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Ingredient Dictionary and Handbook* (wINCI; *Dictionary*).[1] This safety assessment includes relevant published and unpublished data that are available for each endpoint that is evaluated.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 extensive 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 Unpublished data are provided by the cosmetics industry, as well as by other interested parties.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]

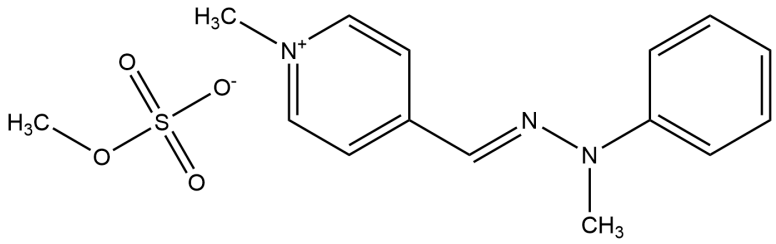

Figure 1. Basic Yellow 87

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.[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 2023 VCRP survey data, Basic Yellow 87 is used in a total of 33 formulations (Table 2).[5] Of these reported uses, the majority (27) are in rinse-off hair coloring products. Five 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).[6,7] 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.[8,9] 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%.[10] 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.[4,11]

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 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 derivation; 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 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 the 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, 48, or 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 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 another 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.[12] 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.[13] 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.[14]

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.[15] 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 2023 VCRP survey data, Basic Yellow 87 is used in a total of 33 formulations. Of these reported uses, the majority (27) 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. A dermal ADME study of Basic Yellow 87 (91.6% pure; 0.2 mg/cm^2) in rats reported that Basic Yellow 87 was poorly absorbed through the skin; 0.3% of the applied dose was absorbed from the skin into the systemic circulation. In an oral ADME study in rats of Basic Yellow 87 (91.6% pure; 10 mg/kg bw) performed in conjunction with the dermal study, Basic Yellow 87 did not readily absorb through the gastrointestinal tract; the test material was rapidly excreted, mainly in the feces. In a separate oral bioavailability study in mice, Basic Yellow 87 (91.6% pure; 40 mg/kg bw) rapidly absorbed in the gastrointestinal tract; the maximum concentration in plasma, corresponding to 4.823 ppm equivalents/g, was observed 0.5 h after exposure.

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 the 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 five 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 of a color additive 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	[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 (2023)[5] and concentration of use (2022)[6] according by product category.

	# of Uses	Max Conc of Use (%)
Totals	**33**	**0.0007-1**
Hair Preparations (non-coloring)		
Hair Conditioner	1	NR
Shampoos (non-coloring)	1	NR
Other Hair Preparations	3	NR
Hair Coloring Preparations		
Hair Dyes/Colors (all types requiring caution statements and patch tests)	12	0.0007-1
Hair Rinses (coloring)	4	NR
Hair Shampoos (coloring)	5	0.02
Hair Color Sprays (aerosol)	1	NR
Other Hair Coloring Preparation	6	NR

NR – not reported

Table 2. 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 3. 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	[12]
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 4. 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 5. 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%	[13]
		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.	[14]

Table 5. 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 6. 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	[15]
			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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