File No.: LTD/2150

September 2020

AUSTRALIAN INDUSTRIAL CHEMICALS INTRODUCTION SCHEME (AICIS)

PUBLIC REPORT

Phenol, 2-chloro-4-[(1*E*)-2-(1-methyl-1*H*-pyrazol-5-yl)diazenyl]- (INCI name: HC Yellow No. 16)

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 public health and occupational health and safety. 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 the AICIS website:

ASSESSMENT REFERENCE	APPLICANT(S)	CHEMICAL OR TRADE NAME	HAZARDOUS CHEMICAL	INTRODUCTION VOLUME	USE
LTD/2150	Kao Australia Pty Ltd	Phenol, 2-chloro-4-[(1*E*)-2-(1-methyl-1*H*-pyrazol-5-yl)diazenyl]- (INCI name: HC Yellow No. 16)	Yes	≤ 0.07 tonne per annum	Oxidative hair dye ingredient for professional use only

CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard Classification
Based on the information available in the SCCS Opinion (2016), the assessed chemical is a hazardous chemical according to the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia. The hazard classification applicable to the assessed chemical is presented in the following table.

Hazard Classification	*Hazard Statement*
Specific target organ toxicity, repeated exposure (Category 2)	H373 – Causes damage to organs through prolonged or repeated exposure

Human Health Risk Assessment
Under the conditions of the occupational settings described, the assessed chemical is not considered to pose an unreasonable risk to the health of workers.

When used in the proposed manner, 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

REGULATORY CONTROLS

Hazard Classification and Labelling

- The assessed chemical should be classified as follows:
  - Specific target organ toxicity, repeated exposure (Category 2): H373 – Causes damage to organs through prolonged or repeated exposure

  The above should be used for products/mixtures containing the assessed chemical, if applicable, based on the concentration of the assessed chemical present.

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.

- 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.

Storage

- The handling and storage of the assessed chemical should be in accordance with the Safe Work Australia Code of Practice for *Managing Risks of Hazardous Chemicals in the Workplace* (SWA, 2012) or relevant State or Territory Code of Practice.

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 chemical 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 applicant 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 for professional use, or is likely to change significantly;
- the importation volume exceeds one tonne per annum assessed chemical;
- the 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 1%;
- 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 SDSs of products containing the assessed chemical provided by the applicant were reviewed by AICIS. The accuracy of the information on the SDSs remains the responsibility of the applicant.

ASSESSMENT DETAILS

1. APPLICANT AND APPLICATION DETAILS

APPLICANT(S)
Kao Australia Pty Ltd (ABN: 59 054 708 299)
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: specific other names, analytical data, degree of purity, introduction and use concentrations and import volume.

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

NOTIFICATION IN OTHER COUNTRIES
EU (2009)

2. IDENTITY OF CHEMICAL

MARKETING NAME
HC Yellow No. 16 (INCI Name)

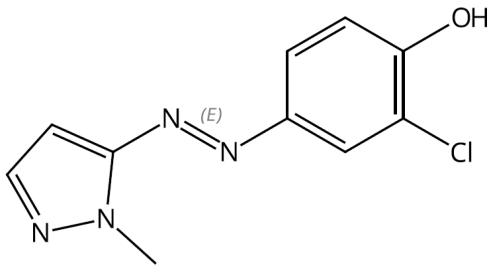
CAS NUMBER
1184721-10-5

CHEMICAL NAME
Phenol, 2-chloro-4-[(1*E*)-2-(1-methyl-1*H*-pyrazol-5-yl)diazenyl]-

OTHER NAME(S)
T44P2
Colipa No. B123

MOLECULAR FORMULA
$C_{10}H_9ClN_4O$

STRUCTURAL FORMULA



MOLECULAR WEIGHT
236.66 g/mol

ANALYTICAL DATA
Reference NMR, IR and UV spectra were provided.

3. COMPOSITION

DEGREE OF PURITY
> 99%

IMPURITIES

Chemical Name	4 unknown impurities		
CAS No.	N/A	*Weight %*	< 0.9 (total)

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: yellow powder (SCCS 2016)

Property	***Value***	***Data Source/Justification***
Melting Point	266.15 °C	Calculated (US EPA MPBVP (v1.43))
Boiling Point	361.93 °C	Calculated (US EPA MPBVP (v1.43))
Density	~1,100-1,200 kg/m^3	Estimated by applicant
Vapour Pressure	1.99 x 10^{-7} kPa at 25 °C	Calculated (US EPA MPBVP (v1.43))
Water Solubility	134.5 mg/L at 25 °C	Calculated (US EPA (2012) WSKOW (v1.42))
Hydrolysis as a Function of pH	Not determined	Contain no functionality susceptible to hydrolysis. Found to be stable in alkaline peroxide for 45 min (EU 2015).
Partition Coefficient (n-octanol/water)	log Pow = 2.89 at 25 °C	Calculated (US EPA (2012) KOWWIN (v1.68))
Adsorption/Desorption	log K_{oc} = 3.52 at 25 °C	Calculated (US EPA (2012) KOCWIN (v2.0))
Dissociation Constant	pKa = 7.75	Calculated (ACD/labs)
Flash Point	Not determined	Not expected to form flammable vapours (information provided by the applicant)
Flammability	Not determined	Not expected to be flammable
Autoignition Temperature	Not determined	Not expected to autoignite
Explosive Properties	Not determined	Contains no functional groups that would imply explosive properties
Oxidising Properties	Not determined	Contains no functional groups that would imply explosive properties

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 oxidative hair dye products at ≤ 1% concentration.

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

Year	*1*	*2*	*3*	*4*	*5*
Tonnes	0.02-0.07	0.02-0.07	0.02-0.07	0.02-0.07	0.02-0.07

PORT OF ENTRY
Major ports in Australia

IDENTITY OF MANUFACTURER/RECIPIENTS
Kao Australia Pty Ltd

TRANSPORTATION AND PACKAGING
The assessed chemical will be imported as a component of finished hair dying products (at ≤ 1% concentration) in containers, such as tubes (50-120 g) or tubs (500 g), for professional use.

USE
The assessed chemical will be used as an oxidative dye in hair dye formulations. The assessed chemical will be introduced in finished oxidative hair dye products at ≤ 1% concentration The hair dye product will be mixed with a developer to give a maximum on-head concentration of 0.33% for the assessed chemical. The hair dye products will be available for use by professionals only (e.g. hairdressers or hair salon workers).

OPERATION DESCRIPTION
The assessed chemical will not be reformulated or repacked in Australia. Hair dye products containing the assessed chemical at ≤ 1% concentration will be used by professionals only (such as hairdressers and hair salon workers). Professional hairdressers and hair salon workers will mix the hair dye products with a developer and then apply the dye mixture containing the assessed chemical at ≤ 0.33% concentration to the customer's 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 warehouse	2	12
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 ≤ 1% concentration in hair dying products may occur in 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
Hair dye products containing the assessed chemical will not be made available for home use. The public will be exposed to hair dye products containing the assessed chemical during hair dye treatments in hair salons. The main route of exposure will be dermal, with some potential for accidental ocular exposure. The maximum on-head concentration of the assessed chemical will be 0.33%.

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 the Scientific Community on Consumer Safety (SCCS, 2016). Study dossiers were not provided by the applicant.

Endpoint	***Result and Assessment Conclusion***
Dermal percutaneous absorption – *in vitro* pig dermatomed skin (2% mixture)	0.51 ± 0.21 µg/cm^2 or 0.18 ± 0.07% (oxidative conditions)
Skin irritation – rabbit	non-irritating
Eye irritation – rabbit	slightly irritating

Endpoint	*Result and Assessment Conclusion*
Skin sensitisation – mouse local lymph node assay	no evidence of sensitisation (up to 20%)
Repeat dose oral toxicity – rat, 90 days	NOAEL = 15 mg/kg bw/day (males) NOAEL = 3 mg/kg bw/day (females)
Mutagenicity – bacterial reverse mutation	non mutagenic
Genotoxicity – *in vitro* mammalian cell gene mutation test (*hprt* locus)	non genotoxic
Genotoxicity – i*n vitro* micronucleus test using V79 cells	genotoxic
Genotoxicity – i*n vitro* micronucleus test using human lymphocytes	non genotoxic
Genotoxicity – *in vivo* mammalian bone marrow micronucleus test - rat	non genotoxic
Prenatal developmental toxicity – rat	NOAEL = 15 mg/kg bw/day (maternal toxicity) NOAEL = 50 mg/kg bw/day (developmental toxicity) No teratogenic potential up to 150 mg/kg bw/day

The SCCS Opinion (2016) indicated that there are discrepancies and uncertainties related to the purity of test substance used in the toxicological studies.

Dermal / percutaneous absorption
The dermal penetration of the assessed chemical under oxidative conditions from a formulation containing the assessed chemical at 2% concentration was investigated in dermatomed pig ear skin according to OECD TG 428. Under the reported conditions, the dermal delivery of the assessed chemical was 0.51 ± 0.21 μg/cm² (0.18 ± 0.07% of applied dose).

Toxicokinetics
Under the conditions of an *in vivo* toxicokinetic study, an oral absorption of 84% was determined for the assessed chemical, based on the results from the bile-duct cannulated rats showing an excretion of the assessed chemical of about 37% and 47% of the dose in bile and urine, respectively.

Acute Toxicity
No data were submitted for acute oral, dermal and inhalation toxicity.

Based on the mortalities (1 out of 5 males and 1 out of 5 females on days 6 and 8 respectively) in rats treated at 300 mg/kg bw/day via oral gavage in a 14-day dose range-finding study, the assessed chemical is considered to have moderate acute toxic potential via the oral route.

Irritation
The assessed chemical caused no skin reactions in rabbits when tested according to OECD TG 404. Slight yellow staining of the skin occurred and it was not noted in the SCCS Opinion 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 mouse local lymph node assay (LLNA, OECD TG 429), when tested up to 20% concentration. The test substance induced stimulation index (SI) values of 0.78, 0.93, 0.79 and 0.88 at concentrations of 1, 5, 10 and 20%, respectively and the estimated concentration that elicits a three-fold increase in lymphocyte proliferation (EC3) could not be calculated. The SCCS (2016) commented that the highest dose tested was the maximum concentration that could be technically achieved and based on the negative results, the assessed chemical is not a skin sensitiser.

Repeated Dose Toxicity
In a 14-day dose range finding study, the assessed chemical was administered by oral gavage to rats (5/sex/group) at dose levels of 0, 75, 150, 300 mg/kg bw/day (reduced to 200 mg/kg bw/day from day 8 in males due to deaths) and 600 mg/kg bw/day (reduced to 450 mg/kg bw/day from day 4 in males and from day 7 in females due to deaths) once daily for 14 days.

Deaths occurred included 1 male and 4 females treated at 600 mg/kg bw/day died on day 3 and days 5-7 respectively, 3 males treated at 450 mg/kg bw/day died on days 5-6, and 1 male and 1 female treated at 300 mg/kg bw/day died on days 6 and 8, respectively.

Clinical signs of toxicity, laboratory findings and effects in organs included:

- Several animals that died exhibited a decrease in locomotor activity, prone position, tremor, irregular respiration, hypothermia, chromaturia (yellow urine), and remarkable decreases in body weight and food consumption before death.
- In the surviving animals, a decrease in locomotor activity, emaciation, tremor, irregular respiration, and/or were noted in one male at 300 (200) mg/kg bw/day from day 7 and in one female at 600 (450) mg/kg bw/day at days 5-10. Chromaturia was noted sporadically in 1 male and in 1 female each at 300 (200) mg/kg bw/day and 600 (450) mg/kg bw/day.
- In the surviving animals, a statistically significantly lower body weight was observed in males treated at 300 (200) mg/kg bw/day or more and in females treated at 150 mg/kg bw/day or more on day 3. However, individual body weight increased from day 6 in females treated at 150 mg/kg bw/day and from day 9 in males and females treated at 300 (200) mg/kg bw/day or more. Food consumption decreased correspondingly but increased gradually and was not statistically significant on day 14.
- Several changes related to the test substance were noted in urinalysis, haematology and clinical chemistry in males and/or females treated at 75 mg/kg bw/day and/or more.
- Statistically significant increases in mean kidney and spleen weights were noted in males and females treated at 150 mg/kg bw/day or more. Liver weight increased in males treated at 300 (200) mg/kg bw/day and in females treated at 300 mg/kg bw/day or more. Adrenal weight increased in males treated at 150 and 300(200) mg/kg bw/day. Thymus weight decreased in females treated at 300 mg/kg bw/day.
- Histopathological changes were observed in the kidney, spleen, liver and bone marrow in males and/or females treated at 75 mg/kg bw/day and/or more.

The No Observed Adverse Effect Level (NOAEL) for the assessed chemical is lower than 75 mg/kg bw/day, based on the results obtained in the 14-day dose range-finding study.

In a 90-day repeated dose toxicity study, rats (10/sex/group) were treated by the assessed chemical via oral gavage once daily for at least 13 weeks at the doses 0, 3, 15, 75 mg/kg bw/day according to OECD TG 408, with 5 animals per sex of the control group and high dose group were allowed a 4-week treatment-free recovery period.

No deaths or treatment-related clinical signs of toxicity were observed and no abnormalities were noted in the function tests (sensory reactivity to stimuli and grip strength), or in the motor activity test, body weight, food consumption and ophthalmology.

In the final week of the dosing period, an increase in epithelial cells in urinary sediment was noted in 2 females treated at 75 mg/kg/day and an increase in urinary glucose in 1 female of the same group, which recovered at the end of the recovery period.

The following laboratory finding were noted at the end of the dosing period but were reversed at the end of the recovery period (SCCS, 2016):

- Statistically significant decreases in red blood cell count, haematocrit, haemoglobin concentration, and MCHC in males and females treated at 75 mg/kg/day
- Decreases in red blood cell count, haemoglobin concentration and MCHC in females treated at 15 mg/kg bw/day
- Statistically significant increases in MCV, MCH, and reticulocyte ratio and count in males and females treated at 75 mg/kg bw/day
- A statistically significant increase in total bilirubin in females at 75 mg/kg bw/day

Statistically significant increases in the relative spleen weights were noted in males and females treated at 75 mg/kg bw/day, and in the relative kidney weights in males treated at 75 mg/kg bw/day, which were reversed at the end of the recovery period.

At the end of the dosing period, the following treatment-related histopathological changes were noted in the kidney, spleen, liver and bone marrow. At the end of the recovery period, treatment-related changes were still noted in the kidney and spleen:

- In the kidneys of animals treated at 75 mg/kg bw/day, increased incidence and severity (minimal to mild grade) of basophilic tubule, and cell infiltration (lymphocyte, interstitium; minimal grade) in males,

necrosis of proximal tubular epithelium (minimal grade) and regeneration of tubular epithelium (minimal grade) in females, and interstitium mineralisation (minimal grade), hyaline cast (minimal grade), and brown pigment deposition in the tubular epithelium (minimal grade) in males and in females
- In the spleen, increased incidences of extramedullary haematopoiesis of erythroid lineage (minimal grade) and of haemosiderin deposition in splenic macrophages (minimal grade) in females treated at 15 mg/kg bw/day and in males and females treated at 75 mg/kg bw/day.
- In the liver, increased incidences of focal hepatocyte necrosis (minimal grade) in males and of haemosiderin deposition in Kupffer cells (minimal grade) in females treated at 75 mg/kg bw/day
- In the femoral bone marrow, an increase in erythrocytic cells (minimal grade) in males and females treated at 75 mg/kg bw/day.

The NOAEL was considered to be 15 mg/kg bw/day for males and 3 mg/kg bw/day for females. The treatment-related changes noted in the kidney and spleen following the recovery period warrants a hazard classification for specific target organ toxicity, repeated exposure (Category 2).

Mutagenicity/Genotoxicity
The assessed chemical was tested negative for the induction of gene mutations in strains of *Salmonella typhimurium* and *Escherichia coli* according to OECD TG 471.

The assessed chemical was negative for gene mutations at the *hpr*t locus of Chinese hamster V79 cells both in the absence and presence of metabolic activation according to OECD TG 476.

The assessed chemical was tested negative in the absence of metabolic activation but positive in the presence of metabolic activation (≥ 138.8 µg/ml) for the induction of micronuclei in V79 cells according to draft OECD TG 487 (2009).

In another experiment, the assessed chemical was negative in the absence or presence of metabolic activation for the induction of micronuclei in human lymphocytes up to 150 µg/ml concentration, according to OECD TG 487.

SCCS (2016) commented that the positive results on V79 cells and the negative outcome with human lymphocytes were contradictory and much lower concentrations were used for the main experiment in the study on human lymphocytes, compared to the micronucleus test on V79 cells.

The assessed chemical was found to be negative for induction of micronuclei in the bone marrow cells of rats treated by oral gavage once daily for 14 days at dose levels of 0, 75, 150, 300 and 600 mg/kg bw/day, according to OECD TG 407 (integrated in the 14-day oral repeated dose toxicity study).

SCCS (2016) commented that the assessed chemical can be considered to have no genotoxic potential and additional tests are unnecessary.

Developmental Toxicity
In a dose range finding study for prenatal developmental toxicity, the assessed chemical was administered by oral gavage to mated female rats (6 females/group) at dose levels of 0, 10, 25, 50, 100 and 150 mg/kg bw/day from gestation day 6 to 19.

No mortalities, clinical signs of toxicity or gross pathological changes were observed. Decreased (not statistically significant) body weight, food consumption and gravid uterus weight were observed in animals treated at 150 mg/kg bw/day. No treatment-related effects were noted on the number of corpora lutea, implantations, pre- and post-implantation loss index, early and late resorption index, dead foetus index, live foetuses, or sex ratio. Decreases in the body weight of the live male and female foetuses were recorded in 100 and 150 mg/kg bw/day dose groups, but without statistical significance compared to the control group. No treatment-related placental or foetal anomalies (external, visceral or skeletal) were observed in any live foetus. No effects were observed in the examination of the progress of ossification using sternebrae and sacrocaudal vertebrea. Based on the results, dose levels of 15, 50 and 150 mg/kg bw/day were proposed for the main study on embryo-foetal development.

In the main study for prenatal developmental toxicity, the assessed chemical was administered by oral gavage to mated female rats (20 females/group) at dose levels of 0, 15, 50 and 150 mg/kg bw/day from gestation day 6 to 19 according to OECD TG 414.

No mortalities, clinical signs of toxicity, significant differences in gravid uterus weight, or gross pathological changes were observed. Statistically significant decreases in mean body weight and food consumption were observed in animals treated at 50 or 150 mg/kg bw/day. No treatment-related effects were noted on the number of corpora lutea, implantations, pre and post-implantation loss index, early and late resorption index, dead foetus index, live foetuses, or sex ratio of live foetuses. No placental anomalies were observed. The body weights of live male and female foetuses in the 150 mg/kg bw/day group were statistically significantly lower, compared to the control. No treatment-related foetal anomalies (external, visceral or skeletal) were observed in any live foetus. No effects were observed in the examination of the progress of ossification using sternebrae and sacrocaudal vertebrea (SCCS, 2016).

The NOAEL was considered to be 15 mg/kg bw/day for general toxicity of the dams and 50 mg/kg bw/day for the embryo-foetal development and the assessed chemical did not reveal any teratogenic potential up to 150 mg/kg bw/day.

Health Hazard Classification
Based on the information available in the SCCS Opinion (2016), the assessed chemical is a hazardous chemical according to the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia. The hazard classification applicable to the assessed chemical is presented in the following table.

Hazard Classification	***Hazard Statement***
Specific target organ toxicity, repeated exposure (Category 2)	H373 – Causes damage to organs through prolonged or repeated exposure

6.3. Human Health Risk Characterisation
Based on the toxicity data evaluated by the SCCS (2016), the assessed chemical is considered to have acute and repeated dose toxicity potential via the oral route and is a mild eye irritant. However, eye irritation effects are not expected at the low end-use concentrations (≤ 1%).

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 1%. 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 only. Therefore, members of the public may potentially be exposed to the assessed chemical when having the product applied to their scalp (at ≤ 0.33% 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 1%) in hair dyes.

Systemic effects from repeated use
The assessed chemical was the subject of a SCCS Opinion (SCCS, 2016) which calculated the margin of safety (MOS) for the use of the assessed chemical (oxidative conditions, in formulation, on-head concentration of 1%) as follows:

Absorption through the skin	A	0.72 μg/cm^2
Skin area surface	SAS	580 cm^2
Dermal absorption per treatment	SAS × A × 0.001	0.418 mg
Typical body weight of human		60 kg

Systemic exposure dosage (SED)	SAS × A × 0.001/60	0.0070 mg/kg bw/day
No Observed Adverse Effect Level	NOAEL	3 mg/kg bw/day (derived from sub-chronic oral toxicity study in rats)
84% bioavailable*		2.52 mg/kg bw/day
MOS	adjusted NOAEL/SED	360

* based on the toxicokinetic study.

The SCCS (2016) concluded that the use of the assessed chemical at a maximum on-head concentration of 1% in oxidative hair dye formulations does not pose a risk to the health of the consumer.

The proposed Australian use of the assessed chemical in oxidative hair dye products at a maximum on-head concentration of 0.33% is lower than the concentration assessed by the SCCS (2016). Therefore, systemic repeated dose risks from use of the assessed chemical by members of the general public at ≤ 0.33% on-head concentration in oxidative 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, reformulated or repacked in Australia. It will be 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 based on its estimated soil adsorption coefficient (log Koc = 3.52). The assessed chemical is not expected to bioaccumulate based on the estimated moderate partition coefficient (log Pow = 2.89). 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 chlorine.

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/Manufactured Volume	70	kg/year
Proportion expected to be released to sewer	100%	
Annual quantity of chemical released to sewer	70	kg/year

Days per year where release occurs	365	days/year
Daily chemical release:	0.19	kg/day
Water use	200	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:	0.04	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 1000 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 1500 kg/m^3). Using these assumptions, irrigation with a concentration of 0.04 µg/L may potentially result in a soil concentration of approximately 0.00026 mg/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 0.0013 mg/kg and 0.0026 mg/kg, respectively.

7.2. Environmental Effects Assessment

No ecotoxicity studies on the assessed chemical were submitted.

7.2.1. Predicted No-Effect Concentration

The Predicted No-Effect Concentration (PNEC) has not been calculated as no ecotoxicity studies were available.

7.3 Environmental Risk Assessment

A risk quotient (PEC/PNEC) for the assessed chemical was not calculated as no ecotoxicity data were available. The assessed chemical is unlikely to reach ecotoxicologically significant concentrations in the environment based on its annual importation quantity and use pattern. On the basis of the low import volume, the assessed chemical is not considered to pose an unreasonable risk to the environment.

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