

File No: NA/952

October 2001

**NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION  
AND ASSESSMENT SCHEME**

**FULL PUBLIC REPORT**

**Chemical in Catalyst MC**

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For enquiries please contact the Administration Section at:

*Street Address:* 92 -94 Parramatta Rd CAMPERDOWN NSW 2050, AUSTRALIA

*Postal Address:* GPO Box 58, SYDNEY NSW 2001, AUSTRALIA

*Telephone:* (61) (02) 9577 9514 FAX (61) (02) 9577 9465

Director  
Chemicals Notification and Assessment

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**FULL PUBLIC REPORT****Chemical in Catalyst MC****1. APPLICANT**

Basell Australia Pty Ltd of Level 13, 90 Collins St, Melbourne VIC 3000 (ABN 42 004 327 762) has submitted a limited notification statement in support of their application for an assessment certificate for Chemical in Catalyst MC.

**2. IDENTITY OF THE CHEMICAL**

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

**3. PHYSICAL AND CHEMICAL PROPERTIES**

<b>Appearance at 20°C &amp; 101.3 kPa:</b>	white powder; imported in mineral oil solution
<b>Melting Point:</b>	102.25°C
<b>Boiling Point:</b>	252°C
<b>Specific Gravity:</b>	not determined
<b>Vapour Pressure:</b>	$5.3 \times 10^{-2}$ kPa at 30°C
<b>Water Solubility:</b>	< 10 mg/L at 25°C
<b>Particle Size:</b>	not relevant as the notified chemical is only imported in solution
<b>Partition Co-efficient (n-octanol/water):</b>	$\log P_{ow} = 1.8$ at 25°C
<b>Hydrolysis as a Function of pH:</b>	not determined
<b>Adsorption/Desorption:</b>	$\log K_{oc} \sim -1.42$ (estimated)
<b>Dissociation Constant:</b>	no dissociable groups are present
<b>Flammability Limits:</b>	not flammable; combustible

**Autoignition Temperature:** no self ignition to 400°C

**Explosive Properties:** sensitive to friction

**Reactivity/Stability:** not oxidising

### 3.1 Comments on Physico-Chemical Properties

The density of the notified chemical could not be measured by the pycnometer method because no suitable liquid with a combination of properties including wettability, insolubility and density lower than the notified chemical could be found. The notified chemical is imported in a solution with specific gravity between 0.9 and 1.1.

Water solubility measurements were performed by a modified flask method with gas chromatographic determination of the solute (Centro Di Saggio Montell Italia 1997). The detection limit of the method was stated to be 10 mg/L. Based on values reported in the ecotoxicity tests, the water solubility of the notified chemical is between 6.82 and 8.58 mg/L.

The notified polymer contains no linkages that could be expected to undergo hydrolysis under the environmental pH range of 4 to 9.

The partition coefficient of the notified polymer has not been determined due to its expected low water solubility, and its likely hydrophobic nature, indicative of partitioning into the octanol phase. While, the MSDS supplied by the notifier indicates that the log P value for the notified chemical is expected to be greater than 1.7, the real value may be higher than this. The log P for the parent hydrocarbon is stated at being approximately 4.2 (Vershueren, 1996).

No adsorption/desorption test was conducted for this notification. The notifier estimates a log Koc for the notified chemical of -1.42. However, an estimate of adsorption/desorption potential of the notified chemical based on its water solubility ( $\log K_{oc} = -0.55\log S + 3.64$  using  $S = 10 \text{ mg/L}$ ) suggests that the log Koc is 3.09 (Lyman et al., 1990). This estimate is consistent with the value for Koc reported for the parent hydrocarbon (Vershueren, 1996).

No dissociation constant tests were conducted for this notification because the notified chemical does not contain any ionisable groups.

The notified chemical could be ignited, but did not sustain combustion beyond 26 seconds. Measurement of the explosive properties showed that the notified chemical was not sensitive to flame or shock, but measurements of friction sensitivity in accordance with 92/69/EEC Test A.14 with a loading of 360 N gave two positive results (sparks observed) from six tests. The notified chemical is therefore considered explosive.

A test of oxidising properties according to 92/69/EEC Test A.17 gave results indicative of oxidising properties, in that the burning rate of a 50:50 mixture of notified chemical and cellulose was higher than that of the reference mixture of  $\text{Ba}(\text{NO}_3)_2$  and cellulose (60:40). A repeat of the test using kieselguhr (an inert material) in place of cellulose also showed high burning rates at mixing ratios around 50:50, indicating that burning of the notified chemical itself may be enhanced on dilution.

#### 4. PURITY OF THE CHEMICAL

<b>Degree of Purity:</b>	high
<b>Hazardous Impurities:</b>	none
<b>Non-hazardous Impurities (&gt; 1% by weight):</b>	none at > 1 %
<b>Additives/Adjuvants:</b>	none as produced

#### 5. USE, VOLUME AND FORMULATION

The notified chemical will be used as part of a catalyst formulation known as MC126 or MC406, which is used in the production of polypropylene. The notified chemical will be present in the imported formulation at > 10 %, with the remainder being primarily mineral oil.

The notified chemical will only be imported as part of the slurry catalyst formulation, in Dangerous Goods approved drums. The catalyst formulation is a dangerous good due to the presence of titanium tetrachloride, which requires airtight storage. The slurry will be transferred under nitrogen into a mixing vessel containing other ingredients used in the manufacture of polypropylene. These ingredients will be blended and the resulting polypropylene dried and repackaged for distribution to customer sites. The notified chemical is stated to be completely consumed during the polypropylene production process.

The notifier expects that the volume to be imported will be less than one tonne per annum for the first five years of importation. The product containing the notified chemical will only be used at the notifier's site.

#### 6. OCCUPATIONAL EXPOSURE

##### *Transport and Storage*

The notifier indicated that one waterside worker, one transport driver and one storage worker will handle the drums containing the notified chemical. For the waterside and transport workers, handling will occur for a maximum of 4 hours per day, 6 days per year. The storage worker may handle drums containing the notified chemical for 2 hours per day, daily. No exposure of these workers to the notified chemical is expected, as they will handle only unopened drums, and the Dangerous Goods approved drums will be resistant to damage so as to prevent exposure to titanium tetrachloride.

##### *Polypropylene Manufacture*

The notifier indicated that two process workers will supervise the production of polypropylene using the catalyst containing the notified chemical. The estimated frequency of handling the notified chemical is 4 hours per day, 48 days per year. Laboratory staff may also handle the notified chemical on 3 days per year, in a fume cupboard.

The slurry containing the notified chemical will be transferred from the drums into a mixing tank by nitrogen displacement. From the mixing tank, it will be automatically dosed into the reactor. The entire process occurs under nitrogen, to avoid decomposition of the catalyst, and therefore has to remain enclosed. The notifier stated that the factory has appropriate ventilation.

The enclosed process minimises the risk of spills of the notified chemical, however there is the possibility of drips of decomposed catalyst mixture, containing the notified chemical at > 10 %, near the transfer hose connections. The notifier indicated that overalls, impervious gloves, eye goggles and safety boots will be used while handling the notified chemical.

During polypropylene manufacture, the notified chemical is incorporated in the polymer matrix at very low levels (2.06 µg/g), and is completely consumed. Negligible risk is expected for workers handling the finished polypropylene.

## **7. PUBLIC EXPOSURE**

There is little potential for public contact with the notified chemical. It is transported from the port of entry in especially designed drums over a single and relatively short transport route. The likelihood of transport accidents and any subsequent public contact with the notified chemical is very low. The escape of the notified chemical to the environment during the industrial process is most unlikely. The notified chemical is consumed in the industrial process for which it is intended and the manufactured consumer products do not contain the notified chemical. The potential for public exposure to the notified chemical is therefore negligible.

## **8. ENVIRONMENTAL EXPOSURE**

### **8.1 Release**

During formulation of polypropylene, the notifier estimates that up to 29 kg per annum of notified chemical waste will be generated. This will be derived from:

Spills:  $\leq 5$  kg/annum  
Residues in the import containers:  $\leq 24$  kg/annum

Spills of the notified chemical that occur during formulation will be collected and disposed of to a licensed waste landfill site. Empty import drums with any residual solid will also be disposed of in a licensed waste landfill site.

The remainder of the notified polymer will be incorporated into polypropylene, which at the end of its useful life will be disposed of in landfill.

### **8.2 Fate**

The notifier provided a test report on the biodegradation of the notified chemical by microorganisms in aqueous media (TNO, 1997e). The test was carried out in accordance with

## EC Test Guidelines C.5 and C.6.

The test used inoculum collected from an oxidation ditch located in the municipality of Berkel Rodenrijs, The Netherlands. The biodegradation tests were performed on solutions containing 0.99 and 1.99 mg/L of the notified chemical and were prepared by dilution of a stock solution (144.9 mg in 25 mL ethanol) with ethanol. The required amount of solution (100 µL) was deposited on to filter paper, the ethanol evaporated and the paper was placed into an empty test bottle to which the required amount of seawater was added. The test substance was left to cultivate (degrade) in a closed vessel for a period of 28 days, at a temperature of 20 °C. After 28 days,  $\leq 5\%$  biodegradation of the test substance was observed. Over the same period the reference substances, glucose/glutamic acid, exhibited 57% degradation. The test substance was found not to be degraded by microorganisms under these test conditions.

The majority of the notified chemical will share the fate of the polypropylene products in which it is bound. The notifier indicates that the notified chemical will remain bound within the polymer matrix. At the end of their useful lives polypropylene products containing the notified chemical will be disposed of in landfill or incinerated. Wastes generated from manufacturing and spills will also be disposed of in landfill.

In landfill, based on the low water solubility and estimated Koc of the notified chemical, it will associate with the soil matrix and not leach into the aquatic environment. The incineration of polypropylene products containing the notified chemical would yield water vapour and oxides of carbon.

The polymer is not expected to cross biological membranes due to its low water solubility and should not bioaccumulate (Connell, 1990).

## 9. EVALUATION OF TOXICOLOGICAL DATA

### 9.1 Summary of Toxicological Investigations

<i>Endpoint &amp; Result</i>	<i>Assessment Conclusion</i>
Rat, acute oral LD50 > 2000 mg/kg bw	low toxicity
Rat, acute dermal LD50 > 2000 mg/kg bw	low toxicity
Rat, acute inhalation	not conducted
Rabbit, skin irritation	non-irritating
Rabbit, eye irritation	slightly irritating
Guinea pig, skin sensitisation - adjuvant test.	no evidence of sensitisation.
Rat, Oral Repeat Dose Toxicity - 90 Days.	NOEL = 253 mg/kg bw/day
Genotoxicity - bacterial reverse mutation	Non mutagenic
Genotoxicity – in vitro Chromosome Aberration	Genotoxic

Genotoxicity – in vitro HPRT Locus Test	Non genotoxic
Genotoxicity – in vivo Mouse Micronucleus	Non genotoxic
Genotoxicity – in vivo Mouse Micronucleus	Non genotoxic
Genotoxicity – in vivo Rat DNA Repair	Non genotoxic
Pharmacokinetic/Toxicokinetic Studies	Not a scheduled data requirement under the Act. At the time of this assessment no data were available for review.
Developmental & Reproductive Effects	Not a scheduled data requirement under the Act. At the time of this assessment no data were available for review.
Carcinogenicity	Not a scheduled data requirement under the Act. At the time of this assessment no data were available for review.

## 9.2 Acute Toxicity

### 9.2.1 Acute Oral Toxicity (TNO, 1997d)

TEST SUBSTANCE	notified chemical
METHOD	OECD 401 Acute Oral Toxicity – Limit Test. EC Directive 92/69/EEC B.1 Acute Toxicity (Oral) – Limit Test.
Species/Strain	Rat/Wistar; CrI:(WI) WU BR
Vehicle	Suspension in maize oil
Remarks - Method	No significant protocol variations

#### RESULTS

<i>Group</i>	<i>Number &amp; Sex of Animals</i>	<i>Dose mg/kg bw</i>	<i>Mortality</i>
I	5/sex	2000	1/10

LD50	> 2000 mg/kg bw
Signs of Toxicity	One female was found dead on day 3; this animal had showed emaciation, sluggishness, blepharospasm, dyspnea and coma at 24 and 48 hours after dosing. Two males showed blepharospasm at 1 hour after dosing, one of these was also sluggish.
Effects in Organs	No treatment related effects on organs were found; the animal which died during the study could not be examined



Remarks - Results	due to autolysis.
CONCLUSION	The notified chemical is of low toxicity via the oral route.
TEST FACILITY	TNO Nutrition and Food Research Institute

### 9.2.2 Acute Dermal Toxicity (TNO, 1997b)

TEST SUBSTANCE	notified chemical
METHOD	OECD 402 Acute Dermal Toxicity – Limit Test. EC Directive 92/69/EEC B.3 Acute Toxicity (Dermal) – Limit Test.
Species/Strain	Rat/Wistar; CrI:(WI) WU BR
Vehicle	Suspension in maize oil
Type of dressing	Occlusive
Remarks - Method	No significant protocol variations

#### RESULTS

<i>Group</i>	<i>Number &amp; Sex of Animals</i>	<i>Dose mg/kg bw</i>	<i>Mortality</i>
I	5/sex	2000	0/10

LD50	> 2000 mg/kg bw
Signs of Toxicity - Local	For all animals, slight erythema was seen on day 1. On day 3, the females alone showed slight to moderate erythema and very slight to slight oedema; moderate encrustations were also observed. One male on day 3 and one female on day 7 also showed slight encrustations.
Signs of Toxicity - Systemic	No clinical signs of systemic toxicity were observed.
Effects in Organs	No treatment related effects on organs were found.
Remarks - Results	

CONCLUSION	The notified chemical is of low toxicity via the dermal route.
TEST FACILITY	TNO Nutrition and Food Research Institute

### 9.2.3 Acute Inhalation Toxicity

Test not conducted.

#### 9.2.4 Skin Irritation (TNO, 1997a)

TEST SUBSTANCE	notified chemical
METHOD	OECD 404 Acute Dermal Irritation/Corrosion. EC Directive 92/69/EEC B.4 Acute Toxicity (Skin Irritation).
Species/Strain	Rabbit/New Zealand White
Number of Animals	3 male
Observation Period	3 days
Vehicle	none
Type of Dressing	Semi-occlusive.
Remarks - Method	No significant protocol variations
RESULTS	
Remarks - Results	No non-zero Draize scores were recorded at 1hr, 24 hr, 48 hr or 72 hr.
CONCLUSION	The notified chemical is non-irritating to skin.
TEST FACILITY	TNO Nutrition and Food Research Institute

#### 9.2.5 Eye Irritation (TNO, 1997c)

TEST SUBSTANCE	notified chemical
METHOD	OECD 405 Acute Eye Irritation/Corrosion. EC Directive 92/69/EEC B.5 Acute Toxicity (Eye Irritation).
Species/Strain	Rabbit/New Zealand White
Number of Animals	3 male
Observation Period	3 days
Remarks - Method	A Chicken Enucleated Eye Test (CEET) was used as an irritation pre-screen. No significant protocol variations occurred during the main test.

#### RESULTS

<i>Lesion</i>	<i>Mean Score* Animal No.</i>	<i>Maximum Value</i>	<i>Maximum Duration of Any Effect</i>	<i>Maximum Value at End of Observation Period</i>
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	1	2	3			
<i>Conjunctiva: redness</i>	0.67	0.67	0.67	2	48 hr	0
<i>Conjunctiva: chemosis</i>	0.33	0.33	0.33	1	24 hr	0
<i>Conjunctiva: discharge</i>	0	0	0	1	1 hr	0
<i>Corneal opacity</i>	0	0	0	0		0
<i>Iridial inflammation</i>	0	0	0	0		0

\*Calculated on the basis of the scores at 24, 48, & 72 hours for EACH animal.

Remarks - Results	The CEET test showed results consistent with those from the Draize test. Low scores were recorded for corneal swelling, opacity and fluorescein retention. In the Draize test, conjunctival redness, swelling and discharge were observed at 1 hr; discharge resolved by 24 hr, swelling by 48 hr and redness by 72 hr.
CONCLUSION	The notified chemical is slightly irritating to the eye.
TEST FACILITY	TNO Nutrition and Food Research Institute

## 9.2.6 Skin Sensitisation (TNO, 1997h)

TEST SUBSTANCE	notified chemical
METHOD	OECD 406 Skin Sensitisation – Maximisation Test. EC Directive 96/54/EC B.6 Skin Sensitization - Maximisation Test.
Species/Strain	Guinea pig/Dunkin Hartley CrI:(HA)BR
PRELIMINARY STUDY	Maximum Non-irritating Concentration: Intradermal: 1 % Topical: 30 %
MAIN STUDY	
Number of Animals	Test Group: 5 per sex      Control Group: 3 per sex
INDUCTION PHASE	Induction Concentration: Intradermal: 3 % Topical: 30 %
CHALLENGE PHASE	
1st challenge	topical application: 30 %
Remarks - Method	Sodium lauryl sulphate was applied to induce irritation on the day prior to topical induction.

Signs of Irritation	<p>Moderate erythema was seen at all sites intradermally treated with mixtures including Freund's Complete Adjuvant (FCA). Slight erythema was seen at the injection site for diluted notified chemical in two animals; one control animal showed slight erythema at the site injected with diluent alone.</p> <p>Topical pre-treatment with sodium lauryl sulphate produced erythema; after topical application of the test material, very slight erythema was seen in the test animals; very slight erythema with or without very slight oedema was seen in the controls.</p>
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## RESULTS

<i>Animal</i>	<i>Challenge Concentration</i>	<i>Number of Animals Showing Skin Reactions after challenge</i>	
		<i>24 h</i>	<i>48 h</i>
<i>Test Group</i>	30 %	0/10	0/10
<i>Control Group</i>	30 %	0/6	0/6

Remarks - Results	No reactions were seen at challenge in any test or control animals.
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CONCLUSION	There was no evidence of reactions indicative of skin sensitisation to the notified chemical under the conditions of the test.
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TEST FACILITY	TNO Nutrition and Food Research Institute
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### 9.3 Repeat Dose Toxicity (TNO, 1997j)

TEST SUBSTANCE	notified chemical
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METHOD	OECD 407 Repeated Dose 28-day Oral Toxicity Study in Rodents. EC Directive 96/54/EC B.7 Repeated Dose (28 Days) Toxicity (Oral).
Species/Strain	Rat/Wistar; Crl:(WI) WU BR
Route of Administration	Oral – diet
Exposure Information	Total exposure days: 28 days; Dose regimen: 7 days per week; Post-exposure observation period: none
Remarks - Method	Histopathological examinations were carried out on the adrenals, heart, kidneys, liver, spleen and any gross lesions in animals of the control (I) and high dose (IV) groups only. There were no other significant protocol variations.

## RESULTS

Group	Number & Sex of Animals	Dose/Concentration (% w/w)		Mortality
		Nominal	Actual	
I	5 per sex	0	0	0/10
II	5 per sex	0.075	0.067	0/10
III	5 per sex	0.3	0.272	0/10
IV	5 per sex	1.2	1.06	0/10

#### *Mortality & Time to Death*

No unscheduled deaths occurred during the study.

#### *Clinical Observations*

Sparsely haired skin was seen in groups I and IV; occasional soiling of the perineum was seen in group II females. No clinical signs of toxicity were evident. No statistically significant differences in body weights, mean food intake or food conversion efficiency were seen.

#### *Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis*

No changes in haematological parameters were observed. For males of group IV, several clinical chemistry changes were seen. These were a decrease in alanine aminotransferase and aspartate aminotransferase activity, a decrease in creatinine concentration, and an increase in total protein concentration. A decrease in plasma glucose was seen for group III but not for group IV males.

#### *Effects in Organs*

The relative liver weight was increased for the group IV males and females, and the absolute liver weight was increased for group IV males only. A decrease in absolute adrenal weight was seen for group III males but not for group IV males.

No treatment related gross abnormalities were observed at necropsy. Only scattered histopathological variations were observed in both group I and group IV animals, except for the presence of accessory adrenals in 3 group IV males and 2 group IV females, compared with no control animals.

#### *Remarks – Results*

The actual dosages measured from food intake were: Group I, males and females 0 mg/kg bw/day, Group II males 63.5 mg/kg bw/day, females 69.0 mg/kg bw/day, Group III males 253.1 mg/kg bw/day, females 265.6 mg/kg bw/day, Group IV males 1050.8 mg/kg bw/day, females 1106.4 mg/kg bw/day.

The study authors indicated that the presence of accessory adrenals is a spontaneous anatomical variation, and that the incidence in the high dose group is likely to be a chance occurrence.

#### CONCLUSION

Due to liver weight changes in both sexes in group IV and clinical chemistry differences in group IV males, and as the observations for animals of Group III were not replicated in Group IV, the No Observed Effect Level (NOEL) was established to be 253 mg/kg bw/day for males and 266 mg/kg bw/day for females.

TEST FACILITY

TNO Nutrition and Food Research Institute

## 9.4 Genotoxicity

### 9.4.1 Genotoxicity-Bacteria (TNO, 1995b)

TEST SUBSTANCE	notified chemical
METHOD	OECD 471 Bacterial Reverse Mutation Test. EC Directive 2000/32/EC B. 14 Mutagenicity – Reverse Mutation Test using Bacteria. Plate incorporation procedure
Species/Strain	<i>S. typhimurium</i> : TA1535, TA1537, TA98, TA100
Metabolic Activation System	10 % S9 fraction from Aroclor 1254 induced rats
Concentration Range in Main Test	a) With metabolic activation: 0 – 5000 µg/plate. b) Without metabolic activation: 0 – 5000 µg/plate.
Vehicle	dimethyl sulphoxide (DMSO)
Remarks - Method	Two independent tests were performed in triplicate. No preliminary test to establish toxicity was performed. No significant protocol variation occurred.

#### RESULTS

Metabolic Activation	Test Substance Concentration (µg/plate) Resulting in:			
	Cytotoxicity in Preliminary Test	Cytotoxicity in Main Test	Precipitation	Genotoxic Effect
<i>Present</i>				
Test 1	-	185	185	-
Test 2	-	222	74	-
<i>Absent</i>				
Test 1	-	185	185	-
Test 2	-	222	74	-

Remarks - Results	No significant increases in the number of revertant colonies were observed for any strain either in the presence or absence of metabolic activation. The positive controls gave significant increases in revertant colonies indicating that the test system responded appropriately.
CONCLUSION	The notified chemical was not mutagenic to bacteria under the conditions of the test.
TEST FACILITY	TNO Nutrition and Food Research Institute

### 9.4.2 Genotoxicity-In Vitro (TNO, 1995a)

TEST SUBSTANCE	notified chemical
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METHOD	OECD 473 In vitro Mammalian Chromosomal Aberration Test.
Cell Type/Cell Line	Chinese hamster ovary (CHO)
Metabolic Activation System	40 % S9 fraction from Aroclor 1254 induced rats
Vehicle	DMSO
Remarks - Method	The test was carried out in accordance with an in house protocol based on the OECD guidelines. Protocol deviations included the use of the same cultures for preliminary toxicity testing and metaphase analysis. A repeat test was not carried out due to the positive results of the first test.

<i>Metabolic Activation</i>	<i>Test Substance Concentration (µg/mL)</i>	<i>Exposure Period</i>	<i>Harvest Time</i>
<i>Present</i>	0*, 1.25, 2.5, 5, 10*, 20, 30, 40, 50*, 75*, 100, 125	3 hr	18 hr
<i>Absent</i>	0*, 1.25, 2.5*, 5, 10*, 20, 30*, 40, 50, 75, 100, 125	18 hr	18 hr

\*Cultures selected for metaphase analysis.

## RESULTS

<i>Metabolic Activation</i>	<i>Test Substance Concentration (µg/mL) Resulting in:</i>			
	<i>Cytotoxicity in Preliminary Test</i>	<i>Cytotoxicity in Main test</i>	<i>Precipitation</i>	<i>Genotoxic Effect</i>
<i>Present</i>	75	-	75	50
<i>Absent</i>	40	-	75	-

Remarks - Results

Cytotoxicity was reported above in terms of cell appearance and growth; reduction in mitotic index was apparent at 5 µg/mL in the absence of metabolic activation and at 50 µg/mL in the presence of metabolic activation.

In the presence of metabolic activation, clear increases in the percentage of cells with chromosomal aberrations were observed at 50 and 75 µg/mL; the positive controls gave significant increases in percentage of cells with chromosomal aberrations indicating that the test system responded appropriately.

CONCLUSION

The notified chemical was clastogenic to Chinese hamster ovary cells treated in vitro under the conditions of the test.

TEST FACILITY

TNO Nutrition and Food Research Institute

### 9.4.3 Genotoxicity-In Vitro (TNO, 1995c)

TEST SUBSTANCE

notified chemical

METHOD	OECD 476 In vitro Mammalian Cell Gene Mutation Test.
Cell Type/Cell Line	Chinese hamster ovary (CHO)
Metabolic Activation System	40 % S9 fraction from Arochlor 1254 induced rats
Vehicle	DMSO
Remarks - Method	No significant protocol deviations. Two independent assays were performed, without a preliminary cytotoxicity test.

<i>Metabolic Activation</i>	<i>Test Substance Concentration (µg/mL)</i>	<i>Exposure Period</i>	<i>Expression Time</i>	<i>Selection Time</i>
<i>Present</i>				
Test 1	0*, 2.5*, 5, 25, 50*, 75*, 100*, 200*, 300, 400, 500	4 hr	18-21 hr	7 days
Test 2	0*, 5*, 10, 25, 50, 75*, 100*, 200*, 300, 400*, 500	4 hr	18-21 hr	7 days
<i>Absent</i>				
Test 1	0*, 3.125*, 6.25*, 12.5, 25*, 50, 75*, 100, 150*, 200	4 hr	18-21 hr	7 days
Test 2	0*, 3.125*, 6.25*, 12.5*, 25*, 50, 75, 100, 150, 200	4 hr	18-21 hr	7 days

\*Cultures used for mutant selection.

## RESULTS

<i>Metabolic Activation</i>	<i>Test Substance Concentration (µg/mL) Resulting in:</i>			
	<i>Cytotoxicity in Preliminary Test</i>	<i>Cytotoxicity in Main test</i>	<i>Precipitation</i>	<i>Genotoxic Effect</i>
<i>Present</i>				
Test 1	-	75	100	-
Test 2	-	100	200	-
<i>Absent</i>				
Test 1	-	50	50	-
Test 2	-	50	75	-

Remarks - Results	<p>Cytotoxicity in the second assay in the absence of metabolic activation resulted in very low initial cell yield at and above 50 µg/mL. In this assay, the highest dose evaluated (25 µg/mL) did not reach the level of cytotoxicity or insolubility specified in the protocol, however the next higher dose showed excessive cytotoxicity and was discarded. For the other assays, the concentration producing cytotoxicity is reported from cell observations while initial cell yields and cloning efficiencies were generally above 50 %.</p> <p>No concentration related or reproducible increase in mutant colony frequency was observed for the notified chemical under any conditions; the positive controls gave significant increases in mutant frequency indicating that the test system responded appropriately.</p>
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CONCLUSION The notified chemical was not clastogenic to CHO cells treated in vitro under the conditions of the test.

TEST FACILITY TNO Nutrition and Food Research Institute

#### 9.4.4 Genotoxicity-In Vivo (TNO, 1996a)

TEST SUBSTANCE notified chemical

METHOD OECD 475 Mammalian Bone Marrow Chromosomal Aberration Test.

EC Directive 2000/32/EC B.11 Mutagenicity - In vivo Mammalian Bone-Marrow Chromosome Aberration Test.

Species/Strain Rat/Wistar; CrI:(WI) WU BR

Route of Administration Oral – gavage

Vehicle Corn oil

Remarks - Method The animals were fasted for 16 hr rather than 2-4 hr; signs of reactions were not recorded daily; no other significant protocol deviations occurred.

<i>Group</i>	<i>Number &amp; Sex of Animals</i>	<i>Dose mg/kg bw</i>	<i>Sacrifice Time hours</i>
I	15 per sex	0	6, 24, 48
II	15 per sex	2000	6, 24, 48
III	5 male	M; 2.5	24

M=mitomycin C.

#### RESULTS

Doses Producing Toxicity The only signs of toxicity observed were blepharospasm and lethargy 1-4 hours after treatment; signs were observed in 5 control and 25 treated animals

Genotoxic Effects A reduction in mitotic index from 2.94 % to 1.62 % in females was observed at 6 hr, and a reduction from 2.80 % to 2.04 % was observed in females at 48 hr.

Remarks - Results No statistically significant increase in the percentage of cells with structural chromosome aberrations was observed in any group of animals treated with the notified chemical; the positive control produced a significant increase in structural aberrations indicating that the test system responded appropriately.

CONCLUSION The notified chemical was not clastogenic in this in vivo Mammalian Bone Marrow Chromosomal Aberration Test under the conditions of the test.

TEST FACILITY TNO Nutrition and Food Research Institute

#### 9.4.5 Genotoxicity-In Vivo (TNO, 1996c)

TEST SUBSTANCE	notified chemical
METHOD	OECD 474 Mammalian Erythrocyte Micronucleus Test. EC Directive 2000/32/EC B.12 Mutagenicity Mammalian Erythrocyte Micronucleus Test.
Species/Strain	Mouse/Charles River CD-1
Route of Administration	Oral – gavage
Vehicle	Maize oil
Remarks - Method	No significant protocol deviations.

<i>Group</i>	<i>Number &amp; Sex of Animals</i>	<i>Dose mg/kg bw</i>	<i>Sacrifice Time hours</i>
I	15 per sex	0	24, 48, 72
II	15 per sex	2000	24, 48, 72
III	5 male	M; 0.75	24

M=mitomycin C.

#### RESULTS

Doses Producing Toxicity In a preliminary test, sluggishness and piloerection were observed at 400 mg/kg bw; pallor was also observed at 2000 mg/kg bw. In the main test, sluggishness was observed in all group II animals at 1-4 hr after treatment; two group II females at 48 hr and one at 72 hr had light coloured femurs; the latter had little marrow.

Genotoxic Effects No statistically significant differences in the ratio of polychromatic erythrocytes (PCE) to total erythrocytes was observed in the group I and II males; the females showed a weakly significant decrease (only at 48 hr sacrifice) in the ratio indicative of genotoxicity at 2000 mg/kg bw.

Remarks - Results No statistically significant increase in the proportion of PCEs containing micronuclei was observed in any group of animals treated with the notified chemical; the positive control produced a significant increase in micronuclei indicating that the test system responded appropriately.

CONCLUSION The notified chemical was not clastogenic in this in vivo Mammalian Erythrocyte Micronucleus Test under the conditions of the test.

TEST FACILITY TNO Nutrition and Food Research Institute

#### 9.4.6 Genotoxicity-In Vivo (TNO, 1996b)

TEST SUBSTANCE	notified chemical
METHOD	based on 1995 draft OECD 486 Unscheduled DNA Synthesis (UDS) Test with Mammalian Liver Cells in vivo.
Species/Strain	Rat/Wistar Crl:[WI] WU BR

Route of Administration	Oral – gavage
Vehicle	0.5 % carboxymethylcellulose in phosphate buffered saline
Remarks - Method	An in house protocol was based on the draft OECD guideline. A number of deviations from the protocol were reported. An initial test was stopped after one day because of low viability of hepatocytes, and recommenced a week later with the remaining animals, which were then older than the age range specified in the protocol. The positive control was given by gavage rather than IP injection. Several deviations in cell collection and scoring which were not considered to affect the results were also reported.

<i>Group</i>	<i>Number &amp; Sex of Animals</i>	<i>Dose mg/kg bw</i>	<i>Sacrifice Time hours</i>
I	12 male	0	1-4, 12-16
II	12 male	2000	1-4, 12-16
III	6 male	AAF: 50	12-16

AAF=2-acetylaminofluorene

#### RESULTS

Doses Producing Toxicity	No data on clinical observations were presented.
Genotoxic Effects	Hepatocyte viability was affected by fasting time but not by treatment with the notified chemical.
Remarks - Results	Results of less than 5 net grains per nucleus (NG) were observed for both test and control animals at both sacrifice times; similar proportions of cells in repair were observed for both test (5.33 % at 1-4 hr, 15.33 % at 12-16 hr) and control (6.67 % at 1-4 hr, 10.67 % at 12-16 hr) groups; for the positive control 20.94 NG was observed, with 81.33 % of cells in repair, indicating that the test system responded appropriately.

#### CONCLUSION

The notified chemical was not clastogenic in this in vivo Unscheduled DNA Synthesis Test under the conditions of the test.

#### TEST FACILITY

TNO Nutrition and Food Research Institute

### 9.5 Overall Assessment of Toxicological Data

The notified chemical was of low toxicity in rats by the dermal and oral routes (in both cases, LD50 > 2000 mg/kg bw). It was not irritating to rabbit skin, and a slight irritant to rabbit eyes. In the dermal toxicity test in rats, with a prolonged contact time with skin, moderate dermal irritation was observed in the females while slight irritation was observed in the males. The notified chemical was not sensitising to the skin of guinea pigs in an adjuvant type test.

In a 28-day feeding study in rats, liver weight changes were observed at the highest dose in both sexes and clinical chemistry differences were observed at the highest dose for males, the No Observed Effect Level (NOEL) was established to be 253 mg/kg bw/day for males and 266 mg/kg bw/day for females.

A number of in vitro and in vivo mutagenicity tests were performed using the notified chemical. In a bacterial point mutation test, the notified chemical was found to be non-mutagenic. In an in vitro chromosome aberration study, clear and significant increases in the incidence of chromosome aberrations were seen in the presence of metabolic activation. An in vitro HPRT Locus Test and three in vivo tests each gave results indicating that the notified chemical was not clastogenic under the conditions of the test.

The notified chemical would not be classified as a hazardous substance in accordance with the NOHSC *Approved Criteria for Classifying Hazardous Substances* (Approved Criteria) (NOHSC, 1999a) based on the results of the toxicological studies submitted. The notified chemical may have potential for genotoxicity as one test gave clear evidence that it may be genotoxic, and as it has structural alerts giving rise to concern over genotoxicity.

## 10. ASSESSMENT OF ENVIRONMENTAL EFFECTS

Full test reports on the ecotoxicity studies for the notified chemical were provided by the notifier.

<i>Test</i>	<i>Species</i>	<i>Results</i>
Acute Toxicity	Zebra Fish <i>Brachydanio rerio</i>	LC <sub>50</sub> could not be calculated NOEC (96 h) = 4.55 mg/L
Acute Immobilisation	Water Flea <i>Daphnia magna</i>	EC <sub>50</sub> could not be calculated NOEC (48 h) = 4.42 mg/L
Growth Inhibition [OECD 201]	Algae <i>Selenastrum capricornutum</i>	E <sub>r</sub> B <sub>50</sub> (96 h) > 6.8 mg/L E <sub>b</sub> B <sub>50</sub> (96 h) = 5.9 mg/L NOEC (96 h) = 2.4 mg/L

\* NOEC - no observable effect concentration

The ecotoxicity tests were performed on the Water Accommodated Fraction (WAF) of the notified chemical. The WAFs were prepared by adding an excess of the notified chemical to water and stirring the resulting solution for 20 hours. The mixture was then allowed to stand for 4 hours after which the medium was drawn off.

The tests on fish were performed using a semi-static methodology in which test preparations were renewed daily to ensure that concentrations of test material were maintained near nominal and to prevent the accumulation of nitrogenous wastes (TNO, 1997g). Observations were performed at 0, 3, 24, 48, 72 and 96 hours. The test was performed using ten specimen fish per loading rate at a temperature of 24°C. The aqueous solubility of the notified chemical in the test was determined to be 8.12 mg/L. The tests were conducted at 0, 10, 18, 32, 56 and 100 volume percent WAF. The results of the definitive study showed that no mortalities were observed at any test concentration. At 100 volume percent WAF, fish showed slow disturbed

swimming behaviour. A LC<sub>50</sub> value could not be calculated because no mortality was experienced during the period of the test. The 96 hr NOEC for the notified chemical to *Brachydanio rerio* is 4.55 mg/L.

The immobilisation test with *Daphnia magna* was performed under static conditions with observations performed at 24 and 48 hours (TNO, 1997i). The test was performed in quadruplicate using 5 daphnids per flask at a temperature of 21°C. The aqueous solubility of the notified chemical in the test was determined to be 8.66 mg/L. The tests were conducted at 0, 10, 18, 32, 56 and 100 volume percent WAF. After 48 h, no immobilised daphnids were observed in any of the test vessels. However, the mortality of one daphnid was observed in the control, 18, 56 and 100 volume percent WAF. These deaths were not statistically significant and were not attributed to the toxicity of the test chemical. Although all daphnids were mobile according to the definition given in the OECD TG 202, at 100 volume percent WAF, the daphnids swam slower and with irregular movements suggesting the test substance may exhibit some chronic toxicity. A LC<sub>50</sub> value could not be calculated because no mortality was experienced during the test period that could be attributed to the toxicity of the test chemical. The 48 hr NOEL for the notified chemical to *Daphnia magna* is 4.42 mg/L.

In the algal growth test, concentrations of 0, 1, 3.2 and 10 mg/L of the test substance were prepared with the aid of dimethyl sulfoxide (DMSO), and water accommodated fractions (WAF) were prepared at nominal concentrations of 0, 18.7, 31.9, 56.5 and 102 mg/L (TNO, 1997f). Algae were exposed to the test substance at a concentration of 0, 1, 3.2, 10, 18.7, 31.9, 56.5 and 102 mg/L for 96 h at 24°C under constant illumination and shaking (TNO 1997f). Six replicate test flasks were prepared for the test substance and two controls. No abnormalities were detected in any of the replicate test samples. The growth rate of *Selenastrum capricornutum* was significantly affected by the test substance, giving a 96 h ErC<sub>50</sub> of greater than 6.8 mg/L and NOEC of 2.4 mg/L. Analysis of the WAF after 96 h showed a measured concentration of 6.82 mg/L.

The ecotoxicity data indicates the notified chemical is moderately toxic to algae up to the limit of its water solubility, but appears to be less toxic to fish and daphnia, based on measured concentrations.

## 11. ASSESSMENT OF ENVIRONMENTAL HAZARD

The majority of the notified chemical will share the fate of the polypropylene products in which it is bound. The notifier indicates that the notified chemical is bound within the polymer matrix during the polypropylene production process. Once incorporated into the polypropylene matrix the notified chemical poses little risk to the environment.

Polypropylene products containing the notified chemical will be disposed of in landfill or incinerated, as to will wastes from spills during manufacture. In landfill, based on the low water solubility and estimated K<sub>oc</sub> of the notified chemical, it will associate with the soil matrix and is not expected to leach into the aquatic environment. The incineration of polypropylene products containing the notified chemical would yield water vapour and oxides of carbon.

The ecotoxicity data indicates the notified chemical is moderately toxic to algae up to the limit of its water solubility, but appears to be less toxic to fish and daphnia, based on

measured concentrations. However, exposure of the notified chemical to the aquatic compartment should be low.

The polymer is not expected to cross biological membranes due to its low water solubility and should not bioaccumulate (Connell, 1990).

Given the above considerations, the overall environmental risk is expected to be low.

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

### *Hazard Assessment*

The notified chemical was of low toxicity in rats by the dermal and oral routes, and was at most a slight irritant to rabbit skin and eyes. It was not sensitising to the skin of guinea pigs. In a 28-day feeding study in rats, the NOEL was established to be 253 mg/kg bw/day for males and 266 mg/kg bw/day for females.

A number of in vitro and in vivo mutagenicity tests were performed using the notified chemical. In an in vitro chromosome aberration study, clear and significant increases in the incidence of chromosome aberrations were seen in the presence of metabolic activation. The remainder of the tests gave results indicating that the notified chemical was not genotoxic under the conditions of the test.

The notified chemical would not be classified as a hazardous substance in accordance with the Approved Criteria based on the results of the toxicological studies submitted. The notified chemical has structural alerts giving rise to potential concerns about genotoxicity. Based on the clear positive result in one of genotoxicity studies submitted by the notifier, it is recommended that strict precautions be taken to avoid dermal or other contact with the notified chemical.

### *Occupational Health and Safety*

The notified chemical will be imported as part of a formulated catalyst slurry for the preparation of polypropylene. The slurry is a hazardous substance and a dangerous good, primarily due to the presence of titanium tetrachloride, which is corrosive and produces hazardous fumes of hydrogen chloride on contact with moist air (NOHSC, 1999b).

Due to the air-sensitivity of the catalyst slurry, and the health hazards associated with exposure of the slurry to air, use of the notified chemical involves transfer under nitrogen, minimising the risk of worker exposure. The enclosed process minimises the risk of spills of the notified chemical, however there is the possibility of drips of decomposed catalyst mixture, containing the notified chemical at around 20 %, near the transfer hose connections. Protection including overalls, impervious gloves, eye goggles and safety boots should be used where contact with the notified chemical is possible.

During polypropylene manufacture, the notified chemical is incorporated in the polymer matrix at very low levels, and is completely consumed. Negligible risk is expected for workers handling the finished polypropylene.

### *Public Health*

Since the notified chemical is consumed in the industrial process for which it is intended, the only likely method of public exposure to the notified chemical is through transport or industrial accidents. Such contact is most unlikely. If contact occurs it is most likely to be dermal, infrequent and transient. The low likelihood of contact and the toxicological profile of the notified chemical suggest that it will not pose a significant hazard to public health when used as proposed.

### 13. RECOMMENDATIONS

#### *Regulatory controls*

- Use the following safety phrases for the notified chemical:
  - S24: Avoid contact with skin
  - S36/37: Wear suitable protective clothing and gloves

#### *Control Measures*

##### Occupational Health and Safety

- Employers should implement the following isolation and engineering controls to minimise occupational exposure to the notified chemical in the product Catalyst MC:
  - The product should be used only in enclosed systems
- Employers should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical:
  - Overalls, impervious gloves, eye goggles and safety boots

Guidance in selection of personal protective equipment can be obtained from Australian, Australian/New Zealand or other approved standards.

- A copy of the MSDS should be easily accessible to employees.
- As the product containing the notified chemical is classified as hazardous to health in accordance with the NOHSC *Approved Criteria for Classifying Hazardous Substances*, workplace practices and control procedures consistent with provisions of State and Territory hazardous substances legislation must be in operation.

#### 13.1 Secondary notification

The Director of Chemicals Notification and Assessment must be notified in writing within 28 days by the notifier, other importer or manufacturer:

- (1) Under Section 64(2) of the Act:
- if any of the circumstances listed in the subsection arise.

The Director will then decide whether secondary notification is required.

No additional secondary notification conditions are stipulated.

## 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. REFERENCES

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TNO (1996b) In vivo/in vitro DNA-repair/Unscheduled DNA-synthesis Test with [notified chemical] in Hepatocytes from Rats, Project No. V96.687, TNO Nutrition and Food Research Institute, Zeist, The Netherlands. (unpublished report)

TNO (1996c) Micronucleus Test with [notified chemical] in Mice, Project No. V95.773, TNO Nutrition and Food Research Institute, Zeist, The Netherlands. (unpublished report)

TNO (1997a) Acute Dermal Irritation/Corrosion Study with [notified chemical] in Albino Rabbits, Project No. V97.067, TNO Nutrition and Food Research Institute, Zeist, The Netherlands. (unpublished report)

TNO (1997b) Acute Dermal Toxicity Study (Limit Study) with [notified chemical] in Rats, Project No. V97.066, TNO Nutrition and Food Research Institute, Zeist, The Netherlands. (unpublished report)

TNO (1997c) Acute Eye Irritation/Corrosion Study with [notified chemical] in Albino Rabbits (Including an ex vivo Prescreen), Project No. V97.068, TNO Nutrition and Food Research Institute, Zeist, The Netherlands. (unpublished report)

TNO (1997d) Acute Oral Toxicity Study (Limit Study) with [notified chemical] in Rats, Project No. V97.065, TNO Nutrition and Food Research Institute, Zeist, The Netherlands. (unpublished report)

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TNO (1997h) Sensitisation Study with [notified chemical] in Guinea Pigs (Maximisation Test), Project No. V97.069, TNO Nutrition and Food Research Institute, Zeist, The Netherlands. (unpublished report)

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## Attachment 1

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

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

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

### ***CORNEA***

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

### ***CONJUNCTIVAE***

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

### ***IRIS***

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

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