BUKI FRANCE

Technical Report: **(8824)365-0040(R1)** Feb 27, 2025

Date Received: Dec 30, 2024

BUKI FRANCE
38 AVENUE FRANCOIS MITTERRAND 72000 LE MANS - FRANCE

Sample Description:	TATTOO PEN		
Vendor:	N/A	Sample Size:	3PCS
Manufacturer:	GUANGDONG AKIA TECHNOLOGY CO., LTD	Style No(s):	GOLD, SILVER
Labeled Age Grade:	NOT RECORD	SKN/SKU No.:	54381&54382
Appropriate Age Grade:	NOT REQUESTED	PO No.:	NOT PROVIDE
Client Specified Age Grade:	7+	Ref #:	54381&54382
Tested Age Grade:	OVER 7 YEARS OF AGE	Country of Origin:	CHINA
UPC Code:	N/A	Assortment No.:	NOT PROVIDE
		Country of Destination:	NOT PROVIDE
Test Starting Date:	DEC 30, 2024	Test Finished Date:	DEC 31, 2024

EXECUTIVE SUMMARY:

Test Requested	Conclusion
CPSR Test	DATA

Remark:

The above result was performed at a Bureau Veritas CPS approved subcontract lab.
This report is to Supersede BV(Dong guan) report No. (8824)365-0040 dated on Dec 31, 2024.

END OF REPORT

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COSMETIC PRODUCT SAFETY REPORT

Product Name:	Tattoo pen
SKU No.:	Gold, Silver
Region of Destination:	EU
Target consumers:	Age above 6 years old
Buyer Name:	BUKI FRANCE
Buyer Address:	38 AVENUE FRANCOIS MITTERRAND 72000 LE MANS - FRANCE
Receiving Date:	Dec 6, 2024

Requirement:

This safety assessment is conducted with reference to the EU Cosmetic Regulation (EC) No 1223/2009 of the European Parliament and its amendment.

Conclusion:

The product is considered acceptable for its intended application. It would not be expected to pose a significant risk of adverse effects in a majority of individuals under normal and reasonably foreseeable conditions of use. The assessment for human health is based on upon the information available at this date and reviews will be made when the information become updated & available.

Reviewer

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Wen SUN
B. Pharm, M. Pharm, ERT, UKRT, DCST
Registered Toxicologists

Date: 31/12/2024

Part A – Cosmetic product safety information

1 Composition of the cosmetic product

The maximum amount of ingredients are as follow:

INCI Name	CAS No.	Intended Function	Amount [%]
WATER	7732-18-5	Solvent	78.38%
STYRENE/ACRYLATES COPOLYMER	25085-19-2	Film former	12.5%
CALCIUM ALUMINUM BOROSILICATE	65997-17-3	Bulking agent	3.925%
BUTYLENE GLYCOL	107-88-0	Skin conditioning	5%
TITANIUM OXIDE	13463-67-7	Colorant / opacifying agent	1%
PHENOXYETHANOL	122-99-6	Preservative	0.5%
1,2-HEXANEDIOL	6920-22-5	Skin conditioning	0.5%
TIN OXIDE	18282-10-5	Bulking agent	0.08%
SODIUM DEHYDROACETATE	4418-26-2	Preservative	0.125%
Ceteareth-25	68439-49-6	Surfactant	0.08%
CAPRYLYL GLYCOL	1117-86-8	Skin conditioning	0.024%
CI 11680	2512-29-0	Colorant	2.12%
GLYCERIN	56-81-5	Skin conditioning	0.96%

2 Physical and chemical stability

The physical and chemical stability of the finished product and the substances or mixtures have been determined by the manufacturer.

12-weeks stability test was conducted at -15°C, ordinary temperature and 50°C. Appearance, color, odor, texture and feeling were observed. All the parameter meet the acceptance criteria at different time periods during the course of test. Therefore, the overall test result was considered as PASS according to manufacturer’s test criteria.

The Period after Opening (PAO) is 6 months and shelf life is 3 years. It is the responsibility of manufacturer or responsible person to determine the finished product's minimum durability and period-after-opening PAO if applicable using the available data.

Physical-chemical characteristics concerning the substances or mixtures is held separately as part of the cosmetic ingredient technical data pack. Responsible person/manufacturer must ensure the physical-chemical properties of the product do not pose significant impact on the toxicological profile of the product under normal and foreseeable conditions of use.

3 Microbiological quality

Based on test result provided for review, the microbiological data reference with USP 61 and 62 was passed and considered to be acceptable. The manufacturer must ensure the microbiological requirement comply with the criteria of product category 2 as required by the SCCS notes of guidance for the testing of cosmetic ingredients and their safety evaluation

Based on test result provided for review, the preservative effectiveness data reference with USP 51 was passed and considered as acceptable.

Microbiological specifications of the substances and mixtures used within the product are not available for review. Responsible person/manufacturer must ensure that all production batches of raw materials and finished product are met with the microbiological requirements that would not contribute a microbial risk to consumers.

4 Impurities, traces and information about the pack material

The packaging material is not provided for the review.

For the formulation, test results of Lead, Cadmium, Mercury, Arsenic, Antimony on the combined products showed ''PASS'' according to Recommendation from German Health Journal No. 28, July 1985.

Details on the purity or grade of the material used in the packaging are not available for review as well as the compatibility test between the formulation and direct packaging. Responsible person/manufacturer must ensure that the appropriate packaging materials are used to be compatible with the formulation and impurities of concerns in the packaging materials are not at levels likely to cause harm to consumers.

Technical information concerning the material that comprises the primary pack holding the finished product is held separately as part of the packaging data pack. This pack may include details about the pack material itself, source and certification, details of additives (including colours) and confirmation with existing legislation, where applicable.

5 Normal and foreseeable usage

The product is designed to be applied on the body

6 Exposure to the cosmetic product

The following assumptions have been made for assessment of exposure based on EU Scientific Committee on Consumer Safety (SCCS) opinion notes of guidance, EPA exposure handbook 2011 and A.S. Ficheux et al. 2014 & A.S. Ficheux et al. 2016:

- Target consumers: Age above 6 years old
- Physical form: Liquid
- Site of application: Body
- Intended use: undiluted before use
- Net quantity: 1-15g
- Product use per day: 1g (assumption)

- Exposure duration: Leave on
- Body weight: 31.8kg
- Retention factor: 1
- Calculated relative daily exposure: 31.4 mg/kg bw/day

7 Exposure to the substance and Margin of Safety MoS

The Margin of Safety MoS and typical exposure of the consumer to each ingredient are calculated based on the cosmetic product exposure in Section 6.

INCI Name	% w/w	PoD	SED	MoS	Dermal penetration
WATER	78.38%	No Data	24.61132	No Data	100%
STYRENE/ACRYLATES COPOLYMER	12.50%	No Data	3.925	No Data	100%
CALCIUM ALUMINUM BOROSILICATE	3.93%	1000	1.23245	811.4	100%
BUTYLENE GLYCOL	5%	2500	1.3188	1895.7	84%
TITANIUM OXIDE	1%	1000	0.314	3184.7	100%
PHENOXYETHANOL	0.50%	357	0.157	2273.9	100%
1,2-HEXANEDIOL	0.50%	500	0.157	3184.7	100%
TIN OXIDE	0.08%	170	0.02512	6767.5	100%
SODIUM DEHYDROACETATE	0.13%	100	0.03925	2547.8	100%
Ceteareth-25	0.08%	50	0.0005024	99522.3	2%
CAPRYLYL GLYCOL	0.02%	150	0.007536	19904.5	100%
CI 11680	2.12%	1000	0.66568	1502.2	100%
GLYCERIN	0.96%	8000	0.30144	26539.3	100%

Columns in the above file relating to the calculation of typical exposure are as follows:

SED

Calculated **S**ystemic **E**xposure **D**ose, SED = (Product Used (mg) x Retention Factor x Concentration of Material in Product x Dermal Penetration) / intended user body weight (kg)

POD

Point of Departure, this may be an animal-derived No Observed Adverse Effect Level (NOAEL) or a value indicated as being safe to humans. In the case of the latter this would typically be in the form of an ADI (Acceptable Daily Intake) or DNEL (Derived No Effect Level) established by a governmental or scientific committee / body.

MOS

Margin **o**f **S**afety, calculated by dividing the POD by the SED

8 Toxicological profile of the substances

See the appendix for each substance in the product.

9 Undesirable effects and serious undesirable effects

This is a new product to market. No previous sales or complaints data and details of consumer user trial or product safety testing data is available for review. Manufacturer / responsible person must monitor details of any concerns or complaints relating to consumer safety post market launch. if undesirable effects or serious undesirable effects are observed, the details of reaction should be provided so that the safety assessment can be updated accordingly.

10 Other information on the cosmetic product

There is no other relevant information.

Part B – Cosmetic product safety assessment

1 Assessment conclusion

The product complies with the requirements for safety specified by or set out in EU Cosmetic Regulation (EC) No 1223/2009 of the European Parliament and its amendment. Assuming the necessary warnings stated in the safety assessment are included on the product packaging it will give consumers the level of safety they can reasonably expect. The product is considered acceptable for its intended application. It would not be expected to pose a significant risk of adverse effects in most individuals under normal and reasonably foreseeable conditions of use.

This safety assessment for human health postulates the application of the Cosmetic GMP Guidelines at the manufacturing level. The Responsible person/manufacturer must ensure that the raw materials used are of suitably cosmetic grade and the purity meets the criteria as set out in relevant regulations for EU and residues and impurities in the raw materials and/or products are not exposed at level that would cause local and/or chronic toxicity on humans.

It is based on the current state of knowledge and information available at this point of time. Reviews or new safety assessment will be made when there's any subsequent change in product composition, any update of information that affects the product safety, which renders this assessment invalid.

There is no nanomaterials and CMR substances are indicated to be used in this formulation.

2 Labelled warnings and instructions for use

Do not use on the lips. Avoid contact with eyes. If product gets into eyes, rinse well with water immediately.

3 Reasoning

The toxicological profiles of ingredient present in the formulation have been reviewed. The ingredients are all common cosmetic raw materials with extensive history of safe usage. Furthermore, a number of ingredients are present at or below the recommended safe levels as established by bodies such as the Scientific Committee on Consumer Safety (SCCS) or Cosmetic Ingredients Review (CIR) expert panel, or maximum legal limits from the relevant regulations.

All significant toxicological routes of absorption have been considered as well as the systemic effects. Where applicable, Margin of Safety (MoS) has been calculated for all ingredients except those which No

Observed Adverse Effect Levels (NOAELs), or other suitable Points of Departure (PoD) were not available for review. The MoS values for these ingredients were well above 100 to indicate they are systemically safe for use in the product. For those materials where a Margin of Safety (MoS) was not derived, their safety could be substantiated by history of safe use at similar levels in related products, reference dose, The Threshold of Toxicological Concern (TTC) approach, or justified in the ingredient toxicological summary in Annex I.

The product is considered to have adequate stability and microbial quality. Also, any interactions between substances have been considered.

Based on the ingredients used within this product, and their respective concentrations of inclusion in the final formulation, it is not expected to be irritating & sensitizing to the skin and produce systemic toxicity following skin contact under normal and reasonably foreseeable conditions of use. Accidental exposure into eyes may cause slight transient irritation but is expected to be minimal after rinsing with water. The risk of inhalation and oral consumption are considered unlikely.

4 Assessor's credential and approval

Signed on behalf of STANDARDS COMPLIANCE AND TECHNOLOGY(INTERNATIONAL) CO LIMITED

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Wen SUN
B. Pharm, M. Pharm, ERT, UKRT, DCST
Registered Toxicologists

APPENDIX I TOXICOLOGICAL PROFILES OF INGREDIENTS

Aqua

CAS No.	7732-18-5
Regulatory listing	-
Function	Solvent
Appearance/physical state	Clear colourless liquid
Melting point	0°C
Boiling point	100°C
Vapour pressure	-
Partition coefficient	-
Water solubility	-
pH	7
Dissociation constant	-
Molecular weight	18Da
Tox data summary	
Aqua is a ubiquitous liquid that is the basis for all known forms of life. It is normally used as solvent in cosmetic products. Use in consumer products is not expected to result in any Acute or Chronic Toxicity following typical exposures.	

Styrene/Acrylates Copolymer

CAS No.	9010-92-8; 25085-34-1; 25034-86-0
Regulatory Listing	Not listed in EU cosmetic regulation Annex
Function	Film former
Appearance/physical state	White liquid emulsion
Melting point	No data available
Boiling point	No data available
Vapour pressure	No data available
Partition coefficient	No data available
Water solubility	No data available
pH	5 - 8
Dissociation constant	No data available
Molecular weight	115,000 – 200,000 Da
Tox data summary	
Styrene/acrylates copolymer is formed by the polymerisation of styrene and acrylic acid, methacrylic acid or one of their simple esters. It was found to be non-irritating and non-sensitizing in human studies. Two in-vitro eye irritation assay indicated slightly irritating. It is not mutagenic in Ames test with or without metabolic activation. A NOAEL was not available for review. However, CIR concluded to be safe in the current practices of use and concentration up to 35% in leave on and 12% in rinse off products. Based on very high molecular mass and inert nature, absorption of polymers is not expected via physiological exposure routes (inhalation, dermal or	

oral), causing systemic toxicity.
Unreacted monomer may give rise to irritating or allergenic potential, but it is unlikely to occur in the fully polymerized material.
Overall, this compound is not considered to pose an undue risk of adverse effects when included in cosmetic products at typical concentrations.
Reference:
1. CIR 2014 - Safety Assessment of Styrene and Vinyl-type Styrene Copolymers as Used in Cosmetics

Calcium Aluminum Borosilicate

CAS No.	65997-17-3 (generic) 94891-31-3; 155775-82-9 (CIR, 2013)
Regulatory listing	Not regulated in EU/UK
Function	Bulking agent
Appearance/physical state	Hollow, nonporous spheres
Melting point	~730 °C
Boiling point	Not available
Vapour pressure	Not available
Partition coefficient	Not available
Water solubility	17 - 684 µg/L @ 21.1 - 21.5 °C and pH 4.4 - 8
pH	Not available
Dissociation constant	Not available
Molecular weight	328.045
Tox data summary	

Calcium Aluminium Borosilicate, also known as fibrous glass or glass, is a glass consisting essentially of calcium and aluminium borosilicate. This synthetic product is formed by the fusion of boron oxide, silica, sodium oxide, aluminium oxide, and calcium oxide, or combined sources thereof. It is predominantly used in makeup and nail polish product (CIR, 2013).
Where data was not available for certain endpoints, data was read-across to calcium sodium borosilicate, magnesium aluminium silicate and calcium borosilicate since these are also borosilicate glass ingredients with similar structure, properties, functions, and uses of available toxicological data supported to assess the safety of the entire group (CIR, 2013).
Calcium borosilicate was found to be weak irritant to rabbit skin while calcium sodium borosilicate and calcium aluminium borosilicate showed no eye irritation or skin sensitization (CIR, 2013).
Calcium borosilicate reported low potential for acute toxicity with a dermal LD50 of >2000 mg/kg for rabbits and an oral LD50 of >5000 mg/kg for rats. Various silicates and silicate clays used in cosmetics are not significantly toxic in repeated-dose studies (CIR, 2013). In short-term oral toxicity studies, no adverse effects were seen in mice or rabbits dosed up to 5000 mg/kg magnesium aluminium silicate (CIR, 2015).
There was no direct data available on any mutagenicity or genotoxicity on calcium aluminium borosilicate. However, the supernatant of calcium borosilicate steeped in DMSO was not genotoxic in an Ames test (CIR, 2013). No lesions were found in rats dosed orally up to 1000 mg/kg of magnesium aluminium silicate for 104 weeks; and it had neither teratogenic nor adverse effects on the mouse fetus when administered up to 6000 mg/kg/day on days 7-12 of gestation (CIR, 2015). Based on carcinogenicity study, a NOAEL of 1000

mg/kg/day has been considered as point of departure.
Borosilicate ingredients are insoluble, inert, and will not significantly penetrate the skin.
Concluded by the CIR to be safe when used in cosmetic products with concentration up to 33% in leave on and 6% in rinse off described at the time of their report (CIR, 2013).
Overall, this compound is not considered to pose an undue risk of adverse effects when included in cosmetic products at typical concentrations.
References:
1. Cosmetic Ingredient Review (CIR) 2013 - Final report: On the safety assessment of Calcium Aluminum Borosilicate. IJT 32(Suppl. 3):65-72, 2013.
2. European Chemicals Agency (ECHA). REACH Registered Substances Factsheet (Glass, oxide, chemicals; CAS# 65997-17-3).

BUTYLENE GLYCOL

CAS No.	107-88-0 / 6290-03-5
Regulatory Listing	Not regulated in EU regulation
Function	as fragrance, skin conditioning agent, humectant, solvent and viscosity controlling agent
Appearance/physical state	Clear, practically colorless, viscous, hygroscopic liquid
Melting point	-57 °C
Boiling point	209 °C
Vapour pressure	26 Pa at 20 °C
Partition coefficient	-0.9 at 25 °C
Water solubility	500 g/L at 20 °C, miscible in all proportions with water
pH	6.1
Dissociation constant	15.1 at 20 °C
Molecular weight	90.12 g/mol
Tox data summary	

Butylene glycol (also known as 1,3-butanediol) is an aliphatic diol used in cosmetics. Where toxicity data are not available at certain endpoints (in vitro genotoxicity), data was read across to 1,4-butane diol.
Undiluted or diluted form of butylene glycol was reported to be non-irritant to minimal irritant in several ocular and skin irritation studies using rabbits. Reported data on human states that it caused stinging, when it was applied to the human eye and there was a rapid complete relief after rinsing-off the material. Human data reveal no or only minimal skin irritating properties of the undiluted substance or a 50% aqueous solution.
Butylene glycol was a non-sensitiser under the conditions of an HRIPT; and a nail lotion containing 5% butylene glycol was not a photosensitizer.
It shows low potential for acute toxicity with oral LD50 of 18610 to 22800 mg/kg in rats, 11460 mg/kg bw in guinea pigs, 23430 to 25150 mg/kg bw in mice, dermal LD50 of >20 g/kg in rabbits and inhalation LC50 of 292 mg/m3 in rats.
In a 13-week repeated dose oral toxicity study, a NOAEL of 6000 mg/kg/day was reported in dogs. No systemic effects observed in 4 days to 4 weeks dermal toxicity study in rats (formulation containing 3% butylene glycol) or in guinea pigs (20100 mg/kg/day for 2 hrs/day) to the intact or scarped skin.
Butylene glycol is considered negative genotoxicity potential. Two-year feeding studies conducted at doses up

to 5000 mg/kg/day in rats and up to 750 mg/kg/day in dogs did not reported treatment related carcinogenic and non-carcinogenic effects; and therefore, these highest tested doses were established as NOAELs in these studies. Based on outcomes of a multi-generation reproductive study in rats, a NOAEL of 5000 mg/kg/day for fertility and 2500 mg/kg/day for fetotoxicity (based on delayed ossification of sternebral noted at higher dietary dosed tested). Based on available dataset, a conservative NOAEL of 2500 mg/kg/day has been selected as the point of departure for risk assessment.
Percutaneous absorption study in mice and rats suggested that the dermal absorption can vary over a wide range (26% -84%) within 96 hours under occlusive test conditions
CIR Concluded to be safe as used in the practices of use and concentrations up to >50% in rinse off and 25% leave on products described at the time of their report
Overall, this compound is not considered to pose an undue risk of adverse effects when included in cosmetic products at typical concentrations.
Reference:

1. Cosmetic Ingredient Review (CIR 1985). Final report on the safety assessment of Butylene Glycol, Hexylene Glycol, Ethoxydiglycol, and Dipropylene Glycol. Journal of the American college of toxicology. Volume 4, Number 5.
2. ECHA REACH Registration dossier. Butane-1,3-diol (CAS# 107-88-0)

CI 77891 (Titanium Dioxide)

CAS No.	1317-80-2 (Rutile); 13463-67-7; 1317-70-0 (Anatase)
Regulatory Listing	Permitted pigment: Annex IV item 143 - All products. Purity criteria as set out in Commission Directive 231/2012/EC (E 171); Permitted UV Agent - Annex VI Item 27, Max 25%.
Function	Abrasive; Absorbent; Anti-Caking; Bulking; Viscosity Modifying; Opacifying
Appearance/physical state	White powder
Melting point	1560°C (anatase), 1843°C (rutile), 1825°C (brookite)
Boiling point	Not available
Vapour pressure	melting point is above 300°C
Partition coefficient	Substance is inorganic.
Water solubility	0.04 to 0.287 µg TiO2/L.
pH	Not available
Dissociation constant	Substance is insoluble
Molecular weight	79.88 g/mol
Tox data summary	

Titanium dioxide (CI 77891; Pigment White) is the inorganic oxide; classed chemically as an inorganic colour. It is reported to function as a colorant, opacifying agent, UV absorber and UV filter in cosmetics. In OTC drug products, it is used as a sunscreen agent (21CFR352.10). The color additive TiO2 may be safely used for coloring foods in general at levels not to exceed 1% (21CFR73.575).
It is not irritating to the eyes and skin of rabbits. It was not sensitizing under the conditions of a Buehler test or LLNA assay. Its use in sunscreens at high concentrations over a long period has not been associated with reporting of human skin sensitization.

It shows low acute toxicity with reported oral LD50 >5 g/kg bw and inhalation LC50 >3.43 mg/L in rats. In rat oral studies, the NOAEL of 1000 mg/kg bw/day was established in several developmental toxicity studies and in one 28-day repeated dose toxicity. A NOAEC of 0.5 mg/m3 from 90-day rat study was selected by the SCCS as the point of departure (PoD).

The genotoxic effects of TiO2 most probably manifest through an indirect mechanism (e.g. oxidative stress and inflammation) for which there is a practical threshold. In EU, titanium dioxide [in powder form containing 1 % or more of particles with aerodynamic diameter ≤ 10 μm] is classified as Category 2 carcinogen (via inhalation). TiO2 is not a reproductive and developmental toxicant in rats.

Titanium dioxide is classified as carcinogenic (Group 2B) in the powder form via inhalation based on sufficient evidence in experimental animals and inadequate evidence from epidemiological studies by the IARC. However, this product is in the format of liquid. As such, the likelihood of the product being inhaled is negligible thus the inhalation toxicity potential is low.

Overall, it is not considered to pose an undue risk of adverse effects when included in cosmetic products at typical concentrations.

References

1. ECHA Registration Dossier – Titanium dioxide (EC No. 236-675-5 / CAS No. 13463-67-7). Registration Dossier No. 15560. European Chemicals Agency, Helsinki. URL: https://echa.europa.eu/registrationdossier/-/
2. registered-dossier/15560).
3. European Commission. Regulation (EC) No 1333/2008 of the European Parliament and of the Council of 16 December 2008 on food additives (Text with EEA relevance)
4. JECFA 1969. Titanium Dioxide (13463-67-7), Report: NMRS 46/TRS 445-JECFA 13/12. Tox Monograph: FAS 70.36/NMRS 46A-JECFA 13/55. Available at: http://apps.who.int/food-additives-contaminantsjecfa-
5. database/chemical.aspx?chemID=2723 (Accessed 18 Dec 2019)
6. SCCS/1516/13 OPINION ON Revision of the opinion on Titanium Dioxide, nano form.
7. SCCS/1580/16 OPINION ON additional coatings for Titanium Dioxide (nano form) as UV-filter in dermally applied cosmetic products

Phenoxyethanol

CAS No.	56257-90-0; 37220-49-8; 122-99-6
Regulatory Listing	Approved Preservative - Annex V/29 - Maximum 1% all Products
Function	Preservative
Appearance/physical state	Liquid
Melting point	14°C
Boiling point	245°C
Vapour pressure	0.007 mm Hg at 25°C
Partition coefficient	1.16
Water solubility	In water, 10 to 50 mg/mL at 68° F
pH	-
Dissociation constant	pKa = 15.10 at 25°C
Molecular weight	138.16 g/mol
Tox data summary	

Phenoxyethanol is the aromatic ether alcohol, used as antimicrobial and preservative in cosmetics and topical pharmaceutical formulations at a concentration up to 1%.
CIR concluded to be safe as used in the practices of use and concentrations, generally <1%.
Undiluted phenoxyethanol is an eye irritant, but was non-irritating when tested at 2.2%. It is reported to slightly irritate skin in animal studies, particularly following repeated exposure. It was not a sensitizer in guinea pigs. In clinical studies, substance was neither a primary nor a cumulative irritant, and it did not cause delayed hypersensitivity. It was also nonphototoxic.
It shows moderate acute oral toxicity with LD50 of 1386 mg/kg or greater in rats. Multiple oral repeated dose toxicity studies from three species (mouse, rat and rabbit) are available. These studies indicate that the rabbit is the most sensitive of the species tested, mainly due to its susceptibility to haematotoxic effects. Target organs in rats and mice were the kidney and liver. A key 13-week dermal toxicity study in rabbits identified a NOAEL of 357 mg/kg/day which was used as the point of departure by the SCCS because the dermal route is the relevant route for cosmetic ingredients and rabbit being most sensitive species.
It does not pose a genotoxicity hazard based on in vitro and in vivo test results. It was not carcinogenic in rats and mice. It was not a reproductive toxicant in rats and rabbits following oral or dermal exposure.
In vitro skin penetration studies shows dermal absorption of 47% for a rinse-off formulation containing 0.2% phenoxyethanol and 85% for a leave-on formulation containing 1% phenoxyethanol.
Based on the available data it is considered that the use of phenoxyethanol at typical levels within a consumer product would be unlikely to produce significant localised or systemic toxicity.
References:

1. CIR (1990). Final Report on the Safety Assessment of Phenoxyethanol. JACT, 9(2).
2. SCCS (2016). Opinion on phenoxyethanol SCCS/1575/16
3. European Chemicals Agency (ECHA). REACH Registered Substances Factsheet (2-phenoxyethanol; CAS# 122-99-6)
4. NICNAS, Australia. Ethanol, 2-phenoxy-: Human health tier II assessment, (CAS# 122-99-6), 12 September 2013
5. Organization for Economic Co-operation and Development (OECD). Ethylene Glycol Phenyl Ether (CAS# 122-99-6). SIDS initial assessment report 18th SIAM

1,2-HEXANEDIOL

CAS No.	6920-22-5
Regulatory Listing	Not regulated in EU regulation
Function	Solvent
Appearance/physical state	Liquid
Melting point	Not available
Boiling point	223 - 224 °C
Vapour pressure	Not available
Partition coefficient	0.25
Water solubility	Insoluble in water
pH	Not available
Dissociation constant	Not available
Molecular weight	118.17 Da

Tox data summary	
1,2-Hexanediol is likely to undergo a range of metabolic modifications in the body. In vitro data suggest that it penetrates the skin upon dermal application and that it can act as a penetration enhancer in mixtures. 1,2-Hexanediol displayed no, or at most a low, potential to cause skin irritation in human studies, but slight skin irritation was noted in laboratory animals. It was irritating to the eyes of rabbits, findings which are supported by an in vitro assay. The compound has shown no evidence of skin sensitization in a number of studies in humans involving repeated dermal application, and this is supported by data from a mouse local lymph node assay. No acute or repeated dose inhalation data were identified. Laboratory animal studies suggest that 1,2-hexanediol is of low acute oral toxicity, while acute dermal data are limited. Fairly minor toxic effects were reported in rats on repeated exposure, with NOAELs of 700 mg/kg bw/day (90-day dermal toxicity study in rabbits) and 500 mg/kg bw/day (oral), the respective LOAELs being 1000 and 750 mg/kg bw/day. Prenatal developmental study derived a NOAEL of 500 mg/kg bw/day in rats, based on the reduced body weight gain and reduced relative feed consumption of mothers at 750 mg/kg bw/day. No effects on reproduction or foetal development were noted in the respective studies at the highest doses tested (1000 mg/kg bw/day and 750 mg/kg bw/day, respectively). The lowest NOAEL of 500 mg/kg bw/day is conservatively taken as a Point of Departure. No evidence of genotoxicity was observed in in vitro chromosome aberration or gene mutation tests in mammalian cells, or in a bacterial mutagenicity (Ames) assay. No developmental toxicity was seen in two limited oral studies in rats. In its assessment of 1,2-glycols, a US Cosmetic Ingredient Review Expert Panel concluded that “the following cosmetic ingredients [including 1,2-hexanediol] are safe in the present practises of use and concentration described in this safety assessment”, i.e. ranging from 0.00005 to 10% for 1,2-hexanediol. Reference: 1. CIR, (2012). Safety assessment of 1,2-glycols as used in cosmetics. International Journal of Toxicology 31(suppl 2)	

Tin oxide

CAS No.	18282-10-5; 1332-29-2
Regulatory listing	Not regulated in EU/UK
Function	abrasive, bulking, and opacifying agent
Appearance/physical state	White/Grey powdered solid
Melting point	1630°C
Boiling point	Sublimes at 1800 - 1900°C
Vapour pressure	Not available
Partition coefficient	Not available
Water solubility	Not available
pH	Not available
Dissociation constant	Not available
Molecular weight	150.7 Da
Tox data summary	

Tin Oxide is inorganic oxide.
Tin Oxide is not a skin irritant or a sensitizer but can cause mild eye irritation.
Tin Oxide has a low acute toxicity with high oral LD50 greater than 2000 mg/kg.
A NOAEL of 510 mg/kg bw/day is selected from a 4-week oral repeated dose toxicity study. The value is divided by three to extrapolate to long term study (SCCS opinion) to become 170 mg/kg bw/day as point of departure. The NOAEL is derived from the highest dose of the study, this is not a true NOAEL but can be taken as a conservative and protective value for calculating MoS.
Data is not available for genotoxicity and carcinogenicity for Tin Oxide.
There is no evidence to support the lack of dermal penetration of silica and as such the dermal absorption is assumed as 100%.
The Cosmetic Ingredient Review (CIR) reports that Tin Oxide was used up to 1.3% in leave on products (Incidental ingestion was 0.2%; Incidental inhalation was 1%, Eye area was 1.3%) and 0.4% in rinse off products. The CIR Expert Panel concluded that Tin Oxide is safe in the present practices of use and concentration.
Overall the use of this material at low levels within Consumer Products would not be expected to pose an undue risk of significant adverse effects.
References:
1. CIR. Safety Assessment of Tin (IV) Oxide as Used in Cosmetics. IJT 33(Suppl 4):40-46, 2014.
2. SCCS notes of guidance 10th revision SCCS/1602/18

Sodium Dehydroacetate

CAS No.	4418-26-2
Regulatory Listing	Listed in EU cosmetic regulation Annex V 13 - Maximum authorized concentration 0.6% (acid) - Prohibited in aerosol dispensers (sprays)
Function	Preservative
Appearance/physical state	Beige powder
Melting point	295 °C
Boiling point	No data
Vapour pressure	No data
Partition coefficient	No data
Water solubility	Soluble
pH	No data
Dissociation constant	No data
Molecular weight	190.13
Tox data summary	

Sodium Dehydroacetate is the sodium salt of dehydroacetic acid. It is a permitted cosmetic preservative in the EU at a maximum as 0.6% as the acid, and not permitted in aerosol products.
Sodium dehydroacetate is minimally irritating to rabbit skin and minimally irritating to rabbit eyes. There was no evidence of skin sensitisation potential in a human repeat insult patch test of an aqueous paste containing 60% sodium dehydroacetate. The compound was found to be not phototoxic or photosensitising in a repeated insult photo patch test.
Oral LD50 of Sodium dehydroacetate in mice was 1.05 g/kg bw.

The NOAEL from a 2-year chronic toxicity study in rats was 100mg/kg bw/day. A study in which humans ingested 10mg/kg bw/day for 150 days showed no adverse health effects. These values are considered relevant point of departure for risk assessment, and would lead to similar margins of safety (as the animal study has a NOAEL which is 10 times the NOAEL of the human study). An oral derived no-effect level (DNEL) of 0.78 mg/kg bw/day for the general population was established by registrant (ECHA registration dossier).
Sodium dehydroacetate was not genotoxic in the Ames test with or without metabolic activation. Regarding reproductive toxicity, a developmental toxicity reports no adverse effects - the effects seen we comparable to control group, therefore, not compound specific.
Little data was available on the dermal absorption of Sodium dehydroacetate.
Cosmetic Ingredient Review (CIR) expert panel concluded Sodium dehydroacetate to be safe at the present uses and concentrations in a cosmetic product at up to 0.6% (CIR 2006).
References:

1. CIR 1985/2006 - Safety Assessment of Sodium Dehydroacetate and Dehydroacetic Acid. J Amer. Coll. Toxicol. Vol 4(3):123-159, 1985.
2. EFSA. Guidance on dermal absorption. EFSA Journal 2017;15(6):4873.
3. ECHA registration dossier of Sodium 1-(3,4-dihydro-6-methyl-2,4-dioxo-2H-pyran-3-ylidene)ethanolate, CAS: 4418-26-2. Available at: https://echa.europa.eu/de/registration-dossier/-/registereddossier/
4. 22401/7/1

Ceteareth-25

CAS No.	68439-49-6
Regulatory listing	Not regulated in EU/UK
Function	Emulsifier, surfactant
Appearance/physical state	Liquids to waxy solids (CIR, 1999)
Melting point	Not Available
Boiling point	Not Available
Vapour pressure	Not Available
Partition coefficient	Not Available
Water solubility	Slightly Soluble (HERA, 2009)
pH	Not Available
Dissociation constant	Not Available
Molecular weight	>1000 g/mol (CIR, 2012)
Tox data summary	

Ceteareth-25 is non-ionic polyoxyethylene ether of higher saturated fatty alcohols (cetyl/stearyl alcohol). There was lack of toxicological data on Ceteareth-25, therefore based on the analogue and chain-length category approach considering similarities and trends in molecular structure, physiochemical properties, uses, and hazard profiles, toxicological data for alcohol ethoxylates (AEs) ranging from C_6-C_{18} and AE_3-AE_{12} were considered appropriate to fill the data gaps.
Based on the available eye irritation studies on several analogue compounds Ceteareth-25 is considered as moderate to severe eye irritant. In a skin irritation study on analogue compounds, Ceteareth-25 is considered as a mild skin irritant. In clinical HRIPT studies, and animal skin sensitisation studies with analogue compounds, Ceteareth-25 was considered as non-sensitiser to animal and human skin.

The oral Lethal Dose (LD_{50}) of analogue compounds ($C_{14\text{-}15}AE_{11}$) was identified as 720 mg/kg and 1800 mg/kg in rats. In a 90 days oral gavage feeding study of Ceteareth ($C_{16\text{-}18}AE_{10}$) in rats, a NOAEL of 100 mg/kg/day was established. In another 90 days dermal toxicity study in rats using $C_{9\text{-}11}AE_6$, a NOAEL of 80 mg/kg/day was established.

Various analogues of alcohol ethoxylates (AEs) were not genotoxic based on *in vitro* and *in vivo* studies conducted (HERA, 2009; NICNAS, 2020). A 2-year feeding study conducted in rats with AEs ($C_{12-13}EO_{6.5}$ and $C_{14-15}EO_7$) did not show tumours or other treatment related toxic effects and a NOAEL of 50 mg/kg/day was established.

Results of pharmacokinetic studies suggest that the oral absorption of analogue compounds was rapid (>75% of the dose), however the percutaneous doses of ^{14}C-labelled $C_{12\text{-}15}AE_6$ and $C_{12\text{-}15}AE_7$ were absorbed slowly and incompletely (about 50% in 72 hours).

Concluded by the CIR to be safe as used in the practices of use and concentrations up to 3% (both in leave-on and rinse-off products described at the time of their report (CIR, 1999).

HERA Expert Panel has assessed the safety of Alcohol Ethoxylates (AE) and demonstrated that its use in household laundry and cleaning detergents is safe and does not cause concern with regard to consumer use (HERA, 2009).

References:

1. Cosmetic Ingredient Review (CIR)- Final Report on the Safety Assessment of Ceteareth-2, -3, -4, -5, -6, -7, -8, -9, -10, -11, -12, -13, -14, -15, -16, -17, -18,-20,-22,-23,-24,-25,-27, -28, -29, -30, -33, -34, -40, -50, -55, -60, -80, and -100. International Journal of Toxicology, 18(Supplement 3) 41-49, 1999.
2. Cosmetic Ingredient Review (CIR)- Safety Assessment of Alkyl PEG Ethers as Used in Cosmetics, International Journal of Toxicology, 31(Supplement 2) 169S-244S
3. Human & Environmental Risk Assessment on ingredients of European household cleaning products. Alcohol Ethoxylates Version 2.0 September 2009
4. NICNAS, IMAP Group Assessment Report, Ethoxylates of aliphatic alcohols (>C6): Human health tier II assessment, 12 December 2019.

Caprylyl Glycol

CAS No.	1117-86-8
Regulatory listing	Not regulated in EU
Function	Skin conditioning
Appearance/physical state	White - May be liquid or solid
Melting point	140°C
Boiling point	30 – 35°C
Vapour pressure	No data
Partition coefficient	No data
Water solubility	Miscible, approx 3 gm/l
pH	No data
Dissociation constant	Log Kow 2.1
Molecular weight	146.13 g/mol
Tox data summary	

Caprylyl glycol is a diol material with a molecular formula of C8H18O2.

It was not irritating to the respiratory tract of rats following an acute inhalation exposure. In general, the substance displayed mild transient skin irritation in rabbits. Neat and diluted solutions of caprylyl glycol produced reversible eye irritation in rabbits, while an in vitro BCOP assay indicated the potential of the substance to induce serious eye damage. Caprylyl glycol showed a consistent lack of skin sensitisation potential in a mouse LLNA and four GPMTs.

In rats, caprylyl glycol showed a low-moderate acute inhalation toxicity, with a 4-hour LC50 value of around 2000-5000 mg/m3, and is of low acute toxicity by the dermal and oral routes. Repeated oral (gavage) exposure of rats for 4 weeks produced effects on motor activity and kidney/liver weights as well as evidence of glandular stomach irritation, though these changes was not observed in a subsequent 13-week investigation, which instead reported effects on growth at and above 300 mg/kg bw/day. The REACH registrants considered the subacute and subchronic systemic NOAELs to be 300 and 150 mg/kg bw/day, respectively. The latter value was used by REACH registration dossier submitters to calculate chronic systemic DNELs for the general population.

Caprylyl glycol was not genotoxic in a range of in vitro assays, including three bacterial reverse mutation tests, and mammalian cell gene mutation and chromosome aberration studies. No carcinogenicity data are available. No evidence of reproductive or developmental toxicity was apparent in a guideline screening test involving exposure of rats at up to 1000 mg/kg bw/day for around 6 weeks (starting 2 weeks prior to mating). In a prenatal developmental toxicity study, foetal effects included reduced body weight and the presence of accessory ribs but these only occurred at the maximum test dose of 1000 mg/kg bw/day and in association with maternal toxicity, the maternal and developmental NOAELs being 150 and 300 mg/kg bw/day respectively.

References:

1. CIR (2012) Safety Assessment of 1,2-Glycols as Used in Cosmetics. Intemational joumal of Toxicology 31 (Supplement 2) 147S-168S.
2. ECHA Registration dossier of Octane-1,2-diol, CAS: 1117-86-8. Available at: https://echa.europa.eu/registration-dossier/-/registered-dossier/14120/1. (Accessed: 30 August 2018)
3. Steiner et al. 2017. Margin of safety of pentylene glycol derived using measurements of cutaneous absorption and volatility. Regulatory Toxicology and Pharmacology 87 (2017) 106-111.
4. Lee et al. 2011. The influence of alkane chain length on the skin irritation potential of 1,2-alkanediols. International Journal of Cosmetic Science, 2011, 33, 421–425

CI 11680

CAS No.	2512-29-0
Regulatory Listing	EU Annex IV/4 - Permitted colour all cosmetic products
Function	Colorant
Appearance/physical state	Yellow powder
Melting point	257°C
Boiling point	Not Available
Vapour pressure	<0.000001 Pa at 25°C
Partition coefficient	Log Pow: 3.1 (calculated)
Water solubility	<13 µg/L at 22 -23°C

pH	Not Available
Dissociation constant	Not Available
Molecular weight	
Tox data summary	

CI 11680 is classed chemically as a monoazo colour.
It is of low acute toxicity. Acute oral LD50 determined to be >10000 mg/kg bw in Wistar-rats. And acute dermal LD50 was >2000 mg/kg bw in the Wistar strain rat too.
The primary skin irritation potential of the test item was investigated according to OECD test guideline no 404. No erythema or edema were observed at any time point (score 0).There was no indication of systemic toxicity.
The test item was subject to an Acute Eye Irritation/Corrosion Test in the rabbit according to OECD TG 405.
Chemosis was observed in all three animals1 h after application. The effect was fully reversible within 48 h. Conjunctival redness was observed in all three animals up to 72 h after application, reversible by seven days. Iridial effects were noted in one animal up to 24 h. Corneal opacity was not observed in any animal.
The test item was assessed for its possible contact allergenic potential in a local lymph node assay according to OECD TG 429. The test was performed using test item concentrations of 2, 4 and 8% (w/v). The animals (5 female mice/dose group) did not show any clinical signs during the course of the study and no cases of mortality were observed and it was not a skin sensitiser under the conditions tested. Skin patch test was conducted according to recommendations of ICDRG (International Contact Dermatitis Research Group),
it showed only slight reactions with erythema in 1 out of 38 Person and erythema with edema in 1 out of 38 Person too. The 2 persons showed also reactivity to various other dyes. 1 out of 34 individuals showed slight erythma in the photo patch test.
A 90-day toxicity study in Fischer F344 rats was performed with the close analogue PY 74. All animals survived until scheduled termination without any toxic signs in life. In haematology, clinical biochemistry and urinalysis some scattered significant differences, altogether without a clear dose response and all only minor in severity, were noted. Post mortem examination including histopathology did not reveal any test substance related toxic alterations. The test substance caused elevated liver weights in the high dosed females. As there were no corresponding histopathological or clinical-biochemical alterations found, the most likely interpretation is an adaptive response by enzyme induction. No parallel trend was present in the males. The effects did not persist until the end of the recovery period. No other test substance-related effect was noted. The No-observed-adverse-effect-level (NOAEL) of the test item was 1000 mg/kg bw/day in both sexes.
It did not cause genotoxic effects in vitro in bacterial or mammalian cells.

To sum up, it is considered unlikely to produce significant localized or systemic toxicity at typical concentration.
References:

1. European Food Safety Authority (EFSA). Scientific Opinion on the re-evaluation Tartrazine (E 102). EFSA Journal 2009; 7(11):1331
2. Evaluations of the Joint FAO/WHO Expert Committee on Food Additives (JECFA). TARTRAZINE (CAS# 1934-21-0). Evaluation Year: 2016.
3. Scientific committee on cosmetic products and non-food products for consumers (SCCNFP). Opinion concerning Acid Yellow 23. 23-Apr-2004. SCCNFP/0786/04.
4. The European Chemical Agency (ECHA) REACH registration dossier (CAS: 1934-21-0).

Glycerin

CAS No.	56-81-5
Regulatory Listing	Not listed in EU cosmetic regulation Annex
Function	Humectant, skin conditioning
Appearance/physical state	Colourless syrup
Melting point	18.2°C
Boiling point	290°C
Vapour pressure	26 Pa
Partition coefficient	-1.75
Water solubility	Soluble (1 000 000 mg/L)
pH	Not available
Dissociation constant	Not available
Molecular weight	92.0932
Tox data summary	

Glycerin is a polyhydric alcohol, which is used in a wide variety of applications including cosmetics, licensed medicines and foods. Typically, in cosmetics it can be used as a humectant and hair conditioner.

Glycerin constitutes around 10% of the Fat found in a typical Human Diet and is readily metabolised on ingestion and has generally recognised as safe (GRAS) status in the US. (FDA, 21CFR§182.1320). Based on the toxicological studies in the ECHA registration dossier, it has low acute toxicity, unlikely to cause skin and eye irritation and is non-mutagenic.

A no-observed-adverse-effect-level (NOAEL) of 8000-10000 mg/kg bw was determined based on the absence of treatment-related effects in rats from the 2-year diet study. The lower of these values of 8000 mg/kg bw is conservatively chosen as the point of departure.

Given the low toxicity profile of this substance, and the fact it is a constituent of a typical human diet, its use in Consumer Products is not expected to produce significant localised or systemic toxicity.

References:

1. CIR 2019 – Safety assessment of Glycerin used in cosmetic
2. ECHA registration dossier of Glycerol CAS 56-81-5

END OF REPORT