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NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME

FULL PUBLIC REPORT

MILLAD 3940

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Director
Chemicals Notification and Assessment

FULL PUBLIC REPORT

MILLAD 3940

1. APPLICANT

ICI Australia (Operations) Pty Ltd, 1 Nicholson St, Melbourne, Victoria.

2. IDENTITY OF THE CHEMICAL

Trade names:	Gel All-MD Gerol MD Millad 3940

3. PHYSICAL AND CHEMICAL PROPERTIES

Appearance at 20°C and 101.3 kPa:	White powder
Melting Point:	249.3 - 249.8°C
Density:	1300 kg/m^3 at 20°C
Water Solubility:	0.70 X 10^{-3} g/L at 20°C
Fat Solubility:	4.7 mg/kg at 37 °C
Partition Co-efficient (n-octanol/water):	log $P_{O/W}$: 2.5
Hydrolysis as a function of pH:	Stable at pH 7 and pH 9 but unstable at pH 4
Flammability Limits:	Not able to be ignited with a flame

Autoignition Temperature:	Not auto flammable
Explosive Properties:	Not explosive
Particle size distribution:	Approximately 70% < 7 µm

Comments on physico-chemical properties

The following comments have been provided by the notifier:

Adsorption/desorption information has not been provided as it is considered inapplicable as the chemical will be encapsulated in a polymer matrix from which it will not significantly leach.

Dissociation constant information has not been provided as it is considered inapplicable as the chemical will be encapsulated in a polymer matrix from which it will not significantly leach.

The above comments provide sufficient justification for the omission of the relevant data.

4. PURITY OF THE CHEMICAL

Degree of purity: Approximately 98%

5. INDUSTRIAL USE

Millad 3940 is used as a clarifying agent for polypropylene homopolymer. The polypropylene is to be used for the manufacture of housewares, bottles, syringes and take away food containers.

Millad 3940 will be imported in quantities of greater than 1 tonne per annum.

6. OCCUPATIONAL EXPOSURE

Millad 3940 will be imported in cardboard cylinders weighing approximately 40 kg. It is manually added to an enclosed blender with other powdered chemicals. The blended mixture is drummed off into 200 L plastic lined drums.

Loading of the blender will be under local exhaust ventilation in a segregated work area. Drumming off will be also performed under local exhaust ventilation to minimise exposure to dust.

The drummed material will be added to an additive feeder which gravimetrically controls the addition of the chemical blend to polypropylene powder. A dust extraction process will keep the fine dust within the system and dust is not allowed to escape into the atmosphere.

The duration of exposure during blending will be 4 hours/day, 30-40 days/year and during addition of the blended material to the additive feeder will be 1-2 hours/day, 30-40 days/year. It is expected that 26 workers will be involved in these operations.

During maintenance, 6 workers will be exposed for 1 hour/month, 12 days/year and during analysis, 3 workers will be exposed for 6 days/year.

7. PUBLIC EXPOSURE

There is low potential for public exposure to Millad 3940 during shipment and reformulation.

There is potential for widespread public exposure to low doses of Millad 3940 in diet, caused by migration from polypropylene food and drink containers. Based on measurements of migration at 100°C from polypropylene containing 0.32% of Millad 3940, the maximum concentrations of Millad 3940 were measured to be 0.414 ppm in aqueous and acidic foods and 4.30 ppm in alcoholic and fatty foods. An estimated daily intake of 0.00165 mg/kg/day was derived, assuming a bodyweight of 60 kg and that 2% of the dietary intake comes in contact with polypropylene containing Millad 3940. Applying a 2000-fold safety factor to the NOEL of 1560 mg/kg/day, determined in a 90 day rat oral toxicity study, yields an ADI of 0.78 mg/kg/day which is approximately 100-fold greater than the estimated daily intake of Millad 3940. Additional exposure may arise from injectable solutions following contact with polypropylene syringes containing Millad 3940. This aspect has not been addressed by the notifier but is likely to result in only low exposure.

8. ENVIRONMENTAL EXPOSURE

. Release

The notifier states that possible release of the notified chemical to the environment cannot occur under normal operating conditions. During such times, the dust-extraction process keeps the fine dust within the system and dust is not released to the atmosphere.

When the system undergoes inspection, cleaning or maintenance, it is emptied thoroughly. The following sections may have remnants of the chemical once opened, but only to trace amounts: additive feeder, additive feed hopper and the diverter feed valve.

The notifier estimate less than 1 kg per annum of waste would be generated from the manufacture of polypropylene. Disposal will occur only at approved land waste site by external waste management authority. Likely disposal site is the secure landfill at Lucas Heights or waste fixation at ICI (bagged and/or kibbled) and burial at land fill.

During the manufacture of finished articles, the notifier estimates about 200 kg per year (combined waste from all customers) of polypropylene granules containing 0.5 kg of encapsulated Millad 3940 will be disposed of as follows:

. Injection moulding; spillage would account for ~100 kg waste per year. The granules would be swept up and disposed of in garbage and buried at land fill. The runner material is either recycled in-house or sold to a recycler.

. Blow moulding; as above, spillage would account for ~100 kg waste per year.

. Thermoforming; the off-cuts of sheet are either recycled in-house or sold to a recycler.

• Fate

Millad 3940 will enter the environment when waste generated from the manufacture of polypropylene and the finished articles, and articles containing Millad 3940 are disposed of to land fill.

It is unlikely that Millad 3940 will migrate from the polymer matrix and leach into groundwater under environmental conditions. Extraction studies provided by the notifier showed very low levels (33 ppb) of migration from polypropylene under exaggerated exposure conditions (exposing test specimens to distilled water at 49°C for 10 days).

Incineration of finished articles containing Millad 3940 will produce oxides of carbon.

- **Biodegradation**

Millad 3940 was tested for its ready biodegradability in the modified Sturm test (OECD Guideline 301B) at nominal concentrations of 10 and 20 $mg.L^{-1}$. After 28 days of incubation the extent of biodegradation amounted to 30% at 10 $mg.L^{-1}$ and 4% at 20 $mg.L^{-1}$. Although substantial biodegradation occurred at the lower concentration, the results indicate that Millad 3940 is not readily biodegradable.

- **Hydrolysis**

The hydrolysis of Millad 3940 was determined according to an EEC directive. Because of the low water solubility of Millad 3940 acetone (70%) was used as a co-solvent. The study indicated the notified chemical was hydrolytically stable at pH 7 and 9 (< 10% hydrolysis after 5 days). At pH 4 the half-life at 50°C and 37°C was 19 and 92 hours, respectively. The half-life time at 25°C was calculated to be 444 hours. The main hydrolysis product of Millad 3940 was detected but not identified.

The results indicate that hydrolysis of Millad 3940 is likely to occur under acidic conditions. However, Millad 3940 is unlikely to hydrolyse readily under environmental conditions because of its low water solubility.

- **Bioaccumulation**

Characteristics of organic chemicals which exhibit bioaccumulation are a molecular weight >100 giving a maximum capacity at about 350, then declining to a low capacity about 600, and a log Kow between 2 and 6 (1). Millad 3940's molecular weight of 386, log Kow of 2.5, low water solubility and low biodegradability, indicates it may bioaccumulate. However,

Millad 3940's low fat solubility may preclude this from occurring. Also, Millad 3940 is unlikely to enter the aquatic environment due to its use pattern. Therefore, the overall bioaccumulation potential of Millad 3940 is likely to be low.

9. EVALUATION OF TOXICOLOGICAL DATA

9.1 Acute Toxicity

Table 1 Summary of the acute toxicity of Millad 3940

Test	Species	Outcome	Reference
Acute Oral	Rat	LD_{50}>5,000 mg/kg	2
Acute Dermal	Rat	LD_{50}>2,000 mg/kg	3
Skin Irritation	Rabbit	Non-irritating	4
Eye Irritation	Rabbit	Slightly irritating	5
Skin Sensitisation	Guinea Pig	Non-sensitising	6

9.1.1 Oral Toxicity (Ref No:2)

Wistar rats (5/sex) were administered by gavage two doses of Millad 3940 in polyethylene glycol each dose at 2,500 mg/kg, 12 hours apart. The rats were observed for a period of 14 days. There were no deaths or treatment related clinical signs. All animals showed body weight gain and there were no macroscopic findings at necropsy.

The oral LD_{50} of Millad 3940 in rats was >5,000 mg/kg.

9.1.2 Dermal Toxicity (Ref No:3)

Millad 3940 in polyethylene glycol was applied to the shaved dorsal area of Wistar rats (5/sex) at a dose of 2,000 mg/kg under occlusive bandage for 24 hours. The animals were observed for a period of 14 days. There were no deaths or treatment related clinical signs. All the animals showed body weight gain. Slight erythema was observed in 1 male following bandage removal. There were no macroscopic findings at necropsy with the exception of a white nodule observed in the forestomach of 1 male.

The dermal LD_{50} of Millad 3940 was >2,000 mg/kg.

9.1.4 Skin Irritation (Ref No:4)

Millad 3940 (0.5g) moistened with water was applied to the shaved dorsal area of each of 3 female New Zealand white rabbits under a semi-occlusive bandage for a period of 4 hours. The application site was examined 50 minutes, 24, 48 and 72 hours after the removal of the dressing and the test substance. No erythema or oedema was observed in any of the animals.

Millad 3940 powder was found not to cause skin irritation.

9.1.5 Eye Irritation (Ref No:5)

Millad 3940 powder (39 mg, equivalent to 0.1 ml) was instilled in the conjunctival sac of the right eye of each of 3 female New Zealand white rabbits. The eyes of each rabbit were examined 1, 24, 48 and 72 hours after instillation of the test substance. Slight erythema and oedema were observed in all 3 animals at the 1 hour examination. The slight erythema persisted for up to 24 hours in 2 animals and up to 48 hours in the remaining animal, but the oedema was no longer evident at 24 hours.

Millad 3940 was slightly irritating to the eye.

9.1.6 Skin Sensitisation (Ref No:6)

Millad 3940 was tested for skin sensitisation potential in the albino guinea pig using the Buehler test method. This strain of

guinea pigs had been tested prior to the commencement of the study with formaldehyde as a positive control.

A skin irritation study was conducted with Millad 3940 in propylene glycol to determine the appropriate induction and challenge doses to be used in the skin sensitisation study. Millad 3940 was applied epicutaneously to the shaved left flank of each guinea pig (1/dose level) at a concentration of 50%, 25%, 10% or 5% under occlusive dressing for a period of 6 hours. There was no erythema or oedema at 24 or 48 hours after removal of the dressing for any of the dose levels. On the basis of these results and the fact that the 50% concentration level was too viscous, the 25% concentration level was chosen for both the induction and the challenge dose for the skin sensitization study.

In the induction phase of the skin sensitisation study, nine repeated epicutaneous applications of Millad 3940 at 25% concentration were made to the same shaved area on the left flank of each of 20 albino guinea pigs over a period of 3 weeks (days 1, 3, 5, 8, 10, 12, 15, 17 and 19). The test substance was applied each time under an occlusive dressing which was kept in place for 6 hours, after which the dressing and the excess test substance were removed. A separate control group consisting of 10 albino guinea pigs was treated in the same way with the omission of the test substance. The treated skin area was examined for erythema and oedema immediately after removal of the dressing on day 19. There were no signs of irritation in any of the animals.

Ten days after the last induction exposure (day 29), both the experimental and the control animals were challenged with Millad 3940 at a concentration of 25% which was applied to a shaved area on the right flank of each animal under occlusive dressing for a period of 6 hours. The application site was examined for erythema and oedema at 24 and 48 hours after removal of the dressing. There were no signs of skin irritation at either time interval in any of the animals in either the test or the control group.

Body weight gain in the treated animals was not affected during this study. One of the treated animals was found dead on day 29 and this was possibly due to an overtight application of the occlusive bandage. Another of the treated animals showed tremors, bradypnoea, dyspnoea and pale skin on day 29. There is

no comment in the report on the possibility of these symptoms being treatment related.

Millad 3940 was found not to cause skin sensitisation under the condition of this experiment.

9.2 Repeated Dose Toxicity

9.2.1 28-Day Oral Toxicity Study (Ref No:7)

Millad 3940 in polyethylene glycol was administered to Wistar rats (5/sex/group) by oral gavage at doses of 0 (vehicle control), 50, 200 or 1000 mg/kg/day for 28 days.

There were no deaths during this study. Clinical signs included transient salivation and rales in mid dose males and high dose females. Body weight gain and food consumption were not affected. Haematology and clinical chemistry did not reveal any adverse effects. Ophthalmoscopy also did not show any effect which could be attributed to the treatment.

At necropsy, absolute and relative organ weights in treated animals were similar to those in the control group. Macroscopic examination did not reveal any treatment related effects. Microscopic examination of the control and high dose groups showed mononuclear cell infiltration of the liver in 2/5 high dose males and 3/5 high dose females and one female in this group showed acute inflammation of the liver. There was no comment in the pathology report on the likelihood of the liver effects being related to the treatment.

9.2.2 90-Day Oral Toxicity Study (Ref No:8)

SLc-Wistar rats (10/sex/dose) were administered with Millad 3940 in the solid feed at a concentration of 0 (control group), 1.25% (750 mg/kg/day), 2.5% (1,500 mg/kg/day) or 5% (3,000 mg/kg/day) for 90 days.

There were no deaths and no apparent clinical signs. There was a decrease in body weight gain in the high dose males from the 5th week onwards which resulted in these males weighing 19% less than the control males by week 13. Haematology and urinalysis did reveal any adverse effects. Clinical chemistry showed a slight increase in the level of ALP in the high dose females.

At necropsy, there was a decrease in absolute and relative pituitary, heart, liver and spleen weights in the high dose males, but these decreases did not reach statistical significance. Histology showed mononuclear cell infiltration of the liver in 4/10 high dose females while the incidence was 1/10 in the control females. The report does not contain any comment as to the likelihood of this finding being related to the treatment.

9.3 Genotoxicity

9.3.1 *Salmonella typhimurium* Reverse Mutation Assay (Ref No:9)

Millad 3940 was tested for its potential to cause gene mutations in the *Salmonella typhimurium* reverse mutation assay using the TA1535, TA1537, TA1538, TA98 and TA100 strains. A pre-test for toxicity for Millad 3940 showed normal background growth for TA98 and TA100 up to a concentration of 1000 µg/plate. Consequently the concentration levels selected for the main test were 10, 100, 333, 1,000 and 5,000 µg/plate. There was no increase in the number of revertants per plate both in the presence or absence of rat liver microsomal fraction with any of the strains tested. Positive controls used were sodium azide, 2-aminoanthracene and 4-nitro-o-phenylene-diamine.

Millad 3940 was found not to cause gene mutation under the conditions of this experiment.

9.3.2 Micronucleus Assay in the Bone Marrow Cells of the Mouse (Ref No:10)

Millad 3940 was assayed for its potential to induce micronuclei in polychromatic erythrocytes in bone marrow of the mouse. Millad 3940 in gummi arabicum (5%) was administered by oral gavage to NMRI mice (5/sex/dose/time interval) at doses of 0 (vehicle control) or 5,000 mg/kg. Bone marrow was examined at 24, 48 and 72 hours after dosing. The ratio of polychromatic to normochromatic erythrocytes in the treated animals was comparable to that of the control group indicating that there was no cytotoxic effect. There was no observed increase in the number of micronucleated cells at any of the time intervals in the treated animals. Cyclophosphamide was used as a positive control

and caused the expected increase in the frequency of micronucleated erythrocytes.

Millad 3940 was found not to have clastogenic activity under the conditions of this experiment.

9.4 Overall Assessment of Toxicological Data

Millad 3940 was found to have low acute toxicity in the rat when given by the oral route with an LD_{50} >5,000 mg/kg and by the dermal route with LD_{50} >2,000 mg/kg. Millad 3940 did not cause primary skin irritation, but was found to be slightly irritating to the rabbit eye. Millad 3940 was negative in the guinea pig skin sensitisation test. A 28-day oral repeat dose toxicity study with Millad 3940 did not reveal any adverse effects. Millad 3940 was devoid of mutagenicity activity when tested in the *Salmonella typhimurium* reverse mutation assay, and did not possess clastogenic activity in the mouse micronucleus assay.

10. ASSESSMENT OF ENVIRONMENTAL EFFECTS

Test	Species	Result
Acute toxicity	Zebra fish	96h LC50 > 1000 $mg.L^{-1}$
Acute toxicity	*Daphnia magna*	24h EC50 > 1000 $mg.L^{-1}$

Reports were provided and these indicate the above tests were satisfactorily conducted according to OECD Guidelines.

Exposure to filtered and unfiltered supersaturated solutions of 1000 $mg.L^{-1}$ did not induce any mortalities or side effects on the above aquatic organisms. It should be noted the test solution used exceeded the water solubility of Millad 3940. Although the actual concentrations are unclear, zebrafish and *Daphnia* are unlikely to suffer acute effects up to the limit of solubility (0.7 $mg.L^{-1}$) of Millad 3940.

11. ASSESSMENT OF ENVIRONMENTAL HAZARD

The proposed use of Millad 3940 as an additive in polypropylene is unlikely to present an environmental hazard as the notified substance is unlikely to migrate from the polymer matrix under environmental conditions.

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

Millad 3940 is not expected to be an acute toxicant, a skin irritant or skin sensitiser. Repeated dose studies in rats indicate that Millad 3940 does not cause significant toxicity from repeated exposure. Millad 3940 may cause slight eye irritation. It is not expected to be genotoxic.

Millad 3940 is a powder and 70% of the particles are in the respirable range. Because Millad 3940 is sparingly soluble in water, it is likely to be a nuisance particulate and the high level of particles in the respirable range may cause irritation in the lower respiratory tract as well as the upper respiratory tract at high dust levels. It is not known whether prolonged high level exposure would lead to lung damage as is the case with other particulates. This uncertainty accentuates the need for work practices which minimise dust generation during transfer of the notified chemical to enclosed systems.

The notifier states that local exhaust ventilation is used to minimise exposure during blending and transfer of the blend to the additive feeder. However, during maintenance operations, local exhaust ventilation may not be operational and it is important that dust generation is kept to a minimum despite the fact that maintenance is carried out for only 36 hours/year. Dermal exposure is not expected to be a problem during these operations.

It is expected that the slight eye irritation potential of Millad 3940 is due to mechanical rather than chemical factors. However, the effect of prolonged exposure to the eye is not known and eye protection should be worn as noted in section 13.

13. RECOMMENDATIONS

To minimise occupational exposure to Millad 3940 the following guidelines and precautions should be observed:

. the workplace should be well ventilated and engineering controls such as local exhaust ventilation should be employed where the powder is handled and where blending takes place. The dust level should be maintained below Worksafe Australia's exposure standard for nuisance particulates of 10 mg/m^3 (11);

. where the powder is blended with other chemicals in bulk or where the blend is added to polypropylene powder in bulk, mechanical handling should be employed;

. where the powder is blended with other chemicals or the blend added to polypropylene powder:

  - a dust mask complying with Australian Standard AS 1716 (12) should be chosen and used in accordance with Australian Standard AS 1715-1991 (13);

  - safety glasses or goggles complying with Australian Standard AS 1337-1984 (14) should be chosen and used in accordance with Australian Standard AS 1336-1982 (15);

  - protective clothing complying with Australian Standard AS 3765.2-1990 (16) should be chosen and used in accordance with AS 3765.3-1990 (17); and

  - gloves complying with Australian Standard AS 2161-1978 (18) should be worn.

. good personal hygiene practices should be observed; and

. a copy of the Material Safety Data Sheet should be easily accessible to employees.

14. MATERIAL SAFETY DATA SHEET

The Material Safety Data Sheet (MSDS) for Millad 3940 (Attachment 1) was provided in Worksafe Australia format (19). This MSDS was provided by ICI Australia (Operations) 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 ICI Australia (Operations) Pty Ltd.

15. REQUIREMENTS FOR SECONDARY NOTIFICATION

Under the *Industrial Chemicals (Notification and Assessment) Act 1989* (the Act), secondary notification of Millad 3940 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) Connell D W, "Bioaccumulation of Xenobiotic Compounds" CRC Press, p56, 1990.

(2) RCC Notox B.V., The Netherlands, Assessment of Acute Oral Toxicity with Millad 3940 in the Rat. Data on file, Project No. 035358, 1990.

(3) RCC Notox B.V., The Netherlands, Assessment of Acute Dermal Toxicity with Millad 3940 in the Rat. Data on file, Project No. 035369, 1990.

(4) RCC Notox B.V., The Netherlands, Primary Skin Irritation/Corrosion Study with Millad 3940 in the Rabbit. Data on file, Project No. 035393, 1990.

(5) RCC Notox B.V., The Netherlands, Acute eye Irritation/Corrosion Study with Millad 3940 in the Rabbit. Data on file, Project No. 035404, 1990.

(6) RCC Notox B.V., The Netherlands, Contact Hypersensitivity to Millad 3940 in the Albino Guinea Pig. Data on file, Project No. 037463, 1990.

(7) RCC Notox B.V., The Netherlands, Subacute 28-Day Oral Toxicity with Millad 3940 by Daily Gavage in the Rat. Data on file, Project No. 035382, 1990.

(8) Drug Safety Test Centre, Japan, Report on a three month oral subacute test of Gerol MD administered to rats by admixture with the feed. Data on file, project no. 360-3358, 1982

(9) Cytotest Cell Research (CCR), Germany, *Salmonella Typhimurium* Reverse Mutation Assay with Millad 3940. Data on file, Project No. 195524, 1990.

(10) Cytotest Cell Research (CCR), Germany, Micronucleus Assay in Bone Marrow Cells of the Mouse with Millad 3940.Data on file, Project No. 195513, 1990.

(11) Exposure Standards for Atmospheric Contaminants in the Occupational Environment. Guidance Note [NOHSC: 3008 (1991)]; National Exposure Standards [NOHSC: 1003 (1991)], 2nd Edition, October 1991.

(12) Australian Standard 1716-1991 *Respiratory Protective Devices*, Standards Association of Australia Publ, Sydney 1991.

(13) Australian Standard 1715-1991 *Selection, use and maintenance of Respiratory Protective Devices*, Standards Association of Australia Publ, Sydney 1991.

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

(15) Australian Standard 1336-1982 *Recommended Practices for Eye Protection in the Industrial Environment,* Standards Association of Australia Publ, Sydney 1982.

(16) Australian Standard 3765.2-1990 *Clothing for Protection against Hazardous Chemicals Part 2 Limited protection against specific chemicals*.Standards Association of Australia Publ, Sydney 1990.

(17) Australian Standard 3765.3-1990 *Clothing for Protection against Hazardous Chemicals Part 3 Selection, Care, and Use*. Standards Association of Australia Publ, Sydney 1990.

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

(19) Guidance Note for Completion of a Material Safety Data Sheet. [NOHSC : 3001 (1991)], 3rd Edition, October 1991.