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**NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION  
AND ASSESSMENT SCHEME**

**FULL PUBLIC REPORT**

**Hostacor IT**

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For enquiries please contact the Administration Coordinator at:

*Street Address:* 92 -94 Parramatta Rd CAMPERDOWN NSW 2050, AUSTRALIA  
*Postal Address:* GPO Box 58, SYDNEY NSW 2001, AUSTRALIA  
*Telephone:* (61) (02) 9577 9514 FAX (61) (02) 9577 9465

Director  
Chemicals Notification and Assessment

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**FULL PUBLIC REPORT****Hostacor IT****1. APPLICANT**

Clariant (Australia) Pty Ltd of 675 Warrigal Rd, Chadstone VIC (ACN 069 435 552) has submitted a standard notification statement in support of their application for an assessment certificate for Hostacor IT.

**2. IDENTITY OF THE CHEMICAL**

The chemical name, CAS number, molecular and structural formulae, molecular weight, spectral data and details of exact import volume, formulations and uses have been exempted from publication in the Full Public Report and the Summary Report.

**3. PHYSICAL AND CHEMICAL PROPERTIES**

The properties listed below are for the product Hostacor IT, containing > 50 % notified chemical, unless otherwise indicated. The notified chemical is an amine salt of an organic acid, and some properties have been calculated or measured for the two components separately.

<b>Appearance at 20°C &amp; 101.3 kPa:</b>	yellowish liquid with a slight, specific odour
<b>Boiling Point:</b>	> 100°C
<b>Specific Gravity:</b>	1.09
<b>Vapour Pressure:</b>	not determined (see comments below)
<b>Water Solubility:</b>	> 500 g/L at 25°C (notified chemical)
<b>Viscosity:</b>	approximately 600 mPa.s at 25°C
<b>Particle Size:</b>	not applicable as the notified chemical will only be produced and used in liquid form
<b>Partition Co-efficient (n-octanol/water):</b>	$\log P_{ow} = -0.1$ (notified chemical, calculated)
<b>Hydrolysis as a Function of pH:</b>	not determined (see comments below)

<b>Adsorption/Desorption:</b>	log $K_{oc}$ = 3.0 (acid, calculated) log $K_{oc}$ = 0.4 (amine, calculated)
<b>Dissociation Constant:</b>	p $K_a$ = 4.43 (acid, see comments below) p $K_a$ = 7.76 (amine, measured)
<b>Flash Point:</b>	> 100°C
<b>Flammability Limits:</b>	not flammable
<b>Explosive Properties:</b>	not explosive
<b>Reactivity/Stability:</b>	expected to be stable under normal environmental conditions

### 3.1 Comments on Physico-Chemical Properties

The chemical is supplied and used as an aqueous solution of an amine salt, and is therefore expected to have negligible vapour pressure.

Although no report on water solubility was submitted, the very high water solubility, demonstrated by the high concentration of notified chemical in the aqueous product (> 500 g/L), is consistent with the ionic nature of the notified chemical when in the form of the amine salt. However, the organic acid component has a large linear hydrocarbon moiety coupled to an anionic carboxylate “head groups”, and compounds with these structural features are known to be surface active and capable of forming micellar aggregates (Tanford, 1960) which are of colloidal dimensions and fully dispersible in water. Consequently the high water solubility of the amine salt is a consequence of formation of micelles or other colloidal aggregates rather than true solubility in the normally accepted sense.

The notifier also supplied calculated data for the parent acid derived from Quantitative Structure Activity Relationships (QSAR) (ACD, 1999) where water solubility is related to the estimated value for the n-octanol/water partition coefficient. The derived estimation for water solubility of this compound is 390 mg/L. The ASTER database (US EPA, 2000) was also used in this assessment to obtain QSAR estimates of important physico-chemical properties, providing a water solubility estimate of 197 mg/L for the parent acid. QSAR estimates for the water solubility of the parent acid are very much lower than for the amine salt (ie. the notified chemical), but as discussed below, data on physico-chemical properties for the parent acid is of only marginal relevance for this submission.

No report on hydrolytic degradation as a function of pH was submitted. However, the notifier indicated that the parent acid contains a group which may be susceptible to hydrolytic cleavage at extreme pH. The ASTER database provided a half life for hydrolysis under environmental conditions of 190 days.

No experimental data on the n-octanol/water partition coefficient ( $P_{ow}$ ) or on the potential of the compound to adsorb/desorb from soil ( $K_{oc}$ ) were provided. The new chemical is expected to be surface active and consequently determination of n-octanol/water partition coefficient and adsorption/desorption data would be difficult. However, the very high water solubility

indicates the chemical would have very little affinity for the oil phase or organic matter, and may also be expected to be very mobile in soils. The notifier provided QSAR estimates for  $\text{Log } P_{\text{ow}} = 3.04$  and  $\text{Log } K_{\text{oc}} = 3.01$  for the parent acid (un-ionised) calculated using ACD software. These values can be considered typical for neutral compounds containing a substantial aliphatic hydrocarbon component, but have no relevance to the notified compound which will be in ionised form. The notified compound is a highly water soluble ionic salt which would not exist in neutral form, except at  $\text{pH} < 4$ . The ASTER database provided similar QSAR estimates for the un-ionised parent acid, of  $\text{Log } P_{\text{ow}} = 3.19$  and  $\text{Log } K_{\text{oc}} = 3.07$ .

No  $\text{pK}_a$  data was provided. A  $\text{pK}_a$  of 4.43 for analogous carboxylic acids was provided by the notifier. The acid group is expected to be ionised (ie anionic) in an aqueous environment, and balanced by the basic amine component which is expected to be protonated.

The notified chemical has a substantial hydrophobic aliphatic group bonded to an anionic carboxylate head group. Such compounds are well known to be surface active (Tanford, 1960) and would be expected to form micellar solutions or emulsions in an aqueous environment with significantly lower surface tension than that of water (around 72  $\text{dyne/cm}^2$ ).

#### 4. PURITY OF THE CHEMICAL

**Degree of Purity:** 30 - 60 %

**Hazardous Impurities:**

<i>Chemical name:</i>	2,2',2''-nitrilotris(ethanol)
<i>Synonyms:</i>	triethanolamine
<i>CAS No.:</i>	102-71-6
<i>Weight percentage:</i>	< 30 %
<i>Toxic properties:</i>	skin and eye irritant; reported to cause contact dermatitis in exposed workers (American Conference of Government Industrial Hygienists, 1998) NOHSC exposure standard 5 $\text{mg/m}^3$ TWA, with sensitiser notation (NOHSC, 1995)

**Non-hazardous Impurities (> 1% by weight):** the identity of non-hazardous impurities have been exempted from publication in the Full Public Report

**Additives/Adjuvants:** none

#### 5. USE, VOLUME AND FORMULATION

The notified chemical will be used as a corrosion inhibitor in coolant/lubricant fluids used in metal working baths during whitegoods and motor vehicle manufacture.

The notified chemical will be manufactured in Australia. The notifier estimates that the manufacture volume will be up to 10 tonnes notified chemical in the first year, increasing to within the range of 10 - 100 tonnes per annum after five years. A significant proportion of this will be exported, ranging from 50 % in the first year to 80 – 90 % by the fifth year.

The product Hostacor IT will contain between 30 % and 60 % notified chemical. It will be stored and transported in 200 L drums. The product as manufactured will be blended at a number of sites to produce concentrates of metalworking fluids, which will contain less than 10 % notified chemical. The concentrates will be further diluted by the end user, and comprise approximately 10 % of the final metalworking fluid. The concentration of the notified chemical will therefore be less than 1 % in the final metalworking fluid bath.

## **6. OCCUPATIONAL EXPOSURE**

### *Transport and Storage*

Warehouse workers and transport drivers will handle the drums of Hostacor IT, but no exposure is expected unless the packaging is ruptured. A total of 15 forklift operators and truck drivers, and 12 storemen are expected to be involved in handling Hostacor IT or the metalworking fluid concentrates, for 1 hour per day, 20 days per year.

### *Manufacture*

The notifier has indicated that 20 plant operators will be exposed to the notified chemical. These will be divided between those involved in manufacture and those involved in reformulation. Manufacture of Hosatcor IT will involve pumping the raw materials into a reaction vessel and filling drums with the finished product. The notifier indicates that exposure is expected to be for 1 hour per day, 10 days per year.

The reactants will be added to an enclosed reactor by pumping from the original packaging. The finished product will be transferred directly to the drums. There is potential for dermal exposure to the product in the form of drips and spills during connection and disconnection of transfer hoses while filling drums. The notifier indicated that safety goggles, rubber safety gloves and coveralls will be worn during these procedures.

### *Reformulation*

As described above, a total of 20 plant operators will handle the notified chemical, including during reformulation. Reformulation will involve pumping the notified chemical from the original drums (after weighing) into tanks where it will be mixed with water and other additives to produce the metalworking concentrates, which will then be pumped into drums for sale to metalworking customers. These operations will be carried out under local exhaust ventilation. There is potential for dermal exposure to the product in the form of drips and spills during connection and disconnection of transfer hoses while transferring the notified chemical into the blending tank and while filling drums. The notifier indicated that safety goggles, rubber safety gloves and coveralls will be worn during these procedures.

### *Laboratory Staff*

During manufacture and reformulation, sampling and testing of the notified chemical and the metalworking concentrates will occur. The notifier indicated that a total of 4 development chemists and 12 quality control staff will handle the notified chemical during these processes.

During quality control testing, exposure to the product Hostacor IT will be for 15 hours per year, and exposure to the blended concentrates will be for 100 hours per year. Development of new products based on the notified chemical will occur for 40 – 75 hours per year.

The notified chemical is likely to be handled in small quantities under laboratory conditions. The notifier states that the chemists will wear safety glasses, PVC or rubber safety gloves and a laboratory dust coat.

#### *Maintenance Personnel*

Maintenance of manufacture and reformulation equipment will occur after the equipment has been washed. The notifier indicated that a total of 14 maintenance personnel will be potentially exposed to the notified chemical, although exposure should be low as the equipment will have previously been washed. Maintenance personnel will wear coveralls.

#### *Metalworking Operators*

The notified chemical will be diluted in metalworking baths of volume between 200 L and 110000 L to a concentration of < 1 %. The baths will be topped up as required. The contents of the baths will be changed every 12 months and the used fluids will be disposed of by waste disposal contractors. The initial dosing will be in bulk from drums or bulk tanks, and maintenance of the concentrate level will be by automatic dosing pump from these sources. Local exhaust ventilation will be used during weighing, chemical transfer, mixing and general metalworking operations.

The notifier expects that approximately 50 metalworkers will be exposed to fluids containing the notified chemical. Exposure is expected for approximately 2 hours per day, 100 days per year. Little contact with the metalworking fluids is expected, and the metalworkers will wear coveralls and PVC or rubber gloves.

## **7. PUBLIC EXPOSURE**

It is expected that during manufacture, formulation, transport, storage and use, public exposure to the notified chemical will be low. Metalworking fluids containing the notified chemical will be for industrial use only and consequently no public exposure is anticipated except in the case of an accidental spill during transport.

## **8. ENVIRONMENTAL EXPOSURE**

### **8.1 Release**

#### *Manufacturing Process*

Some release of the raw materials used in preparation of the new chemical will occur as a result of the vacuum extraction used during the preparation, although no quantities were specified. Unreacted parent acid is stripped from the gases by alkali in a caustic scrubber, and will become incorporated into aqueous waste and treated at the factory on-site treatment plant prior to discharge to the sewer as trade waste. The description of the treatment process was not detailed in the notification statement, and apart from neutralisation of the plant effluent no other treatment operations were indicated.

The notifier indicated that after preparation of each batch of Hostacor IT, around 2 kg of the finished product (containing around 1.2 kg of the new chemical) may be released as a result of tank cleaning and spills incurred during filling of the 200 L drums. This would be washed to the on-site treatment plant, and treated prior to discharge to sewer. Since up to 11 batches of material may be produced each year, up to 13.2 kg of the new chemical may be released in this manner per annum.

#### *Reformulation*

The notifier did not indicate the extent of losses during formulation into metalworking concentrates, but it is not unusual during such reformulation activities for approximately 1 % of the material to be left as residual in drums, while a further 1 % may be lost as result of spills and equipment leaks. Assuming 20 tonne per annum (based on 20 % of the maximum specified manufacture volume) of the new chemical is reformulated into concentrates in Australia, approximately 400 kg may be released during these activities. Drum residue would most likely be removed during drum reconditioning and recycling, and incorporated into waste sludge at the drum recycling facilities. This is expected to be either placed into landfill or be incinerated and may account for around 200 kg each year. Material lost due to spills and leaks (a further 200 kg annually) may be collected in containment bunds at the reformulation sites and would most likely be pre-treated and discharged to sewer.

#### *Use of Metalworking Fluids*

The notifier indicated that spent metalworking fluid is often totally removed from the circuits by liquid waste contractors and presumably disposed of through accepted methods such as biological treatment, prior to discharge of the treated effluent to sewer. During these operations, solid material (eg. fine metal cuttings) which have accumulated in the systems are also removed and are placed into landfill. The notifier indicated that such periodic removal by licensed operators is universal, but while large factories are very likely to periodically have spent metalworking fluid removed in this manner, smaller establishments may not do so. In the case of smaller factories and metal working shops (eg. motor garages) it must be assumed that much of the spent fluid would be disposed of to sewer, or allowed to spill onto the ground. Since a maximum of 20 tonnes of the new chemical are likely to be used each year within Australia, and assuming that 50 % is used by small factories, as a worst case it is possible that up to 10 tonnes of the new chemical may be released to sewer without prior treatment, or disposed of onto land each year.

During use, some metalworking fluids will be lost through splashes and spills. This is likely to be contained within bunds at large establishments, then sent to sewer. At smaller shops spilt material would be most likely absorbed with saw dust and disposed of to landfill with everyday waste. Assuming overall losses due to splashes amount to 20 % of the maximum 20 tonnes of material used annually within Australia, and that 50 % is disposed of to sewer and 50 % to landfill, then each year an additional 2 tonnes may reach the sewer and 2 tonnes may go to landfill.

#### *Summary*

It is not possible to accurately determine the amount of material likely to be released to the various environmental compartments, but of the estimated maximum 20 tonnes likely to be used within Australia each year at least 50 % (or up to 10 tonnes) is likely to be discharged to the sewer, with most probably undergoing some biological pre-treatment prior to discharge. In reality the proportion discharged to sewer may be as high as 90 %. The remainder would most likely be placed into landfill or otherwise released to the land compartment, in a very



diffuse manner across the nation. In the worst case this would amount to 10 tonnes per annum although the real figure would probably be closer to 2 tonnes each year.

## 8.2 Fate

The ready biodegradation of the notified chemical was determined by Geywitz (1997) using the Dissolved Organic Carbon (DOC) Die-away test (OECD TG 301 A). The test was conducted in duplicate over a 22 day period at  $21\pm 1^\circ\text{C}$  and used a formulation containing a slightly lower proportion of notified chemical than that to be manufactured in Australia. The test material was added to unadapted diluted sewage sludge (22.9 mg dry matter per litre) at an initial organic carbon level of 32.15 mg/L.

After one day incubation, the degree of degradation, determined through the decrease in DOC was 10.1 % in one test vessel and 11.4 % in the other. After ten days the degradation levels had increased to 73.7 % and 70.0 %, respectively and after 22 days to 96.1 % and 93.6 %. Since the degradation of the notified chemical had exceeded 60 % within 10 days of achieving 10 %, the criteria for ready aerobic biodegradability were met. Sodium benzoate reference was used to check the viability of the bacterial culture used, and better than 94 % degradation was achieved after around 3 days incubation. In respect of these biodegradation results, the ASTER database (US EPA, 2000) estimated a biodegradation half life of between 3 and 12 days.

The notifier indicated that spent metalworking fluid removed by waste contractors is likely to be treated in a biological (activated sludge) plant, where it is expected to be mineralised to water, carbonate and ammonia, or possibly nitrogen oxides, prior to discharge to metropolitan sewage systems. The environmental assessment expects that this is likely to be a routine scenario only at the larger industrial facilities, and possibly only 50 % of the material used, annually around 10 tonnes, would be disposed of in this manner. The remainder, originating from smaller factories, may be released directly to sewer, storm water drains or landfill.

As the parent carboxylic acid is readily biodegradable, notified chemical released to the environment is not expected to be persistent. The notified chemical is an amine salt of a long chain carboxylic acid, and such acids are well known to form insoluble salts with common divalent cations such as  $\text{Ca}^{2+}$  and  $\text{Mg}^{2+}$ . In this form the calcium and magnesium salts are expected to become associated with soils and sediments. The probable association of the released carboxylic acid with calcium, magnesium and other metal ions may mitigate the toxicity of the notified chemical.

Some sludge containing waste material may be incinerated, although quantitative estimates are not possible. In this case the material would be destroyed with production of water,  $\text{CO}_2$  and oxides of nitrogen.

Due to the high water solubility and ready biodegradability nature, the notified chemical is not expected to bioaccumulate.

## 9. EVALUATION OF TOXICOLOGICAL DATA

## 9.1 Acute Toxicity

The acute oral toxicity, skin irritation potential and eye irritation potential were determined for a formulation containing the notified chemical. The formulation differed from that to be manufactured in Australia and contained a slightly lower proportion of notified chemical. The notifier also provided information on the skin sensitisation potential of the analogue chemical, Hostacor IL. The structure of the analogue was provided and, on this basis, it is considered to serve as a good indication of the skin sensitisation potential of the notified chemical.

Additional toxicity information was provided for the amine counterion and for one of the ingredients of the notified chemical, which is a potential hydrolysis product of the notified chemical and which is a likely metabolite of concern with respect to subchronic effects of exposure to the notified chemical.

### Summary of the acute toxicity of Hostacor IT

<i>Test</i>	<i>Species</i>	<i>Outcome</i>	<i>Reference</i>
acute oral toxicity	rat	LD <sub>50</sub> > 2000 mg/kg	(Jensch, 1996)
skin irritation	rabbit	non-irritating	(Kreiling, 1996)
eye irritation	rabbit	slight to moderate irritant	(Kreiling, 1996)

### Summary of the acute toxicity of Hostacor IL

<i>Test</i>	<i>Species</i>	<i>Outcome</i>	<i>Reference</i>
skin sensitisation	guinea pig	non-sensitiser	(Bury, 1996)

#### 9.1.1 Oral Toxicity (Jensch, 1996)

<i>Species/strain:</i>	rat, Wistar
<i>Number/sex of animals:</i>	5/sex
<i>Observation period:</i>	14 days
<i>Method of administration:</i>	gavage, dose level 2000 mg/kg as a 20 % solution in deionised water
<i>Test method:</i>	OECD TG 401
<i>Mortality:</i>	no deaths were recorded during the study
<i>Clinical observations:</i>	after dosing, the animals showed decreased spontaneous activity, squatting posture and stilted gait; these signs were reversible after 4 to 6 hours

<i>Morphological findings:</i>	no organ abnormalities were observed at necropsy
<i>Comment:</i>	no effect on body weight gain was observed
<i>LD<sub>50</sub>:</i>	> 2000 mg/kg
<i>Result:</i>	the notified chemical was of very low acute oral toxicity in rats

### 9.1.2 Dermal Toxicity

No test results were provided by the notifier.

### 9.1.3 Inhalation Toxicity

No test results were provided by the notifier.

### 9.1.4 Skin Irritation (Kreiling, 1996)

<i>Species/strain:</i>	rabbit/New Zealand albino
<i>Number/sex of animals:</i>	3 female
<i>Observation period:</i>	3 days
<i>Method of administration:</i>	0.5 mL test substance was applied to a clipped test site under semi-occlusive conditions for 4 hr
<i>Test method:</i>	OECD TG 404
<i>Comment:</i>	no signs of irritation were observed at 30-60 minutes, 24 hr, 48 hr or 72 hr; all Draize scores were zero
<i>Result:</i>	the notified chemical was not irritating to the skin of rabbits

### 9.1.5 Eye Irritation (Kreiling, 1996)

<i>Species/strain:</i>	rabbit/New Zealand albino
<i>Number/sex of animals:</i>	3/not stated
<i>Observation period:</i>	7 days
<i>Method of administration:</i>	0.1 mL test substance was placed in the conjunctival sac of

the left eye; the untreated eye served as control

*Test method:* OECD TG 405

*Draize scores of unirrigated eyes:*

<i>Time after instillation</i>															
<i>Animal</i>	<i>1 hour</i>			<i>1 day</i>			<i>2 days</i>			<i>3 days</i>			<i>7 days</i>		
<i>Cornea</i>	all Draize scores were zero														
<i>Iris</i>															
1	1			1			0			0			0		
2	0			0			0			0					
3	0			1			0			0					
<i>Conjunctiva</i>	<i>r</i>	<i>c</i>	<i>d</i>	<i>r</i>	<i>c</i>	<i>d</i>	<i>r</i>	<i>c</i>	<i>d</i>	<i>r</i>	<i>c</i>	<i>d</i>	<i>r</i>	<i>c</i>	<i>d</i>
1	2	2	2	3	2	1	3	1	0	2	0	0	0	0	0
2	2	1	3	1	0	0	0	0	0	0	0	0			
3	3	2	3	3	2	1	0	0	0	0	0	0			

<sup>1</sup> see Attachment 1 for Draize scales

o = opacity a = area r = redness c = chemosis d = discharge

*Result:* the notified chemical was a slight to moderate irritant to the eyes of rabbits

#### 9.1.6 Skin Sensitisation: Hostacor IL (Bury, 1996)

*Species/strain:* guinea pig/Pirbright-White

*Number of animals:* test group: 20/female  
control group: 10/female

*Induction procedure:*

test group:  
days 1, 8, 15 0.5 mL of 100 % test substance was applied by occlusive patch to a clipped area of the left flank for 6 hr

control group: treatment was as for the test group except 0.5 mL 80 % (v/v) ethanol in water was used in place of the test substance

*Challenge procedure:*

day 29 0.5 mL of 100 % test substance was applied by occlusive patch to a clipped area of the right flank for 6 hr, for both test and control groups

*Test method:* OECD TG 406 (Buehler method)

*Challenge outcome:*

<i>Challenge concentration</i>	<i>Test animals</i>		<i>Control animals</i>	
	<i>24 hours*</i>	<i>48 hours*</i>	<i>24 hours</i>	<i>48 hours</i>
100 %	**0/20	0/20	0/10	0/10

\* time after patch removal

\*\* number of animals exhibiting positive response

*Comment:* no signs of irritation were observed during the induction or challenge phases

*Result:* the test substance was not sensitising to the skin of guinea pigs

## 9.2 Summary of Toxicity Data for the Amine Counterion

A summary of data from HSDB (National Library of Medicine, 1997) and RTECS (National Institute of Occupational Safety and Health, 1997) was provided by the notifier, along with reports from the NTP on genetic toxicity and 2 year carcinogenesis studies (NTP, 1999).

The summary of toxicity data indicates that this chemical is of generally low toxicity, with the major effects being ascribed to the alkalinity of the chemical. It was found to be of low oral toxicity ( $LD_{50} = 4920 \mu\text{L/kg}$ ) and low dermal toxicity ( $LD_{50} > 16 \text{ mL/kg}$ ) in rats. It was a slight skin irritant in humans and rabbits, and a slight eye irritant in rabbits at 10 mg applied dose, but a severe eye irritant in rabbits at 20 mg applied dose. It was found to not have skin sensitising activity in guinea pigs. There are reports that this chemical causes skin sensitisation in exposed human populations, and the NOHSC exposure standard for this chemical is therefore annotated to indicate that it is a sensitiser.

During a 14 day inhalation study, the only histopathological result reported was minimal acute inflammation of the laryngeal submucosa in rats and mice. A No Observed Effect Level (NOEL) of 80 mg/kg/day was established in a 90 day feeding study in rats, with alterations in liver and kidney weights being observed at 170 mg/kg/day, and microscopic lesions and deaths at 730 mg/kg/day.

The NTP genetic toxicology testing indicated that this chemical was not genotoxic in a number of tests, including *Salmonella typhimurium* point mutations, Chinese Hamster Ovary cell Sister Chromatid Exchange and Chromosome Aberration, Sex-Linked Recessive Lethal Mutations in *Drosophila melanogaster* and micronucleus induction in mice following 13 week dermal application.

As a preliminary for the NTP 2 year carcinogenesis studies in rats and mice, 13 week dermal repeat dose studies were carried out. It was stated that the dermal absorption at the doses used was extensive. Skin effects at the site of application, including irritation, scaliness, crustiness and discolouration, were observed in both rats and mice. Also inflammation and acanthosis were found in the histopathological examination. In rats administered 500 mg/kg and above, increases in kidney weights were observed. Nephropathy was observed in female rats, and hypertrophy of the pituitary gland pars

intermedia was observed in males and females. Dose related increases in incidence and severity of lesions was observed in both sexes. In mice, the absolute kidney and liver weights were increased for males and females receiving 4000 mg/kg, and the relative kidney weights were increased for males at 1000 mg/kg and above, and all females.

In rats, mild but dose related increases in serum alanine and aspartate aminotransferase activity were seen, suggestive of liver injury, but no corresponding change in sorbitol dehydrogenase activity or histopathological evidence of liver damage was observed. A decrease in urinary protein excretion was observed in male rats, although no corresponding renal histopathological changes were observed. In mice, the clinical chemistry observations were limited to a dose related decrease in sorbitol dehydrogenase activity.

In the 2 year carcinogenesis study in rats, there was equivocal evidence (defined as a study which is interpreted as showing a marginal increase in neoplasms that may be chemical related) of carcinogenic activity in the males, based on an increase in renal tubule cell adenoma. No evidence of carcinogenic activity was observed in the females, at up to 250 mg/kg/day. In mice, the study was confounded by a *Helicobacter hepaticus* infection, which may have been responsible for the observed increase in liver neoplasms.

### 9.3 Summary of Toxicity Data for the Hydrolysis Product

A summary of data from HSDB (National Library of Medicine, 1997) and RTECS (National Institute of Occupational Safety and Health, 1997) was provided by the notifier, along with an Australian National Drug Information Services profile (Australian National Drug Information Services, 1981) and a published paper on a 2 generation study of toxicity of this chemical in rats (Melander, 1965).

The acute oral toxicity of this chemical in rats and mice was found to be very low (rats, LD<sub>50</sub> = 12000 mg/kg, mice LD<sub>50</sub> = 16500 mg/kg). In a 90 day repeat dose oral study, this chemical was found to produce no major gross or microscopic changes in major organs. Changes in a number of haematology parameters and clinical chemistry parameters were observed at all doses used (500, 2500 and 5000 mg/kg/day), and no NOEL was established. In a two generation study, the higher doses (2500 and 5000 mg/kg/day) were found to reduce the number of pregnancies observed. This chemical has been approved in Australia for drug use at doses of up to 30 g in a 24 hour period.

No toxicological information on the other major metabolite which is expected to be produced has been provided by the notifier.

### 9.4 Overall Assessment of Toxicological Data

The notified chemical is of very low oral toxicity in rats. It is non-irritating to rabbit skin, and a slight to moderate irritant to rabbit eyes. An analogue was found to be non-sensitising in guinea pigs. Based on the properties of the amine in the notified chemical, it is expected to have irritant properties in the eye, as observed, but no additional sensitising properties are expected.

Based on repeat dose studies on two components of the notified chemical, the amine and one of the expected metabolites, effects on the liver and kidney may be observed at high doses,

but these are not expected to be severe. The other main metabolite would be expected to have low toxicity, based on its structure.

Genetic toxicity testing and a two year carcinogenesis study have been carried out on the amine counterion. It is not considered genotoxic on the basis of the reported studies, but there is equivocal evidence that it is carcinogenic in male rats.

Based on the submitted data, the notified chemical is not classified as a hazardous substance in accordance with the NOHSC *Approved Criteria for Classifying Hazardous Substances* (Approved Criteria) (NOHSC, 1999).

## 10. ASSESSMENT OF ENVIRONMENTAL EFFECTS

The ecotoxicological studies were performed using a formulation containing the notified chemical. The formulation differed from that to be manufactured in Australia and contained a slightly lower proportion of notified chemical.

<i>Test</i>	<i>Species</i>	<i>Results (nominal)</i>
acute toxicity	<i>Brachydanio rerio</i> zebra barbel	LC <sub>50</sub> (96 h) > 1000 mg/L
respiration inhibition	aerobic waste water bacteria	3 h EC <sub>50</sub> > 1000 mg/L

### *Fish*

A summary report (Zok, 1996) on the acute toxicity of the formulation to zebra barbel was submitted. The acute toxicity was determined in a 96 hour static test at 22°C at a single nominal concentration of 1000 mg/L, although subsequent Total Organic Carbon (TOC) analysis established that the actual concentration was around 853 mg/L. However, it was not clear whether this concentration referred to the notified chemical, or to the formulation containing an excess of amine. Also, while the dissolved oxygen in the test media was stated as being between 7.8 and 8.8 mg/L, and the pH between 8 and 8.2, the hardness of the water was not indicated. OECD TG 203 specifies that water hardness should be between 50 and 250 mg/L as CaCO<sub>3</sub>. As discussed below, this may influence interpretation of the results.

Although the summary report did not specify the number of fish used in the study, it was indicated that there were no mortalities during the entire trial period and that no changes in the appearance and behaviour of the fish were observed when compared with the control group. The 96 hour LC<sub>50</sub> of the notified chemical was therefore determined to be > 1000 mg/L and the highest concentration tested without toxic effects was (nominally) 1000 mg/L. The results indicate that the test material is not toxic to this species of fish.

### *Microorganisms*

The notifier supplied a report (Noack, 1996) on the toxicity of the formulation to sewage bacteria. The bacteria were exposed to nominal concentrations of the test substance of 1000, 1800, 3200, 5800 and 10000 mg/L over a 3 hour period, and the bacterial respiration rate then determined.

No significant inhibition of bacterial respiration rate over that of two controls (no test material) was noted, and consequently the 3 hour EC<sub>50</sub> value for the chemical was determined

as > 1000 mg/L. In contrast to the test material, 3 hour exposure of the bacterial culture to (nominally) 58 mg/L copper sulphate caused 29% inhibition of respiration, while exposure to 100 and 180 mg/L caused 56 and 81 % inhibition respectively, and these results confirmed the viability of the bacterial culture used in the test.

#### *QSAR Toxicity Estimates on Parent Acid*

The notifier supplied some data toxicity data calculated using QSAR data (ACD, 1999) for the parent acid of the notified compound. These results are relevant to the ecotoxicity of the notified chemical, as the salt is expected to dissociate into its constituents under the conditions of environmental release. The results derived using QSARs appropriate to anionic surfactants indicate that the compound may be highly toxic to freshwater fish and daphnia, with the 96 h LC<sub>50</sub> = 0.18 mg/L for fish, and 48 h LC<sub>50</sub> = 0.18 mg/L for daphnia. For green algae the results indicate the material is extremely toxic with a 96 h EC<sub>50</sub> of 0.4 µg/L. The particular set of QSARs used for these estimates are based on the number of aliphatic carbon atoms in the organic component of the molecule, and were stated in information provided to be appropriate for anionic surfactants including those terminated by carboxylate groups.

The ASTER database (US EPA, 2000) also provided QSAR estimates of the potential toxicity of the parent acid to aquatic organisms. The more relevant results were:

96 hour LC <sub>50</sub> for rainbow trout	6.75 mg/L
96 hour LC <sub>50</sub> for bluegill	13.39 mg/L
96 hour LC <sub>50</sub> for fathead minnow	16.69 mg/L
32 day (chronic) MATC for fathead minnow	2.76 mg/L.
48 hour LC <sub>50</sub> for Daphnia magna	9.56 mg/L

MATC = maximum allowable toxic concentration

No data for algae were generated.

The results indicate that the new chemical may be at least slightly acutely toxic to aquatic species, but the values are at least two orders of magnitude higher (ie. indicating lower toxicity) than the ACD software estimates. The differences highlight the uncertainties involved in the use of QSAR methods for estimation of aquatic toxicity. Both sets of QSAR data indicate the potentially toxic nature of the new chemical, and are very different from the limited measured toxicity data which indicates the material to be non toxic. It is possible that the low measured toxicity against zebra fish was due to the presence of high water hardness in the test media. The compound is expected to form insoluble salts with divalent ions such as calcium, and these are likely to become associated with aquatic sediments. Consequently any potential toxicity of the compound may have been mitigated through this mechanism, but since water hardness data was not included in the report this discussion is speculative.

#### *Conclusions*

The ecotoxicity data supplied by the notifier for the notified substance indicates that the notified chemical is practically non-toxic to fish and sewage microorganisms.

In contrast, the ecotoxicity data profiles obtained from QSAR estimates for the free parent acid of the notified chemical indicates that this compound may be extremely toxic to aquatic organisms at all trophic levels. The differences between the measured data for fish and the QSAR estimates were not discussed at length in the submission. However, the notifier stated that the measured data probably reflected the low toxicity of the amine counterion (eg. 48 h



LC<sub>50</sub> > 10000 mg/L for the fish *Leuciscus idus* and 72 h EC<sub>50</sub> = 216 mg/L for algae *Scenedesmus subspicatus*) (Verschueren, 1996) rather than the new anionic material. Confirmatory measured test data is needed for daphnia and algae.

It is possible that complex formation of the compound with divalent ions in hard water was responsible for the low measured acute toxicity against zebra fish, but without additional measured toxicity data it is not possible to resolve the differences. This assessment assumes that the compound may be toxic to aquatic organisms, particularly if released into water with lower concentrations of Ca and Mg than those required for complete reaction with the notified chemical.

## 11. ASSESSMENT OF ENVIRONMENTAL HAZARD

The compound is readily biodegradable under aerobic conditions, and would be mineralised to water, carbonate and ammonia. Up to 13.2 kg of the compound may be released annually as a result of production and packing activities, and this would most likely enter the sewer system.

Up to 20 tonnes of the new chemical may be used in Australia in metalworking fluids, and usually spent fluid will be removed (typically after 12 months) by waste contractors for biological (activated sludge) treatment process and disposal to sewer. However, it is estimated that in a worst case scenario up to 50 % of the material used within Australia (ie. up to 10 tonnes per annum) may be released untreated to the sewer system, storm water drains, placed into landfill or incinerated. Nevertheless, due to its ease of aerobic biodegradation the notified chemical is not expected to persist. Also, when released the compound is expected to form insoluble salts with calcium and other ions in environmental waters, which would become assimilated into aquatic sludges and undergo subsequent biodegradation.

Assuming nationwide use of the material, and that all estimated 20 tonnes are released annually without degradation to the sewer system, and that annual sewage production is 19,000,000 (persons) × 150 (L) × 365 (days) =  $1.04 \times 10^{12}$  L, the worst case Predicted Environmental Concentration (PEC) for the chemical in the sewer is 7 µg/L. Assuming dilution by a factor of 10 on discharge of sewage effluent to receiving waters, the overall PEC is 2.1 µg/L. However, it should be stressed that these estimates assume no degradation of a chemical shown to be readily biodegradable, so PEC values are likely to be significant overestimates.

Although limited ecotoxicity data indicates that the notified chemical is not toxic to zebra fish, two different sets of Quantitative Structure Activity Relationship (QSAR) data indicate that it may in fact demonstrate significant toxicity to aquatic organisms with the notifier indicating extreme toxicity of the parent acid to green algae with an estimated EC<sub>50</sub> of 0.4 µg/L. However, due to the formation of insoluble complexes with calcium and other ions which are usually present in significant concentration in environmental waters, it is likely that potential toxicity would be reduced through association of the insoluble salts with aquatic sediments. Nevertheless, given the estimated EC<sub>50</sub> to algae of 0.4 µg/L the safety margin for toxic effects resulting from release of the notified chemical may be considerably less than 1, indicating significant potential toxicity to aquatic organisms. This could be particularly serious if the spent metalworking fluid containing the notified chemical was to be released to

water bodies containing water with lower concentrations of Ca and Mg than those required for complete reaction with the notified chemical.

Once combined with metal ions and incorporated into sediments, the organic component is expected to undergo biodegradation and not to persist. Due to the high water solubility and its readily biodegradable nature, the notified chemical is not expected to bioaccumulate.

Due to large differences between limited measured toxicity results (to fish and bacteria) indicating low toxicity to aquatic organisms and QSAR estimates provided by the notifier indicating potential extreme toxicity, it is not possible to reach firm conclusions on the likely environmental hazard resulting from the stated use of the new compound in Australia.

## **12. ASSESSMENT OF PUBLIC AND OCCUPATIONAL HEALTH AND SAFETY EFFECTS**

### *Hazard Assessment*

Toxicological information has been provided for acute oral toxicity and skin and eye irritation for the notified chemical, and for skin sensitisation for a close analogue to the notified chemical, differing in amine counterion. The notified chemical is of very low oral toxicity in the rat ( $LD_{50} > 2000$  mg/kg). It was non-irritant to skin, and a slight to moderate eye irritant. The analogue was not a skin sensitiser in guinea pigs, and, based on the known properties of the amine counterion, the notified chemical is also not expected to be a skin sensitiser. The notified chemical cannot be assessed against the Approved Criteria for other toxicity endpoints.

Additional toxicity information was provided by the notifier for the amine counterion, and for one major hydrolysis product of the notified chemical.

The MSDS for the formulation containing the notified chemical, Hostacor IT, indicates that it is not a hazardous substance. It indicates that eye irritation may occur. This is likely to be primarily due to the presence of an excess of triethanolamine in the formulation.

### *Occupational Health and Safety*

There is little potential for significant occupational exposure to the notified chemical in the transport and storage of Hostacor IT or the metalworking fluid concentrates containing the notified chemical. There may be exposure during the manufacture and reformulation of the notified chemical and during use of metalworking fluids containing the notified chemical.

During manufacture, reformulation and end use, the main exposure route for the notified chemical will be dermal. While the mixing and dosing operations are automated, exposure to drips and spills of Hostacor IT (30 - 60 % notified chemical) and the metalworking fluid concentrates (< 10 % notified polymer) is possible at a number of points where these products are transferred. Once the reformulated product has been dosed into metalworking fluids, the final concentration will be very low (< 1 %) and little exposure is likely, as little contact with the fluids is expected.

Precautions should be taken to avoid ocular contact with the products containing the notified chemical, as eye irritation may occur. The MSDS indicates that protective clothing, protective gloves and safety glasses should be worn.

### *Public Health*

Given that the intended use of the notified chemical will be restricted to industrial metalworking, such as motor vehicle and whitegoods manufacture, no public exposure is anticipated except in the event of an accidental spill during transport. It is therefore considered that Hostacor IT will not pose a significant hazard to public health when used in the proposed manner.

## **13. RECOMMENDATIONS**

To minimise occupational exposure to Hostacor IT the following guidelines and precautions should be observed:

- Safety goggles, chemical resistant industrial clothing and footwear and impermeable gloves should be used while handling the product containing the notified polymer; where engineering controls and work practices do not reduce vapour and particulate exposure to safe levels, an air fed respirator should also be used;
- Spillage of the notified chemical should be avoided. Spillages should be cleaned up promptly with absorbents which should then be put into containers for disposal;
- Good personal hygiene should be practised to minimise the potential for ingestion;
- A copy of the MSDS should be easily accessible to employees.

If products containing the notified chemical are hazardous to health in accordance with the NOHSC *Approved Criteria for Classifying Hazardous Substances* (National Occupational Health and Safety Commission 1999), workplace practices and control procedures consistent with State and territory hazardous substances regulations must be in operation.

Guidance in selection of goggles may be obtained from Australian Standard (AS) 1336 (Standards Australia 1994) and Australian/New Zealand Standard (AS/NZS) 1337 (Standards Australia/Standards New Zealand 1992); for industrial clothing, guidance may be found in AS 2919 (Standards Australia 1987) and AS 3765.2 (Standards Australia 1990); for impermeable gloves or mittens, in AS 2161 (Standards Australia/ Standards New Zealand, 1998); for occupational footwear, in AS/NZS 2210 (Standards Australia/ Standards New Zealand, 1994a); for respirators, in AS/NZS 1715 (Standards Australia/ Standards New Zealand, 1994b) and AS/NZS 1716 (Standards Australia/ Standards New Zealand, 1994c).

## **14. MATERIAL SAFETY DATA SHEET**

The MSDS for the notified chemical was provided in a format consistent with the *National Code of Practice for the Preparation of Material Safety Data Sheets* (NOHSC, 1994).

This MSDS was provided by the applicant as part of the notification statement. It is reproduced here as a matter of public record. The accuracy of this information remains the responsibility of the applicant.

## 15. REQUIREMENTS FOR SECONDARY NOTIFICATION

Under subsection 64(1) of the Act, secondary notification will be required if end use of the notified chemical within Australia exceeds 10 tonnes per annum. In this case, measured ecotoxicity data for the notified chemical against daphnia and algae will be required for NICNAS assessment.

Under subsection 64(2) of the Act, the director must be informed if any of the circumstances stipulated under that subsection arise, and secondary notification of the notified chemical may be required.

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## Attachment 1

The Draize Scale (Draize, 1959) for evaluation of skin reactions is as follows:

<b><i>Erythema Formation</i></b>	<b><i>Rating</i></b>	<b><i>Oedema Formation</i></b>	<b><i>Rating</i></b>
No erythema	0	No oedema	0
Very slight erythema (barely perceptible)	1	Very slight oedema (barely perceptible)	1
Well-defined erythema	2	Slight oedema (edges of area well-defined by definite raising)	2
Moderate to severe erythema	3	Moderate oedema (raised approx. 1 mm)	3
Severe erythema (beet redness)	4	Severe oedema (raised more than 1 mm and extending beyond area of exposure)	4

The Draize scale (Draize *et al.*, 1944) for evaluation of eye reactions is as follows:

### ***CORNEA***

<b><i>Opacity</i></b>	<b><i>Rating</i></b>	<b><i>Area of Cornea involved</i></b>	<b><i>Rating</i></b>
No opacity	0 none	25% or less (not zero)	1
Diffuse area, details of iris clearly visible	1 slight	25% to 50%	2
Easily visible translucent areas, details of iris slightly obscure	2 mild	50% to 75%	3
Opalescent areas, no details of iris visible, size of pupil barely discernible	3 moderate	Greater than 75%	4
Opaque, iris invisible	4 severe		

### ***CONJUNCTIVAE***

<b><i>Redness</i></b>	<b><i>Rating</i></b>	<b><i>Chemosis</i></b>	<b><i>Rating</i></b>	<b><i>Discharge</i></b>	<b><i>Rating</i></b>
Vessels normal	0 none	No swelling	0 none	No discharge	0 none
Vessels definitely injected above normal	1 slight	Any swelling above normal	1 slight	Any amount different from normal	1 slight
More diffuse, deeper crimson red with individual vessels not easily discernible	2 mod.	Obvious swelling with partial eversion of lids	2 mild	Discharge with moistening of lids and adjacent hairs	2 mod.
Diffuse beefy red	3 severe	Swelling with lids half-closed	3 mod.	Discharge with moistening of lids and hairs and considerable area around eye	3 severe
		Swelling with lids half-closed to completely closed	4 severe		

### ***IRIS***

<b><i>Values</i></b>	<b><i>Rating</i></b>
Normal	0 none
Folds above normal, congestion, swelling, circumcorneal injection, iris reacts to light	1 slight
No reaction to light, haemorrhage, gross destruction	2 severe

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