant when compared to the vehicle control. No irritation was observed in the mice treated with the test material in these LLNAs. Basic Blue 99 (concentration not reported) was not a sensitizer in a modified repeated-insult patch test in 54 volunteers.*

Additional sensitization studies were not found in the updated literature search, and unpublished data were not submitted.

OCULAR IRRITATION STUDIES

Basic Blue 99 (0.5%) did not cause ocular irritation in 3 rabbits.[2] *Discoloration was noted.*

In an ocular study, undiluted Basic Blue 99 (50.2% pure; 0.1 g) was place in the conjunctival sac of the left eye of a single New Zealand White rabbit.[4] The right eye served as an untreated control. Both eyes were rinsed with tap water after 24 h. The eyes were examined 24, 48, and 72 h after application. No clinical signs were observed. Staining from the test material prevented assessment of the reddening of the conjunctivae and sclera throughout the observation period, and staining made assessment of the cornea and iris not possible 1 and 24 h after treatment. Marked opacity, affecting the whole area, as well as an absent light reflex was noted in the eye at 48- and 72 h. The individual mean score for corneal opacity was 3.00 and the maximum score for the iris was 2.00. The individual mean score for chemosis was 3.67. The study was closed due to the results in the 1 animal, and possible corrosion could not be determined. The SCCS determined that an eye irritant effect from the test material could not be ruled out.

CLINICAL STUDIES

Case Reports

Case reports have documented positive patch test results to 1% Basic Blue 99 in 3 patients.[2] *One of the patients presented with an immediate reaction, while the other two were delayed.*

Several cases of adverse reactions to hair dye products containing Basic Blue 99 have been reported in the published literature and are summarized in Table 5.[13-17] In addition to reports of dermal reactions that have been summarized, a case study review of contact urticaria cases related to cosmetic and industrial dyes included a discussion regarding Basic Blue 99.[18] A case study summarized in the original CIR safety assessment of Basic Blue 99 was analyzed to further categorize the adverse reaction observed as a potential immunologic contact urticaria instead of a general contact urticaria. The authors noted that dyes like Basic Blue 99 may have multiple impurities, whose immunogenicity has not been studied.

RISK ASSESSMENT

Margin of exposure (MOE) is a quantitative factor calculated for cosmetic ingredients by dividing the NOAEL obtained for an ingredient in an animal experiment by the estimated systemic exposure dose (SED) for the ingredient in humans, generally according to US Environmental Protection Agency (EPA) and European Commission SCCS guidelines. The standard MOE value of 100 is derived from multiplying two factors: a 10-fold factor extrapolating data from test animals to human being (interspecies extrapolation) and an additional 10-fold for differences among the human population (intra-species extrapolation). An MOE value greater than 100 has traditionally been considered an indication of safety. The MOE is sometimes referred to as margin of safety (MOS), despite the parameters being definitionally different.

The manufacturer's submissions to the SCCS review provided a calculated MOE value for Basic Blue 99 under non-oxidative conditions in a formulation of 1353.[4] This calculation is based on an adjusted NOAEL of 18 mg/kg bw/d (a 90-d oral rat study; adjust for 50% bioavailability) and an SED of 0.0133 mg/kg bw/d (skin area surface of 580 cm^2 x absorption

through skin of 1.37 μg/cm^2 x 0.001 (unit conversion)/typical human bw of 60 kg). The skin absorption value was estimated from a mean value of 0.8 μg/cm^2 + 2 standard deviations.

The manufacturer's submissions also provided a calculated MOE value for Basic Blue 99 under non-oxidative conditions in aqueous solution of 160.[4] This calculation used the same adjusted NOAEL of 18 mg/kg bw/d and an SED of 0.1123 mg/kg bw/d, this time using a skin absorption value of 11.62 μg/cm^2 (an absorption value of 3.6 μg/cm^2 + 2 standard deviations). The SCCS reported that it could not calculate its own value due to the toxicological data not fully corresponding to the materials specifications provided to the committee and due to concerns of the genotoxicity potential.

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 Blue 99 is reported to be used in direct 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 Blue 99 is reported to function in cosmetics as a hair colorant and a hair conditioning agent. Basic Blue 99 was previously reviewed by the Panel in a safety assessment that was published in 2007. At that time, the Panel concluded that Basic Blue 99 was safe for use as a hair dye ingredient. In accordance with its Procedures, the Panel evaluates the conclusions of previously-issued reports approximately every 15 years, and it has been at least 15 years since this assessment has been issued. In December 2022, the Panel determined that this safety assessment should be re-opened for re-evaluation due to concerns regarding the variability of the composition of the ingredient. In submissions to the SCCS, Basic Blue 99 is comprised of a main naphthoquinoneimine and 4 other major constituents, including a regio isomer of the main naphthoquinoneimine and 3 different dibrominated analogues. The 2 mono-brominated analogues comprise more than 50% this ingredient, while the 3 dibrominated analogues variably comprise approximately another 30%.

According to RLD obtained from the FDA in 2025, Basic Blue 99 is reported in 856 formulations, with the majority of the uses reported in hair coloring preparations (246 in hair dyes and colors, 121 in hair tints, and 226 hair rinses). RLD also indicate that Basic Blue 99 is used in non-coloring hair preparations (78 formulations) and 1 use in a rinse-off personal cleanliness product. With regard to the reported use in non-coloring hair preparations and personal cleanliness products, the FD&C Act mandates that color additives must be approved by FDA for their intended use before they are used. Basic Blue 99 is not approved as a color additive in non-hair dye cosmetic products, and thereby, use in non-coloring hair preparations and personal cleanliness products is not permitted. The results of the concentration of use survey conducted by the Council in 2025 indicate Basic Blue 99 is used at up to 0.88% in hair dyes and colors.

In the EU, the most recent opinion by the SCCS stated that the committee does not consider the use of Basic Blue 99 safe for use as an ingredient in non-oxidative hair dye formulations when used at 1% because the collective evidence indicates a potential for genotoxicity. Additionally, the SCCS regards Basic Blue 99 as a skin sensitizer. The SCCS noted throughout its opinion that many of the studies provided were not representative of the material specifications outlined in the current submission.

In a percutaneous absorption using dermatomed pig skin samples mounted in glass diffusion cells, Basic Blue 99 (43.4% pure) was tested at 1.09% w/w in both the aqueous solution and formulation. The penetration of Basic Blue 99 through the skin was below the limit of quantitation for both the aqueous solution the formulation. The mean recovery was between 74 and 78% for the aqueous solution and between 75 and 79% for the formulation. The majority of the applied Basic Blue 99 was washed from at surface of the skin at 30 min. Small amounts of Basic Blue 99 in both test items were recovered from the remaining epidermis/dermis. The manufacturer's submissions to the SCCS recommended using the percutaneous penetration values of 11.62 μg/cm^2 for the aqueous solution of Basic Blue 99 and 1.37 μg/cm^2 for the formulation with Basic Blue 99. However, the SCCS did not consider this study adequate as it was performed using a batch of material with 43.4% purity and used calculations based on 100% purity. The SCCS also found limitations with materials and methods used.

An NOEL for Basic Blue 99 (62.8% pure) could not be established in a 90-d study in rats that received 0, 10, 60, or 240 mg/kg bw/d in water via gavage. The NOAEL was determined to be 60 mg/kg bw/d for males and females, but due to the material being only 62.8% pure, the NOAEL value was re-calculated to be 37 mg/kg bw/d. A minimal disturbance to the electrolyte (or water) balance in 60 and 240 mg/kg bw/d animals was substantiated by higher sodium, calcium, and chloride concentrations. In females, there was only minimal reversible increase of the chloride concentration. A change in phosphate concentration was noted in 60 and 240 mg/kg bw/d animals (males increased, female decreased) with a poor dose relationship. This finding persisting to the end of the recovery period in high dose males was considered of equivocal toxicological relevance. At the recovery end, accentuated lobular pattern was noted in all 240 mg/kg/d males.

In a developmental toxicity study in rats that received 0, 60, 200, or 500 mg/kg bw/d Basic Blue 99 (62.8% pure), the NOAEL for embryo/fetal toxicity was 200 mg/kg bw/d (due to the purity of the test substance, the NOAEL value was re-calculated to 125.8 mg/kg bw/d) and the NOEL for embryo/fetal toxicity was 60 mg/kg bw/d. No teratological or embryo lethal effects were observed at up to 500 mg/kg bw.

In in vitro gene mutation studies, Basic Blue 99 (62.8% pure in one study and as received in another study) was mutagenic with and without metabolic activation in Ames tests with *S. typhimurium* cells when tested at up to 5000 µg/plate. Basic Blue 99 (62.8% pure; tested at up to 40 µg/ml with and without metabolic activation at up to 24 h exposure) was not mutagenic in a gene mutation assay at the *tk* locus of L5178Y mouse lymphoma cells by the study authors, but the SCCS noted equivocal mutagenic effects. No mutagenicity was observed to Basic Blue 99 (69.5% pure; tested at up to 30 µg/ml with metabolic activation and 11 µg/ml without metabolic activation) in gene mutation assay at the hprt locus of L5178Y mouse lymphoma cells. In studies of chromosomal damage, Basic Blue 99 (62.8% pure) induced a clear increase in the number of micronuclei when tested at up to 300 µg/ml with metabolic activation and up to 50 µg/ml without metabolic activation in a micronucleus assay using V79 cells. Chromosomal damage was not observed in an in vivo micronucleus induction test in mice at up to 5 mg/kg bw Basic Blue 99 (62.8% pure) via intraperitoneal injection.

The utility of the EHE 3D model was studied using Basic Blue 99 (> 63% pure). In this study, Basic Blue 99 had more pronounced necrotic death in monolayer cultures, while apoptosis was observed in a 3D environment. Based on the data generated from the EHE 3D model, the authors stated a decrease in the keratinocytes viability was expected after human dermal exposure to Basic Blue 99, which could result in dermal irritation. (It should be noted that this study was published before the OECD TG on reconstructed human epidermis 3D models was finalized, and it does not meet the OECD TG requirements.) Case reports concerning reactions to Basic Blue 99 in hair dye formulations have been described in published literature.

In a dermal irritation study, undiluted Basic Blue 99 (50.2% pure) was considered to be not irritating to rabbit skin. No corrosive effects were noted and no clinical signs were observed. An ocular study of undiluted Basic Blue 99 (50.2% pure) was limited to one rabbit after marked opacity, affecting the whole area, as well as an absent light reflex was noted. Staining from the material made assessment of ocular effects difficult. Possible corrosion could not be determined and the SCCS determined that an eye irritant effect from the test material could not be ruled out.

Several cases of adverse reactions to hair dye products containing Basic Blue 99 have been reported. In addition to reports of dermal reactions, a case study review of contact urticaria cases related to cosmetic and industrial dyes included a discussion regarding Basic Blue 99. A case study summarized in the original CIR safety assessment of Basic Blue 99 was analyzed to further categorize the adverse reaction observed as a potential immunologic contact urticaria instead of a general contact urticaria. The authors noted that dyes like Basic Blue 99 may have multiple impurities, whose immunogenicity has not been studied.

Manufacturer submissions to the SCCS review provided a calculated MOE value for Basic Blue 99 under non-oxidative conditions in a formulation of 1353. This calculation is based on an adjusted NOAEL of 18 mg/kg bw/d and an SED of 0.0133 mg/kg bw/d. The skin absorption value was estimated from a mean value of 0.8 $\mu g/cm^2$ + 2 standard deviations. In an additional calculation, the MOE value for Basic Blue 99 under non-oxidative conditions in aqueous solution was 160. This calculation used the same adjusted NOAEL of 18 mg/kg bw/d and an SED of 0.1123 mg/kg bw/d, this time using a skin absorption value of 11.62 $\mu g/cm^2$ (an absorption value of 3.6 $\mu g/cm^2$ + 2 standard deviations). The SCCS reported that it could not calculate its own value due to the toxicological data not fully corresponding to the materials specifications provided to the committee and due to concerns of the genotoxicity potential.

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.

Method of manufacturing data and carcinogenicity studies on Basic Blue 99 were not included in the original safety assessment and were not found in an updated search of the published literature, and unpublished data were not submitted.

DISCUSSION

In accordance with its Procedures, the Panel re-evaluates the conclusions of previously-issued reports approximately every 15 years. In 2007, the Panel first published a final report on Basic Blue 99 and concluded that this ingredient was safe as a hair dye ingredient. The Panel considered a re-review of this ingredient at the December 2022 meeting and re-opened the report due to concerns regarding the variability of the composition of this ingredient. In this amended report, the Panel reviewed the safety of Basic Blue 99 in accordance with the product categories and concentrations of use identified in the Use section and Use table, concluded that the available data are insufficient for determining the safety of this ingredient under the intended conditions of use as a hair dye ingredient.

The Panel noted a lack of relevant data and determined that the data needs from the Insufficient Data Announcement issued following the March 2023 Panel meeting remain unmet. In order to come to a conclusion of safety for this ingredient, the following additional data are needed:

- Method of manufacturing
- Composition and impurities data
    - Depending on the results of these data, additional information on toxicological endpoints may be needed (e.g. dermal absorption data)

In the absence of adequate characterization of the composition and impurity profile of the Basic Blue 99 materials used in the dermal absorption and toxicological studies described in this report, the Panel cannot determine whether these studies are applicable to the material currently used in hair coloring formulations. The Panel also noted genotoxic concerns for Basic Blue 99, including positive Ames tests and positive in vitro chromosomal damage findings, specifically chromosome aberration and micronucleus assays in Chinese hamster V79 cells. Although some in vivo genotoxicity studies were negative, the Panel considered the overall weight-of-evidence difficult to interpret because of uncertainty regarding the representativeness of the tested batches. A dermal absorption study conducted with Basic Blue 99 material representative of that currently used in hair coloring formulations is needed to support estimation of systemic exposure and to inform the assessment of threshold-based systemic toxicity endpoints.

The Panel noted that urticarial reactions were observed in several case reports related to Basic Blue 99 exposure. The Panel considered these reports to be relevant to the sensitization profile of this ingredient, particularly because the immunogenicity of some impurities or accompanying constituents may not be fully characterized. The Panel recognizes that coal tar hair dye ingredients are exempt from certain provisions of the 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.

Additionally, Basic Blue 99 has been reported to be used in non-coloring hair preparations and a personal cleanliness product. This ingredient is exempt from certain adulteration and color additive provisions of the FD&C Act ***only*** when used as a coal tar hair dye ingredient. Accordingly, because Basic Blue 99 is not an approved color additive in cosmetics products, use in non-coloring hair preparations and personal cleanliness products is not permitted in the U.S.

Furthermore, at least 1 use for the ingredient assessed in this assessment is reported in the RLD under Category 17, "other preparations." For instances wherein the use of an ingredient in a cosmetic product is only categorized as Category 17, and other information in the RLD is not indicative of use type, the present practices of use for such products remain unknown and the Panel's safety assessment conclusion, therefore, does not apply thereon.

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. Inhalation toxicity data were not available. However, the Panel noted that the majority of droplets/particles would not be respirable to any appreciable amount. Furthermore, droplets/particles deposited in the nasopharyngeal or tracheobronchial regions of the respiratory tract present no toxicological concerns based on the chemical and biological properties of these ingredients. Coupled with the small actual exposure in the breathing zone and the low concentrations at which this 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.

CONCLUSION

The Expert Panel for Cosmetic Ingredient Safety concluded that the available data are insufficient to make a determination of safety for Basic Blue 99 under the intended conditions of use as a hair dye ingredient.

TABLES

Table 1. Chemical properties

Property	Value	Reference
	Basic Blue 99 - General	
Physical Form	Blue-black fine powder	4
Odor	Odorless	2
Density (g/ml @ 20 ºC) (g/ml, no temperature reported)	2.19 1.71	3 4
Vapor pressure (mmHg)	1.965×10^{-19} (estimated)	3
Melting Point (ºC)	300 – 320 > 200	2 4
Boiling Point (ºC)	724.99 (estimated)	3
Water Solubility (g/l)	1.37 (estimated) 10-100 (20 ºC)	3 4
Other Solubility (g/l @ 20 ºC)	Ethanol: 1-10 DMSO: 1-10	4
log K_{ow}	-0.88 (estimated)	3
UV Absorption Maximums (λ_{max}; nm)	268/269, 578/576, 620/616 for 2 different batches	2
	Main Constituent ***3-[(4-amino-6-bromo-5,8-dihydro-1-hydroxy-8-imino-5-oxo-2-naphtyl)amino]-N,N,N-trimethylanilinium chloride***	
Formula Weight (g/mol)	451.8 (as chloride) 416.3 (as cation)	4
Vapor pressure (mmHg @ 25 ºC)	1.97×10^{-19} (MPBPVP v1.43 estimate)	19
Melting Point (ºC)	325.32 (MPBPVP v1.43 estimate)	19
Boiling Point (ºC)	741.32 (MPBPVP v.143 estimate)	19
Water Solubility (g/l @ 25 ºC	8.23 (WSKOW v.142 estimate)	19
log P_{ow}	1.12 (KOWWIN v1.68 estimate) -0.88 (for salt: KOWWIN v.168 estimate)	4 19
	3-((8-amino-7-bromo-5-hydroxy-4-imino-1-oxo-1,4-dihydronaphthalen-2-yl)amino)-N,N,N-trimethylbenzenaminium chloride	
Formula Weight (g/mol)	451.8 (as chloride) 416.3 (as cation)	4
Vapor pressure (mm Hg @ 25 ºC)	1.97×10^{-19} (MPBPVP v1.43 estimate)	19
Melting Point (ºC)	325.32 (MPBPVP v1.43 estimate)	19
Boiling Point (ºC)	741.32 (MPBPVP v.143 estimate)	19
Water Solubility (g/l @ 25 ºC)	8.23 (WSKOW v.142 estimate)	19
log P_{ow}	1.12 (KOWWIN v1.68 estimate) -0.88 (for salt; KOWWIN v.168 estimate)	4 19
	3-((8-amino-3,7-dibromo-5-hydroxy-4-imino-1-oxo-1,4-dihydronaphthalen-2-yl)amino)-N,N,N-trimethylbenzenaminium chloride	
Formula Weight (g/mol)	530.7 (as chloride) 495.2 (as cation)	4
Vapor pressure (mm Hg @ 25 ºC)	1.61×10^{-20} (MPBPVP v1.43 estimate)	19
Melting Point (ºC)	339.67 (MPBPVP v1.43 estimate)	19
Boiling Point (ºC)	772.02 (MPBPVP v.143 estimate)	19
Water Solubility (g/l @ 25 ºC)	0.447 (WSKOW v.142 estimate)	19
log P_{ow}	2.01 (KOWWIN v1.68 estimate) 0.01 (for salt: KOWWIN v.168 estimate	4 19
	3-((8-amino-3,7-dibromo-5-hydroxy-4-imino-1-oxo-1,4-dihydronaphthalen-2-yl)amino)-N,N,N trimethylbenzenaminium chloride	
Formula Weight (g/mol)	530.7 (as chloride) 495.2 (as cation)	4
Vapor pressure (mm Hg @ 25 ºC)	1.61×10^{-20} (MPBPVP v1.43 estimate)	19
Melting Point (ºC)	339.67 (MPBPVP v1.43 estimate)	19
Boiling Point (ºC)	772.02 (MPBPVP v.143 estimate)	19
Water Solubility (g/l @ 25 ºC)	0.447 (WSKOW v.142 estimate)	19
log P_{ow}	2.01 (KOWWIN v1.68 estimate) 0.01 (for salt; KOWWIN v.1.68 estimate)	4 19
	3-((8-amino-6,7-dibromo-5-hydroxy-4-imino-1-oxo- 1,4-dihydronaphthalen-2-yl)amino)-N,N,N-trimethylbenzenaminium chloride	
Formula Weight (g/mol)	530.7 (as chloride) 495.2 (as cation)	4
Vapor pressure (mm Hg @ 25 ºC)	9.88×10^{-21} (MPBPVP v1.43 estimate)	19
Melting Point (ºC)	342.43 (MPBPVP v1.43 estimate)	19
Boiling Point (ºC)	777.94 (MPBPVP v.143 estimate)	19
Water Solubility (g/l @ 25 ºC)	1.19 (WSKOW v.142 estimate)	19
log P_{ow}	1.51 (KOWWIN v1.68 estimate) -0.49 (for salt; KOWWIN v.1.68 estimate)	4 19

Table 2. Anion (%) and heavy metal (ppm) content of Basic Blue 99[4]

Measured Impurity	Range for 4 Batches
Chloride	17.2 - 23.1
Sulfate	trace - 0.53
Antimony	0 - <1
Arsenic	0 - <1
Barium	0 - 1
Cadmium	0 - <1
Chromium	0 - 39
Cobalt	0 - <1
Copper	0 - 18
Iron	14 - 6900
Lead	0 - 2
Manganese	0 - 3
Mercury	0 - 1
Nickel	0 - 5
Selenium	0
Zinc	33,100 - 66,250

Table 3. Frequency and concentration of use of Basic Blue 99 according to likely duration and exposure and by product category

	# of Uses RLD (2025)[7,8]	Max Conc of Use % (2025)[9]
Totals*	**856**	**0.01-0.88**
summarized by likely duration and exposure**		
Duration of Use		
Leave-On	*30*	*NR*
Rinse-Off	*874*	*0.01-0.88*
Diluted for (Bath) Use	*NR*	*NR*
Unknown	*19*	*NR*
Exposure Type		
Baby Products	NR	NR
Children's Makeup	NR	NR
Eye Area	NR	NR
Incidental Ingestion	NR	NR
Mucous Membrane	1	NR
Incidental Inhalation-Spray	6; 166[a]; 20[b]	NR
Incidental Inhalation-Airbrush	NR	NR
Incidental Inhalation-Powder	20[b]	NR
Dermal Contact	1	NR
Deodorant (underarm)	NR	NR
Hair - Non-Coloring	78	NR
Hair-Coloring	830	0.01-0.88
Nail	NR	NR
Other Preparations (Unknown Exposure Type)	19	NR
as reported by product category		
Hair Preparations (non-coloring)		
Hair Conditioners	1 (l.o.); 19 (r.o.)	NR
Hair Straighteners	3	NR
Rinses (non-coloring)	2	NR
Shampoos (non-coloring)	11 (r.o.)	NR
Tonics, Dressings, and Other Hair Grooming Aids	8	NR
Other Hair Preparations	4 (l.o.); 30 (l.o.)	NR
Hair Coloring Preparations		
Hair Dyes and Colors (all types requiring caution statements and patch tests)	246	0.013-0.88
Hair Tints	121	0.3
Hair Rinses (coloring)	3 (l.o.); 223 (r.o.)	0.01-0.062 (r.o.)
Hair Shampoos (coloring)	84 (r.o.)	NR
Hair Color Sprays (aerosol)	6	NR
Hair Lighteners with Color	3	NR
Other Hair Coloring Preparation	8 (l.o.); 136 (r.o.)	NR
Personal Cleanliness		
Other Personal Cleanliness Products	1 (r.o.)	NR
Other Preparations (i.e., those preparations that do not fit another category)	19	NR

NR – not reported

l.o. – leave-on; r.o. – rinse-off

*The sum of the counts given for duration of use and by exposure type, and the sum of the frequency reported by product category, may not equal the sum of total uses because each ingredient may be used in cosmetic formulations that are reported under more than one product category.

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

[a] It is possible these products are sprays, but it is not specified whether the reported uses are sprays.

[b] Not specified whether a spray or a powder, but it is possible the use can be as a spray or a powder, therefore the information is captured in both categories

Table 4. Genotoxicity studies

Test Article	Vehicle	Concentration/Dose	Test System	Protocol	Results	Reference
IN VITRO						
Gene Mutation						
Basic Blue 99, 62.8% pure	DMSO	up to 1000 µg/plate	*S. typhimurium* strains TA98, TA100, TA102, TA1535, TA1537	Ames test with and without metabolic activation in accordance with OECD TG 471	Mutagenic. An increase in the number of revertant colonies with a dose-effect relationship was noted with and without metabolic activation in strains TA 98, TA100, TA 1537. For strains TA 100 and TA1537, mutagenic potential was determined only at concentration where cytotoxicity and/or precipitate could be observed as well.	[4]
Basic Blue 99, tested as received	water	up to 5000 µg/plate with (TA100 and TA102) and without metabolic activation (TA102); up to 2500 µg/plate with (TA1535 and TA1537) and without metabolic activation (TA98 and TA100; up to 1250 µg/plate without metabolic activation (TA1535 and TA1537)	*S. typhimurium* strains TA98, TA100, TA102, TA1535, TA1537	Ames test with and without metabolic activation in accordance with OECD TG 471	Mutagenic. A significant increase (≥ 2- or 3-fold) in revertant numbers was observed in strains TA98, TA100, and TA1537 with metabolic activation and in TA1537 without metabolic activation. No significant increases in revertant numbers were observed in TA98 without metabolic activation or in TA100 or TA1535 with or without metabolic activation.	[4]
Basic Blue 99, 62.8% pure	deionized water	Experiment I: up to 40 µg/ml with and without metabolic activation for 4 h Experiment II: up to 40 µg/ml without metabolic activation for 24 h Experiment III: up to 17.5 µg/ml with and without metabolic activation for 4 and 24 h	L5178Y mouse lymphoma cells	Gene mutation assay at the *tk* locus of mouse lymphoma cells in accordance with OECD TG 476	Not mutagenic. No substantial or reproducible dose-dependent increase in mutant colony number observed in any experiment. No relevant shift of the ratio of small versus large colonies observed up to the maximal concentration of the test material. The SCCS noted a positive result observed in Experiment I after 4 h without metabolic activation at 15 and 20 µg/ml, but the higher dose was too toxic to be considered in Experiments I and II. At 24 h, Experiment II was determined to be unreliable. An inconsistent increase was observed in Experiment III at 4 and 24 h at 15 µg/ml. Overall, it was determined that this study had equivocal mutagenic effects.	[4]
Basic Blue 99, 69.5% pure	purified water	up to 30 µg/ml with metabolic activation up to 11 µg/ml without metabolic activation	L5178Y mouse lymphoma cells	Gene mutation assay at the hprt locus of mouse lymphoma cells in accordance with OECD TG 476; incubation period was 3 h.	Not mutagenic. When tested up to toxic concentrations, no statistically significant increases in mean mutant frequencies, compared to mean vehicle controls, were observed.	[4]
Chromosomal Damage						
Basic Blue 99, 62.8% pure	Dulbecco modified eagle medium	up to 300 µg/ml with metabolic activation up to 50 µg/ml without metabolic activation	V79 cells	Micronucleus assay in accordance with OECD TG 487; 4-h treatment; harvest time 24 h after treatment began	Genotoxic. The test material induced a clear increase in the number of micronuclei with and without metabolic activation. A dose-effect relationship was observed in incubations with metabolic activation. At the end of the incubation period in cells treated without metabolic activation, a decrease in the number for attached cells was observed at 25 and 50 µg/ml. Similar effects were observed with metabolic activation at 150 and 300 µg/ml. Precipitation was observed at 75, 150 and 300 µg/ml with metabolic activation.	[4]

Table 4. Genotoxicity studies

Test Article	Vehicle	Concentration/Dose	Test System	Protocol	Results	Reference
IN VIVO						
Chromosomal Damage						
Basic Blue 99, 62.8% pure	deionized water	0, 1.25, 2.5, or 5 mg/kg bw	groups of 5 male and 5 female NMRI mice per dose	Mammalian erythrocyte micronucleus test in accordance with OECD TG 474; mice received test material intraperitoneally; harvest times were 24 h after treatment for all concentrations and 48 h for the highest dose only	Not clastogenic and/or aneugenic. Treatment with test material did not induce a biologically relevant increase in the number of micronucleated polychromatic erythrocytes in bone marrow cells of treated mice.	[4]

Table 5. Case reports related to Basic Blue 99

Patient(s)	Presentation	Patch/Prick Test Results	Reference
57-yr-old female	Patient had employment history as a hairdresser; presented with eczema on the hands and feet, also reported a history of severe itching on the hands and in the ears, accompanied by a "bad taste" in the mouth following use of a name-brand hair-coloring formulation; previous patch testing positive for *p*-phenylenediamine, nickel, chromium, cobalt, and colophonium and the patient underwent additional patch testing and prick testing with the hair-coloring formulation and the ingredients of the hair-coloring formulation	In additional patch testing, results were positive to *p*-toluenediamine, methyldibromo glutaronitrile, and several extracts of "hypoallergenic leather;" prick testing resulted in strong positive reactions to the hair-coloring formulation and to 1% Basic Blue 99 aq. (+++, > histamine) and 1% Basic Brown 17 aq. (++, = histamine); a repeated prick test several months later resulted in the same results, but a patch test with the ingredients of the hair-coloring formulation was negative; a prick test with components identified by thin-layer chromatography from the formulation indicated that the patient may be sensitized to some impurities present	[10]
56-yr-old female	Patient with history of asthma experienced anaphylaxis following use of a semi-permanent, non-oxidative hair dye product; prick tests with the hair dye product and 0.001 - 0.1% Basic Blue 99 (aq.) were performed	Positive results were observed to hair dye product, 0.1% Basic Blue 99 (with pseudopod development); a slight reaction and a negative results were observed with 0.01 and 0.001% Basic Blue 99, respectively	[11]
61-yr-old male	Patient presented with erosive erythema with swelling and exudation on head; erythema gradually extended to nick and forehead, with redness and pain also appearing inside oral cavity; patient also had fever and redness of the palpebral conjunctiva; symptoms began 11 d following hair coloring treatment; a skin biopsy from the forehead erythema revealed spongiosis in the epidermis and lymphocytic infiltration in the upper dermis; patient patch and prick tested with the hair dye (1% aq.) and the ingredients of the hair dye, including Basic Blue 99 (1% aq.)	Positive results to the hair dye (day 3; intensity not reported) and Basic Blue 99 (+? day 2; + day 6); prick test was negative	[17]
54-yr-old female	Patient experienced a Type I hypersensitivity reaction (pruritic facial rash, throat irritation, sneezing, stomach pain and vomiting) 20 min following use of a hair dye, hair color conditioning agent, and hydrogen peroxide solution; patient had a history of atopic dermatitis, cold urticaria, and contact dermatitis caused by *p*-phenylenediamine-containing hair dye; 4 yr previously, patient experienced a pruritic facial rash from a *p*-phenylenediamine-free hair color conditioning agent; skin prick test was performed with hair color conditioning agents from previous reaction and Type I reaction, the hair dye, the hydrogen peroxide solution, and the ingredients of the hair color conditioning agents, including 0.1% Basic Blue 99 in saline	Positive prick test results were observed within 15 min of application to both hair color conditioning agents and to Basic Blue 99	[15]
1 male and 4 females aged 51 - 81 yr	Patients all developed eczema on the head following use of hair coloring products; in 2 cases, condition was also observed on face, and on the trunk in 1 case; patch testing performed with 1% Basic Blue 99 and open tests were conducted with hair coloring products containing Basic Blue 99	Positive patch reactions of + to ++ observed in all 5 patients; open tests with the hair coloring products were positive in 4 patients; 3 cases were also positive to p-phenylenediamine and 2 cases were positive to *p*-methylaminophenol sulfate	[16]

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