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NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME

FULL PUBLIC REPORT

MIXED C_{18} MONO-/C_{22} TRI-CARBOXYLIC ACID AMINO ALKYL AMIDES

This Assessment has been compiled in accordance with the provisions of *the Industrial Chemicals (Notification and Assessment) Act 1989, as amended* 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 Arts, Sport, the Environment and Territories and the assessment of public health is conducted by the Department of Health, Housing and Community Services.

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Director
Chemicals Notification and Assessment

FULL PUBLIC REPORT

MIXED C_{18} MONO-/C_{22} TRI-CARBOXYLIC ACID AMINO ALKYL AMIDES

1. APPLICANT

Westvaco Pacific Pty Ltd, Charlton House, Suite 2, Level 6, 20 Alfred Street, Milsons Point, NSW 2061.

2. IDENTITY OF THE CHEMICAL

Based on the nature of the chemical and the data provided Indulin MQK-1M is considered to be hazardous. Therefore the chemical name has not been exempted from publication. The molecular formula, molecular weight, spectral data and the import volume have been exempted from publication in the Full Public Report and Summary Report.

Chemical name: Mixed C_{18} mono-/C_{22} tri-carboxylic acid amino alkyl amides

Chemical Abstracts Service (CAS) Registry No.: Not available

Trade name(s): Indulin MQK-1M

Molecular Weight: < 1000

Method of detection and determination:

Separation and structure elucidation by Ultra-violet spectroscopy, Infra-red spectroscopy and Nuclear Magnetic Resonance (NMR).

3. PHYSICAL AND CHEMICAL PROPERTIES

Appearance at 20°C and 101.3 kPa:	Dark brown moderately viscous liquid.
Odour:	Ammoniacal amine type odour.
Boiling Point:	>193°C
Specific Gravity:	1020 kg/m^3 at 20°C
Vapour Pressure:	1.173 kPa at 28°C
Water Solubility:	> 9.24 g/kg at 20°C
Partition Co-efficient (n-octanol/water) log $P_{O/W}$:	Not provided because no test could be devised to analyse concentrations of the notified substance in the emulsion caused when the substance was added to the *n*octanol/water mix.
Hydrolysis as a function of pH:	Not provided because the substance is a complex mixture and any hydrolysis that occurs will be difficult to detect. Hydrolysis is unlikely to occur under environmental conditions.
Adsorption/Desorption:	Not provided because no suitably sensitive analytical method available.
Dissociation Constant	Not provided because it is not possible to measure dissociation constant since there is no mode of chemical dissociation for this reaction mixture of organic compounds.

	However it is noted that there are a number of primary, secondary and tertiary amines. These are likely to have typical basicity
pH:	10.5 - 11.5
Flash Point:	121°C Closed cup method
Flammability Limits:	Not flammable.
Combustion Products:	The combustion products formed are gases such as carbon and nitrogen oxides and ammonia.
Autoignition Temperature:	413°C
Explosive Properties:	The chemical is not explosive under the action of shock or heat. The oxygen balance of the major components of this reaction mixture is -127 to -130 which indicates a negative prediction of explosive properties.
Reactivity/Stability:	Stable under ambient conditions; does not have oxidising properties. It polymerises with epoxy resins and polyisocyanates giving off heat. Oxidising agents react strongly with active hydrogen groups in the amine groups.
Particle size distribution:	Not relevant as the chemical is a liquid

4. PURITY OF THE CHEMICAL

Degree of purity: 99.6%

Toxic or hazardous impurity/impurities: No toxic or hazardous impurities are known

Additive(s)/Adjuvant(s): None

5. INDUSTRIAL USE

Indulin MQK-1M will be imported into Australia and is used as an emulsifier for asphalts used in road repair. It is used in road surface treatments to fill cracks and provide a skid-resistant surface on aged roads.

The purpose of the substance is to act as a surfactant to aid in the formation of a stable asphalt water emulsion for later mixing with aggregate to form the applied road repair mix. The concentration of the notified substance in the environmentally exposed road paving mix is 0.2% by mass.
The asphalt emulsion is specifically designed for slurry seal applications, used in both preventative and corrective maintenance of asphalt pavement surfaces.

Indulin MQK-1M has been in use in United States since 1983.

6. OCCUPATIONAL EXPOSURE

Indulin MQK-1M will be stored in 200 litre drums or bulk containers made of stainless steel or carbon steel. There will be only one initial commercial user site in Australia and the chemical will be transported to this site by road. The asphalt emulsions containing the chemical at a concentration of 2% w/w will be transported to the road repair sites in the storage tanks on truck mounted, slurry-seal mixing units. Therefore, significant risk of worker exposure during transport and storage is unlikely except in an accident.

At the user site, workers involved in the preparation of the emulsifier solution could be exposed to the chemical when it is

transferred from drums to process tanks with five gallon pails. The notifier has stated that two workers per shift could be exposed to the chemical and the time of worker exposure would be less than half hour per batch.

When the chemical is handled in bulk, transfer would take place in closed pipelines and exposure would be minimal.

The major route of exposure to the notified chemical is through skin and eye contact.

During transfer of the chemical to process tanks, there is potential for extensive skin and eye contact with the chemical if splashings and spillages occur.

During preparation of the emulsifier, the chemical is added to an emulsifier solution tank containing water. The emulsifier is mechanically dispersed and the solution is acidified to a pH of 2.5 to 3.0 by the addition of hydrochloric acid. This process is isolated to a remote area of the workplace. Exposure to the chemical during this process is prevented by the use of local exhaust ventilation.

Asphalt emulsions are prepared mechanically by dispersing molten asphalt in water with the aid of a high shear high speed mechanical device, such as a colloid mill. Separate pumps are used to meter asphalt and emulsifier solution into the colloid mill. The emulsion is then fed into a product emulsion storage tank. The notifier has indicated that once the asphalt emulsion is formed, the chemical would be tightly bound in the emulsion.

7. PUBLIC EXPOSURE

Indulin MQK-1M will not be sold to the public. It will be used exclusively by industry and tradespersons. The public may be exposed to the notified chemical infrequently through contact with road surfaces, where the notified chemical will be encapsulated in asphalt.

Disposal of the chemical is to be by landfill or by incineration at a licensed waste treatment processor. Products of incineration are likely to be oxides of carbon, nitrogen, hydrogen and ammonia. The notifier recommends that Indulin MQK-

1M should not be discharged to the sewage system. However, it is possible that slight run-off of the emulsion aggregate mixture may occur during its application, especially under rainy conditions.

Under the expected conditions of use, public exposure to the notified chemical will be negligible. As a result, the severe acute toxicity noted in the laboratory animals is not expected to pose significant hazard to public health.

8. ENVIRONMENTAL EXPOSURE

- **Formulation, handling and disposal**

The notified substance is fully imported, at first in 200 L drums and later in bulk containers. At the asphalt emulsion formulating site the substance is pumped into the mixing tank where water acid and heated asphalt are mixed at high speed to form an emulsion. The asphalt emulsion is then pumped into tanker trucks for transport to the application site. On arrival at the application site, the asphalt emulsion is mixed with the aggregate and spread on the roadbed to be surfaced. Evaporation of water from the mix and the breaking of the emulsion will fix the notified substance within the asphalt aggregate mix.

Bioaccumulation is unlikely due to the moderate water solubility and low exposure to the water compartment.

- **Fate**

Emulsion residues containing the notified substance from the mixing site and road tankers are expected to be minimal. Road tankers using only compatible product types will not require flushing. If spillage does occur, residues in soil are likely to be disposed to licensed landfill. Solid residues may, in some cases, be used as primers in road making. The fate of product drums will be to recyclers.

The bitumen emulsion is transported by road tanker to near the site of use where it is mixed with aggregate for use in road resurfacing. This road construction technique utilising the cationic surfactant, Indulin MKQ-1M , is likely to replace the existing bitumen hot mix

road making (which at present uses organic solvents that are evaporated to the air).

The bitumen/water emulsion is mixed with aggregate in truck mounted application equipment which applies the final mix in a layer 3-6 mm thick across the road surface. Once applied and drying of the mixture commences the electrostatic charge differential between the cation and the anionic aggregate is greater than the differential between the cation and water, resulting in water exclusion and bonding of the asphalt (containing the cation) to the aggregate. This physico-chemical process is consistent with the properties of other cationic surfactants **(1).**

Once the evaporation of the water in the applied road surfacing mixture takes place the emulsion is broken and the notified substance is not available for transport as a free entity into the environment.

Under extreme heat conditions (fire) the notified substance, or bitumen emulsion, would combust emitting oxides of carbon and nitrogen.

The notified substance was tested for biodegradability according to OECD guideline No301D. The percentage biodegradation over 28 days was found to be -4% indicating the substance is not readily biodegradable **(2).**

9. EVALUATION OF TOXICOLOGICAL DATA

9.1 Acute Toxicity

Table 1: Summary of the acute toxicity of Indulin MQK-1M

Test	Species	Outcome	Reference
Oral	Rats	LD_{50}: > 200 mg/kg	3
Dermal	Rats	LD_{50}: > 2000mg/kg	4
Skin Irritation (24 hrs)	Rabbits	Corrosive	5
Skin Corrosion (4 hrs)	Rabbits	Severe irritant	5
Eye Irritation	Rabbit	Severe irritant to corrosive	5
Skin Sensitisation	Guinea-Pig	Sensitising	6

9.1.1 Oral Toxicity (3)

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

Ten Sprague-Dawley rats, 5 male and 5 female, were selected for each dosage. Indulin MQK-1M was administered by gavage as supplied by the at a purity of 99.6%. The animals were observed for gross toxicological effects immediately after administration of the chemical, and at frequent intervals on Day 1. On subsequent days the animals were observed once in the morning and at the end of the day for fourteen days.

From the data supplied, it appears that the groups of animals were added on during the study as those receiving the higher doses died.

Table 2: Number of deaths of rats dosed orally with Indulin MQK-1M

No. of Animals	Dosage (mg/kg)	Mortality M : F
10	200	1 : 0
10	800	5 : 5
10	2000	5 : 5
10	5000	5 : 5

Among surviving rats, all the rats had gained weight at Day 15 but slight bodyweight losses were recorded for all decedents. Piloerection and increased salivation were observed in the rats within five minutes of dosing.

Rats dosed at 800 mg/kg were lethargic and also had a hunched posture, pallor of the extremities and noisy respiration. The hunched posture was also noted in rats dosed at 2000 and 5000 mg/kg. Rats dosed at 5000 mg/kg had pallor of the extremities, lethargy and a decreased respiratory rate. In addition, ptosis was observed among males dosed at 5000 mg/kg while females had an abnormal gait.

At later intervals, rats dosed at 200 mg/kg developed abnormal gait and body carriage, lethargy, pallor of the extremities and decreased respiratory rate. Loss of righting reflex was seen in one male and ptosis in one rat. Rats dosed at 800 mg/kg later developed decreased respiratory rate and prostration and ptosis and clonic convulsions were seen among males. At 2000 mg/kg, the rats had abnormal gait, a decreased respiratory rate, lethargy and prostration. Ataxia was seen in three males and body tremors in one male. Rats treated with 5000 mg/kg developed ataxia and ptosis with cyanosis and clonic convulsions were seen in some males.

At necropsy, animals that died during the course of the study showed congestion of the blood vessels of the intestinal tract at all dose levels, with thickening for two males and two females administered 800 mg/kg. Rats dosed at 800, 2000 and 5000 mg/kg had darkened kidneys, liver and spleen and red fluid in the cranial cavity. Congestion of the blood vessels of the heart and/or lungs among rats treated at 800 mg/kg were observed.

The results of this study indicate that Indulin MQK-1M has moderate acute oral toxicity with an oral LD50 of 200 - 800 mg/kg in male and female rats.

An additional **Acute Oral Toxicity Study (4)** was also submitted. In this study, eight Sprague-Dawley rats (4 males and 4 females) were selected for each dosage. Indulin MQK-1M was administered at doses of 750 mg/kg, 500 mg/kg, 250 mg/kg, 100 mg/kg and 75 mg/kg. The sample was diluted with distilled water 1:10 or 1:20. The animals were observed immediately after administration of the chemical and after one hour, four hours and once daily thereafter for a period of fourteen days. All the animals that died expired within 24 hours post-dosing.

Table 3: Number of deaths of rats dosed orally with Indulin MQK-1M

		14 Day Mortality	
No of Animals	Dosage (mg/kg)	% Total	Ratio M : F
8	75	0	0 : 0
8	100	37	0 : 3
8	250	87	4 : 3
8	500	87	3 : 4
8	750	100	4 : 4

At necropsy, animals that died showed massive haemorrhage of the stomach lining. The GI tract was filled with blood and livers were dark and congested.

The results of this study indicate that Indulin MQK-1M has a moderate acute oral toxicity with a LD_{50} of 200 mg/kg (100 - 400 mg/kg, 95% confidence interval).

9.1.2 Dermal Toxicity (4)

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

A single dose of 2000 mg/kg of Indulin MQK-1M was administered by occlusive application to the shaved backs of 10 Sprague-Dawley rats (five male and five female) for 24 hours. The animals were observed for 14 days. There were no deaths or signs of systemic reaction during the study. A gain in body weight was noted for all rats. Well defined erythema with slight or well defined oedema was noted by day 3 for all rats. Hardening of the skin was seen for two females on day 3 and hyperkeratinisation for three males and all five females from day 4. From day 5 dryness and sloughing was seen in four males and one female. Skins appeared normal from day 4 to day 8. No macroscopic abnormalities were observed at necropsy.

The results of this study indicate that the dermal LD_{50} for Indulin MQK-1M is >2000 mg/kg. The lack of systemic effects may indicate that the notified substance is not absorbed significantly from the skin.

9.1.3 Inhalation Toxicity

An acute inhalation toxicity study was not carried out as the chemical was found to be a severe irritant of the skin and eyes.

9.1.4 Skin Irritation (5)

This study was carried out in accordance with the *US Federal Hazardous Substances Labelling Act* as outlined in the *Code of Federal Regulations, Title 16, Chapter IIc, para 1500.41*.

A single dose of 0.5 ml of Indulin MQK-1M was administered by occlusive application to the clipped back and flank of three New Zealand strain albino rabbits. Patches were applied to the abraded and unabraded skin of the rabbits for 24 hours. The site of application was observed at the end of 24 hours. Necrosis as indicated by blanching, discolouration and sloughing of the skin was observed in all three animals at the abraded area. Two of the animals had necrosis at the unabraded areas while one had moderate to severe erythema and severe oedema.

The results of this study indicate that Indulin MQK-1M is corrosive when applied for 24 hrs to rabbit skin.

In another study (4 Hour Exposure) **(5)** (U.S. Department of Transport) conducted in accordance with the *Code of Federal Regulations, 49, part 173.240 - Hazardous Materials Regulations: Corrosive Materials*, Indulin MQK-1M was administered in a dose of 0.5 ml by occlusive application to the shaved backs and flanks of six New Zealand strain albino rabbits. The patches were removed at the end of four hours. The site of application was observed at the end of 4, 24 and 48 hours after removal of the patch. At the end of 4 hrs, very slight erythema was seen in two animals and one animal had well defined erythema. Four rabbits had very slight oedema while one had slight oedema with well defined edges at the end of four hours. The erythema increased in the animals at the end of 24 hrs with two having well defined and one severe erythema. One more animal developed very slight erythema at the end of 24 hrs. At the end of 48 hrs, 2 rabbits had moderate to severe erythema while one had severe erythema. Four animals had very slight oedema at the end of 48hrs while oedema was absent in two rabbits.

The results of this study indicate that Indulin MQK-1M is a moderate to severe irritant.

9.1.5 Eye Irritation (5)

The National Industrial Chemicals Notification and Assessment Scheme does not require, chemicals which are known irritants to undergo an eye irritation test but however an eye irritation study was conducted by the notifier and the results are presented below.

The test was conducted in accordance with the United States *Federal Hazardous Substances Labelling Act* as outlined in the

Code of Federal Regulations, Title 16, Chapter II, part 1500.42. The test was not conducted in compliance with GLP.

One hundred microlitres of Indulin MQK-1M was instilled into the conjunctival sac of one New Zealand strain albino rabbit with the other eye being used as control. The eyes were examined at the end of 24 and 48hrs. The experiment was terminated after 48hrs. At the end of 24hrs the conjunctiva of the rabbit was a dark

beefy red with marked swelling and lids more than half closed. The cornea showed pearly opacities with no details of the iris visible and the size of the pupil barely discernible. The iris was congested with swelling and markedly deepened folds. Reaction to light was positive.

The results of the test in one animal indicate that Indulin MQK-1M is a corrosive to the eye.

9.1.6 Skin Sensitisation (6)

The study was carried out according to the *OECD Guidelines for testing of Chemicals No: 406*

The test used was the guinea-pig maximisation test of Magnusson and Kligman. The skin reactions were assessed according to a four point scale. The sensitivity of the guinea pig strain used was checked periodically with formalin, a known sensitiser.

Preliminary study

To determine the dose level for intradermal injection in the main study, four concentrations of Indulin MQK-1M were administered in water for irrigation to two groups (four in each group) of female albino guinea pigs of the Dunkin/Hartley strain. The doses used were .01%, .025%, 0.05% and 0.1% and 0.25%, 0.5%, 1.0% and 2.5%. The dose selected was 0.025% v/v in water as this level was well tolerated for the induction phase.

To determine the dose level for topical induction in the main study, four dose levels of Indulin MQK-1M were administered in distilled water to two groups (four in each group) of guinea pigs. The doses used were 10%, 20%, 40% and 60% v/v in one group and 2.5%, 5%, 7.5% and 10% v/v in the second group. Skin reactions were observed at the end of 24 and 48hrs. The dose level selected for topical induction was 10% v/v.

The dose levels selected for topical challenge in the main study were 7.5% and 4% v/v in distilled water.

Induction and Challenge Study

Thirty female albino guinea-pigs of the Dunkin-Hartley strain (20 test and 10 control animals) were used.

Three pairs of intra-dermal injections were made into the clipped inter-scapular region of the guinea-pig. The injected solutions were as follows: Freund's complete adjuvant diluted with equal volume of water for irrigation, Indulin MQK-1M 0.025% v/v in water for irrigation and Indulin MQK-1M 0.025% v/v in a 50:50 mixture of Freund's complete adjuvant and water for irrigation. One week later, a single dose of 10% v/v of Indulin MQK-1M was applied to the clipped scapular region of each test animal for 48 hrs. Control animals were similarly induced but without the use of the test substance.

Two weeks after the topical induction application, the test and control animals were challenged topically using Indulin MQK-1M, 7.5% and 4% v/v in distilled water by occlusive application at two different sites. The challenge sites were evaluated 24, 48 and 72 hours after removal of the patches.

At the end of 24hrs, 4/10 animals in the Freund's treated controls that received 7.5% v/v Indulin MQK-1M developed dryness and sloughing of the epidermis. There was no reaction in the other animals. No necrosis was observed in the control animals.

In the test animals, at the end of 24 hrs all the animals developed moderate to severe erythema and 14/20 receiving 7.5% v/v had thickening, dryness and sloughing of the epidermis while 6/20 given 4.0% developed these changes. Four of the animals receiving 7.5% v/v had necrosis. At the end of 48hrs 16/20 of the guinea pigs receiving 7.5% v/v had developed necrosis of the skin. Necrosis was also seen in 4/20 animals with 4% v/v of Indulin MQK-1M. Gain in bodyweight was unaffected in all animals.

The results of this study indicate that Indulin MQK-1M is a skin sensitiser in guinea pigs at the concentrations tested.

9.2 Repeated Dose Toxicity (7)

This study was carried out according to *OECD Guidelines for Testing of Chemicals No: 407*

Indulin MQK-1M was prepared at concentrations of 0.075, 0.75 and 3.0% w/v. Indulin MQK-1M in distilled deionised water was administered by gavage once daily to groups of five male and five female Sprague-Dawley rats at doses of 15, 150 and 600 mg/kg/day. The animals were treated for twenty-nine days. The control group consisted of five male and five female rats and received only the vehicle. Body weights, food and water consumption and clinical observations were recorded. Blood samples were taken on day 28. Surviving animals were killed and examined macroscopically on Day 30. Microscopic examination of the tissues were carried out for:

(a) animals that died during the study to ascertain the cause of death;

(b) rats of the control group, those receiving 150 mg/kg and the surviving rats administered 600 mg/kg killed at the end of study.

The high dose was selected on the basis of available toxicity data and a preliminary oral toxicity investigation.

Seven rats receiving 600 mg/kg/day died during the treatment period. Two male rats died on day 13, one on day 19 and one on day 23. One rat was sacrificed on day 28. One female rat was found dead on day 25 and three females were sacrificed one each on day 6, day 23 and day 27. Clinical signs observed in all animals in this group were increased salivation, noisy respiration, digitigrade locomotion (walking on toes), wet fur and increased respiration. Five animals were cyanosed and five had pallor of the extremities. Pilo-erection was seen in six of the animals while two had ptosis. For rats treated at 150 mg/kg/day, similar clinical signs were seen however, the signs were slight or moderate in degree except for severely increased salivation observed in one female rat.

The body weight of the animals in this group was comparable to the controls. The overall gain in body weights for both males and females in the groups receiving 150 mg/kg and 15 mg/kg were also similar to controls.

There was no notable differences in the food consumption between control and treated animals in the three groups. Daily water consumption by animals treated at 600 mg/kg/day was consisitently greater than by controls in both sexes. There was no notable differences in the water consumption between control and treated animals receiving 150 mg/kg/day and 15 mg/kg/day.

Macroscopic examination of the animals administered 600 mg/kg showed watery distension of the stomach and small intestine and congestion of the corpus mucosa of the small intestine in all the animals. Patchy congestion of the lungs was seen in two animals and pale lower incisors in two other animals.

Microscopic changes observed in the gastro-intestinal tract were ulcerative changes of the gastric non-glandular epithelium in one male and increased prominence of goblet cells in the ileum and/or jejunum for one male and one female.

Among rats receiving 15 mg/kg/day no toxic signs related to treatment were seen.

No toxic signs were observed among control rats and on macroscopic and microscopic examination of the animals.

The haematological changes noted in animals receiving 600 mg/kg were an elevated eosinophil and lymphocyte counts with an increased total white blood cell count in one female. The biochemical changes seen at this dose were increased glutamic-oxaloacetic transaminase and glutamic-pyruvic transaminase activities for all animals.

Among rats treated at 150 mg/kg a significantly lower total white blood cell and lymphocyte counts were recorded for females in comparison with controls. There was a statistically significant increase in the glutamic-pyruvic transaminase activity for male rats at both the 150 mg/kg and 15 mg/kg dose levels, however these values were within historical controls. Significantly lower blood urea nitrogen levels and increased cholesterol levels were recorded for male rats receiving 150 mg/kg.

Increased serum glutamic-oxaloacetic transaminase and glutamic-pyruvic transaminase activities were common across the three groups. This appears to be dose related as these changes are more marked at the higher dose of 600 mg/kg.

These data indicate that the target organs for toxicity of Indulin MQK-1M with repeated oral doses in rats were the GI tract and the liver.

9.3 Genotoxicity

9.3.1 Salmonella typhimurium Reverse Mutation Assay (8)

This study was carried out according to the *OECD Guidelines for Testing Chemicals No 471.*

Indulin MQK-1M was tested in two independent experiments at dose levels of 5000, 500, 50 and 5µg/plate for the dose range finding test and 500, 150, 50, 15, 5 and 0.5µg/plate for the main study. *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538, both in the presence and absence of S9-mix were used. Positive controls used were 9-aminoacridine, N-ethyl-N'-nitro-N-nitrosoguanidine and 2-nitrofluorene. 2-Aminoanthracene was used as positive control in experiments using S-9.

Revertant colony numbers were increased in the preliminary toxicity test following treatment with Indulin MQK-1M with strains TA1538 in the presence of S-9 mix, and TA98 in the presence and absence of S-9 mix. However, no such increases in revertant colony numbers were observed in subsequent mutation tests.

In the experiment, the test substance did not induce an increase in the revertant colony numbers per plate at any concentration tested with or without metabolic activation.

The results indicate that Indulin MQK-1M is not genotoxic toward *Salmonella typhimurium.*

9.3.2 Analysis of Metaphase Chromosomes (9)

This study was carried out according to the *OECD Guidelines for Testing Chemicals No 473.*

Cultured human lymphocytes were incubated with Indulin MQK-1M for a three hour period, with S-9 mix, or a twenty-one hour period without metabolic activation. Mitotic activity was arrested by the addition of colchicine to the culture two hours before the end of the incubation. Ethyl methanesulphonate 750 µg/ml, and cyclophosphamide 15 and 20 µg/ml were used as positive controls. The dose levels of Indulin MQK-1M selected for the metaphase

analysis were 22.5, 15 and 2.5 µg/ml in the absence of S-9 mix and from 50, 30 and 5 µg/ml in its presence. Cells were fixed, stained and examined for clastogenicity.

No statistically significant increase in the proportion of aberrant cells were observed when Indulin MQK-1M was incubated with S-9 mix. In the absence of S-9 mix Indulin MQK-1M caused a statistically significant increase in the proportion of metaphase figures containing chromosomal aberrations at 2.5 µg/ml compared with the solvent control. However, this increase was not considered to be indicative of clastogenic activity as it was within the historical control range and clastogenicity was not observed at higher doses. Both positive controls caused large increases in the number of aberrant cells.

The results of this study indicate that Indulin MQK-1M is not clastogenic towards cultured human lymphocytes.

9.4 Overall Assessment of Toxicological Data

Indulin MQK-1M has a moderate acute oral toxicity with an oral LD_{50} in the rat of between 200 and 800 mg/kg and is therefore classified as harmful (15) by the oral route. It has low acute dermal toxicity in rats (LD_{50} in rats >2000 mg/kg). Indulin MQK-1M is a severe to corrosive eye irritant and, a skin sensitiser. In the skin irritation study, the chemical was a moderate to severe irritant after a four hour exposure and corrosive on prolonged contact (24 hrs). An acute inhalation study was not carried out but skin and eye irritation results indicate that Indulin MQK-1M may be a respiratory irritant. Indulin MQK-1M was not mutagenic towards *Salmonella typhimurium* and did not cause chromosomal aberrations in vitro in human lymphocytes.

In the 28 day repeated oral dose study in rats, Indulin MQK-1M showed marked clinical signs together with significant changes in the blood chemistry and haematology parameters. Macroscopic and microscopic examination revealed changes particularly in the gastro-intestinal tract when the chemical was administered at doses of 600 mg/kg/day. At 150 mg/kg/day, the animals exhibited moderate clinical signs and increased glutamic-pyruvate transaminase activity. No clinical signs or toxicity were noted in animals receiving 15 mg/kg/day.

10. ASSESSMENT OF ENVIRONMENTAL EFFECTS

The notifier has provided ecotoxicological data for the notified substance. Acute toxicity studies were conducted on three species following the appropriate OECD protocols and guidelines (see table below).

Species	Exposure	Measure	Result
Rat	48 hr	LD_{50}	287 $mg.kg^{-1}$
Rainbow trout	96 hr	LC_{50}	1.3 $mg.L^{-1}$
Daphnia	48hr	EC_{50}	0.35 $mg.L^{-1}$

The results show high acute toxicity to daphnia **(10)** and moderate toxicity to rainbow trout **(11)** and the rat. Nominal concentrations were assumed since a method of analysis of the above concentrations has not been developed. Care should therefore be taken with the interpretation of the results.

There are no results for daphnia reproduction or algal growth inhibition but these will not be required for the proposed use due to the low exposure potential to water.

11. ASSESSMENT OF ENVIRONMENTAL HAZARD

There appears to be some danger of spill of the notified substance in the initial charge of substance to the mixing tank. The potential for this class of compound to bond strongly to soil and aggregate will preclude high exposure to the aquatic compartment and as such the environmental hazard is expected to be low, despite the expected moderate to high toxicity to aquatic organisms.

The resulting predicted environmental hazard from proper use is minimal.

12. ASSESSMENT OF PUBLIC AND OCCUPATIONAL HEALTH AND SAFETY EFFECTS

The notified chemical has been in use in USA and Europe since 1983 but there no information on the effects of the chemical on

human health. The main occupational exposure to Indulin MQK-1M is likely to be by skin and eye contact or inhalation of heated vapours or mists. Based on the results of the animal studies, the chemical is a moderate to severe skin irritant, corrosive on prolonged contact, a skin sensitiser and a severe eye irritant. It is also considered to be harmful if ingested. It may also be a respiratory irritant based on the above findings.

During reformulation, exposure to the chemical should be minimised by engineering measures such as exhaust ventilation and by protective clothing.

The notifier intends to import the chemical in the concentration used in the toxicological tests. The chemical is therefore likely to be a hazard at these concentrations. After reformulation, the chemical is present at a concentration of 2% by mass in the asphalt emulsion and is expected to be less hazardous.

Indulin MQK-1M will not be sold to the public. It will be used exclusively by industry and tradespersons. The public may be exposed to the notified chemical infrequently through contact with road surfaces, where it will be encapsulated in asphalt. Under the proposed conditions of use, public exposure to the chemical will be negligible. As a result, the severe acute toxicity noted in the laboratory animals is not expected to pose significant hazard to public health.

13. RECOMMENDATIONS

To minimise occupational exposure to Indulin MQK-1M the following guidelines and precautions should be observed:

. During transfer of the chemical from drums to process tanks and during reformulation, local exhaust ventilation should be used.

. If engineering controls and work practices do not sufficiently reduce exposure to a safe level then the following personal protective equipment should be used as the chemical is a severe eye and skin irritant and a skin sensitiser:

- Rubber gloves which conform to the Australian Standard 2161-1978: Industrial Safety Gloves and Mittens (excluding Electrical and Medical Gloves) should be worn (8).

- Overalls, PVC apron and eye protection which conforms to the Australian Standard 1337-1984: Eye Protectors for Industrial Applications should be worn (9).

- Protective clothing should conform to Australian Standard 3765-1990: Clothing for Protection Against General or Specific Chemicals(10).

. Contact with strong oxidising agents, acids, anionic surfactants or emulsifiers should be avoided.

. Good work practices should be implemented to avoid spillages or splashings.

. Good personal hygiene should be observed

. The MSDS should be easily accessible to all employees.

14. MATERIAL SAFETY DATA SHEET

The Material Safety Data Sheet (MSDS) for Indulin MQK-1M (Attachment 1) was provided in Worksafe Australia format (16). This MSDS was provided by Westvaco Pacific Pty Ltd 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 Westvaco Pacific Pty Ltd.

15. REQUIREMENTS FOR SECONDARY NOTIFICATION

Under the *Industrial Chemicals (Notification and Assessment) Act 1989* (the Act), secondary notification of Indulin MQK-1M shall be required if any of the circumstances stipulated under subsection 64(2) of the Act arise. No other specific conditions are prescribed.

16. REFERENCES

(1) K van Leeuwen et al, *"Ecological Risk Evaluation of Cationic Fabric Softener DTDMAC. III. Risk Assessment"*, Chemosphere, (1992), 24(5), p629-639.

(2) Assessment of Ready Biodegradability of Indulin MQK-1M (Closed Bottle Test). HRC Report No WVC 7(a)/920093, 1992. Data on File. Huntingdon Research Centre Ltd., Huntingdon, Cambridgeshire, England.

(3) Indulin MQK-1M: Acute Oral Toxicity To The Rat. HRC Report No 91878D/WVC9/AC, 1992. Data on File. Huntingdon Research Centre Ltd., Huntingdon, Cambridgeshire, England.

(4) Indulin MQK-1M: Acute Dermal Toxicity To The Rat. HRC Report No 91565D/WVC2/AC, 1992. Data on File. Huntingdon Research Centre Ltd., Huntingdon, Cambridgeshire, England.

(5) Acute Oral Toxicity, Eye and Skin Irritation Tests on Indulin MQK-IM. Test Report No 05593, 1985. Data on File. United States Testing Company, Inc., Biological Services Division, 1415 Park Avenue, Hoboken, New Jersey 07030.

(6) Indulin MQK-1M: Skin Sensitisation in The Guinea-Pig. HRC Report No.91627D/WVC3/SS, 1992. Data on File. Huntingdon Research Centre Ltd., Huntingdon, Cambridgeshire, England.

(7) Indulin MQK-1M: Twenty-Eight Day Oral Toxicity Study In The Rat. HRC Report No WVC 5/920090, 1992. Data on File. Huntingdon Research Centre Ltd., Huntingdon, Cambridgeshire, England.

(8) Indulin MQK-1M: Bacterial Mutation Assay. HRC Report No WVC 1/901297, 1992. Data on File. Huntingdon Research Centre Ltd., Huntingdon, Cambridgeshire, England.

(9) Indulin MQK-1M: Metaphase Chromosome Analysis Of Human Lymphocytes Cultured In Vitro. HRC Report No. WVC 6/911354, 1992. Data on File. Huntingdon Research Centre Ltd., Huntingdon, Cambridgeshire, England.

(10) The Acute Toxicity of Indulin MQK-1M to Rainbow Trout (Oncorhynchus mykiss). HRC Report No WVC 7(c)/920266, 1992. Data on File. Huntingdon Research Centre Ltd., Huntingdon, Cambridgeshire, England.

(11) The Acute Toxicity of Indulin MQK-1M to Daphnia Magna. HRC Report No WVC 7(b)/920265, 1992. Data on File. Huntingdon Research Centre Ltd., Huntingdon, Cambridgeshire, England.

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

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

(14) Australian Standard 3765-1990, "Clothing for Protection Against Hazardous Chemicals, Part 1: Protection Against General or Specific Chemicals", Standards Association of Australia Publ., Sydney, 1990.

(15) National Occupational Health and Safety Commission, *Approved Criteria for Classifying Hazardous Substances*, AGPS, Canberra, 1993.

(16) National Occupational Health and Safety Commission, *Guidance Note for the Completion of a Material Safety Data Sheet*, 2nd edition, AGPS, Canberra, 1990.