File No: NA/229

Date: 2 June 1995

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME

FULL PUBLIC REPORT

HOSTACOR V4221

This Assessment has been compiled in accordance with the provisions of *the Industrial Chemicals (Notification and Assessment) Act 1989,* and Regulations. This legislation is an Act of the Commonwealth of Australia. The National Industrial Chemicals Notification and Assessment Scheme (NICNAS) is administered by Worksafe Australia which also conducts the occupational health & safety assessment. The assessment of environmental hazard is conducted by the Department of the Environment, Sport and Territories and the assessment of public health is conducted by the Department of Human Services and Health.

For the purposes of subsection 78(1) of the Act, copies of this full public report may be inspected by the public at the Library, Worksafe Australia, 92-94 Parramatta Road, Camperdown NSW 2050, between the hours of 10.00 a.m. and 12.00 noon and 2.00 p.m. and 4.00 p.m. each week day except on public holidays.

For Enquiries please contact the Administration Coordinator at:

Street Address: 92 Parramatta Rd Camperdown, NSW 2050, AUSTRALIA
Postal Address: GPO Box 58, Sydney 2001, AUSTRALIA
Telephone: (61) (02) 565-9466 **FAX (61) (02) 565-9465**

Director
Chemicals Notification and Assessment

FULL PUBLIC REPORT

HOSTACOR V4221

1. APPLICANT

Hoechst Australia Limited, 606 St. Kilda Road, Melbourne, Victoria has submitted a standard notification for assessment of Hostacor V4221.

2. IDENTITY OF THE CHEMICAL

Trade name: Hostacor V4221

Method of detection and determination:

The identity of the chemical was confirmed by Fourier transformed infrared spectroscopy, Nuclear magnetic resonance (NMR) and High pressure liquid chromatography (HPLC).

3. PHYSICAL AND CHEMICAL PROPERTIES

Appearance at 20°C and 101.3 kPa:	Dark-brown, viscous liquid
Odour:	Weak, but characteristic
Melting Point:	-34°C
Boiling Point:	185°C @ 101.3 kPa
Density:	1030 to 1040 kg/m^3
Vapour Pressure:	21.6 kPa at 100°C
Water Solubility:	Between 10 and 30 mg/L at 20°C
Surface Tension:	41.7 mN/m at 20°C, and 8.5 x 10^{-3} g/l
Fat Solubility:	0.3 g/100g fat at 37°C
Partition Co-efficient (n-octanol/water) log P_{OW}:	Not determined
Hydrolysis as a function of pH:	Not determined
Adsorption/Desorption:	Not determined
Dissociation Constant pKa**:**	Not determined
Flash Point:	> 185°C

Flammability Limits:	Not determined
Combustion Products:	Not determined
Pyrolysis Products:	Not determined
Decomposition Temperature:	Not determined
Decomposition Products:	Not determined
Autoignition Temperature:	Not determined
Explosive Properties:	Not determined
Stability:	Stable under ambient conditions; not oxidising and does not react with water
Particle size distribution:	Not applicable

. comments on physico-chemical identity

The notifier submits that the new substance, HOSTACOR V 4221, is similar to an earlier notification (HOSTACOR V 4205), in that both are alkenyl succinic acid derivatives. However, the latter is a salt and lacks the intact succinimide ring of the former, and that the two will therefore have differing chemical and environmetal characteristics.

No test reports have been supplied to support data for melting/boiling points, water solubility or vapour pressure. These tests were conducted using Hoechst in-house methods, but are said to be based on relevant OECD and EEC Guidelines. The notifier has stated that full test reports have not been written up for these tests.

The boiling point was determined using OECD Guideline 115, 1981 (a dynamic method). Again, given the structure of the notified substance, and by analogy with similar compounds, the boiling point appears to be lower than would be expected.

Vapour pressure determinations were made following a dynamic method as outlined by the OECD Guideline 104, Paris 1981.

No hydrolysis data for the notified substance were provided but data were supplied for a closely similar compound, HOE S3981. It was found to be hydrolytically stable at room temperature (22^{o}C) under basic conditions. Hydrolysis occurred more quickly at 100^{o}C. Therefore, it is expected that HOSTACOR V4221 will be stable at pH 4, 7 and 9 at room temperature. Succinimides are not readily susceptible to hydrolysis under environmental conditions.

The notified substance is surface active, based on the value supplied for surface activity, but it is noted that no test report has been supplied. Therefore partition coefficient tests are not applicable.

No data was available regarding the adsorption/desorption of the notified substance. However, given the surface active nature of the substance (as indicated by the surface tension results, determined using the OECD harmonised ring method - Guideline 115), the substance would be expected to adsorb strongly to sediments and soils.

No information was available regarding the dissociation constant of the notified substance. The molecule contains a primary carboxylic functionality that is expected to have typical acidity.

4. PURITY OF THE CHEMICAL

Degree of purity : 96% (w/w)

5. INDUSTRIAL USE

Hostacor V4221 is an emulsifier/corrosion inhibitor added to coolants/lubricants used in car and whitegood manufacture. The notified chemical will be blended into concentrate products in which the chemical is expected to be present at concentrations of approximately 14%. This product is diluted with a high viscosity paraffin oil for sale to end-users. The notified chemical would be expected to be present in the paraffin oil blend at concentrations in the order of 2.6%. This is further diluted with water for use as a metal working fluid where the approximate concentration of the notified chemical is 0.1%.

The estimated import of the notified chemical is > 10 tonnes per annum over the next five years.

6. OCCUPATIONAL EXPOSURE

The notified chemical will be imported into Australia in 200 L steel drums. It will be transported by road, in either individual lots of drums, or as pallets of drums. Hostacor V4221 containing 96% of the notified chemical will be reformulated at six sites in Australia and distributed to 25 outlets.

Approximately 400 workers will be exposed to the chemical during storage, handling, reformulation, production support activities and end-use.

In the reformulation plant 40 workers will be exposed to the notified chemical only during pumping of fluids in and out of sealed mixing vessels due to vessel containment. 25 laboratory personnel involved in quality control operations will be exposed to the notified chemical during blended formulations. The blended formulation is pumped to a packaging area. Weighing , chemical transfer and mixing processes are carried out under exhaust ventilation. Air borne effluents pass through water jet scrubbers and carbon adsorbers prior to atmospheric discharge. 150 workers will be exposed to the metal cutting fluids containing the notified chemical during metal working operations.

7. PUBLIC EXPOSURE

Under normal conditions of use, there will be low potential for public exposure to the notified chemical. Although residues of Hostacor V4221 may be present on metal after removal from the cutting equipment, the concentration of the notified chemical will be low (0.1%), and the cut metal probably would be subject to cleaning, followed by other manufacturing operations prior to entering the public domain. Public exposure to the notified chemical from this source is therefore expected to be negligible.

8. ENVIRONMENTAL EXPOSURE

. Formulation

Reformulation of Hostacor V 4221 will not be carried out by Hoechst. Consequently, Hoechst will not control any reformulation operations and subsequent release of the new chemical to the environment during reformulation. The following estimates of release of Hostacor V 4221 are based on effluent release during reformulation at Hoechst of the related substance, Hostacor V 4205, notification number NA/185.

Spills from formulation and rinsing of blending vessels will pass to on-site effluent treatment pits, which at HOECHST have a capacity of 40 000 L. Effluents from the final pit are constantly trickling into a larger interceptor pit (capacity 60 000 L) which ultimately flows into sewers.

For each batch of product containing HOSTACOR V4205 produced, approximately 200 L of water will be used to rinse mixing vessels. Estimates of environmental release (0.57 kg per batch) are based on a similar chemical (HOSTACOR V4205, notification number NA/185) as reformulation of HOSTACOR V4221 will not be carried out by Hoechst. *A total waste disposal in this manner from all the formulators sites will therefore result in less than 55 kg per year passing into effluent pits (assuming all formulators follow similar practices).*

The HOECHST triple interception pit system is cleaned annually by an EPA licensed waste company. Liquid waste is disposed of to sewers with the semi-liquid sludge being disposed of to a registered landfill.

Other accidental spills during formulation procedures are to be adsorbed onto liquid binding substances, which are subsequently sent for incineration.

• Use

During normal use the blended coolant/lubricant is placed in a large volume recirculating bath. Baths vary in size from 200 L to 110 000 L. Most of the newer baths are enclosed to prevent splashing, but some of the older baths in use may not be covered, and therefore splashing may occur. All lubricant baths are bunded, and waste fluid collected from bunds will undergo treatment in effluent ponds prior to release, as will all other waste metalworking fluids.

HOECHST are unable to provide exact details of the amount of sludge that will be removed from lubricant baths, as the amount will vary with bath size, type and frequency of metal working and so on. Only small amounts of HOSTACOR V4221 are expected in the sludge from each site due to the low concentration of the notified substance in the final lubricant baths. *Estimates of wastes are approximately 1 kg per year per user, a total of 150 kg for all the anticipated customers*. Sludge will be disposed of by licensed waste contactors to landfill sites.

The amount of liquid waste to be removed also varies, as above. Liquids removed from lubricant baths, which will contain an estimated 0.1% of the notified substance, will be treated with an inorganic acid. The notified substance has a low hydrophilic/lipophilic balance, and therefore, it is claimed by the notifier will be preferentially soluble in the oil fraction. The notifier additionally claims that over time none of the notified substance will remain in the water phase. This acid treatment procedure results in the formation of non-ionic acid derivatives which are water insoluble. These exist in the oil phase. This waste is disposed of by registered liquid waste contractors. The water fraction will be disposed of via the sewage system, after passing through effluent ponds.

A large-scale anticipated user (based on information received for a similar substance, HOSTACOR V 4205) of the notified substance, will empty lubricant baths into an effluent lagoon of 500,000 L approximately every two years. 30 000 L of effluent per week are removed to be treated in a separate tank with acid prior to release of the water phase to sewers.

. Fate

The notified substance is claimed to be relatively insoluble and hydrolytically stable. These features, combined with surface activity mean that in the case of accidental spillage, or when the product is disposed of to landfill, there is little possibility of the substance leaching into waterways. In addition, the routine procedures to be conducted by end-users, resulting in the pre-treatment prior to release of the substance, are reported to further reduce the solubility of the substance prior to release.

. Biodegradation

Biodegradation studies have been conducted using a structurally similar compound to the notified substance, HOSTACOR V 3981 (also called HOE S 3981). HOSTACOR V 3981 is a pentapropenyl derivative.

Biodegradability was assessed using a respirometer test. A test report was not supplied to detail either this test method or its results. The biodegradability of the related substance HOSTACOR V 3981 was found to be less that 20% (no time of test supplied). Therefore, it was concluded that substance was not readily biodegradable, and that by analogy, HOSTACOR V 4221 would also not readily biodegrade.

. Bioaccumulation

The low solubility of the notified substance and its low potential for biodegradation are indicative of a bioaccumulative substance. However, the surface active nature of the substance, and the expected low quantities to be released should minimise the potential for bioaccumulation of this substance. In addition, the expected adsorption to sediment will limit the bioavailability of the substance.

9. EVALUATION OF TOXICOLOGICAL DATA

In the absence of toxicology data for the notified chemical, studies carried out with structurally similar chemicals were provided by the notifier under variation for schedule requirements and are reported here.

. Hoe S3981 (pentapropenyl derivative of Hostacor V4221) for Acute Oral Toxicity, Skin Irritation and Eye Irritation; and

. Hostacor V4205 (salt of alkenyl succinic acid derivative) for Acute Dermal Toxicity, Skin Sensitisation, 28-Day Repeated Dose Toxicity, *Salmonella typhimurium* and *Escherichia coli* Reverse Mutation Assay.

9.1 Acute Toxicity

Table 1 Summary of the acute toxicity of Hoe S3981 and Hostacor V4205

Test	Species	Outcome	Reference
Oral toxicity	rats	LD_{50} >2000 mg/kg	(2)
Dermal toxicity	rats	LD_{50} >2000 mg/kg	(4)
Skin irritation	rabbit	slight-irritant	(6)
Eye irritation	rabbit	moderate irritant	(7)
Skin sensitisation	guinea pig	non-sensitiser	(9)

9.1.1 Oral Toxicity (2)

This study was carried out according to OECD Guidelines for Testing of Chemicals No.: 401 (3).

A single dose of 2000 mg/kg of Hoe S 3981 in deionised water was administered by gavage to Wistar rats (5/sex). The animals were observed at 1 and 4 hours after dosing and subsequently once daily for 14 days. No deaths were noted during the study. All animals showed the expected gain in body weight over the study period. No abnormalities were noted at necropsy.

The results of this study indicate an oral LD_{50} of >2000 mg/kg for Hoe S3981 in male and female rats.

9.1.2 Dermal Toxicity (4)

This study was carried out in accordance with OECD Guidelines for Testing of Chemicals No: 402 (5).

A single dose of 2000 mg/kg of Hostacor V4205 was administered by semi-occlusive application to the shaved skin of Wistar rats (5/sex) for 24 hours. The animals were observed for 14 days after removal of the bandage. No deaths were noted during the study. All animals showed the expected gain in body weight during the study. There was no evidence of systemic toxicity but skin irritation was noted. No abnormalities were noted at necropsy.

The results of this study indicate a dermal LD_{50} of >2000 mg/kg for Hostacor V4205 in male and female rats.

9.1.3 Skin Irritation (6)

This study was carried out in accordance with OECD Guidelines for Testing of Chemicals No.: 404 (7).

A single dose of 0.5 g Hoe S3981 moistened with water was administered by occlusive application to the clipped flank of three male New Zealand White rabbits for four hours.

The site of application was examined approximately 30 to 60 minutes and 1, 2 and 3 days after removal of the dressing. Because of the persistent erythema in all animals additional examinations were done on 7 and 14 days. Skin reactions were assessed according to Draize (8).

In all animals slight erythema was observed 30-60 minutes after exposure which persisted as well defined erythema in one animal on day 3. Erythema was found to be reversible by day 7. In all animals slight oedema was observed 30-60 minutes post exposure which was reversible on day 1.

The results of this study indicate that Hoe S 3981 is a slight skin irritant in rabbits.

9.1.5 Eye Irritation (9)

This study was carried out in accordance with OECD Guidelines for Testing of Chemicals No.: 405 (10).

Three male New Zealand White rabbits were used in the study. Initially, a single dose of 0.1 g of Hoe S 3981 was instilled into the conjunctival sac of the left eye of each rabbit. The other eye, which remained untreated, served as the control. Ocular reactions were assessed according to Draize (8) after 1 hour and 1, 2, 3, 7 and 14 days post-exposure.

In all eyes, moderate erythema and chemosis of the conjunctivae with considerable discharge was noted one hour after treatment. In two animals, moderate erythema and chemosis and discharge persisted up to day 2. In the other animal these effects persisted up to day 3.

Slight to moderate opacity was observed covering more than half the corneal area up to day 3 in one animal.

Changes to the iris were observed during first three days after treatment in one animal and on day 1 in another animal.

The results of this study indicate that Hoe S 3981 is a moderate eye irritant in rabbits.

9.1.6 Skin Sensitisation (11)

This study was carried out according to the OECD Guidelines for Testing of Chemicals No: 406 (12).

The maximisation test (13) was used to assess the skin sensitisation potential of Hostacor V4205. Reactions were assessed according to a four-point scale (14). The sensitivity of the strain of guinea pig used in this study was periodically tested with a known skin sensitiser, 2,4-dinitrochlorobenzene. Positive sensitisation responses were observed in the animals tested with 2,4-dinitrobenzene.

<u>Preliminary study</u>

To determine the concentration for intradermal injection in the study, three dose levels of Hostacor V4205 (0.2%, 1.0% and 5% w/v in isotonic saline) were administered to three Pirbright-White guinea pigs. Skin reactions were assessed at 24, 48 and 72 hours post-exposure. The dose level selected was 0.2% w/v as this dose is considered to be the minimum irritating dose.

To determine the dose level for topical induction in the main study, four dose levels of Hostacor V4205 (0.2%, 1.0%, 5.0% and 25.0%) in isotonic saline were administered to a group of six animals which had been injected with Freund's Complete Adjuvant previously. Skin reactions were assessed 1, 24 and 48 hours post-exposure. Well

defined to moderate erythema and very slight oedema were observed with 5 and 25% concentration. As there was no reaction observed with 1.0%, this concentration was selected for topical application.

To determine the dose level for topical challenge in the main study, 0.2% Hostacor V4205 in (this dose level was selected since Freund's Adjuvant can lower the threshold value for primary irritation determined in preliminary tests) isotonic saline was administered to group of five animals which had been injected with Freund's Complete Adjuvant previously. Skin reactions were assessed 1, 24 and 48 hours post-exposure. As there was no skin irritation, the dose level selected for the topical challenge was 0.2% (w/w).

Induction

Thirty female Pirbright-White guinea pigs (20 test and 10 control) were used.

A row of three injections of: 1) 50% Freund's Complete Adjuvant (FCA), 2) a 0.2% w/v suspension of the test substance in isotonic saline; and 3) a 0.2% w/v suspension of test material in a 1:1 preparation of FCA, was made on each side of the mid-line of the test animals. One week later, a single dose of 1% w/w of the test substance in isotonic saline was administered by occlusive application to the clipped scapular area of each test animal for 48 hours. Twenty-four hours after the removal of the dressing, the application sites were examined for reactions. Control animals were similarly treated but without the test substance.

Forty-eight hours after induction, erythema and oedema, indurated and encrusted skin and necrosis were observed at the sites previously treated with Freund's Adjuvant. The injection sites treated with the test substance in the vehicle showed well-defined erythema, slight oedema and indurations and encrustations. No effects were observed with the control groups.

Challenge

Two weeks after induction, both the test and control animals were challenged with a single dose of 0.2% w/v of the test substance in isotonic saline by occlusive application for 24 hours on the right flank of each animal. Only the vehicle was applied to the left flank of each animal.

No adverse skin reactions were noted at 48 hours after application. Gain in body weight was unaffected in all animals.

The results of this study indicate that Hostacor V4205 is not a skin sensitiser in guinea pigs at the concentration tested.

9.2 28-Day Repeated Dose Toxicity (14)

This study was carried out according to OECD Guidelines for Testing of Chemicals No: 407 (15).

Hostacor V4205 in deionised water was administered by gavage once daily to groups of Wistar rats (5/sex) at dose levels of 62.5, 250 or 1000 mg/kg/day over 28 days. The control group received only distilled water. The volume of test and control material administered to each animal was based on the most recent body weight and was adjusted at weekly intervals.

Food consumption and body weight gain in test animals were comparable with that seen in controls.

Clinical chemistry examinations revealed a slight increase in glutamic pyruvate transaminase activities in both sexes of the high dose group but were not considered to be toxicologically significant. No haemotology changes observed in any animal in the study.

At necropsy there were no organ weight changes attributable to treatment with the test material, treatment-related macroscopic abnormalities or histopathological changes. However, a spotted spleen was observed in one female of the high dose group.

It can be concluded that no target organ toxicity occurs in rats dosed repeatedly with the notified chemical for 28 days at doses up to 1000 mg/kg/day.

9.3 Genotoxicity

9.3.1 Salmonella typhimurium and Escherichia coli Reverse Mutation Assay (16)

This study was carried out according to OECD Guidelines for Testing of Chemicals No: 471 (17).

Hostacor V4205 at dose levels of 10000, 2500, 500, 100, 20 or 4 µg/plate were tested for gene mutation using *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538 and *Escherichia coli* strain WP2*urvA* both in the presence or absence of metabolic activation (S9-mix). The experiment was also conducted using Hostacor V4205 at dose levels of 5000, 2500, 500, 100, 20, or 4 µg/plate. Positive controls used were sodium azide with TA100 and TA1535, 9-aminoacridine with TA1537, 2- nitrofluorene and MNNG with WP*uvrA* (without S-9 mix) and 2-aminoanthracene (with S-9 mix). Deionised water was used as the diluent for the test substance and as the negative control.

In both experiments, the test substance did not induce statistically significant dose-related increases in the number of revertant colonies of *Salmonella typhimurium* or *Escherichia coli* strains either in the absence or presence of S-9 mix. The positive controls showed the expected increases in all strains tested.

The results of this study indicate that Hostacor V4205 is not mutagenic in bacteria.

9.3.2 Chromosomal Aberration Assay in Chinese Hamster V79 Cells *in vitro* (18)

This study was carried out according to OECD Guidelines for Testing of Chemicals No: 473 (19).

Hostacor V4205 was investigated for its potential to cause chromosomal aberrations in the chinese hamster V79 cell line.

Preliminary experiments were performed in order to determine the toxicity of Hostacor V4205 to the cells. Cytotoxicity was not observed in the presence or absence of rat liver S9 mix at 100 µg/ml. The culture medium and culture medium with solvent were used as negative conrtols; ethylmethanesulphonate (1500 µg/ml) without metabolic activation and cyclophosphamide (5 µg/ml) with metabolic activation dissolved in nutrient medium were the positive controls utilized.

Two experiments were performed using cultures in the absence or presence of S9 metabolic activation provided by rat liver S9. A single cell suspension of V79 was prepared from 2 day old, exponentially growing stock. Cells were subsequently treated with Hostacor V4205 and chromosomes prepared 18 hours or 28 hours after treatment. Cultures with the S9 mix were treated for 6 hours and cultures without the S9 mix were treated for the 6, 28 or 48 hour period between the start of treatment and fixation.

The results indicate the test substance does not show a reproducible enhancement of chromosomal aberrations at concentrations of 10, 50 and 100 µg/ml tested with S9 mix and 10, 25, 50 and 100 µg/ml without S9 mix.

The positive control substances both elicited a significant increase in chromosomal aberrations.

In conclusion, Hostacor V4205 was found to be non-clastogenic *in vitro* in the V79 chinese hamster cell line.

9.4 Overall Assessment of Toxicological Data

Hoe S 3981 has low acute oral toxicity in rats. It is a slight skin irritant and moderate eye irritant.

Hostacor V4205 has low acute dermal toxicity in rats. It is not a skin sensitiser in guinea pigs. A 28-day repeated dose study showed no treatment-related effects at doses of up to 1233 mg/kg/day. Hostacor V4205 was found to be non-mutagenic in the *Salmonella typhimurim* and *Escherichia coli* reverse mutation assay and non-clastogenic in the chinese hamster V79 cell assay.

On the basis of submitted data, the notified chemical would not be classified as hazardous in accordance with *Approved Criteria for Classifying Hazardous Substances* in relation to Acute lethal effects (oral, dermal) ; Severe effects after repeated or prolonged exposure (oral route); Irritant effects (skin, eye) and Sensitising effects (skin).

10. ASSESSMENT OF ENVIRONMENTAL EFFECTS

No data were supplied for the notified substance. A test was made using HOSTACOR V 3981 to assess effects of the substance on zebra fish (20). The test was conducted according to OECD Guideline 203 (Acute Toxicity test), and according to Good Laboratory Practice regulations.

The zebra fish (*Brachydanio rerio*) were exposed to a number of nominal concentrations of the test substance - 10, 18, 32, 58, 100 and 180 $mg.L^{-1}$, for 96 hours. Tests solutions were noted to be turbid, and the test substance to precipitate as droplets on the walls of the vessels, dependent on concentration.

The LC_{50} (96 hour) was determined to be 100 $mg.L^{-1}$. The lowest concentration to cause 100% mortality was found to be 180 $mg.L^{-1}$, with the highest concentration to cause no mortality 58 $mg.L^{-1}$. These results should be treated with caution as the actual concentrations to which the test organisms were exposed are unclear due to turbidity problems.

No *Daphnia* or algal tests were made available. A related substance, HOSTACOR V4205 was found to be moderately toxic to *Daphnia*, but any inferences as to the likely toxicity of Hostacor V4221 are tentative given the different chemical and environmental characteristics of the two substances.

The results for fish indicate that HOSTACOR V 3981, and by analogy, HOSTACOR V 4221 will be at worst slightly toxic to the fish species tested, up to the limits of solubility. It is possible that there may be a moderately toxic effect to *Daphnia,* but the low expected exposure of this substance to the aquatic compartment should limit such toxicity. No conclusions can be drawn for algal toxicity.

11. ASSESSMENT OF ENVIRONMENTAL HAZARD

All the expected re-formulation sites are located in either metropolitan Sydney or Melbourne. The predicted environmental concentrations (PEC's) following releases by one plant after formulation, and one plant after use, are shown in the tables below. The information for these calculations is based on information supplied within the current package, and for the previously assessed HOSTACOR V4205. In these calculations, the effects of biodegradation have not been taken into account, as the level of ready biodegradability for HOSTACOR V 3981 was found to be less than 20%.

Table 1. Predicted Environmental Concentrations following release from typical formulation processes.

Factor	Given Value	Concentration
Amount of waste anticipated per batch (includes splashes and rinsings)	0.57 kg	-
Total discharge to effluent pits per year (assuming 15 batches per year)	8.55 kg	-
Effluent pit capacity	40 000 L	231.75 ppm
Final interceptor pit capacity	60 000 L	142.5 ppm*
Dilution in sewage treatment works (Melbourne)	500 ML	17 ppb*

* Note that these figures do not take into account possible adsorption to sediments or any possible biodegradation that may occur, and assume discharge of a year's waste on one day. They therefore represent a worst case scenario.

Further dilution is expected when the sewage effluent passes into receiving waters. Thus release of the notified substance following treatment in both the effluent pits and sewage treatment plants should pose little threat to aquatic species. Similar PECs are expected should the substance be formulated in Sydney.

Much smaller releases are expected from individual end-users of the notified substance (although the total amount released by all customers is greater). The notifier estimates that approximately 1 kg per year will result from splash clean up and general cleaning of tanks at individual plants (eg. cleaning/discharge of lubricant baths and so on). The following table shows the calculated PECs based on a effluent pond capacity and sewage treatment water flows that will be found at one of the plant in which the notified substance is used.

Table 2. Predicted environmental Concentrations following release from typical users plant.

Factor	Given Value	Concentration
Amount of waste anticipated from baths and cleaning per year	1 kg	-
Dilution of 30 000 L in sewage treatment works	50 ML	0.02 ppm*

* This value represent an extreme worst-case scenario, as it assumes the entire 1 kg of waste will pass straight to the sewage treatment works, without first being treated in either effluent pits, or acid treatment tanks.

The two examples outlined above demonstrate that the proposed release concentrations, from both formulation and typical use are far below the toxic levels noted in the test fish species used for the related substance HOSTACOR V 3981. Even if flow through rates (in the order of 5 ML) of smaller sewage plants are considered , with a PEC of 0.2 ppm resulting, aquatic fauna are not expected to be a risk.

Use of the notified substance in the prescribed manner should ensure that there is little risk to aquatic organisms. However, in the absence of data regarding the toxicity to *Daphnia* or algae, if either the conditions and/or volumes of and areas of use change significantly, such tests may be required for a secondary notification.

12. ASSESSMENT OF PUBLIC AND OCCUPATIONAL HEALTH AND SAFETY EFFECTS

No work-related effects on human health, due to production of Hostacor V 4221, have become known and there are no health conditions for which use of the new chemical should be avoided. It has been shown in animal studies done with structurally similar chemicals that

. Hoe S 3981, exhibits low acute oral toxicity in rats, slight skin and moderate eye `irritation in rabbits and

. Hostacor V 4205, exhibits low acute dermal toxicity in rats, is not a skin sensitisation in guinea pigs and not genotoxic when tested in *Salmonella typhimurim and Escherichia coli* strains.

Therefore, possible eye contact with the notified chemical should be avoided.

Hostacor V4221 has a low vapour pressure, is not explosive and non-reactive under normal use conditions.

Workers at the reformulation plant will be exposed to the chemical during weighing, filling and emptying of the mixing tank. Since these processes are carried under exhaust ventilation the potential for exposure is low. Laboratory personnel will be exposed to small quantities of the chemical during quality control operations.

Workers in metal working operations being the largest group of workers handling the product containing the chemical will not be exposed to more than 0.14% of the notified chemical. Exposure to the notified chemical should therefore be negligible

There is low potential for public exposure to Hostacor V4221, either from blending or manufacturing operations, or from disposal of wastes containing the notified chemical.

Therefore, under normal conditions, the notified chemical is not expected to pose any significant health or safety risk to workers or to the public.

13. RECOMMENDATIONS

To minimise occupational exposure to Hostacor V4221 the following guidelines and precautions should be observed:

. the work place should be well ventilated and local exhaust ventilation should be used during filling and emptying the mixing vessel;

. good personal hygiene should be observed;

. good work practices to avoid contact with the chemical;

. if engineering controls and work practices are insufficient to reduce exposure to a safe level, the following personal protective equipment which complies with Australian Standards should be worn such as safety spectacles (AS 1336-1982 (21), AS 1337-1982 (22)) gloves (AS 2161-1978 (23) and overalls ;

. any spillages should be promptly cleaned up and disposed according to local or state regulations; and

. a copy of the Material Safety Data Sheet (MSDS) should be easily accessible to all employees.

14. MATERIAL SAFETY DATA SHEET

The Material Safety Data Sheet (MSDS) for the product Hostacor V4221 (Attachment 1) was provided in Worksafe Australia format (24). This MSDS was provided by Hoechst Australia Limited, as part of their notification statement. It is reproduced here as a matter of public record. The accuracy of this information remains the responsibility of Hoechst Australia Limited.

15. REQUIREMENTS FOR SECONDARY NOTIFICATION

Under the *Industrial Chemicals (Notification and Assessment) Act 1989* (the Act), secondary notification of Hostacor V4221 shall be required if any of the circumstances stipulated under subsection 64(2) of the Act arise. A secondary notification should be made if the substance were to be used in a manner resulting in either the conditions, increased quantities and/or areas of use change significantly. Such a notification should include both clarified physico-chemical data and toxicity tests (using the notified substance) for aquatic organisms.

16. REFERENCES

1. OECD (1989) Summary of Considerations in the Report from the OECD Expert Group in Physical Chemistry - OECD Test Guideline 105 "Water Solubility".

2. Pharma Development Central Toxicology, "Hostacor V4205: Acute Oral Toxicity to the Rat". Data on file, Report No: 93.0276, July 1993.

3. OECD Guidelines for Testing of Chemicals, "Acute Oral Toxicity" No: 401, 1981.

4. Pharma Development Central Toxicology, "Hostacor V4205": Acute Dermal Toxicity to the Rat". Data on file, Report No: 93.0277, June 1993.

5. OECD Guidelines for Testing of Chemicals, "Acute Dermal Toxicity" No: 402, 1987.

6. Pharma Development Central Toxicology, "Hostacor V4205: Skin Irritation to the Rabbit". Data on file, Report No: 93.0450, July 1993.

7. OECD Guidelines for Testing of Chemicals, "Acute Dermal Irritation/Corrosion" No: 404, 1981.

8. Draize, J.H., et. al, "The Appraisal of Chemicals in Food, Drugs and Cosmetics", Association of Food and Drug Officials of the United States, Austin, Texas, 1959.

9. Pharma Development Central Toxicology, "Hostacor V4205: Eye Irritation to the Rabbit". Data on file, Report No: 93.0451, July 1989.

10. OECD Guidelines for Testing of Chemicals, "Acute Eye Irritation/Corrosion" No: 405, 1987.

11. Pharma Development Central Toxicology, "Hostacor V4205: Skin Sensitisation to the Guinea Pig". Data on file, Report No: 93.0372, June 1993.

12. OECD Guidelines for Testing of Chemicals, "Skin Sensitisation" No: 406, 1981.

13. Magnusson B. and Kligman A.M., "Allergic Contact Dermatitis in the Guinea Pig" Thomas Publ, USA 1970.

14. Pharma Development Central Toxicology, "28-day Oral Toxicity to the Rat". Data on file, Report No: 93.0619, September 1993.

15. OECD Guidelines for Testing of Chemicals, "Repeated Dose Oral Toxicity - Rodent: 28-day or 14-day Study" No: 407, 1981.

16. Pharma Development Central Toxicology, "Hostacor V4205: An Evaluation of Mutagenic Potential Using Salmonella typhimurium & Eschericia coli". Data on file, Report No:93.0271, June 1993.

17. OECD Guidelines for Testing of Chemicals, "Genetic Toxicology: Salmonella typhimurium, Reverse Mutation Assay" No: 471, 1983.

18. Pharma Development CentralPharma Development Central, "Hostacor V4205: An Evaluation in the V79 Chinese Hamster Cells for Chromosomal Aberration". Data on file, Report No: 93.0467, August 1993.

19. OECD Guidelines for Testing of Chemicals, "Genetic Toxicology: Micronucleus Test" No: 474, 1983.

20. Fish Acute Toxicity Test (Zebra-fish) of Hoe S3981 according to OECD 203. August 5-9, 1991. Journal No. 1989. DR U NOACK-Laboratorium Für Angewandte Biologie, Hildesheim.

21. Australian Standard 1336-1982, "Recommended Practices for Eye Protection in the Industrial Environment", Standards Association of Australia Publ., Sydney, 1982.

22. Australian Standard 1337-1984, "Eye Protectors for Industrial Applications", Standards Association of Australia Publ., Sydney, 1984.

23. Australian Standard 2161-1978, "Industrial safety Gloves and Mittens (excluding Electrical and Medical Gloves)", Standards Association of Australia Publ., Sydney, 1978.

24. National Occupational Health and Safety Commission, *National Code of Practice for the Preparation of Material Safety Data Sheets* [NOHSC:2011(1994)], AGPS, Canberra, March 1994.