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June 2011

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

FULL PUBLIC REPORT

2-Propenoic acid, 2-[2-(ethenyloxy)ethoxy]ethyl ester

This Assessment has been compiled in accordance with the provisions of the *Industrial Chemicals (Notification and Assessment) Act 1989* (Cwlth) (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 Ageing, and conducts the risk assessment for public health and occupational health and safety. The assessment of environmental risk is conducted by the Department of Sustainability, Environment, Water, Population and Communities.

For the purposes of subsection 78(1) of the Act, this Full Public Report may be inspected at our NICNAS office by appointment only at Level 7, 260 Elizabeth Street, Surry Hills NSW 2010.

This Full 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:

Street Address:	Level 7, 260 Elizabeth Street, SURRY HILLS NSW 2010, AUSTRALIA.
Postal Address:	GPO Box 58, SYDNEY NSW 2001, AUSTRALIA.
TEL:	+ 61 2 8577 8800
FAX	+ 61 2 8577 8888
Website:	www.nicnas.gov.au

Director
NICNAS

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This notification has been carried out under the approved foreign scheme provisions (Canada) of Section 44 of the Act. The health and environment hazard assessment of the Canadian report was provided to NICNAS and where appropriate used in this assessment report. The other elements of the risk assessment and recommendations on safe use of the notified chemical were carried out by NICNAS.

2-Propenoic acid, 2-[2-(ethenyloxy)ethoxy]ethyl ester

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Agfa-Gevaert Limited (ABN 12000 404 722)
15 Dalmore Drive, Scoresby VIC 3179

NOTIFICATION CATEGORY
Standard: Chemical other than polymer (more than 1 tonne per year).

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
Data items and details claimed exempt from publication: other names, analytical data, impurities and additives/adjuvants

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
Canada 2009, Japan 2005, TSCA 2007, REACH 2010 (ELINCS 2004), Korea 2008, China 2008

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
VEEA

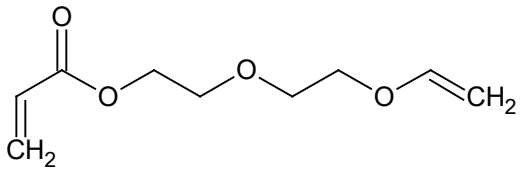
CAS NUMBER
86273-46-3

CHEMICAL NAME
2-Propenoic acid, 2-[2-(ethenyloxy)ethoxy]ethyl ester

OTHER NAME(S)
2-(2'-Vinyloxy ethoxy) ethyl acrylate
2-(2-Vinyloxy ethoxy) ethyl acrylate
FX-VEEA

MOLECULAR FORMULA
$C_9H_{14}O_4$

STRUCTURAL FORMULA



MOLECULAR WEIGHT
186.20 Da

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

3. COMPOSITION

DEGREE OF PURITY 99.6%

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20ºC AND 101.3 kPa: colourless liquid

Property	Value	Data Source/Justification
Freezing Point	< -70.9ºC	Measured
Boiling Point	94ºC at 0.33 kPa	Measured
Density	1045.8 kg/m^3 at 20ºC	Measured
Vapour Pressure	4.13 × 10^{-3} kPa at 25ºC	Measured
Water Solubility*	18.4 g/L at 20°C	Measured (OECD TG 105)
Hydrolysis as a Function of pH*	$t_{1/2}$ < 3 min at 37°C (pH 1.2) $t_{1/2}$ < 1 day at 25°C (pH 4) $t_{1/2}$ = 8 days at 25°C (pH 7) $t_{1/2}$ = 3 days at 25°C (pH 9)	Measured (OECD TG 111)
Partition Coefficient (n-octanol/water)*	log Kow = 1.7	Measured (OECD TG 117)
Adsorption/Desorption*	log K_{oc} = 1.21	Measured (OECD TG 121)
Dissociation Constant*	Not determined	The notified chemical has no dissociable functions
Particle Size	Not determined	Liquid
Flash Point	118.6ºC at 101.3 kPa	Measured
Flammability (Contact with Water)	Non-hazardous	Measured
Autoignition Temperature	About 175ºC at 97.3-98.2 kPa	Measured
Autoignition Temperature	214ºC at 102.2 kPa	Measured
Explosive Properties	Not expected to be explosive	Estimated
Surface Tension	63.4 mN/m at 20.8ºC	Measured
Oxidizing Properties	Non-oxidising	Estimated

*Performed on the notified chemical with a purity of > 99.7%

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

Reactivity
Under normal conditions of storage and use the notified chemical is not expected to be reactive.

Dangerous Goods classification
Based on the submitted physical-chemical data in the above table the notified chemical is not classified according to the Australian Dangerous Goods Code (NTC, 2007). However the data above do not address all Dangerous Goods endpoints. Therefore consideration of all endpoints should be undertaken before a final decision on the Dangerous Goods classification is made by the introducer of the chemical.

5. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
The notified chemical will be imported as a component (< 60%) of ink in 1 L or 5 L plastic bottles or jerry cans in cardboard boxes.

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

Year	*1*	*2*	*3*	*4*	*5*
Tonnes	2	4.5	5	5.5	10

PORT OF ENTRY
Sydney or Melbourne

IDENTITY OF RECIPIENTS
Agfa-Gevaert Limited

TRANSPORTATION AND PACKAGING
The inks containing the notified chemical at < 60% in 1 L or 5 L plastic bottles or jerry cans in cardboard boxes will be transported from port of entry to the notifier's warehouse facilities or directly to printing industry customers.

USE
Component of UV curing ink.

The notified chemical will be used for the digital printing of large format images for use on front lit and backlit billboards, truck-side advertising, stadium and arena displays, shopping mall displays, exterior bus posters, airport terminal displays, exhibition graphics and displays, wall murals, banners, movie and stage backdrops and point of sale displays.

OPERATION DESCRIPTION
There will be no local manufacture, reformulation or repackaging of the imported inks. The inks containing the notified chemical at up to 60% will be used in industrial printers for the digital printing of large format images on a variety of substrates, such as vinyl, canvas, paper, mesh vinyl, shade cloth and a variety of other substrates capable of holding images.

The imported ink containers are opened and poured manually into an ink reservoir which is then sealed with a screw cap. The inks are then automatically pumped to the print heads. Once the ink has been deposited into the substrate it is immediately exposed to UV-light which is fitted to the print head. The curing process is rapid and the printed substrate leaves the printer in a touch-dry state.

Periodically the printers require maintenance and cleaning. The printer is flushed with the notified chemical at < 60% through the same circuit as the inks. The notified chemical is printed and cured onto the substrate in the same manner so that there are no uncured wastes generated.

6. HUMAN HEALTH IMPLICATIONS

6.1 Exposure assessment

6.1.1 Occupational exposure

NUMBER AND CATEGORY OF WORKERS

Category of Worker	*Number*	*Exposure Duration (hours/day)*	*Exposure Frequency (days/year)*
Transport and storages	10-20	4-8	200
Service technicians	200	8	200
Printer operators	> 1000	0.5	5
Wholesale printer supplies	> 1000	8	200

EXPOSURE DETAILS
Dermal exposure of transport, warehousing and wholesale workers to the imported notified chemical will occur only in the event of an accident where the packaging is breached.

The most likely route of exposure of service technicians is dermal as they will come in contact with the notified chemical during printer maintenance and cleaning. Inhalation exposure is unlikely due to the low vapour pressure of the notified chemical (4.13×10^{-3} kPa). Printer maintenance and cleaning personnel are expected to wear disposable gloves.

Printer operators will have limited exposure to the notified chemical, as the process is mainly automated. Dermal and ocular exposure is possible during the replacement of ink containers (manual process) and cleaning residual ink from printers. Inhalation exposure will be limited due to the low vapour pressure of the notified chemical and because of local exhaust ventilation employed in areas surrounding printing machines.

After application to the substrate, the ink containing the notified chemical is UV-cured (chemically reacted) and hence the notified chemical will not be bioavailable.

6.1.2. Public exposure

The printer inks containing the notified chemical will not be sold to the public. After application to the substrate and cured, the notified chemical is expected to remain bound to the substrate print matrix and will not be available for exposure.

6.2. Human health effects assessment

6.2.1. Toxicology studies on the notified chemical

The results from toxicological investigations conducted on the notified chemical are summarised in the table below.

Endpoint	*Result and Assessment Conclusion*
Rat, acute oral toxicity	LD50 300-2000 mg/kg bw for females; harmful
Rat, acute oral toxicity	LD50 > 2026 mg/kg bw for males LD50 > 1790 mg/kg bw for females, harmful
Rat, acute dermal toxicity	LD50 > 2000 mg/kg bw; low toxicity
Rat, acute inhalation toxicity	LC50 > 5.82 mg/L/4 hour; low toxicity
Rabbit, skin irritation	non-irritating
Rabbit, eye irritation	slightly irritating
Mouse, skin sensitisation – Local lymph node assay	evidence of sensitisation
Rat, repeated dose oral toxicity – 28 days	NOEL = 50 mg/kg bw/day NOAEL = 160 mg/kg bw/day
Rat, repeated dose oral and combined reproductive/developmental toxicity – 90 days	NOAEL = 50 mg/kg bw/day for systemic toxicity NOEL = 400 mg/kg bw/day for reproductive developmental effects
Mutagenicity – bacterial reverse mutation	not mutagenic
Genotoxicity – in vitro chromosomal aberration assay	not clastogenic
Genotoxicity – in vitro mouse lymphoma assay	not mutagenic nor clastogenic
Genotoxicity – in vivo micronucleus test	Not clastogenic

Acute Toxicity:

An acute toxicity assay was performed on female rats using the acute toxic class method (administered by oral gavage at doses of 300 or 2000 mg/kg bw). There were no mortalities or clinical signs of systemic toxicity in the animals dosed at 300 mg/kg bw. However, all six animals treated at 2000 mg/kg bw had ruffled fur, hunched posture at 3 hours post-treatment and were found dead at the 5 hour observation point. Surviving animals gained the expected bodyweight and did not have any gross abnormalities at necropsy. Based on the available information, the LD_{50} for the notified chemical is between 300 and 2000 mg/kg bw, which is considered harmful.

An additional acute oral toxicity assay was performed on rats with the notified chemical using a protocol similar to OECD 401. The notified chemical was administered to overnight fasted animals (5/sex/group) at doses of 1024, 1280, 1600, 2000 and 2500 mg/kg bw. Mortalities occurred at 1600 mg/kg bw (1 male and 2 females) and at 2000 mg/kg bw (1 male and 3 females). At a dose of 2500 mg/kg bw all 5 males and all 5 females died on day 2 of the observation period. There were no clinical signs of systemic toxicity observed at 1024 mg/kg bw. At 1280 mg/kg bw and higher doses, decreased locomotor activity and abnormal gait were observed in males and females from 3-6 hours after treatment. At 2000 mg/kg bw and higher, prone position, panting, sedation and hypothermia were observed in males and/or females from 3-6 hours after treatment. Surviving animals gained normal bodyweight. Among decedent animals, stomach distension and dark redness of the glandular stomach were observed at necropsy. The LD_{50} was determined to be 2026 mg/kg bw for males and 1790 mg/kg bw for females, which is considered to be harmful to females.

An acute dermal toxicity assay was performed using rats (5/sex). The notified chemical was applied to the intact, shaved dorsal skin of the animals at a dose of 2000 mg/kg bw and covered with a semi-occlusive dressing for 24 hours. There were no mortalities during the test period or during the observation period. Clinical signs included vocalisation, erythema, crusts, fissures and necrosis. Vocalisation was noted in all males and females during the removal of the dressing on day 2 of the observation period and four males and 4 females also vocalised during examination of the skin on day 3. One female also vocalised on days 4 and 5. Slight to moderate erythema was noted in all males from days 2 to 9 and persisted up to the end of the observation period in one male. Slight to marked general erythema was noted in all females from test days 2 or 3 to test day 8 and persisted up to test day 13 in three females. Slight to moderate focal erythema was also noted in 2 females. Slight to moderate scaling was noted in one male on test days 6-7 and slight scaling was noted in another male from test days 9 to 15. Slight to moderate scaling was noted in all females on test day 6 and persisted as slight scaling up to test day 7, 8 or 15. Slight fissures were noted in three males and one female from test days 4 to 5. Skin necrosis was noted in two animals throughout the study period. Slight to moderate crusts were noted in all males and all females from test day 5 and 6 respectively. All animals gained the expected body weight during the observation period and no macroscopic abnormalities were noted at necropsy. The LD_{50} was determined to be greater than 2000 mg/kg bw which is indicative of low acute dermal toxicity.

An acute inhalation assay was performed using Wistar rats. The animals (5/sex) were exposed to an aerosol atmosphere using a nose only exposure at a mean dose concentration of 5.82 mg/L for 4 hours. One male died the first day after exposure. Clinical signs for all animals included decreased or increased respiratory rate, noisy respiration, laboured respiration, hunched posture, pilo-erection and wet fur. There were occasional or isolated instances of gasping, ataxia, sneezing and red/brown staining around the eyes or snout. All males and four females showed a loss in bodyweight during the first week but showed normal gains during the second week. There were no macroscopic abnormalities detected in any of the animals which survived until the scheduled necropsy. The male which died had abnormally dark lungs, a patchy, pallor liver with accentuated lobular pattern, a pale spleen and a gaseous distension of the stomach. The $LC_{50} > 5.82$ mg/L is indicative of low acute inhalation toxicity.

Primary Irritation:
A skin irritation assay was performed on Japanese white rabbits. The test chemical (0.5 ml) was applied to intact and abraded dorsal skin of 3 male rabbits and covered with an occlusive dressing for a period of 4 hours. There were no mortalities during the test period or during the 14 day observation period. There were no clinical signs of systemic toxicity and all animals gained the expected bodyweight during the observation period. A very slight erythema and very slight oedema were observed at the intact treated site 4 hours after application. No further evidence of irritation was observed at intact sites. At abraded sites, well-defined to moderate-to-severe erythema and oedema were observed at 4 hours. Very slight to well-defined erythema and very slight to slight oedema were observed between 24-72 hours. Very slight oedema persisted in one animal for 11 days while very slight oedema persisted in the same animal for 7 days.

A primary eye irritation assay was performed using New Zealand white rabbits (1 male and 2 females). The notified chemical (0.1 ml) was instilled in the conjunctival sac of the left eye and left unwashed. There were no mortalities or clinical signs of systemic toxicity during the 14 day observation period. Moderate conjunctival redness was observed in all animals at 1 hour, accompanied by slight to moderate chemosis and slight to moderate discharge. Moderate conjunctival redness persisted at 24 hours in all animals and was accompanied by slight chemosis in a single animal. Slight conjunctival redness was observed among all animals at 48 hours in 2 of 3 animals at 72 hours. There was no evidence of iridial or corneal injury.

Skin Sensitisation:
A local lymph node assay was performed in mice (4 females/group) to determine the sensitisation potential of the notified chemical. The test substance (25µl) was applied to the external ear of the animals at concentrations of 5, 10 and 25% for 3 consecutive days. On day 5 the animals were injected with 20.3 µCi ^{3}H-methyl thymidine and sacrificed 5 hours later. There were no mortalities or clinical signs of systemic toxicity during the test period. There were no changes in body weight, however, slight swelling of the external ear was observed at the doses of 10 and 25%. The notified chemical generated SI values of 4.3, 9.8 and 6.7 at doses of 5, 10 and 25% respectively. An extrapolation of the SI values generated an EC_3 value of 2.4 which classifies the notified chemical as a skin sensitiser. The positive control, α-hexylcinnamaldehyde, generated SI values of 1.5, 3.2 and 6.9 at concentrations of 5, 10 and 25% respectively, while the vehicle control had no effects.

Repeat Dose Toxicity:

A 5-day range finding study was performed using Wistar rats (2/sex/dose). The notified chemical was administered by oral gavage at doses of 200, 600 and 1000 mg/kg bw/day for 5 consecutive days. One female treated at 1000 mg/kg bw/day died on day 5. All other animals dosed at 1000 mg/kg bw/day had a slight to moderate weight loss and ruffled fur. One female also showed hunched posture. There was a reduction in the mean daily food consumption in both males and females treated with 1000 mg/kg bw. Females treated with 200 and animals treated at 600 mg/kg bw/day also showed a slight reduction in food consumption during the first days of the study. There was an increase in the relative liver weights (to body weight) in high dose males and females. An increase in the absolute and relative adrenal weights (to body weight) in both males and females treated at 1000 mg/kg bw/day and reduction in absolute and relative thymus weight in both males and females treated with 600 and 1000 mg/kg bw/day are considered stress related as a result of treatment. There was an increase in the relative kidney weights in males treated at 200 and 1000 mg/kg bw/day as well as females treated with 1000 mg/kg bw/day. Macroscopic findings included isolated cateriform retractions of the stomach which were observed in a single male treated with 600 mg/kg bw/day and one with 1000 mg/kg bw/day. One female treated with 600 mg/kg bw/day had a discoloured stomach and one treated at 1000 mg/kg bw/day had foci on the stomach and on the liver. This study established the dosing levels and testing regime for the following 28 day study.

A 28-day repeated dose subchronic assay was performed using Wistar rats (5/sex/dose). The notified chemical was administered once daily by oral gavage at doses of 50, 160 and 400 mg/kg bw/day (dose volume of 5 ml/kg bw) for 28 consecutive days. There were no mortalities or clinical signs of systemic toxicity noted during the test period. There was a slight decrease in the mean hind limb grip strength in females (significant at the high dose) and an increase in total locomotor activity in mid and high dose males at nearly all measurement intervals. There were no differences in the mean food consumption and relative food consumption or in body weights between control and treated groups. Results from haematological examination demonstrated a reduction in RBC count, haemoglobin level and mean corpuscular haemoglobin concentration in high dose female rats. There was an elevated mean absolute and relative reticulocyte counts, correlating to the reduction of haemoglobin, accompanied by a shifted reticulocyte maturity index toward high fluorescent reticulocytes in both high dose males and females although statistical significance was not observed in males. There were no toxicologically relevant differences in the clinical biochemistry of treated females. There were increases in the absolute and relative (liver to body weight and liver to brain weight) liver weight at the mid and high dose groups in females and males which were considered treatment related. There were no corresponding histological observations, therefore the toxicological significance of the increases was considered equivocal. Microscopically, high dose animals had indications of irritation consisting of basal cell and epithelial hyperplasia in combination with or without hyperkeratosis, chronic inflammation in the submucosa of the forestomach and occasionally with ulceration at all doses. The NOEL was considered to be 50 mg/kg bw/day due to the observations in the mid and high dose groups.

A 90-day repeated dose and combined reproductive/developmental toxicity assay was performed using Wistar rats (12/sex/dose). With respect to dose administration in males, the notified chemical was administered by oral gavage over a 91-day period at doses of 50, 140 and 400 mg/kg bw/day before, during and after the mating period. Females were dosed before and during mating and during the gestation period, up to day 5 after parturition. Additional females were selected for the recovery period and dosed for an additional period of 43-52 days. Five additional males and females were dosed with the vehicle or 400 mg/kg bw/day of the notified chemical and kept for an additional 14 days after termination of dosing (recovery animals).

There were no mortalities during the test or recovery period. General clinical observations included sporadic salivation in mid-dose males and high-dose females and males. There were no significant changes in the functional observational battery in males or females at study termination. There were no toxicologically significant changes in body weight changes or food consumption in any of the treated males or females as compared to controls. At week 13 of administration, there were no significant changes in the urinary parameters in any of the treatment groups as compared to controls in either males or females in week 2 of recovery.

At the end of the administration period there were no changes in the haematological parameters in males except for a slight increase in white blood cells in high dose males. High dose recovery males had a significant decrease in red blood cells count which was not observed at the end of the administration period and the toxicological significance of this finding was considered equivocal. High dose males had a significant increase in γ-GTP and β-globulin**.** In high dose females, albumin and the A/G ratio were significantly decreased and potassium and β-globulin were significantly increased. Other changes were noted but were not considered toxicologically significant.

Among the gross necropsy findings, slight thickening of the limiting ridge of the stomach was observed in all 12 low dose males. This was considered secondary to the treatment procedure and irritating nature of the test substance. In the mid dose males, thickening of the limiting ridge of the stomach was observed in all 12 animals,

and diffuse (3 males) and multifocal (6 males) papillary thickening of the forestomach mucosa was observed. In high dose animals, thickening of the limiting ridge of the stomach, diffuse papillary thickening of the forestomach mucosa, and hypertrophy of the pancreaticosplenic lymph nodes were observed in all 7 males. Multifocal black patches (1 male) and firm black patches (2 males) in the glandular stomach mucosa were observed. Thickening of the limiting ridge of the stomach was observed in 8 mid dose females. In high dose females, thickening of the limiting ridge of the stomach and hypertrophy of the pancreaticoplenic lymph nodes were observed in all of the 12 females on day 6 of lactation. Diffuse and multifocal papillary thickening of the forestomach mucosa was also observed in high dose females. High dose recovery males and females continued to show thickening of the limiting ridge of the stomach and focal thickening of the forestomach mucosa.

At the end of the administration period, there was a decrease in absolute and relative thymus weight of high dose males. These reductions were minimal and were attributed likely to stress experienced during the dosing regime. Other changes were noted but not considered toxicologically significant.

Histopathological findings included squamous cell hyperplasia in 1 low dose and all mid and high dose males. Squamous cell hyperplasia was observed in 3 low dose and all mid and high dose females. Ulcers were also observed in 3 low dose, 3 mid dose and high dose females. Submucosal cellular infiltration of inflammatory cells and submucosal fibrosis and oedema were also observed in several treated males and females. High dose recovery males and females also demonstrated squamous cell hyperplasia of the forestomach, submucosal cellular infiltration of inflammatory cells and submucosal fibrosis. The findings in the low dose group were infrequent, mild and are considered secondary to the treatment of the test substance (related to the local irritation of the test substance at the site of application).

With respect to the reproductive and developmental toxicity, there were no changes in the examination of the oestrous cycle, examination of the reproductive performance, gestation, parturition and nursery conditions, viability of pups, general clinical observations, bodyweights changes or necropsy findings in pups.

In conclusion, based on the severity of the gross and histopathological observations in the stomachs of mid and high dose animals, the NOAEL for toxicity is 50 mg/kg bw/day and the NOEL for developmental and reproductive toxicity is 400 mg/kg bw/day.

Genotoxicity:

A bacterial reverse mutation assay was performed using *Salmonella typhimurium* strains TA 98, TA 100, TA 1535, TA 1537 and *Escherichia coli* WP2uvrA using the pre-incubation method. The bacterial strains were treated with the notified chemical at a concentration range of 156.3 -5000 µg/plate in the absence of metabolic activation and at a concentration range of 312.5 -5000 µg/plate in the presence of metabolic activation. No precipitation of the test substance was present at any of the concentrations tested however evidence of cytotoxicity was present at 2500 and 5000 µg/plate in the absence of metabolic activation. Positive controls generated significant increases in the number of revertant colonies in either the presence or absence of metabolic activation. The notified chemical did not cause increases in the number of revertant colonies in any of the strains tested at any concentration in either the presence or absence of metabolic activation; therefore under the present test conditions, the notified chemical is not mutagenic.

A chromosomal aberration assay was performed with Chinese hamster lung cells. The cells were treated at concentrations of 2.5, 5 and 10 µg/ml in the absence of metabolic activation and at 105, 210 and 420 µg/ml in the presence of metabolic activation. The cells were exposed to the notified chemical for a period of 6 hours in the presence and absence of metabolic activation with a harvest time of 24 hours. The cells were also incubated for a continuous 24 hours in the absence of metabolic activation (harvest at 24 hours) and for 6 hours in the presence of metabolic activation with harvest at 48 hours. A toxicity greater than 50% was observed at concentrations greater than 10 µg/ml in the absence of metabolic activation and at concentrations greater than 250 µg/ml in the growth inhibition assay. Positive controls generated a significant increase in the number of chromosomal aberrations at the tested concentrations. The notified chemical did not increase the number of chromosomal aberrations in either the presence or absence of metabolic activation at any of the concentrations tested; therefore, the notified chemical is not clastogenic under the present test conditions.

An *in vivo* mouse micronucleus assay was performed in CD1 mouse. The animals (7 males/dose) were dosed once by oral gavage at 375, 750 and 1500 mg/kg bw (dose volume 10 ml/kg). The animals were sacrificed at 24 and 48 hours. There were no mortalities during the test period. Clinical signs observed in animals dosed at 750 mg/kg bw in both the 24 and 48 hour groups were hunched posture and ptosis. A statistically significant decrease in the PCE/NCE ratio was observed at the 24-hour, 375 mg/kg bw test group as compared to controls. Positive

controls showed a marked increase in the number of micronucleated polychromatic erythrocytes. There was no evidence of a significant increase in the incidence of micronucleated polychromatic erythrocytes in any of the treated animals, therefore the notified chemical is not clastogenic in this *in vivo* assay.

A mouse lymphoma assay was performed using L5178Y TK +/- mouse lymphoma cells. In Experiment 1, the cells were treated with the notified chemical for an exposure period of 4 hours at a dose range of 2.5 – 60 μg/ml in the absence of metabolic activation and at a dose range of 27.5 – 460 μg/ml in the presence of metabolic activation (2% S9), in duplicate. In Experiment 2, the cells were treated with the notified chemical for an exposure period of 4 hours at a dose range of 10 – 60 μg/ml in the absence of metabolic activation and a dose range of 27.5 – 460 μg/ml in the presence of metabolic activation (1% S9). Toxicity was noted at the high dose in both the presence and absence of metabolic activation, however no precipitate was noted at any of the concentrations tested. Positive controls generated a statistically significant increase in the mutant frequency in both the presence and absence of metabolic activation. The notified chemical induced a modest and statistically significant increase in the mutant frequency in both the presence and absence of metabolic activation. However, the response was at a dose where the toxicity was at the limit of acceptability. It is considered that the responses observed are due to a cytotoxic mechanism rather than a true genotoxic response and are not toxicologically significant. Therefore the notified chemical is not considered mutagenic or clastogenic under the present test conditions.

6.2.2 Summary of human health effects

Toxicokinetics

Although the notified chemical has a low molecular weight, its low measured octanol-water partition coefficient (log K_{ow} = 1.7) suggests that the notified chemical would be poorly absorbed via the dermal route. However the fact that the notified chemical was shown to be a skin sensitiser when applied to the skin of mice (see below) is evidence of dermal absorption having occurred.

Acute toxicity

The notified chemical is harmful via the oral route. It is of low toxicity via the dermal (LD_{50} > 2000 mg/kg bw) and inhalation (LC50 > 5.82 mg/L/4 hour) routes in rats.

Irritation

The notified chemical is non-irritating to the skin and slightly irritating to eyes.

Sensitisation

The notified chemical is a skin sensitiser in a local lymph node assay. There is no information available regarding potential respiratory sensitisation.

Repeated Dose Toxicity

The notified chemical has a moderate toxicity in a 28-day repeated dose assay in rats with an NOEL of 50 mg/kg bw/day. A NOAEL of 50 mg/kg bw/day for systemic toxicity and a NOEL of 400 mg/kg bw/day for reproductive and developmental toxicity was also obtained in a 90 day repeated dose combined with a reproductive/developmental assay.

Mutagenicity

The notified chemical was not mutagenic in a bacterial reverse mutation assay or clastogenic in a chromosomal aberration assay. It was not clastogenic in an *in vivo* micronucleus test or mutagenic/clastogenic in an *in vitro* mouse lymphoma assay.

Health hazard classification

Based on the data provided the notified chemical is classified as hazardous according to the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004) with the following risk phrases:

Xn; R22 Harmful if swallowed
Xi; R43 May cause sensitisation by skin contact

6.3. Human health risk characterisation

6.3.1. Occupational health and safety

The notified chemical is a skin sensitiser and is slightly irritating to eyes. It is harmful via the oral route.

Workers most at risk will be those handling ink products containing up to 60% of the notified chemical, particularly during manual replacement of ink containers, cleaning of ink residuals and servicing the printing machine.

In order to mitigate the sensitisation risk the use of impervious gloves and protective clothing would be required during any manual handling processes where dermal exposure is likely. The use of local exhaust ventilation during any process that could generate aerosols would also be required. Ingestion is not expected to be a significant route of exposure and therefore the risk of harmful effects via the oral route is considered negligible.

The risk to workers handling printed material is considered to be negligible due to the notified chemical being cured onto the print matrix and not bioavailable.

Overall the risk to workers is not considered to be unreasonable if the recommended workplace controls are in place.

6.3.2. Public health

The inks containing the notified chemical at up to 60% will not be sold to the public. No exposure is expected from the dried printed materials. Therefore, risk to the public from the notified chemical is considered to be negligible.

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 as a component of industrial printing inks. As manufacturing and reformulation will take place overseas, no release of the notified chemical will occur in Australia from these activities. In the unlikely event of a spill of ink containing the notified chemical during transport, spills are expected to be collected using inert solids and disposed of to landfill.

RELEASE OF CHEMICAL FROM USE

The majority of the release of the notified chemical to the environment from use (≤ 5% of total imported volume) will be from ink spills, wash-downs of printing equipment and from the washing of residual ink in empty containers which will be recycled. The notified chemical is likely to be stable within an inert matrix on printed substrate once UV-cured. Spilled notified chemical is likely to polymerise on exposure to UV light.

RELEASE OF CHEMICAL FROM DISPOSAL

The majority of the notified chemical will be used in inks for printing on a variety of substrates and will share the fate of the printed articles which are expected to be disposed of to landfill. A minor amount of ink containing notified chemical (up to 5%) will be used for paper printing and half of this amount is expected to be recycled. Formulated ink products will not be released directly to the environment. Hence, the total import volume of the notified chemical will predominately be disposed of to landfill with a minor amount potentially reaching the sewer.

7.1.2 Environmental fate

The majority of the notified chemical will be bound in an inert print matrix on various substrates and is not expected to be bioavailable nor mobile. The majority of articles containing the notified chemical are anticipated to be disposed of to landfill, where the notified chemical is expected to degrade by biotic and abiotic processes to form water and oxides of carbon.

An estimated maximum of 7.5% of the imported notified chemical may be disposed of to the sewer due to ink spills, washing of printing equipment and empty containers and paper recycling. During paper recycling processes, waste paper is repulped using a variety of chemical agents which, amongst other things, enhance detachment of ink from the fibres. In a worst case scenario, it is assumed that due to its high water solubility the notified chemical will partition to the supernatant water which is released to sewerage treatment plants (STPs).

In STPs the notified chemical is expected to be mobile due to its high water solubility and low soil adsorption/desorption coefficient, and will therefore potentially be released to surface waters. However, as the notified chemical is readily biodegradable (82.1% BOD; OECD TG 301C) and susceptible to hydrolysis under environmental conditions, it is therefore not expected to persist in the aquatic environment. It is not likely to bioaccumulate based on its high water solubility and low n-octanol/water partition coefficient.

7.1.3 Predicted Environmental Concentration (PEC)

Under a worst case scenario, it was assumed that 7.5% of the total import volume of notified chemical would be released to sewers (2.5% from paper recycling and 5% from spills and washings) with no removal of the notified chemical by sewerage treatment plants (STPs). It was assumed the release of the notified chemical will occur over 260 days per annum into the total Australian effluent volume. This corresponds to release only on working days, based on a 5 day work week.

Predicted Environmental Concentration (PEC) for the Aquatic Compartment		
Total Annual Import/Manufactured Volume	10,000	kg/year
Proportion expected to be released to sewer	7.5%	
Annual quantity of chemical released to sewer	750	kg/year
Days per year where release occurs	260	days/year
Daily chemical release:	2.88	kg/day
Water use	200.0	L/person/day
Population of Australia (Millions)	21.161	million
Removal within STP	0%	
Daily effluent production:	4,232	ML
Dilution Factor - River	1.0	
Dilution Factor - Ocean	10.0	
PEC - River:	0.68	µg/L
PEC - Ocean:	0.068	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 notified 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 0.682 µg/L may potentially result in a soil concentration of approximately 4.544 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 22.72 µg/kg and 45.44 µg/kg, respectively.

7.2. Environmental effects assessment

The results from ecotoxicological investigations conducted on the notified chemical are summarised in the table below. All studies were conducted on the notified chemical at a purity > 99.7%. Validity criteria were satisfied and no significant deviations from guideline protocols were reported.

Study	Duration	Endpoint	Value (mg/L)	Test Method	Assessment Conclusion
Fish Toxicity (Zebra fish)	96 h	LC50 NOEC	6.8 2.2	OECD TG 203; EEC 92/69 C.1	Toxic

Study	Duration	Endpoint	Value (mg/L)	Test Method	Assessment Conclusion
Daphnia Toxicity (*Daphnia magna*)	48 h	EC50	55	OECD TG 202; EEC 92/69 C.2	Harmful
		NOEC	25		
Algal Toxicity (*Scenedesmus subspicatus*)	72 h	E_bC50	5.0	OECD TG 201; EEC 92/69 C.3	Harmful*
		E_rC50	10		
		NOEC	0.78		
Activated Sludge Respiration Inhibition	3 h	IC50	741	OECD TG 209	Not inhibitory to sludge respiration
		NOEC	82		

*Based on E_rC50

Under the Globally Harmonised System of Classification and Labelling of Chemicals (United Nations, 2009) the notified chemical is classified as acutely toxic to fish and acutely harmful to aquatic invertebrates and algae. The notified chemical is therefore formally classified 'Acute Category 2; Toxic to aquatic life'. As the notified chemical is readily biodegradable and has a log Kow < 4, it is 'Not classified for long-term hazard' under the GHS.

7.2.1 Predicted No-Effect Concentration

The endpoint for the most sensitive species (fish) from ecotoxicological studies conducted on the notified chemical was used to calculate the PNEC. An assessment factor of 100 was used as acute toxicity endpoints are available for the effects of the notified chemical on aquatic species from three trophic levels.

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
LC50 (Fish, 96 h)	6.8	mg/L
Assessment Factor	100	
PNEC:	68	µg/L

7.3. Environmental risk assessment

Risk Assessment	PEC µg/L	PNEC µg/L	Q
Q - River	0.68	68	0.01
Q - Ocean	0.068	68	0.001

The Risk Quotients (Q = PEC/PNEC) for the worst case discharge scenario have been calculated to be << 1 for the river and ocean compartments. This indicates the notified chemical is not expected to pose an unreasonable risk to the aquatic environment based on its reported use pattern.

8. CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard classification
Based on the available data the notified chemical is classified as hazardous according to the *Approved Criteria for Classifying Hazardous Substances* [NOHSC:1008(2004)]. The classification and labelling details are:

Xn; R22 Harmful if swallowed
Xi; R43 May cause sensitisation by skin contact

and

The classification of the notified chemical using the Globally Harmonised System for the Classification and Labelling of Chemicals (GHS) (United Nations 2009) is presented below. This system is not mandated in Australia and carries no legal status but is presented for information purposes.

	Hazard category	*Hazard statement*
Acute toxicity	4	Harmful if swallowed
Skin sensitisation	1	May cause sensitisation by skin contact
Aquatic Environment	Acute Category 2	Toxic to aquatic life
	Not classified for long-term hazard	N/A

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

REGULATORY CONTROLS
Hazard Classification and Labelling

- Safe Work Australia, should consider the following health hazard classification for the notified chemical:
  - Xn; R22 Harmful if swallowed
  - Xi; R43 May cause sensitisation by skin contact

- Use the following risk phrases for products/mixtures containing the notified chemical:
  - Conc ≥ 25%: R22; R43
  - ≥ 1% concentration < 25%: R43

Health Surveillance

- As the notified chemical presents a skin sensitisation health hazard, employers should carry out health surveillance for any worker who has been identified in the workplace risk assessment as having a significant risk of sensitisation.

CONTROL MEASURES
Occupational Health and Safety

- Employers should implement the following engineering controls to minimise occupational exposure to aerosols of the notified chemical:
  - Local exhaust ventilation should be in place during ink application. .

- Employers should implement the following safe work practices to minimise occupational exposure during handling of the notified chemical:
  - Avoid contact with eyes and skin.

- Employers should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical during handling of ink products containing up to 60% of the notified chemical, particularly during manual replacement of ink containers, cleaning of ink residuals and servicing the printing machine:
  - Impervious gloves
  - Protective clothing

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

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

- If products and mixtures containing the notified chemical are classified as hazardous to health in accordance with the *Approved Criteria for Classifying Hazardous Substances* [NOHSC:1008(2004)] workplace practices and control procedures consistent with provisions of State and Territory hazardous substances legislation must be in operation.

Disposal

- The notified chemical should be disposed of to landfill.

Emergency procedures

- Spills or accidental release of the notified chemical should be handled by physical containment, 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(2) of the Act; if
  - the function or use of the chemical has changed from component of ink, or is likely to change significantly;
  - the amount of chemical being introduced has increased from 10 tonnes per annum, 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.

No additional secondary notification conditions are stipulated.

Material Safety Data Sheet
The MSDS of the products containing the notified chemical provided by the notifier were reviewed by NICNAS. The accuracy of the information on the MSDS remains the responsibility of the applicant.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Hydrolysis as a Function of pH $t_{½} \leq 43.0$ h at 40°C

Method Modified OECD TG 111 Hydrolysis as a Function of pH

pH	*T (°C)*	$t_{½}$
1.2	37	< 2.9 min
4	40	39 min
7	40	43.0 h
9	40	13.5 h

Remarks Only a brief summary of the study was provided. The notified chemical was dissolved in buffered solutions and its concentration was monitored over time (in duplicate) by GC.

The results are consistent with the hydrolysis study summarised in the Canadian report which where half lives were reported at 25°C for tests conducted at pH 4-9 (see Section 4). The notified chemical is expected to hydrolyse rapidly at environmental temperature and pH.

Test Facility Nippon Shokubai Co Ltd (2005)

Flash Point 118.6°C at 101.3 kPa

Method EC Directive 92/69/EEC A.9 Flash Point.
Remarks The Pensky-Martens flash point tester was used.
Test Facility RCC Ltd (2004b)

Flammability Non-hazardous

Method EC Directive 92/69/EEC A.12 Flammability (Contact with Water).
Remarks The test substance has been determined to be non-hazardous as it did not produce gas at a rate greater than 1 L/kg/hour.
Test Facility Harlan Laboratories Limited (2009a)

Autoignition Temperature About 175°C at 97.3-98.2 kPa

Method DIN 51794, "testing of mineral oil hydrocarbons, determination of ignition temperature", January 1978.
Remarks Auto-ignition temperature analyser according to DIN 51794 was used.
Test Facility RCC Ltd (2006a)

Autoignition Temperature 214°C at 102.2 kPa

Method ASTM E659
Test Facility Tokyo Laboratory (2006)

Explosive Properties Not expected to be explosive

Remarks The explosive properties were estimated based on the UN Recommendations on the Transport of Dangerous Goods (Manual of Test and Criteria, Annex 6, Orange Book, 3rd edition, 1999) where a set criteria is compiled to identify materials being potential explosive.

Reactive Groups
The appraisal of the molecular structure indicates that the molecule contains unsaturated C-C linkage which might be associated with explosive properties according to the UN Recommendations and the Handbook of Reactive Chemical Hazards. Other chemical groups associated with explosive properties as compiled in these documents are not present. In absence of other criteria or in case of reasonable doubt with respect to rapid decomposition, this finding would lead to the recommendation for experimental testing.

Oxygen Balance
The oxygen balance was calculated using the equation given in the UN Recommendations. Based on the molecular formula of $C_9H_{14}O_4$ and a molecular weight of 186.2 Da, the oxygen balance is about -181.

Calorimetric Tests
The exothermic decomposition energy was determined using differential scanning calorimetry in a closed, gold plated high pressure vessel (DSC). The calorimetric test is of special importance for the evaluation of compounds containing chemical groups associated with explosive properties (see reactive groups). The decomposition energy (ΔH_{Dec} determined between room temperature and 500°C) was found to be about 485 J/g thus being below the UN limit of 500 J/g. One exothermic peak has been found with an onset point at about 162°C.

Based on calorimetric tests, the notified chemical is not classified as explosive material and no experimental determination according to the EC test guideline A.14 has to be performed.

Test Facility RCC Ltd (2006b)

Surface Tension 63.4 mN/m at 20.8°C

Method OECD TG 115 Surface Tension of Aqueous Solutions.
EC Directive 92/69/EEC A.5 Surface Tension.
Remarks Concentration: 90% of saturation concentration
Test Facility RCC Ltd (2006c)

Oxidizing Properties Non-oxidising

Remarks The oxidising properties of the notified chemical were screened based on the UN Recommendations on the Transport of Dangerous Goods (Orange Book, 3rd edition, 1999) where a set criteria is compiled to evaluate the need for classification of materials as oxidising substances. According to the criteria described in the above mentioned UN documents:
-the classification procedure using experimental testing need not be applied for organic compound if the compound does not contain oxygen, fluorine or chlorine.

As the notified chemical contains oxygen the second criterion for of the Orange Book UN Recommendations has to be applied:
- the classification procedure using experimental testing need not be applied for organic compounds if the compound contains oxygen, fluorine or chlorine and these elements are chemically bonded only to carbon and hydrogen.

This second criterion is fulfilled for the test chemical.

Additionally, it can be stated that the oxygen balance of the notified chemical is negative as calculated based on the UN Recommendations on the Transport of Dangerous Goods. In principle this means, that there is a surplus of carbon atoms for a complete reaction according to the following reaction scheme: $C_xH_yO_{z_z} + [x + (y/4) - (z/2)] O_2 \rightarrow x CO_2 + (y/2) H_2O$ where $C_xH_yO_{z_z}$ is the test substance.

Applying the internationally recognized UN Recommendation criteria, the notified chemical is found to be non-oxidising and therefore is not tested experimentally for the classification under division 5.1 as oxidising substances. Thus it can be concluded beyond a reasonable doubt that the notified chemical is not capable of causing fire or enhancing the risk of fire when in contact with combustible material.

Test Facility RCC Ltd (2006d)

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