File No: NA/693

January 2001

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME

FULL PUBLIC REPORT

Vanquish

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

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For enquiries please contact the Administration Coordinator at:

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Director
Chemicals Notification and Assessment

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FULL PUBLIC REPORT

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1. APPLICANT

Orica Australia Pty Ltd of 1 Nicholson St Melbourne VIC 3000 (ACN 004 117 828) has submitted a standard notification statement in support of their application for an assessment certificate for Vanquish.

2. IDENTITY OF THE CHEMICAL

The chemical name, CAS number, molecular and structural formulae, molecular weight, spectral data and details of impurities and additives have been exempted from publication in the Full Public Report and the Summary Report.

Marketing Name: Vanquish

3. PHYSICAL AND CHEMICAL PROPERTIES

The following physico-chemical data were supplied with the notification. These data were generated by the manufacturer (Williams, 1996), and unless otherwise indicated, the data were generated using EU test methods. Some information for the molecule was also obtained from the ASTER data base of the US EPA (US EPA, 2000) which employs Quantitative Structure Activity Relationships (QSARs) based on the molecular structure in order to estimate physico-chemical and ecotoxicological properties of an unknown compound. This data is also presented and discussed below.

Appearance at 20°C and 101.3 kPa: brown viscous oily liquid, odourless

Boiling Point: decomposes at 300°C

Specific Gravity: 1.17 at 20°C

Vapour Pressure: 1.5×10^{-5} kPa at 20°C

Water Solubility: 330 mg/L (approximately, see comments below)

Surface Tension: reported to be 49.5 mN/m (see comments below)

Partition Co-efficient (n-octanol/water): log P_{ow} = 2.86

Hydrolysis as a Function of pH:	no hydrolysis observed over pH range 0 to 14 no significant hydrolysis (< 10 %) over 6 days at pH 4, 7 and 9
Adsorption/Desorption:	log K_{oc} = 2.7
Dissociation Constant:	no dissociable groups present
Flash Point:	178°C (closed cup)
Flammability Limits:	not determined (see comments below)
Autoignition Temperature:	425°C
Explosive Properties:	not expected to be explosive
Reactivity/Stability:	stable for 2 weeks at 54°C indicating a shelf life of 2 years; 4 % and 3 % decomposition respectively in the presence of $CuCl_2$ and $FeCl_3$ for 24 hours; stable in the presence of Al, Cu, Fe and Zn metals and Al and Zn ions

3.1. Comments on Physico-Chemical Properties

The water solubility was determined by Williams (1996) as < 0.5 mg/L using European Community test guideline A6 (column elution method) which is equivalent to OECD TG 105. However, as described below it is probable that the results of the experiment were misinterpreted and the true water solubility is more likely to be around 330 mg/L at 25°C.

In the column elution method (which is appropriate for poorly soluble materials) a known weight of the test substance is coated onto an inert substrate (glass beads) in an elution micro column, then a fixed volume of distilled water at 25°C circulated through the column at approximately 25 mL/hour. In the present experiment, 59 mg of the notified chemical were coated onto the beads, which were placed in the column, then water sufficient to cover the bed was introduced and the entire apparatus left to equilibrate overnight in a water bath at 25°C. Following equilibration it appears that water was run through the column, and periodic sampling begun. However, the report did not state that eluent water was reintroduced to the column as required by the protocol or the total water volume used in the experiment and although 15 samples were collected there was no indication of the time between each sample.

Surprisingly the highest concentration of test material (377 mg/L) was found in the first fraction, with successive fractions having substantially lower concentrations. No test material was detected in the final four fractions, and since the detection limit of the analytical apparatus was stated as 0.5 mg/L, the water solubility was inferred as being less than this value.

The conduct of this experiment and/or the interpretation of the analytical results appear to be erroneous, and it is likely that the water solubility is closer to the 377 mg/L found in the first fraction. This is supported by the fact that this fraction was apparently the first taken after the

test material had equilibrated with the water overnight.

Further support for this conclusion is found in elsewhere in the Williams report (1996), which concerned the measurement of surface tension of aqueous solutions of the notified chemical. Two separate determinations of surface tension were conducted with solutions prepared at nominally 6.29 g/L and 5.0 g/L (very large excess of solute). Following surface tension measurements, the solutions were filtered through 0.1 micron cellulose nitrate to remove undissolved material, and the filtrates analysed for test material using HPLC. It may be assumed that the filtrates would have been saturated with respect to the notified chemical, and the analytical results gave 324 and 334 mg/L for the nominal 6.29 and 5.0 g/L preparations, respectively. These analytical results are of similar magnitude to the 377 mg/L found in the first fraction of the elution experiment and support the conclusion that water solubility at 25^{o}C is around 330 mg/L.

Other reports submitted with the notification (eg. those concerned with biodegradation and photo-degradation), also considered aqueous solutions of the notified chemical, and information in these reports suggests that water solubility is in excess of 100 mg/L. In a Risk Assessment for the Aquatic Compartment (Din, 2000), it was also indicated that the water solubility of the chemical is given as 744 mg/L, and although the source of this value was not indicated it is likely that it was derived from a QSAR estimate. The ASTER QSAR data provides a water solubility of 2730 mg/L.

The class of chemicals including the notified chemical are not susceptible to hydrolysis under normal pH, so the material is expected to be stable in aqueous environments where $4 < pH < 9$.

The n-octanol/water partition coefficient (P_{ow}) was determined by Williams (1996) using the "shake flask" method (EEC test method A8). A stock solution (519 mg/L) of the notified chemical was prepared in n-octanol previously saturated with water. Various volumes of this stock solution (or dilutions of this solution) were then stirred with different volumes of water for 2 hours at 25^{o}C, the phases allowed to separate and equilibrate at 25^{o}C overnight, then the concentration of notified chemical in each phase determined using UV spectroscopy. The P_{ow} for all test systems (six in all) was between 656 and 808. The mean value for Log P_{ow} was 2.86, indicating some preference of the chemical for the oil or fat phase over water.

The notified chemical was found to be miscible in all proportions with chloroform, acetone, ethanol, n-octanol, dimethyl sulphoxide and toluene; it was soluble to 0.41 % in n-hexane.

The soil adsorption/desorption constant (K_{oc}) was determined by Roberts and Stanley (1995) using the draft OECD test guideline HPLC method, where the retention time of the chemical on a C18 column is compared with those of a series of reference compounds having known K_{oc}. The value of Log K_{oc} was determined as 2.7 indicating the material has modest affinity for the organic components of soils and sediments and is likely to be mobile in these media. This conclusion is in accord with the low value of Log P_{ow} and appreciable apparent water solubility of around 330 mg/L.

Surface tension data by Williams (1996) for saturated solutions was also provided. The material was found to be surface active. The surface tension of the solutions was measured as between 49 and 55 mN/m, significantly lower than that of water (72.2 mN/m). The surface active nature of the chemical probably results from the combination of the hydrophobic alkyl

group with the dipolar ring system, since these structural features are known to give rise to surface activity (Tanford, 1991).

Flammability limits were not reported. The vapour pressure at room temperature appears to be too low for the lower explosive limit to be reached.

ASTER DATA (QSAR Generated) (US EPA, 2000)

Property	*Value*
Boiling Point:	317°C
Vapour Pressure:	5.58×10^{-5} mm Hg.
Water Solubility:	2,730 mg/L
Partition Coefficient:	Log P_{ow} = 2.17
Adsorption/Desorption:	Log K_{oc} = 2.52
Henry's Law Constant:	H = 5.58×10^{-9} atm.m^3/mole
Hydrolysis:	$T_{1/2}$ = 190 days

Comparisons of estimated data with experimental data are in acceptable agreement, except for water solubility, where the reported value is < 0.5 mg/L. The QSAR result is closer to 330 mg/L, which appears to be more correct based on other test reports.

4. PURITY OF THE CHEMICAL

Degree of Purity: > 90 %

Toxic or Hazardous Impurities:

Chemical name:	toluene
CAS No.:	108-88-3
Weight percentage:	up to 0.03 %
Toxic properties:	On the *List of Designated Hazardous Substances* (NOHSC, 1999b) R20 Harmful by inhalation NOHSC exposure standard 100 ppm TWA, 150 ppm STEL (NOHSC, 1995)

A variety of impurities related to the notified chemical have been identified at concentrations of less than 1 %, and one major impurity was found at up to 5.8 %. The toxic properties of these impurities are unknown. The toxic or hazardous impurities are present as a result of the manufacture process and are likely to have been present in typical concentrations in the samples used for toxicity testing.

The identity of the impurities has been claimed as confidential information by the notifier on the basis of their structural similarities to the notified chemical.

Non-hazardous Impurities (> 1% by weight): none

Additives/Adjuvants: none

5. USE, VOLUME AND FORMULATION

The notified chemical will be used as a broad spectrum fungicide and bactericide for prevention of microbial spoilage of plastic articles. It will potentially be used in a wide variety of polymers including PVC and polyurethanes. Some applications for the polymers incorporating the notified chemical include footwear, pond liners, tarpaulins, awnings and matresses.

The notified chemical will be incorporated in the final plastic articles at a level of 500 – 5000 ppm. The addition of the notified chemical could occur at a variety of stages in the production process, and in a variety of forms. The notifier indicates that it could be added during production of the polymer pellets, or added as part of a plasticiser mixture or as an additive premix. The wide variety of possible applications and the range of polymers in which it may be used would result in a range of formulation approaches being used.

The notified chemical will also be used as a preservative in metalworking fluids at a concentration of around 0.2 % in metal working fluid concentrates and 100 ppm in the final emulsion.

The notified chemical will not be manufactured in Australia. It will be imported in > 90 % purity in 25 kg plastic liquor drums or 200 kg plastic lined metal drums. The notifier estimates that the import volume will be approximately 10 tonnes notified chemical per annum, comprised of 5 tonnes for use in plastic articles, and 5 tonnes for use in metalworking fluids.

6. OCCUPATIONAL EXPOSURE

As the notified chemical is likely to be used in a variety of formulations and in the manufacture of a wide variety of articles, specific occupational exposure details could not be provided. Indications of the types of processes in which the notified chemical is used have been provided by the notifier. The notifier has estimated numbers of workers in each of a number of categories who may be exposed to the notified chemical throughout Australia.

Transport and Storage
The notified chemical will normally be imported by sea, in shipments of between 5 kg and 830 kg, in Dangerous Goods approved packaging. Up to 12 shipments per year are expected. The containers including the notified chemical will be transported to warehouses, where the chemical is stored for road dispatch to the customer site. It is estimated that 1 waterside worker (1 hour per day maximum, for 4 days per year) and 4 warehouse and transport workers (1 hour per day, 10 days per year) will be involved in handling the notified chemical.

Exposure is only expected in the case of an accident causing rupture of the packaging.

Plastics Industry
The manufacture of plastic articles generally occurs in two stages, primary manufacture and secondary manufacture. The primary manufacture involves the synthesis of the polymer itself and the production of suitable forms such as pellets for the use of the secondary manufacturers. The secondary manufacture involves the production of the final articles from the pre-prepared polymer forms.

Addition of the notified chemical to the polymer mixture can occur at either manufacture stage. Once the chemical has been added to the polymer, it will be bound within the polymeric matrix and no longer available for separate exposure.

Primary Manufacture
This normally occurs in large automated facilities, and the additives may be introduced in a manual, semi-automated or automated fashion. The notifier has estimated that 5 workers will be involved in weighing and transferring the additive (for 8 hour per day, 20 days per year), 2 workers will be involved in quality control testing (for 2 hours per day, 20 days per year) and 5 workers will be involved in equipment maintenance (for 4 hours per day, 20 days per year).

In the case of automated addition, exposure would normally only be expected during the connection and disconnection of containers of the notified chemical, and the most probable exposure route would be dermal. Manual or semi-automated addition would generally involve weighing the additive followed by transfer to the reactor. The notified chemical could then be added directly to the reactor, or mixed with other additives prior to addition. The weighing and transfer operations would involve possible dermal or ocular exposure to the notified chemical. The notifier states that workers involved in these activities should wear overalls, rubber boots, elbow length impervious gloves and a face shield. Inhalation is not likely to be a major exposure route because of the low vapour pressure of the notified chemical.

Quality control and maintenance workers will be potentially exposed to the notified chemical on an irregular basis. The most likely exposure routes are likely to be dermal and ocular.

Secondary Manufacture (with notified chemical addition)
This is generally conducted as a batch process, using smaller quantities of polymer and notified chemical than in primary manufacture. There are a larger number of sites in Australia where secondary manufacture occurs compared with primary manufacture, and a larger number of workers are potentially exposed. The batch manufacture is stated to be automated to varying degrees; it is probable that the degree of automation is less than that for primary manufacture in large facilities.

The routes of exposure and type of workers who are potentially exposed will be the same as for primary manufacture, but larger numbers of workers would be involved. The notifier estimates that 50 workers will be involved in weighing and transferring the additive (for 8 hour per day, 46 days per year), 10 workers will be involved in quality control testing (for 2 hours per day, 46 days per year) and 20 workers will be involved in equipment maintenance (for 2 hours per day, 20 days per year). The notifier states that workers involved in these activities should wear overalls, rubber boots, elbow length impervious gloves and a face shield.

Secondary Manufacture (without notified chemical addition)
Secondary manufacture of plastic articles using previously prepared polymer which already contains the notified chemical will occur at numerous sites, and is estimated to involve between 100 and 500 workers. Exposure to the notified chemical is not expected as by this stage it is bound within the polymer matrix and is not separately available for exposure.

Reformulation of Metalworking Concentrates
The notified chemical will be handled during reformulation to produce metalworking fluid concentrates. The notifier indicates that the reformulation may occur in a closed system or in an open addition system.

In a closed system, the notified chemical is added through a dedicated discharge line, which is attached to the shipping container using a connection which allows no aerosol or liquid to escape. Exposure to very small quantities of the notified chemical may still occur as there may be a film of the notified chemical on the exposed sections of the connection. No exposure is expected in the remainder of the enclosed blending operation until the metalworking fluid concentrated is packed.

In an open addition system, the notifier specifies that the system should be designed to minimise spills and dermal or inhalation exposure, and that dispensing should occur under low pressure to prevent splashing. Dermal exposure to drips and spills can occur during manual addition, and the notifier has specified that coveralls, aprons, gloves, arm covers and boots should be worn.

End Use of Metalworking Concentrates
The notifier has provided estimates of exposure during handling of metalworking fluid concentrates containing the notified chemical. The following assumptions have been used.

(a) addition of concentrate to bath

Concentration of notified chemical:	2000 ppm
Exposed area of hands (palms only):	500 cm^2
Handling of concentrate:	twice per shift
Contaminant retention:	2.1 mg/cm^2/event (US EPA Exposure Assessment Division, 1992)

In addition, no skin protection or hand washing has been assumed. This gives an exposure of 8 μg notified chemical per square centimetre of skin, or a total of 4 mg notified chemical over the entire hand per day. The notifier indicates that protective gloves should however be used during handling of the concentrates.

(b) aerosol spread

Impaction ratio:	50 %
Aerosol concentration:	1 mg/m^3
Exposure time:	8 hr
Concentration of notified chemical:	100 ppm
Mean workplace air velocity:	3000 m/hr

In addition, it is assumed that all impacted material remains on the skin for the duration of the

shift. This gives an exposure of 0.12 μg notified chemical per square centimetre of skin. Assuming exposure of the head, neck and hands, with a total area of 2500 cm^2 (US EPA, 1996), this gives a total aerosol exposure of 0.3 mg notified chemical per day.

(c) handling of articles contaminated with metalworking fluid

The assumptions below are based on an exposure assessment for liquid handling without immersion of the hands in the liquid (US EPA Exposure Assessment Division, 1992).

Concentration of notified chemical:	100 ppm
Exposed area of hands (palms only):	500 cm^2
Handling of articles:	30 per shift
Specific gravity of fluid:	1
Contaminant retention:	2.1 mg/cm^2/event (US EPA Exposure Assessment Division, 1992)

In addition, no skin protection or hand washing has been assumed. This gives an exposure of 50 μg notified chemical per square centimetre of skin, or a total of 25 mg notified chemical over the entire hand per day.

(d) inhalation of aerosols

The assumptions below are based on measured data for the mean total particulate concentrations for metalworking fluids in 38 plant based Health Hazard Evaluation surveys within the USA (NIOSH, 1998) and from monitoring metalworking fluid particulates at 28 sites within the UK (UK Health and Safety Executive, 1998).

Aerosol concentration:	1 mg/m^3
Concentration of notified chemical:	100 ppm
Exposure time:	8 hr
Volume of air inhaled:	10 m^3
Absorption from lungs:	100 %
Body weight:	70 kg

This gives an inhalation exposure of 0.009 g/kg/day notified chemical. For short term peak exposure, with a concentration of aerosol of 3 mg/m^3 for 1 hr, the exposure during this time will be 0.005 g/kg.

Transport and Storage
The notified chemical will normally be imported by sea, in shipments of between 5 kg and 830 kg, in Dangerous Goods approved packaging. Up to 12 shipments per year are expected. The containers including the notified chemical will be transported to warehouses, where the chemical is stored for road dispatch to the customer site. It is estimated that 1 waterside worker (1 hour per day maximum, for 4 days per year) and 4 warehouse and transport workers (1 hour per day, 10 days per year) will be involved in handling the notified chemical. Exposure is only expected in the case of an accident causing rupture of the packaging.

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Handling of concentrate:	twice per shift
Contaminant retention:	2.1 mg/cm^2/event (US EPA Exposure Assessment Division, 1992)

In addition, no skin protection or hand washing has been assumed. This gives an exposure of 8 μg notified chemical per square centimetre of skin, or a total of 4 mg notified chemical over the entire hand per day. The notifier indicates that protective gloves should however be used during handling of the concentrates.

(b) aerosol spread

Impaction ratio:	50 %
Aerosol concentration:	1 mg/m^3
Exposure time:	8 hr
Concentration of notified chemical:	100 ppm
Mean workplace air velocity:	3000 m/hr

In addition, it is assumed that all impacted material remains on the skin for the duration of the shift. This gives an exposure of 0.12 μg notified chemical per square centimetre of skin. Assuming exposure of the head, neck and hands, with a total area of 2500 cm^2 (US EPA, 1996), this gives a total aerosol exposure of 0.3 mg notified chemical per day.

(c) handling of articles contaminated with metalworking fluid

The assumptions below are based on an exposure assessment for liquid handling without immersion of the hands in the liquid (US EPA Exposure Assessment Division, 1992).

Concentration of notified chemical:	100 ppm
Exposed area of hands (palms only):	500 cm^2
Handling of articles:	30 per shift
Specific gravity of fluid:	1
Contaminant retention:	2.1 mg/cm^2/event (US EPA Exposure Assessment Division, 1992)

In addition, no skin protection or hand washing has been assumed. This gives an exposure of 50 μg notified chemical per square centimetre of skin, or a total of 25 mg notified chemical over the entire hand per day.

(d) inhalation of aerosols

The assumptions below are based on measured data for the mean total particulate concentrations for metalworking fluids in 38 plant based Health Hazard Evaluation surveys within the USA (NIOSH, 1998) and from monitoring metalworking fluid particulates at 28 sites within the UK (UK Health and Safety Executive, 1998).

Aerosol concentration:	1 mg/m^3
Concentration of notified chemical:	100 ppm
Exposure time:	8 hr

Volume of air inhaled:	10 m^3
Absorption from lungs:	100 %
Body weight:	70 kg

This gives an inhalation exposure of 0.009 g/kg/day notified chemical. For short term peak exposure, with a concentration of aerosol of 3 mg/m^3 for 1 hr, the exposure during this time will be 0.005 g/kg.

7. PUBLIC EXPOSURE

The potential for public exposure during transport and manufacturing operations, use in metal working fluids and disposal is assessed as negligible. Consumer products such as footwear, pond liners, tarpaulins, awnings and mattresses will be manufactured from polymers containing the notified polymer.

Leaching studies have shown that the leaching of the notified chemical from polyurethane foam (at 0.3 % notified chemical) occurs rapidly, with 19 %, 13 % and 14 % leaching into water, synthetic perspiration and synthetic urine, the majority within 2, 21 and 48 hours, respectively. Normally moisture would not penetrate beyond the top layers of bedding. However, in the event of a foam mattress being unusually wet over a period of several hours, there is the potential for leaching of the notified chemical into the liquid, with subsequent deposition into the mattress and release into the air or upper layers of bedding when the mattress is compressed.

Since the notified polymer is present at low levels (≤ 0.2 %) in plastics, and is bound in the polymeric matrix, it is expected that public exposure to the notified chemical from polymer degradation or leaching from the polymer matrix during normal use is likely to be very low.

8. ENVIRONMENTAL EXPOSURE

8.1. Release

Polymer/Plastic Manufacture
During manufacture of polymers or plastic products containing Vanquish some release is possible as a result of spills and accidents. This is estimated to be a maximum of 1 % (50 kg per annum), all of which is likely to be released. During processing occurring in bunded areas (as would be expected in the case of incorporation into the polymer during primary polymer production), waste would most likely be discharged to the sewer via industrial trade waste. However, losses by spillage incurred in non-bunded areas (eg. during blending and extrusion of plastic articles) would be adsorbed by sawdust, vermiculite or other inert materials and placed into landfill or incinerated.

Plastic Product Usage
The notified chemical will be incorporated into plastic articles likely to be used in moist situations where inherent fungicidal/biocidal action is desirable, such as shower curtains, shoes and boots. For the chemical to be effective in its fungicidal role, it must be available near the surface of the articles, and so given that the water solubility is moderate (around 330 mg/L), some loss during use is inevitable, and would be made up through diffusion of more

chemical from the interior of the article.

The notifier provided some information on the rate of leaching of the chemical from two PVC formulations containing di-octyl phthalate plasticiser (DOP) and/or additional inorganic filler (Blake, 2000b). The experiments were conducted under static conditions using PVC plastics containing 0.2 % Vanquish, with one sample containing a high (32 %) content of the plasticiser and the other containing 13 % plasticiser and 20 % calcium magnesium carbonate. HPLC analysis of the aqueous solutions found that the sample containing 32 % plasticiser reached equilibrium between the plastic and aqueous solution within 100 hours at 22^{o}C, while the material containing filler and lower plasticiser content did not reach equilibrium after 140 hours, although it was clear that leaching was progressing. No aqueous phase volumes were mentioned in the summary report, so actual solution concentrations cannot be estimated. However in the case of the high plasticiser content sample it was reported that around 17 % of the Vanquish had leached into the water after 100 hours.

A second report (Zegrour, 2000) conducted using similar methodology on samples of polyurethane formulations containing 0.1-0.5 % Vanquish typical of those used for soles of boots also established that significant leaching occurs for this polymer matrix. Between 4 and 10 % of the contained Vanquish entered the water phase after approximately 50 hours. Again no water volumes were presented, so solution concentrations could not be determined.

Two other leaching reports were also submitted. The first report (Sudworth, 2000) investigated the leaching of Vanquish (present at 0.3 %) from polyurethane foam under static conditions in water, synthetic perspiration and synthetic urine. It found that after 23 hours equilibrium had been reached in all three systems with 19, 13.4 and 10.5 % of the contained chemical having been leached to the aqueous phase for the water, synthetic perspiration and urine, respectively. The second report (Blake, 2000a) also investigated the leaching of the chemical (again present at 0.3 %) from polyurethane by water, synthetic perspiration and synthetic urine, but this test was performed under dynamic conditions. The results of this test confirmed rapid and significant leaching, with 59, 51.4 and 45.9 % of the Vanquish originally present in the samples having leached into the water, synthetic perspiration and urine, respectively after 48 hours.

The results of these leaching tests indicate that the notified chemical is mobile in the plastic and polymer matrices. In wet environments (eg bathrooms, pool liners, caravan tarpaulins) a high proportion of the contained chemical is expected to be released to the environment by leaching. It is probable that prolonged exposure to water would remove most of the chemical from plastic articles into which it has been incorporated.

Disposal of Plastic Products

Most products containing the notified chemical, such as tarpaulins, mattresses and shoes, would most likely be placed into landfill at the end of their useful lives. Over time the polymer matrix would break down through either biological or abiotic processes, releasing the entrapped chemical. It is to be noted that the notified chemical is a biocide and while this may slow biological attack on the polymer matrix, ultimately all the notified chemical (around 5 tonne per annum) is expected to be released from the plastic articles. Since plastic products incorporating the notified chemical will be used throughout Australia, this release will be very diffuse. However, once released from the articles in a land fill the notified chemical is not expected to adsorb strongly to clay minerals or organic matter although it may become assimilated into biomass (see further below). Consequently it is possible that

landfill leachate could have elevated localised concentrations of the chemical.

Use in and Disposal of Metalworking Fluids
Metal cutting fluids are widely used in manufacturing industry for cooling and lubricating machine tools (eg. drill bits, mechanical hacksaws), and are normally used in semi-enclosed circulatory systems. While small quantities of the fluids are lost during use from splashes and leaks, large scale release during use is unlikely. Usually the cutting fluids are replaced periodically (typically every 12 months), and the notifier indicated that spent cutting oil is removed by waste contractors for disposal, and subjected to oil/water separation procedures prior to the aqueous component being released to metropolitan sewage systems and the oily sludge being sent for incineration. Given the partition coefficient Log K_{ow} of 2.86, most of the notified chemical would remain associated with the oil component, and be incinerated. Alternatively, the fluid may be treated in a biological (activated sludge) plant prior to discharge of the treated effluent to sewer. If the used oil is treated biologically, much of the chemical is expected to become associated with the biomass and degrade through biological processes.

However, while the notifier indicated that the disposal practices described above are universal, in reality these are likely to be routine only at the larger industrial facilities using cutting fluids, and possibly only 50 % of the material used (annually up to 2.5 tonnes) would be disposed of in this manner. The remainder (originating from smaller factories) may be released directly to sewer, storm water drains or be placed into landfill.

8.2. Fate

Release of the chemical will be primarily be to the aquatic compartment, so the fate of the chemical in this compartment is of primary importance.

Biodegradation
The notifier provided two reports concerned with assessment of biodegradation of the notified chemical, and although both studies were conducted in the same laboratory the conclusions were not consistent. The first report (Gilbert & Roberts, 1995c) described a manometric respirometry test (OECD TG 301 F) with sewage sludge, and found 0 % biodegradation after 28 days incubation of the chemical. The reference material (sodium acetate) was 61 % degraded within 5 days and 73 % degraded after 28 days.

The lack of biodegradation was confirmed by HPLC analysis for the notified chemical conducted at the conclusion of the test. The concentrations of the test solution, the poisoned control ($HgCl_2$) and abiotic control were 80, 90 and 87 % of the respective nominal starting concentrations. HPLC data did not indicate the presence of metabolites.

The second, more recent study (Dunseath et al., 1999) was conducted using procedures based on OECD TG 301 B (Modified Sturm CO_2 evolution test), although the primary aim of the study appeared to be for assessment of potential adsorption to sludge rather than biodegradation. The test differed from the standard procedure in that it was conducted using two markedly different concentrations of activated sludge (30 mg/L and 2500 mg/L) and employed ^{14}C labelled test chemical. From the information contained in the report, all carbon atoms of the test material were ^{14}C, so the distribution of the radioactivity between the aqueous phase and the biomass (sludge) could be quantified. The tests were conducted using

sufficient of the radio-labelled test chemical to give (nominally) 150 mg/L of carbon in the test media. The test volumes were 130 mL, and the results indicated that equilibrium of the chemical or its metabolites between the sludge and aqueous phase was rapidly achieved within 30 minutes for the high sludge concentration, with 32-40 % of the radioactivity becoming associated with the sludge, and 55-64 % remaining in the aqueous phase. The partitioning was neither as rapid or as marked for the 30 mg/L sludge system, with only 11-12 % of the radioactivity adsorbed to sludge after 72 hours.

In addition to the partitioning experiments, Thin Layer Chromatography (TLC) of the aqueous phases was undertaken periodically throughout the 72 hour experiment to estimate the decrease in concentration of the test material in the water and identify possible metabolites. The results showed that biodegradation in the aqueous phase was very rapid in the 2500 mg/L sludge preparation, with almost all the notified chemical disappearing after 30 minutes accompanied by concomitant formation of a number of metabolites. Over time these metabolites underwent further chemical changes, and overall five different degradation products were detected but not chemically identified. A similar pattern, with the same metabolites, was observed in the 30 mg/L sludge preparation, although overall degradation was slower requiring closer to 24 hours for primary degradation of the Vanquish.

In contrast to the earlier biodegradation study, this work indicated that biodegradation does take place under aerobic conditions, and in addition indicates that appreciable quantities of the chemical may become incorporated into biomass, particularly at high biomass concentrations. It is possible that while the notified chemical is rapidly metabolised by bacteria, ultimate degradation of the metabolites to CO_2 is a slow process, and this may partly explain the negative result obtained in the CO_2 evolution study.

Abiotic Degradation Processes
The class of chemicals including the notified chemical are not susceptible to hydrolysis under normal environmental pH conditions, and so if released to the aquatic compartment the notified chemical is unlikely to degrade by hydrolysis.

However, the notified chemical is susceptible to photolytic degradation (Gilbert, 1996). Solutions of the notified chemical in distilled water (20 mg/L) were exposed to artificial sunlight from a Heraeus Suntest Xenon Lamp. Each hour of exposure was stated to be equivalent to 1 hour exposure to Florida sun, or 1.4 hours exposure to European sunlight. The solutions were then periodically analysed for the test chemical using HPLC, and the course of the photo-degradation could be well fitted to a first order kinetic model with characteristic half life ($t_{1/2}$) of 8.25 hours. In contrast to the solutions exposed to light, control solutions kept in the dark showed no appreciable decrease in concentration, indicating that the observed degradation in the samples exposed to light was unlikely to be due to biological or other processes. The HPLC peak corresponding to the Vanquish decreased with time, with concomitant appearance of at least six other peaks corresponding to degradation products which were not identified.

If the notified chemical is incinerated, eg. as a result of incineration of the organic component of cutting oils, it would be destroyed with production of water vapour and oxides of carbon, nitrogen and sulphur.

The values for water solubility and n-octanol/water partition coefficient indicate little potential for bioaccumulation (Connell, 1990).

9. EVALUATION OF TOXICOLOGICAL DATA

9.1 Acute Toxicity

Summary of the acute toxicity of Vanquish

Test	*Species*	*Outcome*	*Reference*
acute oral toxicity	rat	LD_{50} = 4267 - 4732 mg/kg	(Lees, 1996b)
acute dermal toxicity	rat	LD_{50} > 2000 mg/kg	(Lees, 1996a)
skin irritation	rabbit	corrosive	(Lees, 1996c)
eye irritation		not performed	
skin sensitisation	guinea pig	sensitiser	(Lees, 1996d)

9.1.1 Oral Toxicity (Lees, 1996b)

Species/strain: rat/Alpk:AP_fSD

Number/sex of animals: 5/sex/group

Observation period: 14 days

Dose range: 2000, 5000, 7500 mg/kg

Method of administration: gavage

Test method: OECD TG 401

Mortality:

Dose	Males	Females
2000 mg/kg	0/5	1/5
5000 mg/kg	3/5	1/5
7500 mg/kg	5/5	5/5

all deaths occurred between day 1 and day 4

Clinical observations: piloerection and upward curvature of the spine was seen for the low dose group; in the surviving animals of the mid dose group, decreased activity, salivation and urinary incontinence were also observed; signs of extreme systemic toxicity were seen in all high dose animals prior to death

all animals showed a decrease in bodyweight after dosing; the surviving animals exceeded their initial bodyweight by the termination of the study

Morphological findings: in the animals which died during the study, severe inflammation of the stomach, adhesions, excess watery fluid in the chest and abdomen and discolouration of intestinal

	contents were observed other observations were stated to be often seen in dead and moribund animals, including staining of the nose, discolouration of the liver and lung and empty rectum in the animals which survived to study termination, stomach lesions and adhesions were observed
Comment:	the morphological findings were considered to be suggestive of an irritant effect to the stomach
LD_{50}:	4267 mg/kg for males, 4732 mg/kg for females
Result:	the notified chemical was of very low acute oral toxicity in rats

9.1.2 Dermal Toxicity (Lees, 1996a)

Species/strain:	rat/Alpk:AP_fSD
Number/sex of animals:	5/sex
Observation period:	14 days
Dose:	2000 mg/kg
Method of administration:	semi-occluded patch; 24 hour exposure test material used as supplied
Test method:	limit test, OECD TG 402
Mortality:	there were no deaths during the study
Clinical observations:	no significant signs of toxicity were observed; signs of moderate irritation were observed in all animals, including erythema, oedema, desquamation, thickening, scabbing and wrinkling all animals lost weight between days 1 and 3 but for most animals the initial weight was exceeded by day 6
Morphological findings:	scabbing of the skin was observed in 5 animals two animal showed specked thymus or red areas on the thymus; this was considered to be common for the strain of rat and not treatment related
LD_{50}:	> 2000 mg/kg

Result: the notified chemical was of low dermal toxicity in rats

9.1.3 Inhalation Toxicity

No inhalation toxicity study was submitted by the notifier.

9.1.4 Skin Irritation (Lees, 1996c)

Species/strain: rabbit/New Zealand White

Number/sex of animals: 1 female

Observation period: 21 days

Method of administration: 0.5 mL of test material as supplied was applied to clipped intact skin of the dorsal flank and secured under a gauze patch for 4 hours; at the end of this time, residual material was removed with warm water and cotton wool; the animal was examined for skin lesions 1, 24, 48 and 72 hours following application of the test substance; due to persistence of reactions the observation time was extended to 21 days

Test method: OECD TG 404

Draize scores:

Time after treatment	***Animal #***								
	30-60 min	***1 day***	***2 days***	***3 days***	***4 days***	***8 days***	***14 days***	***17 days***	***21 days***
Erythema									
	2[a]	1	1	2	2	2	1	1	0
Oedema									
	4	4	4	4	4	0	0	0	0

[a] see Attachment 1 for Draize scales

Comment: due to the type and persistence of the reactions, no further animals were dosed

erythema persisted for more than 17 days, while oedema regressed completely by day 8

additional signs of irritation including desquamation, sparse hair growth, new skin with no hair growth, scabbing, thickening and wrinkling were observed; a sample of skin from the test site and a control sample from the opposite

	flank were tested on day 21; slight acanthosis and marked sub-epithelial fibrosis were observed, showing that the notified chemical caused severe and permanent damage to rabbit skin
Result:	the notified chemical was considered corrosive to rabbit skin

9.1.5 Eye Irritation

No eye irritation study was submitted by the notifier, as the notified chemical was found to be corrosive in the skin irritation study.

9.1.6 Skin Sensitisation (Lees, 1996d)

Species/strain:	guinea pig/Crl (HA) BR
Number of animals:	20 female (test group) 10 female (control)
Induction procedure:	
test group: day 1	to a clipped area of the scapular dorsal skin, each animal received 3 pairs of 0.1 mL injections as follows – • 1:1 (v/v) mixture of Freund's Complete Adjuvant and corn oil • the test material diluted to 0.1 % (w/v) in corn oil • the test material diluted to 0.1 % (w/v) with a 1:1 (v/v) mixture of Freund's Complete Adjuvant and corn oil
day 8	a filter paper patch with 0.2 - 0.3 mL of a 30 % (w/v) preparation of test material in corn oil was placed over the injection area and covered with impervious adhesive tape; this was left in place for 2 days
vehicle control group:	The induction procedure was identical to that for the test group, except that corn oil only was used in place of the corn oil solution of test substance in both induction phases
Challenge procedure:	
day 22	undiluted test material (0.05 – 0.1 mL) and 30 % (w/v) test material in corn oil were applied to patches of filter paper and the two patches were applied to the left and right flanks, respectively, of both the test and control groups and secured under rubber sheeting, for a period of 24 hours
Test method:	OECD TG 406

Challenge outcome:

Challenge concentration	Test animals			Control animals		
	24 hours*	48 hours	72 hours	24 hours*	48 hours	72 hours
100 %	0/20**	14/20	16/20	0/10	0/10	5/10
30 %	0/20	8/20	1/20	0/10	0/10	0/10

* time after patch removal
** number of animals exhibiting positive response

Comment: scattered mild to moderate and diffuse redness was observed in 18/20 animals of the test group and 5/10 of the control group for the undiluted material following the challenge application; the net percentage response was calculated to be 40 %; the responses in the control animals indicated that the undiluted test material was an irritant

scattered mild to moderate and diffuse redness was observed in 8/20 animals of the test group and 0/10 of the control group for the 30 % solution; the net percentage response was calculated to be 40 %

Result: the notified chemical was moderately sensitising to the skin of guinea pigs

9.2 Human Repeat Insult Patch Test (Smith, 1999)

Test Material: S123386 (notified chemical) 200 ppm in ethanol

Number of panelists: 103 (22 in pilot study, 81 in main study; 98 completed the study)

Observation period: induction, 20 days
challenge, 4 days

Preliminary irritation study: the notified chemical was applied in ethanol at 200 and 300 ppm under both semi-occlusive and occlusive conditions to 6 subjects for increasing periods; excessive irritation was observed under occlusive conditions

the notified chemical was applied in ethanol at concentrations of 50, 100, 200 and 300 ppm to 6 subjects under semi-occlusive conditions in a 3 patch application study; a concentration of 200 ppm was identified as being appropriate for the main study

Method of administration: semi occluded patch, 0.5 mL test material as supplied, nine 2×2 cm induction patches applied to one arm for 24 hours at 48 to 72 hour intervals over three weeks; challenge patches

	are applied to both the original and alternate arm for 24 hours 12 to 14 days after the end of induction; test material as supplied
Test method:	in house test method
Induction and Challenge Outcome:	during the induction phase approximately 50 % of subjects in the pilot study and approximately 40 % of subjects in the main study exhibited responses of grade 1; during the challenge phase 1 subject exhibited a response of grade 1; the response pattern was concluded to be indicative of primary irritation
Result:	it was concluded that the notified chemical at 200 ppm did not cause contact hypersensitivity

9.3 Repeated Dose Toxicity (Rattray, 1996)

Species/strain:	rat/Alpk:AP$_f$SD
Number/sex of animals:	5/sex/group
Method of administration:	test material was blended with rodent diet at the required concentration; the animals were fed the appropriate diet *ad libitum*
Dose/Study duration:	0, 200, 800, 2500 ppm; administered for 28 consecutive days; the 2500 ppm level was reduced to 2000 ppm on day 10 0, and 2500 ppm; administered for 35 consecutive days; the 2500 ppm level was reduced to 2000 ppm on day 10; the animals in these groups were then allowed 14 days recovery time
Test method:	OECD TG 407

Clinical observations:

No clinical changes considered to be related to the treatment were observed.

Food Consumption/Body Weight:

Initially, the groups treated with 2500 ppm failed to eat the test diet. After 4 days, the food consumption was improving and animals were gaining weight. After 9 days, the 2500 ppm groups showed a marked reduction in bodyweight compared with controls. The maximum effects observed were a 25 % reduction for males on day 5 and an 18 % reduction for females on day 4. The dose was reduced to 2000 ppm on day 10. Both bodyweight and food consumption improved markedly after this, but the bodyweights were still low at the end of treatment. For the main test group at 28 days, the males showed a 9 % reduction, and the females a 4 % reduction; for the recovery group at 29 days, the males showed a 7 % reduction, and the females a 10 % reduction; after 35 days treatment and 14 days recovery, the males showed a 4 % reduction, and the females an 8 % reduction.

There were no significant changes in bodyweight or food consumption in the groups treated with 800 or 200 ppm test material.

The actual doses determined from food consumption were:

Dose	Males	Females
200 ppm	20.1 mg/kg/day	19.5 mg/kg/day
800 ppm	79.9 mg/kg/day	79.3 mg/kg/day
2500/2000 ppm	207.1 mg/kg/day	208.8 mg/kg/day
2500/2000 ppm (recovery)	179.4 mg/kg/day	185.8 mg/kg/day

Clinical chemistry/Haematology

A slight increase in red cell distribution width was seen in males of the 800 and 2500/2000 ppm groups, but no other red cell parameters were changed and the effect was not seen in the 2500/2000 ppm recovery group. Recovery group females showed a slight increase in platelet count compared with the controls, but the value was within the range seen for the main study groups. No toxicological significance was therefore attached to either of these observations.

All the male treated groups in the main study showed a significant increase in plasma alkaline phosphatase activity compared with controls; this effect was not seen in the recovery group. A similar significant increase in plasma alanine aminotransferase activity and a smaller increase in plasma aspartate aminotransferase activity were also seen in the males of the treated groups. No clear dose-response relationship was observed. These effects were not seen in the females, or in the recovery groups. All other statistically significant changes were considered toxicologically unimportant because they were slight or they showed no dose-response relationship.

Urine volumes were higher and urine specific gravity was lower generally in the treated animals compared with the controls; the effects were only seen in one male of the recovery group.

Histopathology:

No treatment related changes were observed in organ weights, gross pathology or histopathology.

Comment:	the study author indicated that the blood chemistry changes were possibly indicative of some perturbation of liver metabolism, but considered them to be of little toxicological importance in the absence of any change in liver weight or histopathology
	the study author indicated a No Observed Adverse Effect Level (NOAEL) of 800 ppm (79.9 – 79.3 mg/kg/day) was established on the basis of food consumption and body weights; considering the perturbation of liver metabolism this does not appear appropriate
Result:	no No Observed Effect Level (NOEL) or NOAEL could be established in this study; the blood chemistry changes which were observed were found to be reversible; the Lowest Observed Effect Level (LOEL) was 19.5 mg/kg/day

9.4 Genotoxicity

9.4.1 *Salmonella typhimurium* and *Escherichia coli* Reverse Mutation Assay (Callander, 1996)

Strains:	*Salmonella typhimurium*: TA98, TA100, TA1535, TA1537 *Escherichia coli*: WP2P, WP2P *uvrA*
Concentration range:	5, 10, 20, 50, 100, 200, 500 μg/plate (without S9) 20, 50, 100, 200, 500, 1000, 2500 μg/plate (with S9)
Metabolic Activation System:	rat liver S9 fraction from animals pretreated with phenobarbital and β-napthoflavone
Test method:	OECD TG 471 and TG 472
Positive controls	*Salmonella typhimurium*: 2-aminoanthracene (2AA) 3 concentrations per strain – all strains with metabolic activation sodium azide 3 concentrations per strain – TA1535, TA100, without metabolic activation daunomycin HCl (DR) 3 concentrations – TA 98 without metabolic activation Acridine Mutagen ICR191 50 3 concentrations –TA 1537, without metabolic activation

	Escherichia coli: 2-aminoanthracene (2AA) 3 concentrations per strain – all strains with metabolic activation mitomycin C (MMC) – WP2P without metabolic activation N-ethyl-N-nitro-N-nitrosoguanidine (ENNG) – WP2P *uvrA* without metabolic activation
Comment:	the background lawn was found to be sparse or absent at 200 μg/plate and above in the absence of metabolic activation and at 1000 μg/plate and above in the presence of metabolic activation; a decrease in the number of revertant colonies was also observed at higher doses in some cases; no substantial increase in the number of revertant colonies or indication of clear dose response was observed the positive controls produced clear positive results indicating that the test system responded appropriately
Result:	the notified chemical was not considered mutagenic in the bacterial strains tested in the absence or presence of metabolic activation provided by rat liver S9 fraction

9.4.2 *In Vitro* Cytogenetic Assay in Human Lymphocytes (Wildgoose, 1996)

Cells:	human lymphocytes from two donors (one male, one female)
Doses:	2.0, 5.0, 10 μg/mL (without S9) 2.0, 7.5, 15 μg/mL (with S9)
Metabolic Activation System:	rat liver S9 fraction from animals pretreated with phenobarbital and β-napthoflavone
Treatment Regime:	test material or positive controls were added to cell cultures for 3 hour incubation with or without S9 mix; the cells were then washed and incubated in fresh complete medium for the remainder of the 68 hour incubation time; cells from one donor were also sampled at 92 hours following a culture medium change at 68 hours; colcemid was added two hours before harvest to arrest cells in metaphase
Test method:	OECD TG 473
Positive controls	mitomycin C 1.0 μg/mL (for cells treated without metabolic activation) cyclophosphamide 50 μg/mL (for cells treated with metabolic activation)
Comment:	two independent assays were performed

for donor 1, the toxicity, by mitotic inhibition, was approximately 48 % at the top dose (10 μg/mL) without S9 and approximately 55 % at the top dose (15 μg/mL) with S9; for donor 2, the toxicity, by mitotic inhibition, was approximately 48 % at the top dose (10 μg/mL) without S9 and approximately 55 % at the top dose (15 μg/mL) with S9

in both assays a statistically significant increase in the percentage of cells with structural aberrations was observed at the highest concentration both with and without metabolic activation for the 68 hour harvest; a small but statistically significant increase was observed for donor 2 at 92 hours but this observation was not considered biologically significant by the study authors

clear positive results were obtained with the positive controls in both assays indicating that the test system responded appropriately

Result: the notified chemical induced chromosomal damage in human lymphocytes *in vitro* both in the presence and absence of metabolic activation

9.4.3 Mouse Lymphoma Forward Mutation Assay (Clay, 1996)

Cells: mouse lymphoma L5178Y

Doses:

phase 1
0, 0.2, 0.4, 0.8, 1.6, 3.1 μg/mL (without S9)
0, 1.6, 3.1, 6.3, 12.5, 25 μg/mL (with S9)

phase 2
0, 0.1, 0.2, 0.4, 0.8, 1.6 μg/mL (without S9)
0, 3.1, 6.3, 12.5, 25, 50 μg/mL (with S9)

phase 3
0, 0.4, 0.5, 0.6, 0.8, 1.1, 1.5, 2.0 μg/mL (without S9)

Metabolic Activation System: rat liver S9 fraction from animals pretreated with phenobarbital and β-napthoflavone

Treatment Regime: cell culture was treated with test material in the presence or absence of metabolic activation for 4 hours; the cells were then recultured in fresh medium for 48 hours; samples were then grown in both selective and non-selective medium for 10 – 13 days to determine the mutant frequency per cell

Test method:	OECD TG 476
Positive controls	ethyl methanesulphonate 750 μg/mL (for cells treated without metabolic activation) N-nitrosodimethylamine 600 μg/mL (for cells treated with metabolic activation)
Comment:	cytotoxicity was observed with the survival percentage falling below 10 % above 1.6 μg/mL (phase 1, -S9), 25 μg/mL (phase 1, +S9), 0.4 μg/mL (phase 2, -S9), 25 μg/mL (phase 2, +S9) and 0.6 μg/mL (phase 3, -S9); concentrations where the survival was lower than 10 % were not evaluated for mutant frequency no significant increases in mutant frequencies were observed with and without metabolic activation and the chemical was considered to be non-mutagenic appropriate increases in mutant frequency were observed for the positive controls indicating that the test system responded appropriately
Result:	the notified chemical did not induce forward mutations in mouse lymphoma L5178Y cells *in vitro* with or without metabolic activation

9.4.4 Micronucleus Assay in the Bone Marrow Cells of the Mouse (Fox, 1996)

Species/strain:	mouse/CD-1
Number and sex of animals:	5/sex/group (positive and negative controls) 5 males (1250 mg/kg) 5 females (2000 mg/kg)
Doses:	0, 1250 , 2000 mg/kg
Method of administration:	gavage, single dose
Study duration:	24 hours, 48 hours
Positive controls	cyclophosphamide 65 mg/kg
Test method:	OECD TG 474
Comment:	clinical signs of toxicity were observed in both treated groups; for the 1250 mg/kg males these included ungroomed appearance and piloerection; for the 2000 mg/kg females these included subdued nature, abnormal respiratory noises, hunched posture and ungroomed appearance; 3 females were

	found to have gas distended intestines on examination of internal organs
	there was no significant difference in micronuclei formation in any of the test animals; the positive control induced a statistically significant increase indicating that the test system responded in an appropriate manner
Result:	the notified chemical did not induce a significant increase in micronucleated polychromatic erythrocytes in the bone marrow cells of the mouse

9.5 Overall Assessment of Toxicological Data

The acute oral toxicity of the notified chemical in rats is very low (LD_{50} ~ 4500 mg/kg) and the acute dermal toxicity in rats is low (LD_{50}>2000 mg/kg).

The notified chemical was considered corrosive (caused severe and permanent damage) to rabbit skin. Erythema persisted for more than 17 days, and slight acanthosis and marked sub-epithelial fibrosis were observed. On the basis of the severe damage, the notifier has included the risk phrase R34 "Causes burns" on the MSDS and label. No eye irritation study was performed because of the results of the skin irritation test.

The notified chemical gave a clear positive result in a maximisation type skin sensitisation study, and therefore should be classified as a skin sensitiser with the risk phrase R43 "May cause sensitisation by skin contact". A negative result was obtained for the notified chemical at 200 ppm (0.02 %) in a human repeat insult patch test, and therefore the notified chemical at this concentration is not classified as a sensitiser in humans.

In a 28 day repeat dose oral toxicity study in rats, the animals were administered the notified chemical in food at 200, 800 and 2500 (later reduced to 2000) ppm. The main findings were a decrease in food consumption with a corresponding decrease in body weight at the highest dose. Changes in a number of clinical biochemistry parameters were observed at all doses in the males. Considering only the effects on food consumption and body weight, the study authors indicated a NOAEL of 800 ppm (79.9 – 79.3 mg/kg/day). As blood chemistry changes possibly indicative of some perturbation of liver metabolism were observed at all doses no NOEL can be established. The Lowest Observed Effect Level (LOEL) was 19.5 mg/kg/day.

A number of genotoxicity studies were submitted as part of the notification. The notified chemical was not considered mutagenic in bacterial test systems. The notified chemical induced chromosomal aberrations in the presence and absence of metabolic activation in an *in vitro* human lymphocyte cytogenetic assay. Additional tests were performed to attempt to clarify the mutagenic potential of the notified chemical. It was not considered mutagenic in an *in vitro* mouse lymphoma forward mutation assay, nor was it clastogenic in an *in vivo* mouse bone marrow micronucleus test.

On the basis of the negative result of the *in vivo* test, and the negative results in two of the *in vitro* tests, the notified chemical would not be classed as a mutagen according to the NOHSC

Approved Criteria for Classifying Hazardous Substances (Approved Criteria) (NOHSC, 1999a).

The notified chemical is a Type 1 hazardous substance on the basis of skin sensitisation and because it also has potential to cause severe and permanent skin and eye damage.

10. ASSESSMENT OF ENVIRONMENTAL EFFECTS

The notifier supplied the following ecotoxicity data for Vanquish against a variety of freshwater aquatic organisms. The tests were performed using standard OECD test methods.

Test	***Species***	***Result***
Acute Toxicity to Freshwater Fish [OECD 203]	Rainbow trout *Oncorhynchus mykiss*	LC_{50} (96 h) = 150 µg/L NOEC (96 h) = 31 µg/L
Acute Immobilisation to Freshwater invertebrates [OECD 202]	*Daphnia magna*	EC_{50} (48 h) = 93 µg/L NOEC (48 h) = 41 µg/L
Inhibition of Freshwater Algal growth [OECD TG 201]	*Selenastrum capricornutum*	E_bC_{50} (72 h) = 0.24 mg/L E_rC_{50} (72 h) = 0.45 mg/L

* NOEC - no observable effect concentration

Fish
The tests on rainbow trout were conducted under semi static conditions over a 96 hour test period at 15±1°C with daily renewal of the test media (Gilbert & Roberts, 1995b). The nominal concentrations of the chemical were 0 (control), 17.5, 35, 70,140, 280 and 560 g/L. Measurements of the real concentration were made over the test period using HPLC and the mean measured values were always between 93 and 104 % of the nominal ones. The test solutions were clear after preparation. Ten fish were used in each test, and the pH and dissolved oxygen levels of the test media were always 7.9-7.7 and 9.2-9.8 mg/L, respectively while the water hardness was around 60 mg/L as $CaCO_3$. No mortalities or aberrant behaviour of the test animals was observed for 96 hour exposures at and below the (nominal) 70 g/L concentration, but after 48 hours exposure at the (nominal) 140 g/L test concentration some of the fish had died or showed signs of distress, and all fish had died after 48 hours exposure to the (nominal) 280 g/L solution. The data was analysed using the methods of Stephan (Mount & Stephan, 1967) to provide the 96 hour LC_{50} of 150 g/L and the associated No Observed Effect Concentration (NOEC) of (nominally) 31 g/L. These data indicate that the chemical is highly toxic to this species (Mensink et al., 1995).

Invertebrates
An acute toxicity test of notified chemical against *Daphnia magna* was conducted under static conditions over a 48 hour period using one control (no test chemical) and six test solutions made up at nominal concentrations of 0 (control), 10, 18, 32, 56, 100 and 180 g/L (Gilbert & Roberts, 1995a). The actual concentrations were measured using HPLC at the beginning and end of the 48 hour test period, and the mean measured concentrations were between 73 and 81 % of the nominal values. The test was conducted in duplicate using 5 daphnia in each test vessel. During the tests the water hardness was around 225 mg/L (as

$CaCO_3$), the temperature between 19.7 and 20.3°C, the pH 8.1±0.1 and the dissolved oxygen levels between 8.6 and 8.8 mg/L. No immobility was observed over the 48 hour test period for the nominal test concentrations of 56 g/L and below, but after 48 hours exposure at (nominal) 100 g/L two of the test animals were immobile, while after 48 hours exposure at 180 g/L all animals were dead. The data were analysed using the methods of Stephan (Mount & Stephan, 1967) to provide the 48 hour EC_{50} of 93 g/L and a No Observed Effect Concentration (NOEC) of 41 g/L. These results indicate that the notified chemical is very highly toxic to this species.

The notifier was asked to provide a report or scientific comment on the chronic toxicity (reproduction) of the chemical to daphnia. On the basis of data in the Risk Assessment submitted (Din, 2000) it was concluded that the ratio of Predicted Environmental Concentration to Predicted No Effect Concentration (PEC/PNEC) was 1.15×10^{-5} (using the measured daphnia EC_{50} of 93 g/L as the PNEC). Since this ratio is very low it was concluded that release of the notified chemical would not be of environmental concern and that provision of a chronic daphnia test was not necessary. The risk assessment undertaken was based on the EUSES model (European Union) which incorporates biodegradation and photo-degradation data, and the true applicability of this analysis in respect of Australian use patterns of the chemical will be discussed in Assessment of Environmental Hazard.

Notwithstanding the above, it is likely that the chronic MATC (maximum allowable toxic concentration) of the chemical would be significantly less than the acute 48 hour EC_{50} of 93 g/L.

Algae
Tests on algal growth inhibition using *Selenastrum capricornutum* were performed with solutions of the notified chemical made up in nutrient media at nominal concentrations of 0 (control), 0.32, 0.056, 0.10, 0.18, 0.32, 0.56, 1.0 and 1.8 mg/L, and three replicate tests were conducted at each concentration over a 72 hour test period (Smyth et al., 1995). The actual concentrations in the test media were measured using HPLC prior to starting the tests, and the mean measured concentrations were always within 6 % of the nominal ones. After preparation, all test solutions were clear and colourless. Throughout the test the mean temperature was between 23.9 and 24.0°C, and the pH of the media containing algae was always between 7.4 and 9.5. Growth of algal biomass was monitored by counting the cell density over the 72 hour test period, and significant inhibition of growth in algal biomass was observed at all test concentrations above 1.0 mg/L. The data was analysed using standard statistical procedures to give the 72 hour E_bC_{50} of 0.24 mg/L and corresponding E_rC_{50} (inhibition of rate of biomass growth) of 0.45 mg/L. These results indicate that the notified chemical is highly toxic to this species of green algae.

Summary
The notified chemical is at least highly toxic to those aquatic organisms against which it has been tested, with the 48 hour LC_{50} of the most sensitive species (daphnia) being 93 g/L. No chronic toxicity data was submitted, but the chemical is likely to have chronic toxic properties against aquatic species at low concentrations.

The toxicity estimates provided by the ASTER profile (US EPA, 2000) have substantially underestimated toxicity compared with experimental data. For example, the estimated 48 hour EC_{50} against daphnia was 55 mg/L and the estimated 96 hour LC_{50} against rainbow trout was 47 mg/L. The QSAR toxicity estimates were apparently based on estimated water

solubility and/or Log P_{ow}, and have not considered toxic mechanisms specific to this class of chemical.

11. ASSESSMENT OF ENVIRONMENTAL HAZARD

Use in Plastic Articles
The notified chemical has been shown to be appreciably mobile in the plastics and polymers, and is very susceptible to leaching. Accordingly, it is expected that much (if not all) of the chemical will be removed from articles over their lifetimes, with most entering the sewer system. Release will be widespread and diffuse.

It is not possible to accurately estimate the rate of loss, but in a worst case scenario if it is assumed that 70 % of the 5 tonne annual import used in plastic are released each year, then based on an Australian population of 19000000, each of whom contributes 150 L of sewage per day, then the global predicted environmental concentration (PEC) in sewage from this use pattern is found to be 10 g/L. The notified chemical is readily incorporated into and degraded by sewage biomass, so on exiting the sewage treatment plants the effluent is expected to contain a significantly lower concentration than 10 g/L of the chemical, which would be further diluted on release and mixing with the receiving waters.

The chemical is highly toxic to aquatic species with the 48 hour acute LC_{50} against daphnia (the most sensitive species) being 93 g/L, and it is likely that the chronic MATC of the chemical would be significantly less than this concentration. However, as discussed below, it is unlikely that the chemical would persist in receiving waters so chronic effects would probably not be realised.

Although the global PEC estimate for sewage of 10 g/L indicates a safety margin of around one order of magnitude, release to receiving waters is likely to be at significantly lower concentrations which will increase the safety margin. Also, the chemical is rapidly degraded by photolysis ($t_{1/2}$ = 8.25 hours), so once released to surface waters is not expected to persist.

The notified chemical is metabolised and degraded by sewage biota, although the metabolites themselves may only be slowly mineralised to CO_2, nitrate and sulphate (or sulphide).

It is concluded that although the notified chemical is highly toxic to aquatic organisms and a high percentage of the material is likely to be released from plastic articles in wet or moist environments, use of the notified chemical as a fungicide in plastics does not constitute a large environmental hazard because of the susceptibility to degradation through biological and abiotic (particularly photolysis) processes.

Use in Metal Cutting Fluids
An additional 5 tonnes (maximum) of the notified chemical may be used as a biocide in metal cutting fluids, and it is expected that in many cases spent fluid will be removed (typically after 12 months) by waste contractors and disposed of to sewer after either biological (activated sludge) or physico-chemical treatment. The notified chemical would be expected to be degraded through biological processes, or be removed in association with waste sludge and be destroyed by incineration. However, it is estimated that in a worst case scenario up to 50 % of the material used in cutting oils (ie. around 2.5 tonnes per annum) may be released untreated to the sewer system, storm water drains, placed into landfill or incinerated. In such

cases local concentrations of the chemical in affected surface waters may be significant, and toxic concentrations may be exceeded. Nevertheless, because of the apparent ease of biodegradation under aerobic conditions and susceptibility to photolytic degradation, the notified chemical is not expected to persist in these systems.

Inappropriate disposal of used cutting oils would appear to have potential for local environmental hazard, although the toxic effects are not expected to persist.

EUSES Risk Assessment Predictions
The notifier provided Risk Assessments for use of the chemical in both plastic articles and in metal working fluids within Australia (Din, 2000), based on outputs from the EUSES model which is widely used in the European Union, and uses input data of biodegradation and photo-degradation half lives, acute ecotoxicity, and the leaching tests discussed above. However, in all cases where release of the chemical from plastic articles was considered (ie. leaching) it was estimated that less than 10 % of the contained Vanquish would be released each year. In most cases these conclusions appear to have been reached through consideration of static leaching scenarios, which are probably inappropriate for most release scenarios (eg. bathroom curtains and tarpaulins used for prolonged covering of damaged roofs). In any case, the static leaching data used was based on results from the experiments discussed above and appears to be arbitrary since the liquid volumes used in the experiments were not specified.

Nevertheless, the overall conclusion on environmental release was that the chemical poses no hazard due to the predicted low release, and most importantly to the low persistence attributable to rapid biodegradation and photolysis. Although, the methodology used for arriving at release figures is questionable, the overall conclusion on environmental hazard from use of the chemical in plastics is essentially in accord with that reached during the present assessment.

The risk assessment provided for use of the chemical in metal working fluids correctly concluded that potential for release is greatest during activities associated with disposal of used cutting fluid. However, this assessment assumed that all spent fluid would be collected and treated by contractors, and that some localised release to the aquatic compartment (ie. the sewer) would result from the recycling and/or disposal activities. The release of the chemical to sewer was estimated as 2.7 % of the 5 tonnes per annum treated, and the resultant PEC to the local sewer from the treatment was estimated from the EUSES model to be 0.063 g/L. Based on the 48 hour acute LC_{50} against daphnia of 93 g/L, this gives a relatively low PEC/PNEC ratio of 0.0007 indicating a safety margin of three orders of magnitude which would be further increased on release to receiving waters. However, while this assessment appears reasonable assuming total collection and disposal of the used fluid, it is unlikely to be realistic as a large fraction of used cutting fluid may not be treated as indicated.

Conclusion
When used as a component of plastic/polymer articles, the notified chemical is unlikely to present a hazard to the environment. However, inappropriate disposal of used metal cutting oil may lead to transitory localised environmental damage.

12. ASSESSMENT OF PUBLIC AND OCCUPATIONAL HEALTH AND SAFETY EFFECTS

Hazard Assessment
The notified chemical is of very low oral toxicity in the rat (LD_{50} ~ 4500 mg/kg) and low dermal toxicity in rats (LD_{50} > 2000 mg/kg). The notified chemical was considered corrosive (caused severe and permanent damage) to rabbit skin, with erythema persisting for more than 17 days, and sub-epithelial fibrosis was also observed. The notified chemical is therefore classified as corrosive, with the risk phrase R34, in accordance with the Approved Criteria. The notified chemical was found to be a moderate skin sensitiser, and is classified with the risk phrase R43, in accordance with the Approved Criteria. A negative result was obtained for the notified chemical at 200 ppm (0.02 %) in a human repeat insult patch test, and therefore the notified chemical at this concentration is not classified as a sensitiser in humans. The notified chemical was not be classed as a mutagen according to the Approved Criteria based on the result of four *in vitro* and *in vivo* studies.

In a 28 day oral repeat dose study in rats, no NOEL could be established, as changes in clinical biochemistry possibly indicative of some perturbation of liver metabolism were observed at the lowest dose used of 19.5 mg/kg/day. A Lowest Observed Effect Level (LOEL) of 19.5 mg/kg/day was established.

Occupational Health and Safety
There is little potential for significant occupational exposure to the notified chemical in the transport and storage of Vanquish or the plastics or metalworking fluid concentrates containing the notified chemical. There may be exposure during the incorporation of the notified chemical into plastics, reformulation to produce metalworking fluid concentrates and during use of metalworking fluids containing the notified chemical.

During reformulation and end use, the main exposure route for the notified chemical will be dermal. The notified chemical has low volatility, but there is potential for exposure by inhalation if aerosols are formed. Exposure to the notified chemical after incorporation into plastic articles or pellets used for further manufacture is likely to be low because the notified chemical will be encapsulated within the polymer matrix, from which it will only slowly be released.

The notified chemical may be used in a wide range of plastics manufacturing facilities, with addition procedures ranging from manual to fully automated. Exposure to the pure notified chemical may occur during weighing and transferring the additive, or during connection and disconnection of transfer hoses is an automated or semi-automated addition system is used. Due to the corrosive and skin sensitising nature of the notified chemical, a high level of precautions is required to prevent dermal and particularly ocular exposure. The MSDS for the notified chemical indicates that a face shield and elbow length impervious gloves should be used, along with overalls, rubber boots and a rubber apron. A respirator is also recommended if the risk of inhalation of spray exists. Chronic skin absorption may be reduced because the corrosive nature of the notified chemical is likely to lead to awareness of contamination and immediate washing.

For metalworking applications, it is possible to calculate a Margin of Exposure (MOE) for the notified chemical in metalworking fluids. The total dermal exposure based on the

calculations in Section 6 is 29.3 mg notified chemical per day (or 0.42 mg/kg/day, based on 70 kg body weight), while the calculated inhalation exposure is 0.009 g/kg/day notified chemical. These estimates assume no use of personal protective equipment, such as gloves and respirator. The exposure is predominantly dermal, and concentrated on the hands (99 % of the dermal exposure).

In the repeat dose toxicity study, no NOAEL was determined, on the basis of changes in the liver biochemistry. The lowest dose used was 19.5 mg/kg/day, and the NOAEL would be below this level. Calculation can be made on the basis of the LOEL of 19.5 mg/kg/day. If 100 % dermal and inhalation absorption is assumed, the MOE is 19.5/0.42 = 46.4. The MOE is therefore low, and the use of personal protective equipment is required to reduce the risk associated with use of the notified chemical in metalworking operations. The use of impervious gloves during handling of articles which have been in contact with the metalworking fluids will be expected to reduce exposure.

In addition, skin contact with the notified chemical at a concentration of 2000 ppm (in the metalworking fluid concentrates) may result in skin sensitisation. The repeat insult patch test indicated that the notified chemical is not a skin sensitiser in humans at 200 ppm, but as the pure notified chemical was found to be a sensitiser in guinea pigs, higher concentrations than that used in the human test must be treated as potential sensitisers, and gloves should be used by workers handling the metalworking fluid concentrates.

Public Health
The public will be exposed to consumer products containing the notified chemical. However, the notified chemical is present at a low concentration in the plastic material (maximum 0.2 %) and, when incorporated in the polymeric matrix, it is expected that the public exposure to the notified chemical during normal use is likely to be very low. In exceptional circumstances, the notified chemical may leach into aqueous solutions; however, the concentration of the notified chemical in the leachate is unlikely to be sufficient to cause skin irritation and is not expected to cause skin sensitisation. Consequently, it is expected that the risk to the public from the use of products containing the notified chemical is very low.

13. RECOMMENDATIONS

- The notified chemical may be recommended to the National Occupational Health and Safety Commission for consideration for inclusion in the NOHSC List of Designated Hazardous Substances.

- Used metalworking fluids containing the notified chemical should be collected by licensed waste disposal contractors for appropriate disposal.

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

- Elbow length gloves, a face shield, chemical resistant industrial clothing and footwear should be used while handling the notified chemical; where inhalation hazards exist, a respirator should also be used;

- Impervious gloves, safety goggles, chemical resistant industrial clothing and footwear should be used while handling the metalworking fluid concentrates containing the notified chemical or articles which are wet with the metalworking fluids;

- 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;

- 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* (NOHSC, 1999a), 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, 1994); for respirators, in AS/NZS 1715 (Standards Australia/Standards New Zealand, 1994) and AS/NZS 1716 (Standards Australia/Standards New Zealand, 1994) or other internationally acceptable standards.

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 the Subsection 64(1) of the Act, secondary notification of the notified chemical shall be required if additional toxicity or ecotoxicity studies, in particular a chronic toxicity test in daphnia, become available. Under the Subsection 64(2) of the Act, secondary notification of the notified chemical shall be required if any of the circumstances stipulated arise.

The Director of NICNAS is to be notified in writing within 28 days of the above circumstances.

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Attachment 1

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

Erythema Formation	*Rating*	*Oedema Formation*	*Rating*
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

Opacity	*Rating*	*Area of Cornea involved*	*Rating*
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

Redness	*Rating*	*Chemosis*	*Rating*	*Discharge*	*Rating*
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.
		Swelling with lids half-closed	3 mod.	Discharge with moistening of lids and hairs and considerable area around eye	3 severe
Diffuse beefy red	3 severe	Swelling with lids half-closed to completely closed	4 severe		

IRIS

Values	*Rating*
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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