File No: LTD/1845

August 2015

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

Cuprate(4-), [[3,3',3'',3'''-[(29*H*,31*H*-phthalocyanine-1,8,15,22-tetrayl-κ*N*^{29},κ*N*^{30},κ*N*^{31},κ*N*^{32})tetrakis(sulfonyl)]tetrakis[1-propanesulfonato]](6-)]-, sodium (1:4), (*SP*-4-1)-

This Assessment has been compiled in accordance with the provisions of the *Industrial Chemicals (Notification and Assessment) Act 1989* (the Act) and Regulations. This legislation is an Act of the Commonwealth of Australia. The National Industrial Chemicals Notification and Assessment Scheme (NICNAS) 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 the Environment.

This Public Report is also available for viewing and downloading from the NICNAS website or available on request, free of charge, by contacting NICNAS. For requests and enquiries please contact the NICNAS Administration Coordinator at:

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Director
NICNAS

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SUMMARY

The following details will be published in the NICNAS *Chemical Gazette:*

ASSESSMENT REFERENCE	APPLICANT(S)	CHEMICAL OR TRADE NAME	HAZARDOUS CHEMICAL	INTRODUCTION VOLUME	USE
LTD/1845	Epson Australia Pty Ltd	Cuprate(4-), [[3,3',3",3"'-[(29*H*,31*H*-phthalocyanine-1,8,15,22-tetrayl-κN^{29},κN^{30},κN^{31},κN^{32})tetrakis(sulfonyl)]tetrakis[1-propanesulfonato]](6-)]-, sodium (1:4), (*SP*-4-1)-	ND*	< 1 tonne per annum	Component of inkjet printing ink

*ND = not determined

CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard classification

Based on the available information, the notified chemical cannot be recommended for classification according to the *Globally Harmonised System of Classification and Labelling of Chemicals* (GHS), as adopted for industrial chemicals in Australia, or the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004).

The environmental hazard classification according to the *Globally Harmonised System of Classification and Labelling of Chemicals* (GHS) is presented below. Environmental classification under the GHS is not mandated in Australia and carries no legal status but is presented for information purposes.

Hazard classification	*Hazard statement*
Acute (Category 3)	H402 - Harmful to aquatic life
Chronic (Category 3)	H412 - Harmful to aquatic life with long lasting effects

Human health risk assessment

Under the conditions of the occupational settings described, the notified chemical is not considered to pose an unreasonable risk to the health of workers.

When used in the proposed manner, the notified chemical is not considered to pose an unreasonable risk to public health.

Environmental risk assessment

On the basis of the PEC/PNEC ratio and the reported use pattern, the notified 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 practice to minimise occupational exposure during handling of the notified chemical as introduced in inkjet printing ink:
  - Avoid contact with eyes

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

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

- If products and mixtures containing the notified 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.

Disposal

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

Emergency procedures

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

Regulatory Obligations

Secondary Notification
This risk assessment is based on the information available at the time of notification. The Director may call for the reassessment of the chemical under secondary notification provisions based on changes in certain circumstances. Under Section 64 of the *Industrial Chemicals (Notification and Assessment) Act (1989)* the notifier, as well as any other importer or manufacturer of the notified chemical, have post-assessment regulatory obligations to notify NICNAS when any of these circumstances change. These obligations apply even when the notified chemical is listed on the Australian Inventory of Chemical Substances (AICS).

Therefore, the Director of NICNAS must be notified in writing within 28 days by the notifier, other importer or manufacturer:

(1) Under Section 64(1) of the Act; if
  - the importation volume exceeds one tonne per annum notified chemical;

or

(2) Under Section 64(2) of the Act; if
  - the function or use of the chemical has changed from a component of inkjet printing ink, or is likely to change significantly;
  - the amount of chemical being introduced has increased, or is likely to increase, significantly;
  - the chemical has begun to be manufactured in Australia;
  - additional information has become available to the person as to an adverse effect of the chemical on occupational health and safety, public health, or the environment.

The Director will then decide whether a reassessment (i.e. a secondary notification and assessment) is required.

(Material) Safety Data Sheet
The (M)SDS of the notified chemical and product containing the notified chemical provided by the notifier were reviewed by NICNAS. The accuracy of the information on the (M)SDS remains the responsibility of the applicant.

ASSESSMENT DETAILS

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Epson Australia Pty Ltd. (ABN: 91 002 625 783)
3 Talavera Road
NORTH RYDE NSW 2113

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

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
Data items and details claimed exempt from publication: other names, analytical data, degree of purity, impurities, use details, and import volume.

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
No variation to the schedule of data requirements is claimed.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
USA (2014) and EU REACH (2015)

2. IDENTITY OF CHEMICAL

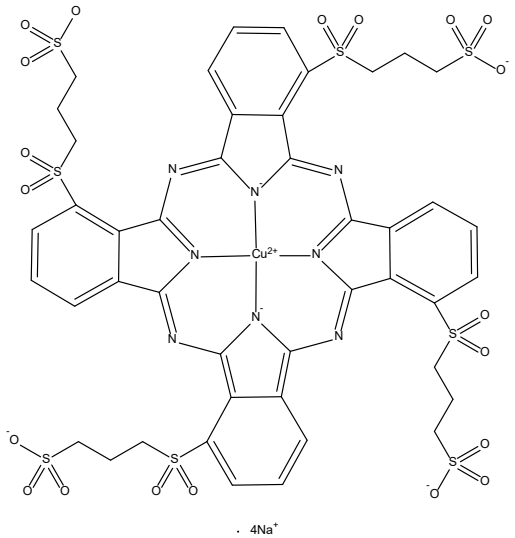
MARKETING NAME
ESI-C002
T6734 (Epson Ink Bottle containing the notified chemical at < 7%)

CAS NUMBER
944730-39-6

CHEMICAL NAME
Cuprate(4-), [[3,3',3",3"'-[(29*H*,31*H*-phthalocyanine-1,8,15,22-tetrayl-
κN^{29},κN^{30},κN^{31},κN^{32})tetrakis(sulfonyl)]tetrakis[1-propanesulfonato]](6-)]-, sodium (1:4), (*SP*-4-1)-

MOLECULAR FORMULA
$C_{44}H_{36}CuN_8O_{20}S_8.4Na$

STRUCTURAL FORMULA



MOLECULAR WEIGHT
1408.8 Da

ANALYTICAL DATA
Reference MS, IR, HPLC and UV/Vis spectra were provided.

3. COMPOSITION

DEGREE OF PURITY
> 90%

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: purple lumpy solid

Property	Value	Data Source/Justification
Melting Point	> 300 °C	Measured
Boiling Point	Not tested	Expected to be high based on based on melting point of > 300 °C
Relative Density	1.69 at 20 °C	Measured
Vapour Pressure	Not tested	Expected to be low based on the high molecular weight and solid form of the chemical
Water Solubility	≥ 300 g/L at pH 5.57	Measured
Hydrolysis as a Function of pH	$t_{½}$ >1 year at 25°C, , pH 4–9	Measured
Partition Coefficient (n-octanol/water)	log Pow < -3.36	Measured
Surface Tension	71.7 mN/m at 25 °C	Measured
Adsorption/Desorption	Not determined	Expected to not significantly partition to soil/sludge based on its high water solubility
Dissociation Constant	Not determined	The notified chemical is a salt. Therefore, the notified chemical will ionise under normal environmental conditions of pH 4 to 9.
Particle Size	Not determined	Introduced as a component of ink
Flammability (Solid)	Not highly flammable	Measured
Autoignition Temperature	350 °C	Measured
Explosive Properties	Predicted negative	Estimated based on the structure
Oxidising Properties	Predicted negative	Estimated based on the structure

DISCUSSION OF PROPERTIES
For full details of tests on physical and chemical properties, refer to Appendix A.

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

Physical hazard classification
Based on the submitted physico-chemical data depicted in the above table, the notified 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 NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
The notified chemical will not be manufactured in Australia. It will be imported as a component of inkjet printing ink at a concentration < 7%. The formulated ink products containing the notified chemical will be imported in individually packed ink bottles for Epson Ink Tank System (ITS) or in ink cartridges and will not require reformulation or repackaging.

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

Year	*1*	*2*	*3*	*4*	*5*
Tonnes	< 1	< 1	< 1	< 1	< 1

PORT OF ENTRY
Melbourne and Sydney

IDENTITY OF RECIPIENTS
Epson Australia Pty Ltd.

TRANSPORTATION AND PACKAGING
Inkjet printing ink containing the notified chemical at < 7% concentration will be imported in ink bottles of 70 mL capacity or individually packed and sealed cartridges in the sizes of 5 to 900 mL. The ink bottles or cartridges will be distributed nationwide by road.

USE
The notified chemical will be used as a component in inkjet printing ink at a concentration < 7%. The ink containing the notified chemical will be imported in sealed ink bottles for Epson Ink Tank System or ink cartridges which will be widely used in commercial and household inkjet printers. The substrate used for printing is expected mainly to be paper (including photos and other office works).

OPERATION DESCRIPTION
No manufacture or reformulation of the notified chemical will occur in Australia.

Sealed ink bottles or cartridges containing the ink with the notified chemical at < 7% concentration will be distributed to commercial and retail centres. Based on the information provided by the notifier, the ink for Epson Ink Tank System will be supplied in 70 mL bottles that have a drip-free nozzle and resealable cap for easy storage. The ink bottles or cartridges will be handled by service technicians, office workers and the public to refill the Epson Ink Tank System or to replace spent cartridges in inkjet printers in accordance with the instructions provided with the packages.

During printing, the ink containing the notified chemical will be transferred from the ink tanks or cartridges to the printing heads where the ink is projected on to the substrates. The printing processes are expected to be fully automated and computerised. After the ink is dry, the notified chemical is expected to be fixed on the substrates printed.

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)*
Importation/Waterside Workers	< 8	10 – 50
Storage and Transport Workers	< 8	10 – 50
Office Workers	< 0.5	2
Service Technicians	1	170

EXPOSURE DETAILS
Transport and storage workers are unlikely to be exposed to the notified chemical except in the event of an accidental package rupture.

Under the proposed use scenario, office workers and service technicians may have the potential for dermal and ocular exposure to the ink containing the notified chemical at < 7% concentration during ink tank refilling, cartridge replacement and printer maintenance/cleaning. As the ink bottles or cartridges are purposely designed to enclose the ink, the potential for exposure to the notified chemical is expected to be limited. Since the printing

processes are automated, the potential for dermal and ocular exposure to the notified chemical during printing is unlikely to be significant. Workers handling articles before the inks have completely dried may come into minor dermal contact with the notified chemical at up to 7% concentration. If dermal exposure to the ink containing the notified chemical is likely to occur, service technicians and office workers are expected to wear protective gloves to minimise the potential for exposure.

Based on the high molecular weight (> 1,000 Da) and anticipated low vapour pressure of the notified chemical, inhalation exposure of workers to the chemical is not expected under normal use conditions.

Once the ink is dried, the notified chemical is expected to be fixed on the substrates printed and the potential for further exposure is not expected to be significant.

6.1.2. Public Exposure

As the ink bottles and cartridges will be sold to the public for household use, members of the public may have the potential for dermal and ocular exposure to the ink containing the notified chemical at < 7% concentration during ink tank refilling or cartridge replacement. However the frequency of ink refilling or cartridge replacement is expected to be low under normal use conditions. Minor dermal contact with the notified chemical at up to 7% concentration may also occur when the printed substrates (mainly photos and office documents) are handled before the ink is completely dry. Once the ink is dry, the notified chemical is expected to be fixed on the substrates and further exposure to the chemical is not expected to be significant.

When the ink bottles with capacity of 70 mL are used in household printers, the possibility of accidental exposure to children cannot be ruled out, if the contents of ink bottle(s) left within their reach are accidentally ingested. However, the low concentration of the notified chemical in printing ink, small size of the bottle and existing label warning against ingesting the ink product would limit the exposure.

6.2. Human Health Effects Assessment

The results from toxicological investigations conducted on the notified chemical are summarised in the following table. For full details of the studies, refer to Appendix B.

Endpoint	*Result and Assessment Conclusion*
Rat, acute oral toxicity	LD50 > 2,000 mg/kg bw; low toxicity
Rabbit, skin irritation	Non-irritating
Rabbit, eye irritation	Slightly irritating
Mouse, skin sensitisation – Local lymph node assay	No evidence of sensitisation (at 25%)
Mutagenicity – Bacterial reverse mutation test	Non-mutagenic
Genotoxicity – *In vitro* mammalian chromosome aberration test	Non-genotoxic

Toxicokinetics, metabolism and distribution

No toxicokinetics, metabolism and distribution information was provided for the notified chemical.

Based on the use scenario proposed, dermal exposure is expected to be the main route for the notified chemical. The notified chemical has a molecular weight of 1,409 Da and a log Pow of -3.36, indicating low potential to cross biological membranes and a low degree of lipophilicity. Therefore, significant dermal absorption of the chemical is not expected after contact with the skin.

Acute toxicity

An acute oral toxicity study report was provided for the notified chemical. Based on the results, the acute oral toxicity of the chemical is considered low (LD50 > 2,000 mg/kg bw).

No information on acute dermal or inhalation toxicity of the notified chemical was provided.

Irritation and sensitisation

Based on the results of the irritation studies on the notified chemical, the chemical is considered non-irritating to the skin but sightly irritating to the eyes. The eye irritation effects recorded in the study report provided do not meet the criteria for classification under the GHS.

A mouse local lymph node assay on the notified chemical was submitted. The results of the assay indicate that the chemical is not a skin sensitiser at concentrations up to 25%.

Repeated dose toxicity
No repeated dose toxicity information on the notified chemical was provided.

Mutagenicity/Genotoxicity
Two study reports were provided for the notified chemical. Neither the bacterial reverse mutation test nor the *in vitro* mammalian chromosome aberration test revealed evidence of mutagenicity or clastogenicity for the notified chemical.

Other considerations
The notified chemical contains copper in the structure. Copper is an essential nutrient; however its presence at high concentration may lead to adverse consequences to the gastrointestinal tract and the liver (ATSDR, 2004).

Health hazard classification
Based on the available information, the notified chemical cannot be recommended for classification according to the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia, or the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004).

6.3. Human Health Risk Characterisation

6.3.1. Occupational Health and Safety
Based on the available information, the notified chemical is a slight eye irritant. It has low acute oral toxicity, is not a skin irritant and was not sensitising to skin when tested up to 25%. *In vitro* mutagenicity / clastogenicity tests were negative.

The notifier stated in the submission that, if dermal exposure to the inks containing the notified chemical is likely to occur, service technicians and workers are expected to wear protective gloves to minimise the potential for exposure. Therefore, repeated or prolonged exposure to the notified chemical is not expected. In addition, the potential for dermal absorption is low.

The enclosed nature of the ink bottle or cartridge packaging containing the notified chemical, the low concentration of use (< 7%) would limit ocular exposure and any associated irritation effects.

Under normal conditions of use, the risk to workers from the use of the notified chemical is not expected to be unreasonable.

6.3.2. Public Health
The ink bottles or cartridges containing the notified chemical at < 7% concentration will be sold to and used by the public. Exposure and risk to the public from use the notified chemical are expected to be less than those of workers (see Section 6.3.1 above), as the frequency of handling items containing the notified chemical by the public is not anticipated to be as high as that of the workers. Minor skin contact with the ink containing the notified chemical at up to 7% concentration may occur; however, the potential for dermal absorption is expected to be low. The slight potential for eye irritation effects would be minimised by the low concentration of use.

When the ink bottles in the capacity of 70 mL are used by the public, the possibility of accidental ingestion of the ink containing the notified chemical at up to 7% concentration by children cannot be ruled out. However, based on the size of the bottle, the low concentration of the notified chemical in the ink, its low acute oral toxicity and limited potential to cross biological membranes, this is not considered to pose a significant additional risk. In addition, the already included label of the ink cartridge contains the warning “Be careful not to get any ink in your eyes or in your mouth”.

Based on the use scenario proposed, the risk of the notified chemical to the health of the public 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 notified chemical will be imported into Australia as a component in inkjet printing ink. Printer ink is imported in ready-to-use cartridges or sealed ink bottles. No manufacturing or repackaging of the notified chemical will take place in Australia. Environmental release of the notified chemical is unlikely to occur during importation, storage and transportation as containers are designed to minimise release.

RELEASE OF CHEMICAL FROM USE

The notified chemical will be contained in ink cartridges and in sealed ink bottles for Epson Ink Tank System. During printing, the ink containing the notified chemical will be transferred from the ink tanks or cartridges to the printing heads where the ink is projected on to the substrates. The printing processes are expected to be fully automated and computerised. As the ink bottles or cartridges are purposely designed to enclose the ink, the potential for environmental release of the notified chemical from use is expected to be limited. If leakage or spillage does occur, the ink is expected to be physically contained with absorbent material and disposed of to landfill.

RELEASE OF CHEMICAL FROM DISPOSAL

Most of the notified chemical will be bound to printed paper and, once the ink has dried, will be contained in an inert matrix. It is assumed that 50% of the waste paper will end up in landfill and the rest will undergo paper recycling processes. It is expected that the majority of the notified chemical will reach landfill as a result of disposal of used paper or sludge waste from paper recycling. The ink cartridges will be contained within the printer until the contents are consumed. The empty ink cartridges and bottles will be disposed of to landfill or sent for recycling.

7.1.2. Environmental Fate

The notified chemical is not readily biodegradable according to the biodegradation study provided. For details of the environmental fate studies please refer to Appendix C.

Approximately half of the paper to which the ink containing the notified chemical is applied to is likely to be recycled. During recycling processes, waste paper is repulped using a variety of chemical agents which, amongst other things, enhance detachment of ink from the fibres. Due to the high water solubility of the notified chemical, a greater proportion can be expected to remain in the aqueous phase released to the sewer. The notified chemical is not readily biodegradable; however, due to its low log Pow (< -3.36) and its high water solubility (≥ 300 g/L), its potential for bioaccumulation is low in the aquatic environment. Eventually, the notified chemical is expected to slowly degrade through biotic and abiotic processes to form water, oxides of carbon, nitrogen, sulphur, and inorganic salts.

Sludge from treatment plants may be collected for disposal to landfill or used in soil remediation where the notified chemical is anticipated to degrade by biotic and abiotic processes. The notified chemical is likely to remain in the ink matrix bound to paper that is disposed of to landfill. In landfill, notified chemical in sludge may leach, due to its high water solubility, although potential cationic functional groups on the notified chemical may result in sorption to negatively charged sites on sediments and soils.

7.1.3. Predicted Environmental Concentration (PEC)

A predicted environmental concentration (PEC) worst case scenario has been calculated. It was assumed that 50% of the annual import quantity of the notified chemical is released to the sewer as de-inking aqueous wastes from paper recycling over 260 days/year, with no removal of the notified chemical by sewage treatment plant (STP) processes.

Predicted Environmental Concentration (PEC) for the Aquatic Compartment		
Total Annual Import/Manufactured Volume	< 1,000	kg/year
Proportion expected to be released to sewer	50%	
Annual quantity of chemical released to sewer	< 500	kg/year
Days per year where release occurs	260	days/year

Daily chemical release:	1.92	kg/day
Water use	200.0	L/person/day
Population of Australia (Millions)	22.613	million
Removal within STP	0%	
Daily effluent production:	4,523	ML
Dilution Factor - River	1.0	
Dilution Factor - Ocean	10.0	
PEC - River:	< 0.43	µg/L
PEC - Ocean:	< 0.04	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 notified 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 0.425 µg/L may potentially result in a soil concentration of approximately 2.84 µg/kg. Assuming accumulation of the notified chemical in soil for 5 and 10 years under repeated irrigation, the concentration of notified chemical in the applied soil in 5 and 10 years may be approximately 14.2 µg /kg and 28.4 µg /kg, respectively.

7.2. Environmental Effects Assessment

The results from ecotoxicological investigations conducted on the notified chemical are summarised in the table below. Details of these studies can be found in Appendix C.

Endpoint	*Result*	*Assessment Conclusion*
Fish Toxicity	96 h EC50 > 120 mg/L	Not harmful to fish
Daphnia Toxicity	48 h EC50 > 120 mg/L	Not harmful to aquatic invertebrates
Algal Toxicity	72 h E_rC50 = 30 mg/L	Harmful to algae
Duckweed Toxicity	7 d EC50 > 120 mg/L	Not applicable

The notified chemical is not considered to be harmful to fish or aquatic invertebrates, but is considered toxic to algae. Therefore, under the *Globally Harmonised System of Classification and Labelling of Chemicals* (GHS; United Nations, 2009), the notified chemical is formally classified as Acute Category 3 - Harmful to aquatic life. Based on the acute toxicity and lack of ready biodegradability of the notified chemical, it has been formally classified under the GHS as Chronic Category 3 - Harmful to aquatic life with long lasting effects.

7.2.1. Predicted No-Effect Concentration

The predicted no-effect concentration (PNEC) for the notified chemical has been calculated and is presented in the table below. The PNEC is calculated based on the endpoint for the most sensitive species for the notified chemical (algae, EC50). An assessment factor of 100 has been used as acute toxicity endpoints for three trophic levels are available.

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
EC50 (Algae)	30	mg/L
Assessment Factor	100	
PNEC:	300	µg/L

7.3. Environmental Risk Assessment

Based on the above PEC and PNEC values, the following Risk Quotient (Q) has been calculated:

Risk Assessment	PEC µg/L	PNEC µg/L	Q
Q - River	0.43	300	0.001
Q - Ocean	0.04	300	0.0001

The Risk Quotients (Q = PEC/PNEC) for a worst case discharge scenario have been calculated to be << 1 for the river and ocean compartments. The notified chemical is not readily biodegradable. The notified chemical has high water solubility and a low log Pow value. It is not expected to bioaccumulate. Therefore, the notified chemical is not considered to pose an unreasonable risk to the environment from the assessed use scenario.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Melting Point > 300 °C

Method OECD TG 102 Melting Point/Melting Range.
Remarks Capillary / metal block method was used and no obvious melting was observed up to 300 °C
Test Facility Intertek (2013)

Relative Density 1.69 ± 0.01 at 20 ± 0.5 °C

Method OECD TG 109 Density of Liquids and Solids.
Remarks Determined using a pycnometer
Test Facility Intertek (2013)

Water Solubility ≥ 300 g/L at pH 5.57

Method Flask method. Visual observation. Flasks containing test material and distilled water were shaken and sonicated for 5 minutes. The test solutions were visually examined after approximately 21 hours standing at 25°C ± 1°C. No excess material was present in the test solutions.
Remarks Water solubility reported as ≥ 300g/L at 25°C ± 1°C with a pH of the test solution at 5.57.
Test Facility Intertek (2013)

Hydrolysis as a Function of pH $t_{½}$ >1 year at 25°C, pH 4–9

Method EC Directive 92/69/EEC C.7 Degradation: Abiotic Degradation: Hydrolysis as a Function of pH.

Test concentrations (1 g/L) at pH 4, 7, and 9 were maintained at 50°C. After 5 days, the concentrations were determined by HPLC.

pH	*T (°C)*	$t_{½}$
4	25	> 1 year
7	25	> 1 year
9	25	> 1 year

Remarks Less than 10% hydrolysis was observed after 5 days at 50°C at pH 4, 7, and 9. Therefore, the test material is considered stable with a half-life greater than 1 year at 25°C.
Test Facility Intertek (2013)

Partition Coefficient (n-octanol/water) log Pow < -3.36

Method EC Directive 92/69/EEC A.8 Partition Coefficient. Flask Method. The partition coefficient was determined by the solubility of the test material in n-octanol and water. Flasks containing test material, n-octanol and water were shaken and, after separation, the concentration of the test material in each phase was determined by HPLC.
Remarks The calculated log Pow of <-3.36 is significantly lower than the recommended range of the method (-2 to 4). However, the reported result is regarded as being an acceptable value for the test substance.
Test Facility Intertek (2013)

Surface Tension 71.7 ± 0.6mN/m at 25 ± 0.5 °C

Method OECD TG 115 Surface Tension of Aqueous Solutions.
Remarks Wilhelmy Plate method
Concentration used: 1 g/L;
The material was found to be not surface active.
Test Facility Intertek (2013)

Flammability (Solid) Not highly flammable

Method	EC Council Regulation No 440/2008 A.10 Flammability (Solids)
Remarks	The test substance failed to ignite during 2 minutes flame application in the preliminary test.
Test Facility	Harlan (2014a)

Autoignition Temperature 350 °C

Method	EC Council Regulation No 440/2008 A.16 Relative Self-Ignition Temperature for Solids
Remarks	On completion of the test, the test substance was a charred black powder with blue specks.
Test Facility	Harlan (2014a)

Explosive Properties Predicted negative

Method	EC Council Regulation No 440/2008 A.14 Explosive Properties.
Remarks	There are no structural alerts within the chemical structure.
Test Facility	Harlan (2014a)

Oxidizing Properties Predicted negative

Method	EC Council Regulation No 440/2008 A.17 Oxidizing Properties (Solids)
Remarks	There are no structural alerts within the chemical structure.
Test Facility	Harlan (2014a)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute toxicity – oral

TEST SUBSTANCE	Notified chemical (96.9% in purity)
METHOD	OECD TG 423 Acute Oral Toxicity – Acute Toxic Class Method. EC Council Regulation No 440/2008 B.1 tris Acute Oral Toxicity – Acute Toxic Class Method.
Species/Strain	Rat/ RccHan:WIST
Vehicle	Distilled water
Remarks - Method	No analysis was conducted to determine the homogeneity, concentration or stability of the test item formulation. No other significant protocol deviations were noted.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	3 F	2,000	0/3
2	3 F	2,000	0/3

LD50	> 2,000 mg/kg bw
Signs of Toxicity	There were no unscheduled deaths of animals during the study. No signs of systemic toxicity were recorded. Blue/green stained faeces were noted in all animals up to six days after dosing.
Effects in Organs	Green discoloration of the kidneys was noted at necropsy in four animals.
Remarks - Results	All animals showed expected gains in body weight.
CONCLUSION	The notified chemical is of low toxicity via the oral route.
TEST FACILITY	Harlan (2014b)

B.2. Irritation – skin

TEST SUBSTANCE	Notified chemical (96.9% in purity)
METHOD	OECD TG 404 Acute Dermal Irritation/Corrosion. EC Council Regulation No 440/2008 B.4 Acute Toxicity (Skin Irritation). EC Directive 2004/73/EC B.4 Acute Toxicity (Skin Irritation).
Species/Strain	Rabbit/New Zealand White (Hsdlf:NZW)
Number of Animals	3 males
Vehicle	None. Test substance was moistened with distilled water.
Observation Period	72 hours
Type of Dressing	Semi-occlusive.
Remarks - Method	No significant protocol deviations were noted. The pH of a 10% aqueous solution of the test substance was determined to be 7.0. The test substance was ground to a powder prior to application. After the test period, the residual test item was wiped off, using cotton wool soaked in distilled water.
RESULTS	No evidence of skin irritation was noted.
Remarks - Results	Blue coloured staining, not preventing evaluation of skin responses, was noted at all treated skin sites throughout the study. Weight gain was as expected.
CONCLUSION	The notified chemical is non-irritating to the skin.
TEST FACILITY	Harlan (2013)

B.3. Irritation – eye

TEST SUBSTANCE	Notified chemical (96.9% in purity)
METHOD	OECD TG 405 Acute Eye Irritation/Corrosion. EC Council Regulation No 440/2008 B.5 Acute Toxicity (Eye Irritation).
Species/Strain	Rabbit/New Zealand White (Hsdlf:NZW)
Number of Animals	3 males
Observation Period	7 days
Remarks - Method	No significant protocol deviations were noted. The pH of 10% aqueous solution of the test substance was determined to be 7.0. The test substance in the amount of 89 mg (equivalent to 0.1 mL as measured in an adapted syringe) was applied to each of the test eyes of the animals.

RESULTS

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			
Conjunctiva: redness	0.67	1	1	1	< 7 days	0
Conjunctiva: chemosis	0	1	1	1	< 7 days	0
Conjunctiva: discharge	0.33	0	0	1	< 48 hours	0
Corneal opacity	0	0	0	0	-	0
Iridial inflammation	0	0	0	0	-	0

* Calculated on the basis of the scores at 24, 48, and 72 hours for EACH animal.

Remarks - Results	Blue coloured staining of the fur was noted around the treated eyes.
CONCLUSION	The notified chemical is slightly irritating to the eye.
TEST FACILITY	Harlan (2014c)

B.4. Skin sensitisation – mouse local lymph node assay (LLNA)

TEST SUBSTANCE	Notified chemical (96.9% in purity)
METHOD	OECD TG 429 Skin Sensitisation: Local Lymph Node Assay (23 July, 2010) Commission Regulation(EC) No. 440/2008 B.42 Skin Sensitisation (Local Lymph Node Assay)
Species/Strain	Mouse/CBA/CaOlaHsd
Vehicle	1% Pluronic L92 in distilled water
Preliminary study	Yes
Positive control	Not conducted in parallel with the test substance, but had been conducted previously in the test laboratory using α-Hexylcinnamaldehyde dissolved in the vehicle.
Remarks - Method	No analysis was conducted to determine the homogeneity, concentration or stability of the test item formulation. Maximum test concentration was determined to be 25% in a preliminary screening test, and was stated to be the maximum attainable concentration.

RESULTS

Concentration (% w/w)	*Number and sex of animals*	*Proliferative response (DPM/lymph node)*	*Stimulation Index (Test/Control Ratio)*
Test Substance			
0 (vehicle control)	4 F	2270.22	1
5	4 F	2043.32	0.90

10	4 F	2501.58	1.10
25	4 F	2947.01	1.30

EC3 Not calculated as none of the resulting stimulation index was above 3.

Remarks - Results Slight blue coloured staining of the ears and fur was noted in all test animals. No signs of systemic toxicity were noted. Resulting stimulation indexes showed slightly dose-response although all were below 3.

CONCLUSION There was no evidence of induction of a lymphocyte proliferative response indicative of skin sensitisation to the notified chemical at a concentration up to 25%.

TEST FACILITY Harlan (2014c)

B.5. Genotoxicity – bacterial reverse mutation test

TEST SUBSTANCE Notified chemical (96.9% in purity)

METHOD OECD TG 471 Bacterial Reverse Mutation Test.
Commission Regulation of 30 May 2008/EC B.13/14 Mutagenicity – Reverse Mutation Test using Bacteria.
Plate incorporation procedure (Test 1) and Pre incubation procedure (Test 2)

Species/Strain *S. typhimurium*: TA1535, TA1537, TA98, TA100
E. coli: WP2*uvrA*

Metabolic Activation System 10% S9 rat liver fraction induced with phenobarbitone /β-naphthoflavone

Concentration Range in Main Test
a) With metabolic activation: 1.5 to 5,000 µg/plate
b) Without metabolic activation: 1.5 to 5,000 µg/plate

Vehicle Distilled water

Remarks - Method No significant protocol deviations were noted. Test concentrations were adjusted for the impurity (3.1 %). No analysis was conducted to determine the homogeneity, concentration or stability of the test item formulation.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:* *Cytotoxicity*	*Precipitation*	*Genotoxic Effect*
Absent			
Test 1	> 5,000	> 5,000	Negative
Test 2	> 5,000	> 5,000	Negative
Present			
Test 1	> 5,000	> 5,000	Negative
Test 2	> 5,000	> 5,000	Negative

Remarks - Results The test system was functional as validated by the results for the vehicle and positive controls. A blue coloration induced by the test substance was observed on plates containing the test substance at 50 µg/plate or above. The coloration was intense at the dose level of 1,500 µg/plate or above but did not prevent the scoring of revertant colonies.

CONCLUSION The notified chemical was not mutagenic to bacteria under the conditions of the test.

TEST FACILITY Harlan (2014e)

B.6. Genotoxicity – *in vitro* mammalian chromosome aberration test

TEST SUBSTANCE Notified chemical (96.9% in purity)

METHOD OECD TG 473 *In Vitro* Mammalian Chromosome Aberration Test.

	Commission Regulation No. 440/2008/EC B.10 Mutagenicity - *In Vitro* Mammalian Chromosome Aberration Test.
Species/Strain	Mammalian cell line
Cell Type/Cell Line	Human lymphocytes
Metabolic Activation System	Induced rat liver homogenate system (S9-mix induced with Phenobarbitone/β-Naphthoflavone) at 2% and 1% for Experiments 1 and 2 respectively.
Vehicle	Eagle's minimal essential medium with HEPES buffer (MEM)
Remarks - Method	No significant protocol deviations were noted. Test concentrations were adjusted for the impurity (3.1 %). Doses were chosen on the basis of a preliminary test.

Metabolic activation	*Test Substance Concentration (μg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	0*, 156.25, 312.5, 625, 1250*, 2500*, 5000*	4	24
Test 2	0*, 156.25, 312.5, 625*, 1250*, 2500*, 5000	24	24
Present			
Test 1	0*, 156.25, 312.5, 625, 1250*, 2500*, 5000*	4	24
Test 2	0*, 156.25, 312.5, 625, 1250*, 2500*, 5000*	4	24

*Cultures selected for metaphase analysis.

RESULTS

Metabolic Activation	*Test Substance Concentration (μg/mL) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	> 5,000	> 5,000	> 5,000	Negative
Test 2	-	> 5,000	> 5,000	Negative
Present				
Test 1	> 5,000	> 5,000	> 5,000	Negative
Test 2	-	> 5,000	> 5,000	Negative

Remarks - Results

The test system was functional as validated by the results for the vehicle and positive controls.

Blue coloration was observed at the end of exposure in groups at and above 156.25 μg/mL. The test substance induced slight dose-related cytotoxicity with maximum 19% mitotic inhibition observed at the dose level of 2,500 μg/mL in the presence of metabolic activation.

In Experiment 2, in the absence of metabolic activation with 24 hour exposure, the maximum dose level for metaphase analysis was limited to 2,500 μg/mL. According to the study authors, at the dose level of 5,000 μg/mL, the metaphase was unscorable.

CONCLUSION

The notified chemical was not clastogenic to human lymphocytes treated *in vitro* under the conditions of the test.

TEST FACILITY

Harlan (2014f)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

C.1.1. Ready biodegradability

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 301 F Ready Biodegradability: Manometric Respirometry Test.
Inoculum	Activated sludge
Exposure Period	28 days
Auxiliary Solvent	Not reported
Analytical Monitoring	A respirometer, CES Multi-Channel Aerobic Respirometer, was used for measurement of the consumption of oxygen.
Remarks - Method	The test was conducted according to the guidelines above using good laboratory practice (GLP). No significant deviations from the test guidelines were reported.

RESULTS

Test substance		*Aniline*	
Day	*% Degradation*	*Day*	*% Degradation*
14	0	14	71
28	6	28	75

Remarks - Results	All validity criteria for the test were satisfied. The reference compound, aniline, reached the 71 % pass level by day 14 indicating the suitability of the inoculum. The toxicity control exceeded 25% biodegradation within 14 days showing that toxicity was not a factor inhibiting the biodegradability of the test substance. The degree of degradation of the test substance was 6% within 28 days. Therefore, the test substance cannot be classified as readily biodegradable according to the OECD (301 F) guideline.
CONCLUSION	The notified chemical is not considered to be readily biodegradable.
TEST FACILITY	Harlan (2014g)

C.2. Ecotoxicological Investigations

C.2.1. Acute toxicity to fish

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 203 Fish, Acute Toxicity Test – Semi-static Test
Species	Rainbow trout (*Oncorhynchus mykiss*)
Exposure Period	96 hours
Auxiliary Solvent	Not reported
Water Hardness	140 mg $CaCO_3$/L
Analytical Monitoring	HPLC/UV
Remarks – Method	The test was conducted according to the guidelines above and good laboratory practice (GLP) principles. No significant deviations from the test guidelines were reported.

RESULTS

Nominal Concentration (mg/L)	*Number of Fish*	*Mortality (%)*				
		3 h	*24 h*	*48 h*	*72 h*	*96 h*
Control	7	0	0	0	0	0
120	7	0	0	0	0	0

LC50	> 120 mg/L at 96 hours
NOEC	120 mg/L at 96 hours
Remarks – Results	All validity criteria for the test were satisfied. The toxicity test was conducted as a limit test. The actual concentrations of the test substance in the test solutions were measured at 0 and 72 hours (fresh media) and 24 and 96 hours (old media). The analyses of the test solutions showed the measured concentrations to be near nominal. Therefore, the test endpoints were calculated based on the nominal concentrations. All validity criteria for the test were satisfied. The end points were determined by visual observations.

CONCLUSION The notified chemical is not harmful to fish.

TEST FACILITY Harlan (2014h)

C.2.2. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE Notified chemical

METHOD	OECD TG 202 *Daphnia* sp. Acute Immobilisation Test – Static Test
Species	*Daphnia magna*
Exposure Period	48 hours
Auxiliary Solvent	Not reported
Water Hardness	250 mg $CaCO_3$/L
Analytical Monitoring	HPLC/UV
Remarks - Method	The test was conducted according to the guidelines above and good laboratory practice (GLP) principles. No significant deviations from the test guidelines were reported.

RESULTS

Nominal Concentration (mg/L)	*Number of D. magna*	*Cumulative % Immobilised*	
		24 h	*48 h*
Control	20	0	0
120	20	0	0

EL50	> 120 mg/L at 48 hours
NOEL	120 mg/L at 48 hours
Remarks - Results	All validity criteria for the test were satisfied. The toxicity test was conducted as a limit test. The actual concentrations of the test substance in the test solutions were measured at 0 and 48 hours. The analyses of the test solutions showed the measured concentrations to be near nominal. Therefore, the test endpoints were calculated based on the nominal concentrations. The end points were determined by visual observations.

CONCLUSION The notified chemical is not harmful to aquatic invertebrates.

TEST FACILITY Harlan (2014i)

C.2.3. *Lemna gibba* test

TEST SUBSTANCE Notified chemical

METHOD	OECD Guidelines for the Testing of Chemicals, No. 221, *Lemna sp.* Growth Inhibition Test, 2006.
Species	Duckweed (*Lemna gibba)*
Exposure Period	7 days
Concentration Range	Nominal: Control and 120 mg/L (Limit test)
Auxiliary Solvent	None

Water Hardness	Not reported
Analytical Monitoring	HPLC/UV.
Remarks - Method	The test was conducted following the test guidelines and good laboratory practice (GLP) principles. The test was to evaluate the impact of the notified chemical on the growth of the freshwater aquatic plant *Lemna gibba* (duckweed). The plants were exposed to the test item for seven days in a semi-static test. The treatments were not renewed as the test substance was shown to be stable over the 7-day test period in the range-finding test. On Day 0, 3, 5 and 7, the number of fronds and yield of the *Lemna gibba* plants were counted. The dry weights of the plants at the start and end of the test were determined. The analyses of the test solutions showed the measured concentrations to be near nominal. Therefore, the test endpoints were calculated based on the nominal concentrations.

RESULTS

Remarks - Results	All validity criteria for the test were satisfied. At the nominal concentration of 120 mg/L, the growth rate and yield based on dry weight were not statistically significantly lower than in the control after the exposure period of 7 days. The 7 day NOEC was determined to be 120 mg/L since the growth of the plants was not inhibited and no abnormalities in appearance of the plants was observed. The 7 day EC50 was determined to be > 120 mg/L based on frond mortality and frond number growth rate. A Students t-test incorporating Bartlett's test for homogeneity of variance was carried out on the average specific growth rate. Yield data at 7 days for the control and 120 mg/L test concentration to determine any statistically significant differences between the test and control groups. All statistical analyses were performed using the SAS computer software package.

CONCLUSION	The 7 day EC50 was > 120 mg/L based on frond mortality and frond number growth rate.
TEST FACILITY	Harlan (2014j)

C.2.4. Algal growth inhibition test

TEST SUBSTANCE	Notified chemical

METHOD	OECD TG 201 Alga, Growth Inhibition Test.
Species	*Pseudokirchneriella subcapitata*
Exposure Period	72 hours
Concentration Range	Nominal: Control, 1.2, 3.8, 12, 38, 120 mg/L
Auxiliary Solvent	None
Water Hardness	Not reported
Analytical Monitoring	HPLC/UV
Remarks - Method	The test was conducted according to the guidelines above and good laboratory practice (GLP) principles. No significant deviations from the test guidelines were reported.

RESULTS

Biomass		*Growth*	
E_bC_{50} (95% confidence interval) mg/L at 72 hours	*NOEC mg/L*	*E_rC_{50} mg/L at 72 hours*	*NOEC mg/L*
9.6 (8.4 – 11)	3.8	30	3.8

Remarks - Results

All validity criteria for the test were satisfied. Analysis of the test treatment solutions at 0 and 72 hours showed measured test concentrations ranged from 99% to 110% of nominal concentrations. Therefore, the results are calculated based on nominal test concentrations only.

It was considered that the effect of the test item on algal growth was not only due to a reduction in light intensity, but also due to the intrinsic toxic properties of the test item.

One way analysis of variance incorporating Bartlett's test for homogeneity of variance and Dunnett's multiple comparison procedure for comparing several treatments with a control was carried out on the growth rate and yield data to determine any statistically significant differences between the test and control groups. All statistical analyses were performed using the SAS computer software package.

CONCLUSION The notified chemical is harmful to algae.

TEST FACILITY Harlan (2014k)

BIBLIOGRAPHY

ATSDR (2004) Toxicological Profile for Copper. U.S. Department of Health and Human Services, Public Health Services, Agency for Toxic Substances and Disease Registry. September 2004. Accessed at http://www.atsdr.cdc.gov/toxprofiles/tp.asp?id=206&tid=37

Harlan (2013) [Notified Chemical]: Acute Dermal Irritation in the Rabbit (Study Number: 41303530, December 2013) Derbyshire, UK, Harlan Laboratories Ltd. (Unpublished report provided by the notifier)

Harlan (2014a) [Notified Chemical]: Determination of Hazardous Physico-Chemical Properties (Study Number: 41303528, March 2014) Derbyshire, UK, Harlan Laboratories Ltd. (Unpublished report provided by the notifier)

Harlan (2014b) [Notified Chemical]: Acute Oral Toxicity in the Rat – Acute Toxic Class Method (Study Number: 41303529, January 2014) Derbyshire, UK, Harlan Laboratories Ltd. (Unpublished report provided by the notifier)

Harlan (2014c) [Notified Chemical]: Acute Eye Irritation in the Rabbit (Study Number: 41303531, February 2014) Derbyshire, UK, Harlan Laboratories Ltd. (Unpublished report provided by the notifier)

Harlan (2014d) [Notified Chemical]: Local Lymph Node Assay in the Mouse (Study Number: 41303532, January 2014) Derbyshire, UK, Harlan Laboratories Ltd. (Unpublished report provided by the notifier)

Harlan (2014e) [Notified Chemical]: Reverse Mutation Assay "Ames Test" Using *Salmonella typhimurium* and *Escherichia coli* (Study Number: 41303533, January 2014) Derbyshire, UK, Harlan Laboratories Ltd. (Unpublished report provided by the notifier)

Harlan (2014f) [Notified Chemical]: Chromosome Aberration Test in Human Lymphocytes *in vitro* (Study Number: 41303534, March 2014) Derbyshire, UK, Harlan Laboratories Ltd. (Unpublished report provided by the notifier)

Harlan (2014g) [Notified Chemical]: Assessment of Ready Biodegradability; Manometric Respirometry Test (Study Number: 41304020, March 2014) Derbyshire, UK, Harlan Laboratories Ltd. (Unpublished report provided by the notifier)

Harlan (2014h) [Notified Chemical]: Acute Toxicity to Rainbow Trout (Study Number: 41304017, February 2014) Derbyshire, UK, Harlan Laboratories Ltd. (Unpublished report provided by the notifier)

Harlan (2014i) [Notified Chemical]: Daphnia sp., 48-Hour Acute Immobilization Test (Study Number: 41304018, February 2014) Derbyshire, UK, Harlan Laboratories Ltd. (Unpublished report provided by the notifier)

Harlan (2014j) [Notified Chemical]: Lemna Growth Inhibition Test (Study Number: 41304019, February 2014) Derbyshire, UK, Harlan Laboratories Ltd. (Unpublished report provided by the notifier)

Harlan (2014k) [Notified Chemical]: Growth Inhibition Test (Study Number: 41304022, February 2014) Derbyshire, UK, Harlan Laboratories Ltd. (Unpublished report provided by the notifier)

Intertek (2014) Substance [Notified Chemical]: Annex VII Registration Data Requirement (Intertek Study 1328086, April 2013), Manchester, UK, Intertek Pharmaceutical Services Manchester (Unpublished report provided by the notifier)

NOHSC (2004) Approved Criteria for Classifying Hazardous Substances, 3rd edition [NOHSC:1008(2004)]. National Occupational Health and Safety Commission, Canberra, AusInfo.

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>.