File No.: LTD/2140

October 2020

AUSTRALIAN INDUSTRIAL CHEMICALS INTRODUCTION SCHEME (AICIS)

PUBLIC REPORT

1-Propanaminium, 3-[(4-amino-9,10-dihydro-3-methyl-9,10-dioxo-1-anthracenyl)amino]-*N,N,N*-trimethyl-, methyl sulfate (1:1) (INCI Name: HC Blue 17)

This Assessment has been compiled in accordance with the provisions of the *Industrial Chemicals Act 2019* (the IC Act) and *Industrial Chemicals (General) Rules 2019* (the IC Rules) by following the *Industrial Chemicals (Consequential Amendments and Transitional Provisions) Act 2019* (the Transitional Act) and *Industrial Chemicals (Consequential Amendments and Transitional Provisions) Rules 2019* (the Transitional Rules). The legislations are Acts of the Commonwealth of Australia. The Australian Industrial Chemicals Introduction Scheme (AICIS) is administered by the Department of Health, and conducts the risk assessment for human health. The assessment of environmental risk is conducted by the Department of Agriculture, Water and the Environment.

This Public Report is available for viewing and downloading from the AICIS website. For enquiries please contact AICIS at:

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Executive Director
AICIS

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SUMMARY

The following details will be published on our website:

ASSESSMENT REFERENCE	APPLICANT(S)	CHEMICAL OR TRADE NAME	HAZARDOUS CHEMICAL	INTRODUCTION VOLUME	USE
LTD/2140	Kao Australia Pty Ltd	1-Propanaminium, 3-[(4-amino-9,10-dihydro-3-methyl-9,10-dioxo-1-anthracenyl)amino]-*N,N,N*-trimethyl-, methyl sulfate (1:1) (INCI Name: HC Blue 17)	ND	≤ 0.05 tonne per annum	Oxidative and non-oxidative hair dye

*ND = not determined

CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard Classification
Based on the information available in the SCCS Opinion (2013), the assessed chemical is not classified according to the *Globally Harmonised System of Classification and Labelling of Chemicals* (GHS), as adopted for industrial chemicals in Australia.

Human Health Risk Assessment
Provided that the recommended controls are being adhered to, under the conditions of the occupational settings described, the assessed chemical is not considered to pose an unreasonable risk to the health of workers.

Provided that the recommended controls are being adhered to by introducers, the assessed chemical is not considered to pose an unreasonable risk to public health.

Environmental Risk Assessment
On the basis of the reported use pattern and import volume of less than one tonne, the assessed chemical is not considered to pose an unreasonable risk to the environment.

Recommendations

CONTROL MEASURES

Occupational Health and Safety

- A person conducting a business or undertaking at a workplace should implement the following safe work practices to minimise occupational exposure during handling of the assessed chemical as introduced in hair dye products:
  - Avoid contact with skin and eyes

- A person conducting a business or undertaking at a workplace should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the assessed chemical as introduced in hair dye products:
  - Impervious gloves

  Guidance in selection of personal protective equipment can be obtained from Australian, Australian/New Zealand or other approved standards.

- The introducer of the end use hair dye products containing the assessed chemical into Australia should make sure that the formulators of hair dye products containing the assessed chemical have followed the following precautionary measures:
  - Not use the assessed chemical with nitrosating agents

- Keep nitrosamine content of the assessed chemical at ≤ 50 µg/kg
- Keep the products containing the assessed chemical in nitrite-free containers
- Keep the levels of any potentially carcinogenic impurities in the assessed chemical below the GHS classification cut-off concentrations

- A copy of the SDS should be easily accessible to employees.

- If products and mixtures containing the assessed chemical are classified as hazardous to health in accordance with the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS)* as adopted for industrial chemicals in Australia, workplace practices and control procedures consistent with provisions of State and Territory hazardous substances legislation should be in operation.

Emergency procedures

- Spills or accidental release of the assessed chemical should be handled by physical containment, collection and subsequent safe disposal.

Disposal

- Where reuse or recycling are not appropriate, dispose of the assessed polymer in an environmentally sound manner in accordance with relevant Commonwealth, state, territory and local government legislation.

Regulatory Obligations

Specific Requirements to Provide Information
This risk assessment is based on the information available at the time of the application. The Executive Director may initiate an evaluation of the chemical based on changes in certain circumstances. Under section 101 of the IC Act the introducer of the assessed chemical has post-assessment regulatory obligations to provide information to AICIS when any of these circumstances change. These obligations apply even when the assessed chemical is listed on the Australian Inventory of Industrial Chemicals (the Inventory).

Therefore, the Executive Director of AICIS must be notified in writing within 20 working days by the applicant or other introducers if:

- the function or use of the assessed chemical has changed from hair dye, or is likely to change significantly;
- the importation volume exceeds one tonne per annum assessed chemical;
- the assessed chemical has begun to be manufactured in Australia;
- the assessed chemical is imported for reformulation in Australia;
- the assessed chemical is imported in solid form;
- the on-head concentration of the assessed chemical has increased from 2%;
- the assessed chemical contains potentially carcinogenic impurities above the GHS classification cut-off concentration;
- additional information has become available to the person as to an adverse effect of the chemical on human health, or the environment.

The Executive Director will then decide whether an evaluation of the introduction is required.

Safety Data Sheet
The SDS of the product containing the assessed chemical provided by the applicant was reviewed by AICIS. The accuracy of the information on the SDS remains the responsibility of the applicant.

ASSESSMENT DETAILS

1. APPLICANT AND APPLICATION DETAILS

APPLICANT(S)
Kao Australia Pty Ltd (ABN: 059 054 708 299)
Level 2, 293 Camberwell Road
CAMBERWELL VIC 3124

APPLICATION CATEGORY
Limited-small volume: Chemical other than polymer (1 tonne or less per year)

PROTECTED INFORMATION (SECTION 38 OF THE TRANSITIONAL ACT)
Data items and details taken to be protected information include: trade name of the full range of products, spectral and analytical data, purity, impurity profile, import volume and concentration in end-use products.

VARIATION OF DATA REQUIREMENTS (SECTION 6 OF THE TRANSITIONAL RULES)
Schedule data requirements are varied for all physical and chemical properties.

PREVIOUS APPLICATION IN AUSTRALIA BY APPLICANT(S)
None

APPLICATION IN OTHER COUNTRIES
EU: REACH
Taiwan Chemical Substance Inventory (TCSI)

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
INCI Name: HC Blue 17

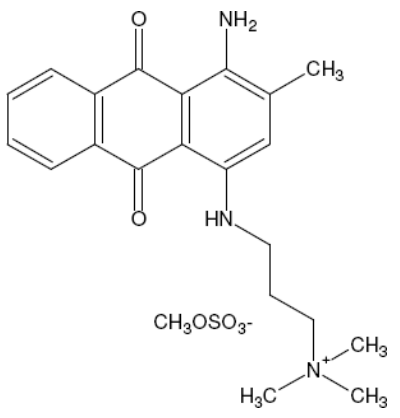
CAS NUMBER
16517-75-2

CHEMICAL NAME
1-Propanaminium, 3-[(4-amino-9,10-dihydro-3-methyl-9,10-dioxo-1-anthracenyl)amino]-*N,N,N*-trimethyl-, methyl sulfate (1:1)

OTHER NAME(S)
Ammonium, [3-[(4-amino-3-methyl-1-anthraquinonyl)amino]propyl]trimethyl-, methyl sulfate
Cationic Blue 347

MOLECULAR FORMULA
$C_{21}H_{26}N_3O_2.CH_3O_4S$

STRUCTURAL FORMULA



MOLECULAR WEIGHT
463 g/mol

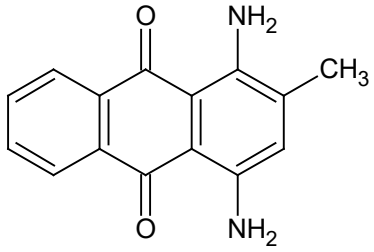
ANALYTICAL DATA
Reference HPLC-UV/MS spectra were provided.

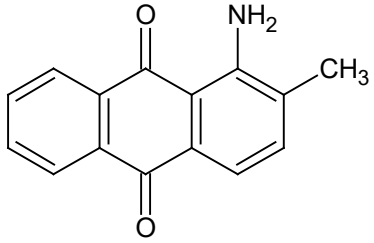
3. COMPOSITION

DEGREE OF PURITY
> 95%

IMPURITIES

Below is information on two of the four impurities detected in the assessed chemical, from analysis of two batches.

Chemical Name	9,10-Anthracenedione, 1,4-diamino-2-methyl-
	
CAS No.	3225-95-4 *Weight %* < 3

Chemical Name	9,10-Anthracenedione, 1-amino-2-methyl-
	
	Disperse Orange 11, 1-Amino-2-methyl-anthra-9,10-quinone
CAS No.	82-28-0 *Weight %* < 1
Hazardous Properties	Carcinogenicity – category 2 H351 (Suspected of causing cancer)

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: blue powder (the Scientific Community on Consumer Safety, SCCS, 2013)

Property	***Value***	***Data Source/Justification***
Melting Point	Approx. 0°C	Product SDS*
Boiling Point	Approx. 100°C	Product SDS*
Density	Approx. 990 kg/m^3	Product SDS*
Vapour Pressure	Not determined	Imported in an aqueous solution
Water Solubility	> 350 g/L at 20 °C	SDS
Hydrolysis as a Function of pH	Not determined	Does not contain hydrolysable functions
Partition Coefficient (n-octanol/water)	Not determined	Expected to partition to the water phase as the assessed chemical is a salt.
Adsorption/Desorption	Not determined	Expected to adsorb to soil due to cationic functionality.

Property	*Value*	*Data Source/Justification*
Dissociation Constant	Not determined	The assessed chemical is a quaternary ammonium salt with a permanent positive charge.
Particle Size	Not determined	Imported in an aqueous solution
Flash Point	Not determined	Not expected to form flammable vapours (information provided by the applicant)
Explosive Properties	Not determined	Not expected to be explosive
Oxidising Properties	Not determined	Not expected to be oxidising

*For product containing the assessed chemical at 35%.

DISCUSSION OF PROPERTIES

Reactivity

The assessed chemical is expected to be stable under normal conditions of use.

Physical Hazard Classification

Based on the information depicted in the above table, the assessed chemical is not recommended for hazard classification according to the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia.

5. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF ASSESSED CHEMICAL (100%) OVER NEXT 5 YEARS

The assessed chemical will not be manufactured in Australia. It will be imported into Australia as a component of hair dye products at ≤ 2% concentration.

MAXIMUM INTRODUCTION VOLUME OF ASSESSED CHEMICAL (100%) OVER NEXT 5 YEARS

Year	*1*	*2*	*3*	*4*	*5*
Kilograms	0.5-50	0.5-50	0.5-50	0.5-50	0.5-50

PORT OF ENTRY

Major ports in Australia

IDENTITY OF RECIPIENTS

Kao Australia Pty Ltd

TRANSPORTATION AND PACKAGING

The assessed chemical will be imported as a component of hair dye products in containers such as tubes (60 - 120 g) for professional and consumer use, or in low pressure cans (250 g) for professional salon use. The products will be distributed throughout Australia by road to beauty salons and retail shops.

USE

The assessed chemical will be used as a component of oxidative and non-oxidative hair dye at ≤ 2% concentration.

OPERATION DESCRIPTION

The assessed chemical will not be reformulated or repacked in Australia. Hair dye products containing the assessed chemical at ≤ 2% concentration will be used by professionals (such as hairdressers and beauty salon workers) and will be available for home use by consumers. The finished products are expected to be applied to the hair by brush.

6. HUMAN HEALTH IMPLICATIONS

6.1. Exposure Assessment

6.1.1. Occupational Exposure

CATEGORY OF WORKERS

Category of Worker	*Exposure Duration (hours/day)*	*Exposure Frequency (days/year)*
Transport and Warehousing	2	2

Retail Workers	0.5	100
Professional salon workers	4	220

EXPOSURE DETAILS
Transport, warehousing and retail workers are not expected to be exposed to the assessed chemical except in the unlikely event of an accident.

Dermal exposure to the assessed chemical at ≤ 2% concentration in hair dye products may occur for professionals (e.g. hairdressers or hair salon workers) where the services provided involve the application of the products to clients. Such professionals may use personal protective equipment (PPE), such as impervious gloves, to minimise dermal exposure, and good hygiene practices are expected to be in place.

6.1.2. Public Exposure
There will be widespread and repeated exposure of the public to the assessed chemical at ≤ 2% concentration through the use of hair dye products which may be mixed with other ingredients before being applied to the hair. The main route of exposure will be dermal, with some potential for accidental ocular or oral exposure. Gloves will be used by the consumers to minimise dermal exposure.

6.2. Human Health Effects Assessment
The results from toxicological investigations conducted on the assessed chemical are summarised in the table and study descriptions below, taken from a report by SCCS (2013). Study dossiers were not provided by the applicant.

Endpoint	***Result and Assessment Conclusion***
Dermal percutaneous absorption: dermatomed pig skin, using assessed chemical in formulations	1.76 ± 2.96 µg/cm^2 or 2% (non-oxidative) 2.18 ± 2.05 µg/cm^2 or 4% (oxidative)
Skin irritation – rabbit	non-irritating
Eye irritation – rabbit	slightly irritating
Skin sensitisation – mouse local lymph node assay	no evidence of sensitisation up to 15%
Repeat dose oral toxicity – rat, 90 days	NOAEL = 200 mg/kg bw/day
Mutagenicity – bacterial reverse mutation	non mutagenic
Genotoxicity – *In vitro* mammalian cell gene mutation test (*tk*-locus)	inconclusive
Genotoxicity – *in vitro* mammalian cell gene mutation test (*hprt* locus)	non genotoxic
Genotoxicity – i*n vitro* micronucleus test	genotoxic
Genotoxicity – *in vivo* mammalian erythrocyte micronucleus test	non genotoxic
Reproductive and developmental toxicity – rat	NOAEL = 200 mg/kg bw/day (maternal toxicity) NOAEL = 1,000 mg/kg bw/day (developmental toxicity)

SCCS (2013) commented that there are discrepancies and uncertainties related to the purity of test substance in the toxicological studies.

Toxicokinetics, Metabolism and Distribution
The dermal penetration of the assessed chemical from two different hair dye formulations (2% in non-oxidative and 4% in oxidative) was investigated in dermatomed pig ear skin according to the OECD TG 428. Under the reported conditions, 1.76 ± 2.96 µg/cm² (0.637 ± 1.056% of the applied dose) and 2.18 ± 2.05 µg/cm² (0.883 ± 0.834% of the applied dose) of the assessed chemical was absorbed through the skin (receptor fluid + epidermis + dermis excluding tape strip) under non-oxidative and oxidative conditions, respectively.

In an *in vivo* micronucleus study (OECD TG 474) systemic distribution and thus bioavailability of the assessed chemical was shown in mice when orally administered the assessed chemical at doses of 0, 6.25, 12.5 and 25 mg/kg bw. Clinical signs included blue-stained urine.

Acute Toxicity
No data were submitted to SCCS for acute oral, dermal or inhalation toxicity.

In the pre-test for the *in vivo* micronucleus test (mentioned below) where mice were treated by intraperitoneal (i.p.) injection of the assessed chemical at 100 mg/kg bw died within 1 hour after treatment. After treatment with an i.p. dose of 50 mg/kg bw, 1 mouse out of 10 died after 6 hours.

Skin and Eye Irritation
The assessed chemical caused no skin reactions on rabbits when tested according to OECD TG 404. Slight blue staining of the skin occurred and it was not noted whether this hindered scoring.

The assessed chemical caused slight and reversible irritation to rabbit eyes, when tested according to OECD TG 405.

Skin sensitisation
The assessed chemical was not sensitising to skin in a local lymph node assay (OECD TG 429), when tested up to 15% concentration. The SCCS commented that this concentration was considered too low, and that a sensitisation potential of the assessed chemical cannot be ruled out at higher concentrations.

Repeated Dose Toxicity
The assessed chemical was tested in a 13-week oral gavage study in rats (n = 10 per sex/dose) with a 4-week recovery period, according to OECD TG 408. Doses of 0, 40, 200 and 1000 mg/kg bw/day were chosen on the basis of a range-finding study. Ophthalmoscopy was mistakenly omitted from the protocol. External peer review of the study was carried out as part of its submission to SCCS.

Premature deaths of three rats in the high dose group and one each in the mid and low dose groups were considered to be due to aspiration of the formulation, or gavage error. Intestinal lesions were found at 1,000 mg/kg bw/day (increased histiocytes in lamina propria and hyaline inclusions in the epithelium of duodenum, jejunum, ileum, cecum, colon or rectum of males and females). After recovery, these lesions disappeared at all doses.

At 200 mg/kg bw/day (this value was not confirmed as there appeared to be a typo in the SCCS opinion) and 1,000 mg/kg bw/day respiratory metaplasia of olfactory epithelium, hyperosteosis of the turbinates, submucosal mineralisation and inflammatory exudates were noted, with similar minor effects at 40 mg/kg bw/day. These findings were considered to result from deposition of minute amounts of dosing solution, which subsequently migrated into the nasal turbinates as the animal exhaled. The external reviewers queried the interpretation of the study authors regarding the occurrence of metaplastic olfactory epithelium, and believed that it should have been interpreted as normal respiratory epithelium. The external reviewers agreed that the degenerative changes in the nasal category were secondary to local deposition of the test substance during dosing, and this effect was not taken into account in determining the NOAEL. The study authors set the NOAEL at 1000 mg/kg bw/day, however SCCS considered the NOAEL for systemic toxicity to be 200 mg/kg bw/day, based on the intestinal lesions.

The SCCS commented that the reported irritant effects in the nasal cavity were quite unusual in an oral gavage study and might be due to technical problems during administration of the test substance. The assessed chemical was not considered a strong mucosal irritant: no signs of stomach irritation were observed and the substance was considered only slightly irritating to the rabbit eyes.

Mutagenicity/Genotoxicity
The assessed chemical was negative in a bacterial reverse mutation study using *Salmonella typhimurium* and *Escherichia coli,* in the absence or presence of metabolic activation. The study was carried out according to OECD TG 471 and used both plate incorporation and pre-incubation methods.

Two *in vitro* mammalian cell gene mutation tests were carried out on the assessed chemical in the absence or presence of metabolic activation, according to OECD TG 476. When tested for gene mutations at the *tk* locus of mouse lymphoma cells, the results were considered inconclusive, as they were negative in the absence of metabolic activation, but inconsistent in the presence of metabolic activation. With metabolic activation, a dose related and statistically significant increase in the mutant frequency occurred in culture 1, however it was considered that a biologically relevant increase did not occur in culture 2. A negative result was obtained in the second gene mutation study (TG 476), which tested for mutations at the *hpr*t locus of mouse lymphoma cells.

The SCCS reviewed a short report on an *in vitro* micronucleus study using Chinese Hamster V79 cells. The study was not conducted in compliance with GLP or according to the draft OECD guideline, and the inducer chemical for S9 extract was not identified. The report only contained the "results and discussion" paragraph but was considered relevant by the SCCS as the most relevant information was described. Under the experimental

conditions used, the test substance induced a biologically relevant and statistically significant increase in the number of V79 cells with micronuclei. This occurred in the absence of S9 at the top three concentrations (1,175, 2,350 and 4,700 µg/mL) but was not clearly dose related, and in the presence of S9 occurred only at the mid concentration (not specified by SCCS). The assessed chemical was considered genotoxic in this study.

The assessed chemical was negative in an *in vivo* micronucleus study in mice carried out according to OECD TG 474. The assessed chemical was orally administered to mice (n = 5 per sex/dose) at doses of 0, 6.25, 12.5 and 25 mg/kg bw. Systemic distribution and thus bioavailability of the chemical was indicated by clinical signs, including blue-stained urine.

The SCCS considered that sufficient investigation of the potential for genotoxicity had been carried out and that overall the assessed chemical was not genotoxic. They noted the negative results in the bacterial gene mutation test and the mammalian gene mutation test using the *hprt*-locus, and the inconclusive result of the *in vitro* mammalian gene mutation test using the *tk*-locus. The positive result in the *in vitro* micronucleus test was not confirmed in the *in vivo* test.

Reproductive /Developmental Toxicity
No data on reproductive effects were submitted to SCCS. A developmental study on the assessed chemical was carried out in rats (n = 22 mated females per test group) according to OECD TG 414 via oral gavage daily from day 6 – 20 *post-coitum.* The doses of 0, 40, 200 and 1,000 mg/kg bw/day were chosen on the basis of a range-finding study using the same maximum concentration, and in which no mortality was observed.

In the main study, there was no mortality or adverse clinical signs in the dams. Discoloured faeces at 1,000 mg/kg bw/day were considered due to the colouring characteristics of the chemical. At this dose there were statistically significant reductions in mean food consumption and mean body weight gain, both considered test substance related. Mean corrected body weight gain (corrected for the gravid uterus weight) was slightly but not statistically significantly reduced at 1,000 mg/kg bw/day (+12.3% compared to +14.5% in the control group), and was considered by the SCCS to be test substance-related.

There was no test substance-related effect on the relevant reproduction parameters in any dose group. No findings were noted during external examination of the foetuses in any group. No test substance-related effects on the sex ratio of the foetuses or mean foetal weights were noted in any group.

During visceral and skeletal examination of the foetuses no test substance-related findings were noted. Due to a skeletal staining error, some foetuses could not be reliably examined. However additional analysis of the data was carried out, and it was considered that the reliability of the study had not been affected. Although there was a statistically significantly higher incidence of rudimentary supernumerary left ribs at 1,000 mg/kg bw/day, when calculated on a foetus basis, this higher incidence was in the range of the historical control data and was considered to be incidental.

The SCCS considered the NOAEL for this study to be 200 mg/kg bw/day for maternal toxicity and 1,000 mg/kg bw/day for developmental toxicity.

Health Hazard Classification
Based on the information available in the SCCS Opinion (2013), the assessed chemical is not classified according to the *Globally Harmonised System of Classification and Labelling of Chemicals* (GHS), as adopted for industrial chemicals in Australia.

Based on analyses submitted for the assessed chemical, it contains an impurity at < 1% (9,10-Anthracenedione, 1-amino-2-methyl-, CAS No 82-28-0), that is classified under HCIS as a Category 2 carcinogen (HCIS, SWA). This impurity is present below the cut-off concentration for classification under the GHS as adopted for use in Australia).

6.3. Human Health Risk Characterisation
Based on the toxicity data evaluated by the SCCS (2013) the assessed chemical is not classified under the GHS. It is a secondary amine, and thus is prone to nitrosation and formation of nitrosamines. It contains a hazardous impurity (Category 2 carcinogen) at < 1%. Although the assessed chemical was not a skin sensitiser in the LLNA

at the highest concentration tested (15%), the SCCS considered that this concentration was too low to rule out the potential for skin sensitisation.

6.3.1. Occupational Health and Safety

Workers involved in professions where the services provided involve the application of hair dye products containing the assessed chemical to clients (*e.g.*, hairdressers and hair salon workers) may be exposed to the assessed chemical at concentrations up to 2%. The greatest potential for exposure is during hair dyeing processes, mainly via skin contact, although ocular exposure may also occur.

Given that the product is a dye, skin contact is expected to be avoided by workers. Workers will use PPE (such as disposable gloves to minimise repeated exposure), and good hygiene practices are expected to be in place.

Overall, based on the low concentration of the assessed chemical in hair dye products and the use of PPE (gloves), the risk to workers from exposure to the assessed chemical is not considered to be unreasonable.

6.3.2. Public Health

Hair dye products containing the assessed chemical will be supplied to hairdressing salons and may also be available for public via retail outlets. Therefore, members of the public may potentially be exposed to the assessed chemical when mixing/applying the product (at ≤ 2% concentration) and when having the product applied to their scalp (at ≤ 2% concentration). The degree and type of exposure may vary depending on the frequency of application, the care taken when applying the dye and amount of dye applied.

Local effects

Irritation or sensitisation effects are not expected from the use of products containing the assessed chemical at the proposed low use concentration (up to 2%) in hair dyes. Possible use of gloves will further reduce exposure and risk.

Systemic effects from repeated use

The assessed chemical was the subject of a SCCS Opinion (SCCS, 2013) which calculated the margin of safety (MOS) for the use of the assessed chemical in hair dyes as follows:

Absorption through the skin under non-oxidative conditions	A	4.72 μg/cm^2
Skin area surface	SAS	580 cm^2
Dermal absorption per treatment	SAS × A × 0.001	2.74 mg
Typical body weight of human		60 kg
Systemic exposure dosage (SED)	SAS × A × 0.001/60	0.05 mg/kg bw/day
No Observed Adverse Effect Level	NOAEL	200 mg/kg bw/day*
50% bioavailable**		100 mg/kg bw/day
MOS	NOAEL/SED	2,000

*Derived for a sub-chronic toxicity study, and for maternal toxicity in a developmental toxicity study
**Standard procedure according to the SCCS's Notes of Guidance for the testing of cosmetic ingredients and their safety evaluation.

Absorption through the skin under oxidative conditions	A	4.23 μg/cm^2
Skin area surface	SAS	580 cm^2
Dermal absorption per treatment	SAS × A × 0.001	2.45 mg
Typical body weight of human		60 kg
Systemic exposure dosage (SED)	SAS × A × 0.001/60	0.04 mg/kg bw/day
No Observed Adverse Effect Level	NOAEL	200 mg/kg bw/day*
50% bioavailable**		100 mg/kg bw/day
MOS	NOAEL/SED	2,500

*Derived for a sub-chronic toxicity study, and for maternal toxicity in a developmental toxicity study
**Standard procedure according to the SCCS's Notes of Guidance for the testing of cosmetic ingredients and their safety evaluation.

The SCCS (2013) concluded that the use of the assessed chemical at a maximum on-head concentration of 2.0% in both oxidative and non-oxidative hair dye formulations does not pose a risk to the health of the consumer. This is reflected in the entry for the assessed chemical in Annex III to Regulation (EC) 1223/2009, which was added in 2015 (EC 2009).

The EC Regulation also specifies the following precautions related to nitrosamines:

- Do not use with nitrosating agents
- Maximum nitrosamine content: 50 µg/kg
- Keep in nitrite-free containers

The EC Regulation recommends label warnings relevant to skin sensitisation for oxidative dye products containing the assessed chemical, in order to better inform consumers about these risks and lower their incidence.

In Australia the proposed use of the assessed chemical in both oxidative and non-oxidative hair dye products at a maximum on-head concentration of 2%, is same as that assessed by the SCCS (2013). When the assessed chemical is used in products at up to 2%, the concentration of the hazardous impurity in the final product is estimated to be < 0.02%. Reduction of the level of hazardous and potentially hazardous impurities in the assessed chemical, and precautions against the formation of nitrosamines throughout the life cycle of the chemical would reduce hazard and risk.

The assessed chemical will not be manufactured, reformulated or repacked in Australia. The finished hair dye products containing the assessed chemical will be imported into Australia for end use. The applicant has confirmed that the product formulations which are being supplied in Germany are those that will be supplied in Australia.

If the formulators of hair dyes containing the assessed chemical are following the above precautions (as specified in the EC Regulation – stated above), the risk to the public from the proposed use of the assessed chemical in hair dyes is not considered to be unreasonable.

7. ENVIRONMENTAL IMPLICATIONS

7.1. Environmental Exposure & Fate Assessment

7.1.1. Environmental Exposure

RELEASE OF CHEMICAL AT SITE

The assessed chemical will not be manufactured in Australia and imported as a component of finished hair dye products. Some release of the assessed chemical may be from spills during the transport and storage of the finished products containing the assessed chemical. Accidental spills will be collected for disposal, in accordance with local government regulations.

RELEASE OF CHEMICAL FROM USE

The majority of the assessed chemical will be rinsed into the sewer system as a result of its use in hair dye products.

RELEASE OF CHEMICAL FROM DISPOSAL

Residues of the assessed chemical in empty product containers are likely to either share the fate of the containers and be disposed of to landfill or be released to the sewer system when containers are rinsed before recycling through an approved waste management facility.

7.1.2. Environmental Fate

The majority of the assessed chemical is expected to enter the sewer system before potential release to surface waters on a nationwide basis.

A proportion of the assessed chemical may be applied to land when effluent is used for irrigation or when sewage sludge is used for soil remediation, or disposed of to landfill as a waste (see Predicted Environmental Concentration). Minor amounts of the assessed chemical may also be disposed of to landfill as collected spills and empty container residues. The assessed chemical residues in landfill and soils are expected to have low mobility and adsorb to soils. The assessed chemical is not expected to bioaccumulate based on its moderate log Pow of 3.47. In the aquatic and soil compartments, the assessed chemical is expected to degrade through biotic and abiotic processes to form water and oxides of carbon, nitrogen and sulphur.

7.1.3. Predicted Environmental Concentration (PEC)

The use pattern will result in most of the assessed chemical being washed into the sewer. The predicted environmental concentration (PEC) has been calculated assuming the realistic worst-case scenario with 100% release of the assessed chemical into sewer systems nationwide over 365 days per annum. The extent to which the assessed chemical is removed from the effluent in STP processes based on the properties of the assessed chemical has not been considered for this scenario, and therefore no removal of the assessed chemical during sewage treatment processes is assumed. The PEC in sewage effluent on a nationwide basis is estimated as follows:

Predicted Environmental Concentration (PEC) for the Aquatic Compartment		
Total Annual Import Volume	50	kg/year
Proportion expected to be released to sewer	100%	
Annual quantity of chemical released to sewer	50.000	kg/year
Days per year where release occurs	365	days/year
Daily chemical release:	0.14	kg/day
Water use	200.0	L/person/day
Population of Australia (Millions)	24.386	million
Removal within STP	0%	
Daily effluent production:	4,877	ML
Dilution Factor – River	1.0	
Dilution Factor – Ocean	10.0	
PEC - River:	0.03	µg/L
PEC - Ocean:	0.00	µg/L

STP effluent re-use for irrigation occurs throughout Australia. The agricultural irrigation application rate is assumed to be 1,000 L/m^2/year (10 ML/ha/year). The assessed chemical in this volume is assumed to infiltrate and accumulate in the top 10 cm of soil (density 1,500 kg/m^3). Using these assumptions, irrigation with a concentration of 0.028 µg/L may potentially result in a soil concentration of approximately 0.19 µg/kg. Assuming accumulation of the assessed chemical in soil for 5 and 10 years under repeated irrigation, the concentration of assessed chemical in the applied soil in 5 and 10 years may be approximately 0.94 µg/kg and 1.87 µg/kg, respectively.

7.2. Environmental Effects Assessment

No ecotoxicity study was conducted on the assessed chemical. However, cationic chemicals are expected to be toxic to aquatic species.

7.2.1. Predicted No-Effect Concentration

The Predicted No-Effect Concentration (PNEC) has not been calculated as no ecotoxicity studies were conducted on the assessed chemical.

7.3. Environmental Risk Assessment

On the basis of the reported use pattern and low import volume, the assessed chemical is not considered to pose an unreasonable risk to the environment.

BIBLIOGRAPHY

Mery S., Gross EA, Joyner DR, Godo M. and Morgan KT (1994): Nasal diagrams: a tool for recording the distribution of nasal lesions in rats and mice. Toxicol Pathol 22 (4): 353-372

SCCS (2013) Opinion on HC Blue 17. Colipa No A184. SCCS/1471/12. Scientific Committee on Consumer Safety, Directorate General for Health of Consumers. Office B232, B1049 Brussels Belgium. 26 February 2013.

EC (2009) Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on Cosmetic Products (recast) (Text with EEA relevance) (OJ L 342, 22.12.2009, p. 59), see https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:02009R1223-20190813&from=EN, accessed 26 August 2020.

HCIS (2020) Hazardous Chemical Information System (HCIS) see http://hcis.safeworkaustralia.gov.au/ accessed on 31 August 2020.

United Nations (2009) Globally Harmonised System of Classification and Labelling of Chemicals (GHS), 3rd revised edition. United Nations Economic Commission for Europe (UN/ECE), <http://www.unece.org/trans/danger/publi/ghs/ghs_rev03/03files_e.html >