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NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

Chemical in Hydraulan Dot 4

This Assessment has been compiled in accordance with the provisions of the *Industrial Chemicals (Notification and Assessment) Act 1989* (Cwlth) (the Act) and Regulations. This legislation is an Act of the Commonwealth of Australia. The National Industrial Chemicals Notification and Assessment Scheme (NICNAS) is administered by the Department of Health, and conducts the risk assessment for public health and occupational health and safety. The assessment of environmental risk is conducted by the Department of the Environment.

For the purposes of subsection 78(1) of the Act, this Public Report may be inspected at our NICNAS office by appointment only at Level 7, 260 Elizabeth Street, Surry Hills NSW 2010.

This Public Report is also available for viewing and downloading from the NICNAS website or available on request, free of charge, by contacting NICNAS. For requests and enquiries please contact the NICNAS Administration Coordinator at:

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Director
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SUMMARY

The following details will be published in the NICNAS *Chemical Gazette:*

ASSESSMENT REFERENCE	APPLICANT(S)	CHEMICAL OR TRADE NAME	HAZARDOUS CHEMICAL	INTRODUCTION VOLUME	USE
STD/1496	BASF Australia Limited	Chemical in Hydraulan Dot 4	ND*	≤ 1000 tonnes per annum	Component of brake fluid

*ND = not determined

CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard classification
Based on the available information, the notified chemical is not recommended for classification according to the *Globally Harmonised System for the Classification and Labelling of Chemicals* (GHS), as adopted for industrial chemicals in Australia, or the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004).

Human health risk assessment
Under the conditions of the occupational settings described, the notified chemical is not considered to pose an unreasonable risk to the health of workers.

When used in the proposed manner, the notified chemical is not considered to pose an unreasonable risk to public health.

Environmental risk assessment
On the basis of the assessed use pattern, the notified chemical is not considered to pose an unreasonable risk to the environment.

Recommendations

CONTROL MEASURES

Occupational Health and Safety

- A person conducting a business or undertaking at a workplace should implement the following safe work practices to minimise occupational exposure to the notified chemical:
  - Avoid eye contact

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

- A copy of the (M)SDS should be easily accessible to employees.

- If products and mixtures containing the notified chemical are classified as hazardous to health in accordance with the *Globally Harmonised System for the Classification and Labelling of Chemicals (GHS)* as adopted for industrial chemicals in Australia, workplace practices and control procedures consistent with provisions of State and Territory hazardous substances legislation should be in operation.

Disposal

- The notified chemical should be disposed of in accordance with local regulations for recycling, re-use or recovery of calorific content.

Emergency procedures

- Spills or accidental release of the notified chemical should be handled by physical containment, collection and subsequent safe disposal.

Regulatory Obligations

Secondary Notification
This risk assessment is based on the information available at the time of notification. The Director may call for the reassessment of the chemical under secondary notification provisions based on changes in certain circumstances. Under Section 64 of the *Industrial Chemicals (Notification and Assessment) Act (1989)* the notifier, as well as any other importer or manufacturer of the notified chemical, have post-assessment regulatory obligations to notify NICNAS when any of these circumstances change. These obligations apply even when the notified chemical is listed on the Australian Inventory of Chemical Substances (AICS).

Therefore, the Director of NICNAS must be notified in writing within 28 days by the notifier, other importer or manufacturer:

(1) Under Section 64(2) of the Act; if
- the function or use of the chemical has changed from a component of brake fluid, or is likely to change significantly;
- the amount of chemical being introduced has increased, or is likely to increase, significantly;
- the chemical has begun to be manufactured in Australia;
- additional information has become available to the person as to an adverse effect of the chemical on occupational health and safety, public health, or the environment.

The Director will then decide whether a reassessment (i.e. a secondary notification and assessment) is required.

(Material) Safety Data Sheet
The (M)SDS of the product containing the notified chemical provided by the notifier was reviewed by NICNAS. The accuracy of the information on the (M)SDS remains the responsibility of the applicant.

ASSESSMENT DETAILS

This notification has been conducted under the cooperative arrangement with Canada. The health and environmental hazard assessment components of the Canadian report were provided to NICNAS and, where appropriate, used in this assessment report. The other elements of the risk assessment and recommendations on safe use of the notified chemical were carried out by NICNAS and the Department of the Environment.

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
BASF Australia Limited (ABN: 62 008 437 867)
Level 12
28 Freshwater Place
SOUTHBANK VIC 3006

NOTIFICATION CATEGORY
Standard: Chemical other than polymer (more than 1 tonne per year) – Comparable agency modular assessment.

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
Data items and details claimed exempt from publication: chemical name, other names, CAS number, molecular and structural formulae, molecular weight, analytical data, degree of purity, impurities, use details, import volume and identity of manufacturer/recipients.

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed as follows: partition coefficient, dissociation constant, adsorption/desorption, flash point, flammability, autoignition temperature, explosive properties, oxidising properties, acute dermal toxicity, acute inhalation toxicity, skin irritation, eye irritation, skin sensitisation, and chromosome damage *in vitro*.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
Canada (1999)
EU (2010)

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
Hydraulan Dot 4 (contains 40-65% notified chemical)

MOLECULAR WEIGHT
< 600 Da

ANALYTICAL DATA
Reference NMR, IR, and UV-VIS spectra were provided.

3. COMPOSITION

DEGREE OF PURITY
> 95%

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: Light yellow, clear liquid

Property	Value	Data Source/Justification
Melting Point	< -55 °C	Measured (OECD TG 102)
Boiling Point	361 °C (dec)	Measured (OECD TG 103)

Density	1070 kg/m^3	Measured (92/69/EEC, pycnometer)
Vapour Pressure	0.12 kPa at 20 °C 0.41 kPa at 50 °C	Measured (92/69/EEC, static method)
Water Solubility	100% at 20 °C	Observed. Highly soluble according to the notifier. This is consistent with predominantly hydrophilic chemical structure.
Hydrolysis as a Function of pH	Spontaneous at pH 1.2, 4.1, 7.1 and 8.9 at ambient temperature	Measured (OECD TG 111)
Partition Coefficient (n-octanol/water)	Not determined	The notified chemical is anticipated to undergo rapid and complete hydrolysis within minutes.
Adsorption/Desorption	Not determined	The notified chemical is anticipated to undergo rapid and complete hydrolysis within minutes.
Dissociation Constant	Not determined	Does not contain dissociable functionalities.
Flash Point	146 °C at 101.3 kPa	BASF 2010
Flammability	Not determined	Not expected to be flammable based on flash point
Autoignition Temperature	310 ± 5 °C at 101.3 kPa	BASF 2010
Explosive Properties	Not determined	Contains no functional groups that would imply explosive properties
Oxidising Properties	Not determined	Contains no functional groups that would imply oxidising properties

DISCUSSION OF PROPERTIES

Reactivity
The notified chemical is expected to be stable under normal conditions of use; however, it is subject to spontaneous hydrolysis in the presence of water.

Physical hazard classification
Based on the submitted physico-chemical data depicted in the above table, the notified chemical is not recommended for hazard classification according to the *Globally Harmonised System for the Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia.

5. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
The notified chemical will be imported into Australia as a component of finished brake fluid at a concentration of ≤ 65%.

MAXIMUM INTRODUCTION VOLUME OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS

Year	*1*	*2*	*3*	*4*	*5*
Tonnes	100-1000	100-1000	100-1000	100-1000	100-1000

PORT OF ENTRY
Melbourne, Sydney, Brisbane, Perth, Adelaide and Hobart

TRANSPORTATION AND PACKAGING
The notified chemical will be imported into Australia as a major component of finished brake fluid by ship in small packages (< 1 L), in 10 L - 1000 L intermediate bulk containers or in bulk. The products will be transported from the dockside to the approved chemical warehouses and logistics facilities or directly to end-users' sites.

USE
The notified chemical will be used as a component of finished brake fluid formulations at ≤ 65% concentration.

OPERATION DESCRIPTION
The notified chemical will be imported as a component of finished brake fluids at ≤ 65% concentration. Repackaging of the finished products into smaller containers for the after-care market (vehicle service stations or private individuals) will also take place.

Repackaging
Repackaging from bulk containers to smaller containers will be undertaken using dedicated packing lines. This process will be automated and operators will attach and detach suction nozzles that pump the brake fluid directly into the filling line or into header tanks.

End-use
The brake fluids containing the notified chemical at ≤ 65% concentration will be used in car manufacturing to fill brake fluid reservoirs on new cars. This is a one person operation where hoses are connected to a drum and fluid pumped via an automated system.

At vehicle service stations or with private users, brake fluid reservoirs will be refilled manually by pouring from a container. During routine service, brake or clutch repair, fluid in the entire system may be replaced.

6. HUMAN HEALTH IMPLICATIONS

6.1. Exposure Assessment

6.1.1. Occupational Exposure

CATEGORY OF WORKERS

Category of Worker	*Exposure Duration (hours/day)*	*Exposure Frequency (days/year)*
Packaging operators	2-3	< 10
New vehicle production personnel	2-4	< 100
Service station/private users	1	< 50

EXPOSURE DETAILS
Transport and storage workers may come into contact with the notified chemical as a component of finished brake fluids (at ≤ 65% concentration) only in the event of accidental rupture of containers.

Repackaging
Repackaging will be largely automated; however, workers may be exposed (dermal and ocular) to the notified chemical (at ≤ 65% concentration) when manually connecting and disconnecting suction nozzles that pump the brake fluid either directly into the filling line or into header tanks. Dermal and ocular exposure should be mitigated through the stated use by the notifier of personal protective equipment (PPE) including gloves, goggles and protective clothing.

New vehicle production
Addition of brake fluids to reservoirs during new vehicle production will be largely automated; however, workers may be exposed (dermal and ocular) to the notified chemical (at ≤ 65% concentration) during manually connecting hoses to the container. Dermal and ocular exposure should be mitigated through the stated use by the notifier of personal protective equipment (PPE) including gloves, goggles and protective clothing.

Automotive services
Workers may be exposed to the notified chemical (at ≤ 65% concentration) during servicing of automotive brake systems and other hydraulic parts, both during topping up of hydraulic fluids and during servicing of the lines containing the fluid. The conditions of exposure in automotive service centres will vary, and it is not likely that appropriate personal protective equipment (PPE) will be used in all (or, indeed, most) cases. Therefore, it is expected there will be widespread and regular dermal exposure of workers to the notified chemical. Secondary ocular exposure, from contact with material on the hands, is also possible; direct ocular exposure may also occur.

6.1.2. Public Exposure

Public exposure to the notified chemical (at ≤ 65% concentration) is expected to be almost completely restricted to DIY users who conduct automobile maintenance. The more common exposure scenario is expected to be dermal contact with drips and spills while topping up hydraulic fluids, but there may be more extensive dermal and ocular exposure during servicing of hydraulic parts. With regards to occupational exposure during vehicle servicing, the use of personal protective equipment is expected to be variable; however, the frequency of exposure is expected to be much lower for members of the public than for automotive service workers.

6.2. Human Health Effects Assessment

The results from toxicological investigations conducted on the notified chemical and products containing the notified chemical are summarised in the following table. Full study reports were only provided for the following endpoints: bacterial reverse mutation, repeated dose oral toxicity and prenatal developmental toxicity. For full details of these studies, refer to Appendix B. For all other endpoints only study summaries were provided (BASF, 2010).

Endpoint	*Result and Assessment Conclusion*
Rat, acute oral toxicity	LD50 > 10,000 mg/kg bw; low toxicity
Rat, acute dermal toxicity	LD50 > 2000 mg/kg bw; low toxicity
Rabbit, skin irritation	non-irritating
Rabbit, eye irritation	slightly irritating
Guinea pig, skin sensitisation – adjuvant test*	no evidence of sensitisation
Rat, repeat dose oral toxicity – 90 days.	NOAEL = 1000 mg/kg bw/day
Mutagenicity – bacterial reverse mutation	non mutagenic
Genotoxicity – in vitro chromosome aberration	non genotoxic
Rat, oral prenatal developmental toxicity	NOEL = 1000 mg/kg bw/day

* data on products containing the notified chemical

Toxicokinetics.

The notified chemical has a relatively low molecular weight (< 600 Da), hence there is potential for absorption across biological membranes. However, given the expected high water solubility and low partition coefficient (log Pow = -4.37 at 20 °C (calculated Epi Suite v.4.0)), dermal absorption is expected to be limited

Acute toxicity.

In an acute oral toxicity study for the notified chemical, ten rats (five per sex) were administered the notified chemical by gavage. Treated animals were observed for 7 days and then sacrificed for gross pathology. Clinical signs of toxicity observed were dyspnea, slight apathy, staggering and slight exsiccosis. At necropsy, acute dilatation of the heart with passive hyperaemia was noted. In the top dose, 1 male and 1 female rat died. The LD50 value was estimated to be > 10,000 mg/kg bw, indicating low acute oral toxicity in the rats (Canadian assessment report).

Another acute oral toxicity study for the notified chemical also yielded an LD50 greater than 2000 mg/kg bw in both male and female rates (BASF, 2010).

In an acute dermal toxicity study, a group of ten (five per sex) rats was given a single, 24-hour, semi-occluded dermal application of the test substance to intact skin at the limit dose of 2000 mg/kg bw. There were no signs of dermal irritation, deaths, clinical observations or signs of systemic toxicity. All animals showed expected gains in body weight and no abnormalities were detected at necropsy (BASF, 2010).

No acute inhalation toxicity data was provided. Inhalation exposure is unlikely based on the low vapour pressure of the notified chemical (0.12 kPa at 20 °C).

Irritation and sensitisation.

In a skin irritation study conducted on rabbits, the notified chemical was found to be non-irritating (BASF, 2010).

In an eye irritation study conducted on rabbits, the notified chemical was found to be slightly irritating (BASF, 2010). Slight conjunctival irritation was observed which cleared within 3 days.

There are no sensitisation studies available for the notified chemical. However, a guinea pig maximisation study was performed on a brake fluid formulation containing the notified chemical at 37% concentration (BASF,

2010). The animals (two per sex) received 0.6% in water and undiluted test substance for intradermal and topical induction, respectively. Challenge was conducted using a 60% solution of the test substance. No animals showed a positive response at either 24 or 48 h after removal of the challenge patch.

In another guinea pig maximisation test, 20 animals (ten per sex) were treated with a brake fluid containing 37% notified chemical (BASF 2010). The animals received 5% in water and undiluted test substance for intradermal and topical induction, respectively. Challenge was conducted using a 60% solution of the test substance. No signs of sensitisation or irritation were observed during the study.

The results of the studies are consistent with the absence of structural alerts for sensitisation for the notified chemical.

Repeated dose toxicity.
In a 90-day repeated dose oral toxicity study in rats the No Observed Adverse Effect Level (NOAEL) for the notified chemical was established as 1000 mg/kg bw/day based on no test-substance-related changes at any of the doses administered.

Mutagenicity/Genotoxicity.
In an *in vitro* mutagenicity study, *Salmonella* tester strains TA98, TA100, TA1535 and TA1537 were treated with the notified chemical in the concentration range from 20-5000 μg/plate with and without metabolic activation. Both plate incorporation and pre-incubation methods were used. There were no significant increases in the revertant frequency in any of the tester strains at any concentration level with or without metabolic activation and all positive and negative controls yielded expected results (BASF, 2010).

The notified chemical did not induce any statistically significant increases in the frequency of cells with aberrations in a chromosome aberration study on human peripheral lymphocytes both in the presence and in the absence of metabolic activation (BASF, 2010).

Toxicity for reproduction.
In an oral prenatal developmental toxicity study in rats the No Observed Effect Level (NOEL) for the notified chemical was established as 1000 mg/kg bw/day, based on the absence of treatment-related effects at any of the doses administered.

Health hazard classification
Based on the available information, the notified chemical is not recommended for classification according to the *Globally Harmonised System for the Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia, or the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004).

6.3. Human Health Risk Characterisation

6.3.1. Occupational Health and Safety
The greatest risk posed by the notified chemical is as a slight eye irritant. Workers most at risk of eye irritating effects will be those in automotive service centres when handling products containing the notified chemical at < 95% concentration that do not use PPE during vehicle servicing. However, the potential for accidental ocular exposure should be infrequent.

Based on the low hazardous nature of the notified chemical, the risk to workers is not considered unreasonable.

6.3.2. Public Health
The public may be at risk of slight eye irritating effects while servicing their own vehicles with products containing the notified chemical at up to 65% concentration through accidental ocular exposure. However, given the infrequent use of the products containing the notified chemical by the public and the low severity of eye irritation effects, the risk to the general public is not considered to be unreasonable.

7. ENVIRONMENTAL IMPLICATIONS

7.1. Environmental Exposure & Fate Assessment

7.1.1. Environmental Exposure

RELEASE OF CHEMICAL AT SITE

The notified chemical will be imported into Australia as a component of finished brake fluid. Environmental release of the notified chemical during importation, storage and transportation is not expected except in the event of accidental spills or leaks. Spills or leaks of a drum is expected to be collected with inert material and disposed of to landfill.

The brake fluid products may be repackaged in Australia. To contain spills at the repackaging site, bunding is in place in all tank/drum areas, where collection of process spills occurs in onsite collection pits. Spilled material is not expected to be significant and will be either collected by licensed disposal firms or consigned to trade waste sewer under licence.

The 200 L drums when emptied will be sent to a drum recycler. The residues in the empty containers are estimated to be up to 1000 kg per annum and are expected to be consigned to sewer from the cleaning/recycling process.

RELEASE OF CHEMICAL FROM USE

During end use, release of the notified chemical contained in the brake fluid may occur mainly through leakages from the hydraulic systems in vehicles, accidental spills during brake fluid changes, and during disposal of used fluids following renewal. The notifier anticipates that users of the brake fluid formulation will include 70% professional after-care, 20% private after-care, 10% new car manufacturers. The notifier has provided the following estimates of releases for each of these usage patterns:

(a) Professional after-care

Residues in drums, 30% of (70% of 1000 t) with 0.1% residues = 210 kg/annum

Residues in small packaging, 40% of (70% of 1000 t) with 0.1% residues = 280 kg/annum

Spills and leaks, <0.1% of (70% of 1000 t) = 700 kg/annum

(b) Private after-care

Residues in small packaging, 20% of 1000 t with <0.1% residues = 200 kg/annum

Spills and leaks, <0.1% of (20% of 1000 t) = 200 kg/annum

(c) New car manufacturers

Residues in drums, 10% of 1000 t with 0.1% residues = 100 kg/annum

The combined annual total of waste is approximately 1700 kg notified chemical. Car manufacturers recommend draining and refilling of brake fluid systems every two years. It is expected that most brake fluid removed from the reservoirs in vehicles at motor garages will be collected and will be sent for oil recycling.

RELEASE OF CHEMICAL FROM DISPOSAL

Material spilled during repackaging will be either collected by licensed disposal firms or consigned to trade waste sewer under licence, while residues from the cleaning and drum recycling process are consigned to sewer under licence.

Residues of the brake fluid in empty containers in non-industrial locations are expected to be discarded with domestic garbage and disposed of to licensed landfill sites. Used brake fluid remaining after oil changes is likely to be recycled. The SDS recommends disposal in accordance with government regulations for the disposal of special waste, which may include oil recycling or reuse of the calorific value.

7.1.2. Environmental Fate

The notified chemical is expected to be readily biodegradable. For the details of the environmental fate study, please refer to Appendix C. The notified chemical is also expected to hydrolyse rapidly. Since the components of the brake fluid are hygroscopic, it is likely that water would become absorbed during normal usage of the formulations containing the notified chemical, and consequently it is likely that some of the notified chemical will hydrolyse to boric acid and neutral organic chemicals to undergo further biodegradation.

A bioaccumulation study was not provided. The notified chemical is not expected to bioaccumulate given its high water solubility and low predicted log P_{OW}.

Most of the notified chemical is expected to be used as a component in the brake fluid, which may be recycled or reused for the calorific value. The associated notified chemical is expected to be either thermally decomposed during the recycling or to be reused for the calorific value as a component of the reused oil. In either case, the notified chemical is expected to be decomposed into water, oxides of carbon and boron.

A small amount of the notified chemical may also be sent to landfill as residues in empty containers. In landfill, the notified chemical may have potential to leach into public water due to the high water solubility. In water, the notified chemical is expected to hydrolyse rapidly followed with further degradation.

The notified chemical is expected to be released to sewer as residues from container cleaning and recycling, and spills from repackaging. Given the high water solubility, the notified chemical is expected to remain in the effluent water of the sewage treatment plants. In water, the notified chemical is expected to hydrolyse rapidly followed with further degradation. In public water or landfill, the notified chemical is expected to undergo abiotic and biotic degradation processes, forming water, oxides of carbon and boron.

7.1.3. Predicted Environmental Concentration (PEC)

Up to 1700 kg notified chemical may be released to the sewer from residue cleaning and spills, which is not considered to be significant as it will be released to sewer throughout Australia. The notified chemical is readily biodegradable and hydrolysed rapidly; hence, it is not persistent in the aquatic environment. The notified chemical is expected to dissipate quickly via hydrolysis in water. In addition, the notified chemical is considered to be of low concern to aquatic organisms as shown below. Therefore, the calculation of Predicted Environmental Concentration (PEC) is not considered to be necessary.

7.2. Environmental Effects Assessment

The notifier provided the following endpoints for effects of the notified chemical on aquatic organisms (BASF, 2010, for fish, daphnia, algae and Appendix C; microbial activity).

Endpoint	*Result*	*Assessment Conclusion*
Fish Toxicity (96 h)	EC50 > 222.2 mg/L	Not harmful to fish
Daphnia Toxicity (48 h)	EC50 > 211.2 mg/L	Not harmful to aquatic invertebrates
Algal Toxicity (72 h)	EC50 > 224.4 mg/L	Not harmful to alga
Inhibition of Bacterial Respiration (30 min)	EC50 > 1000 mg/L	Not expected to be inhibitory to microbial activity

Under the Globally Harmonised System of Classification and Labelling of Chemicals (GHS; United Nations, 2009) the notified chemical is considered not to be acutely harmful to fish, aquatic invertebrate, and algae. Based on the toxicity to aquatic organisms the notified chemical has not been formally classified for acute toxicity and long-term hazard.

7.2.1. Predicted No-Effect Concentration

The Predicted No-Effect Concentration (PNEC) has not been calculated given no PEC was calculated and the expected low concern of the chemical to aquatic organisms.

7.3. Environmental Risk Assessment

The Risk Quotient (PEC/PNEC) has not been calculated since no PEC or PNEC was available. The potential for rapid hydrolysis and the ecotoxicity data of the notified chemical indicate that it is unlikely to reach ecotoxicologically significant concentrations in the aquatic system based on its proposed use pattern. The notified chemical is expected to have a low potential for bioaccumulation. Therefore, on the basis of the assessed use pattern in brake fluid products, the notified chemical is not expected to pose an unreasonable risk to the environment.

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Genotoxicity – bacteria

Test Substance	Notified chemical
Method	Similar to OECD TG 471 Bacterial Reverse Mutation Test. Plate incorporation procedure (Test 1)/Pre incubation procedure (Test 2)
Species/Strain	*S. typhimurium*: TA1535, TA1537, TA98, TA100
Metabolic Activation System	S9 fraction from Aroclor 1254 rat liver
Concentration Range in Main Test	a) With metabolic activation: 20-5000 µg/plate b) Without metabolic activation: 20-5000 µg/plate
Vehicle	Distilled water
Remarks - Method	A preliminary toxicity test was not conducted. An *E.coli* strain was not included in the study.

Results

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:* *Cytotoxicity in Preliminary Test*	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	-	> 5000	> 5000	negative
Test 2	-	> 5000	> 5000	negative
Present				
Test 1	-	> 5000	> 5000	negative
Test 2	-	> 5000	> 5000	negative

Remarks - Results	The test substance was tested up to the maximum recommended dose level of 5000 µg/plate. No toxicologically significant increases in the frequency of revertant colonies were recorded for any of the bacterial strains, with any dose of the test substance, either with or without metabolic activation. All the positive control chemicals used in the test induced marked increases in the frequency of revertant colonies thus confirming the activity of the S9-mix and the sensitivity of the bacterial strains.
Conclusion	The notified chemical was not mutagenic to bacteria under the conditions of the test.
TEST FACILITY	BASF (1989)

B.2. Repeat dose toxicity

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 408 Repeated Dose 90-Day Oral Toxicity Study in Rodents. EC Directive 88/302/EEC B.26 Sub-Chronic Oral Toxicity Test: 90-Day Repeated Oral Dose Study using Rodent Species.
Species/Strain	Rat/Wistar Han:RccHan:WIST
Route of Administration	Oral – gavage
Exposure Information	Total exposure days: 90 days Dose regimen: 7 days per week
Vehicle	Ethanol, 2-[2-(2-methoxyethoxy)ethoxy]-
Remarks - Method	No significant protocol deviations

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
control	10 per sex	0	0
low dose	10 per sex	10	0
mid dose	10 per sex	100	0
high dose	10 per sex	1000	0

Mortality and Time to Death
No test substance related deaths occurred during the study.

Clinical Observations
No clinical signs of toxicity were noted in the treated animals.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis
No toxicologically significant effects were noted in the haematological and blood chemical parameters in the treated animals.

Effects in Organs
No toxicologically significant effects were detected in the necropsy, histopathology or organ weights in the treated animals.

CONCLUSION
The No Observed Adverse Effect Level (NOAEL) was established as 1000 mg/kg bw/day in this study, based on the absence of treatment-related toxicological significant effects at any of the doses administered.

TEST FACILITY Harlan (2013a)

B.3. Developmental toxicity

TEST SUBSTANCE Notified chemical

METHOD OECD TG 414 Prenatal Developmental Toxicity Study.

Species/Strain	Rat/Sprague-Dawley Crl:CD(SD) IGS BR
Route of Administration	Oral – gavage
Exposure Information	Exposure days: 15 days (Day 5 to Day 19 of gestation) Post-exposure observation period: None
Vehicle	Ethanol, 2-[2-(2-methoxyethoxy)ethoxy]-
Remarks - Method	The study was designed to evaluate the effects of the test item on embryonic and foetal development. Females were euthanized before delivery, on gestation Day 20. All animals were subjected to a full external and internal examination and any macroscopic abnormalities were recorded. The ovaries and uteri of pregnant animals were removed, examined and recoded with number of corpora lutea, number, position and type of intrauterine implantation, foetal sex, external foetal appearance, foetal weight, placental weight and gravid uterus weight. The dose level was determined based on the results of a previous toxicity study. In the previous study conducted by Harlan Laboratories Ltd (Project No. 41204722).

RESULTS

Group	*Number of Animals*	*Dose mg/kg bw/day*	*Mortality*
control	8	0	0
low dose	8	30	0
mid dose	8	300	0
high dose	8	1000	0

Mortality and Time to Death
All animals survived to the scheduled necropsies.

Effects on Dams
No signs of clinical toxicity were detected. No treatment related abnormalities were noted during the macroscopic examination of the pregnant animals at termination on Day 20 of gestation.

Effects on Foetus
No treatment-related effects were noted for foetuses in treated animals when compared to control animals.

CONCLUSION
The No Observed Effect Level (NOEL) was established as 1000 mg/kg bw/day in this study, based on the absence of treatment-related effects at any of the doses administered.

TEST FACILITY Harlan (2013b)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

C.1.1. Ready biodegradability

TEST SUBSTANCE: Notified chemical

METHOD: OECD TG 301 A Ready Biodegradability: DOC Die-Away Test.

Inoculum	Activated sludge
Exposure Period	22 days
Auxiliary Solvent	None reported
Analytical Monitoring	TOC Analysis
Remarks - Method	The test was conducted according to the guidelines above using good laboratory practice (GLP). No significant deviations from the test guidelines were reported.

RESULTS

Test substance		*Aniline*	
Day	*% Degradation*	*Day*	*% Degradation*
1	-7	1	-5
3	6	5	95
14	95	14	97
22	102	22	100

Remarks - Results	All validity criteria for the test were satisfied. The reference compound, aniline, reached the 70% pass level by day 5 indicating the suitability of the inoculum. The toxicity control exceeded 35% biodegradation within 14 days showing that toxicity was not a factor inhibiting the biodegradability of the test substance. The degree of degradation of the notified chemial after the cultivation period was 102% and it reached the pass level within the 10-day window. Therefore, the test substance is classified as readily biodegradable according to the OECD (301 A) guideline.

CONCLUSION: The notified chemical is readily biodegradable

TEST FACILITY: BASF (1999a)

C.2. Ecotoxicological Investigations

C.2.1. Inhibition of microbial activity

TEST SUBSTANCE: Notified chemical

METHOD: OECD TG 209 Activated Sludge, Respiration Inhibition Test.
EC Directive 88/302/EEC C.11 Biodegradation: Activated Sludge Respiration Inhibition Test

Inoculum	Activated sludge
Exposure Period	30 min
Concentration Range	Nominal: 1, 10, 100 mg/L Actual: Not measured
Remarks – Method	The test was conducted according to the guidelines above using good laboratory practice (GLP). No significant deviations from the test guidelines were reported.

RESULTS

EC50	> 1000 mg/L at 30 min
NOEC	≥ 1000 mg/L at 30 min
Remarks – Results	All validity criteria for the test were satisfied.

CONCLUSION	The notified chemical is not inhibitory to microorganisms
TEST FACILITY	BASF (1999b)

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