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NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

Alkane, ethoxy-methyl-

This Assessment has been compiled in accordance with the provisions of the *Industrial Chemicals (Notification and Assessment) Act 1989* (the Act) and Regulations. This legislation is an Act of the Commonwealth of Australia. The National Industrial Chemicals Notification and Assessment Scheme (NICNAS) is administered by the 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 Agriculture, Water and the Environment.

This Public Report is 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
NICNAS

TABLE OF CONTENTS

SUMMARY

The following details will be published on our website:

ASSESSMENT REFERENCE	APPLICANT(S)	CHEMICAL OR TRADE NAME	HAZARDOUS CHEMICAL	INTRODUCTION VOLUME	USE
STD/1719	Race Fuels Pty Ltd	Alkane, ethoxy-methyl-	Yes	< 100 tonnes per annum	Racing fuel additive

CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard Classification
Based on the available information, the notified chemical is a hazardous chemical according to the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia. The hazard classification applicable to the notified chemical/polymer is presented in the following table.

Hazard Classification	*Hazard Statement*
Flammable Liquids (Category 2)	H225 – Highly flammable liquid and vapour
Specific Target Organ Toxicity – Single Exposure (Category 2)	H371 - May cause damage to organs (neurotoxicity)(inhalation)

Human Health Risk Assessment
Provided that the recommended controls are being adhered to, 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
Based on the assessed use pattern the notified chemical is not considered to pose an unacceptable risk to the environment. However, if the notified chemical were to enter the aquatic compartment it may change the taste or odour of ground water.

The public assessment report will therefore be forwarded to the National Health and Medical Research Council (NHMRC) for consideration of any action if needed,

Recommendations

REGULATORY CONTROLS

Hazard Classification and Labelling

- The notified chemical should be classified as follows:
  - Flammable Liquids (Category 2): H225 – Highly flammable liquid and vapour
  - Specific Target Organ Toxicity – Single Exposure (Category 2): H371 - May cause damage to organs (neurotoxicity)(inhalation)

  The above classification should be used for products/mixtures containing the notified chemical, if applicable, based on the concentration of the notified chemical present.

Fuel Quality Standards

- The introducer of racing fuels containing the notified chemical should ensure that any requirements under the *Fuel Quality Standards Act 2000* are met.

CONTROL MEASURES

Occupational Health and Safety

- A person conducting a business or undertaking at a workplace should implement the following engineering controls to minimise occupational exposure to the notified chemical during repackaging:
  - Enclosed, automated processes, where possible
  - Local exhaust ventilation

- A person conducting a business or undertaking at a workplace should implement the following safe work practices to minimise occupational exposure during handling of the notified chemical when repackaging and refuelling automotive vehicles:
  - Avoid contact with skin and eyes
  - Avoid inhalation of vapours or mists
  - Avoid spills
  - Remove all sources of ignition
  - Clean up any spills promptly

- A person conducting a business or undertaking at a workplace should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical during repackaging and refuelling vehicles:
  - Respiratory protection if inhalation exposure may occur

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

- A copy of the 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 of 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.

Environment

- The introducer must comply with Federal, State and Territory regulations and guidelines for site assessment and measures to protect the environment during the operation of motorsport events.

- The introducer must manage any risk factors for:
  - Leaks or spills of chemicals or petroleum hydrocarbons from storage areas and mechanical servicing areas and on the race tracks
  - Contamination of stormwater runoffs
  - Inappropriate containment or disposal of solid waste and wastewater from mechanical servicing and washdown areas

- The Introducer must ensure that other risk management strategies deemed appropriate through site assessment or monitoring programs are put in place.

Transport and Packaging

- Due to the flammable properties of the notified chemical, transport of the chemical should be in accordance with the *Australian Code for the Transport of Dangerous Goods by Road and Rail* (ADG code) (NTC, 2018).

Storage

- The handling and storage of the notified chemical should be in accordance with the Safe Work Australia Code of Practice for *Managing Risks of Hazardous Chemicals in the Workplace* (SWA, 2012) or relevant State or Territory Code of Practice.

- Any relevant party involved in the transport or storage of the notified chemical should comply with Federal, State and Territory legislative frameworks, guidelines and regulations to minimise emission risks to the environment.

Emergency procedures

- Minor spills or accidental release of the notified chemical should be handled by absorbance with appropriate substrate and disposal in accordance with local government regulations. Major spills may need to be addressed through remediation programs determined through site assessments on a case by case basis.

Disposal

- Where reuse or recycling are not appropriate, dispose of the notified chemical in an environmentally sound manner in accordance with relevant Commonwealth, state, territory and local government legislation.

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(1) of the Act; if
- the final use concentration of the notified chemical exceeds 30% in racing fuels;
- fuels containing the notified chemical become available for the public;
- storage of fuels containing the notified chemical has changed, or is likely to change, to underground storage;

or

(2) Under Section 64(2) of the Act; if
- the function or use of the chemical has changed from a racing fuel additive, 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.

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

ASSESSMENT DETAILS

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Race Fuels Pty Ltd (ABN: 23 090 961 265)
37-41 Mark Anthony Drive
DANDENONG SOUTH VIC 3175

NOTIFICATION CATEGORY
Standard: Chemical other than polymer (more than 1 tonne per year)

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

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed for all physico-chemical, toxicological and ecotoxicological endpoints except for explosive properties and oxidising properties.

NOTIFICATION IN OTHER COUNTRIES
Canada (1998)
EU (2018)
Japan (2007)
New Zealand (2006)
South Korea (2014)
Taiwan (2015)
USA (2019)

2. IDENTITY OF CHEMICAL

MARKETING NAME
Alkane, ethoxy-methyl-

OTHER NAME
ELF RACE 102 (product containing < 30% notified chemical)

MOLECULAR WEIGHT
< 500 g/mol

ANALYTICAL DATA
Reference IR and MS spectra were provided.

3. COMPOSITION

DEGREE OF PURITY
< 90%

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: colourless liquid

Property	*Value*	*Data Source/Justification*
Melting Point/Freezing Point	-94 °C	Exempt Information 12
Boiling Point	73.1 °C	Exempt Information 12
Density	745 kg/m^3	Exempt Information 12
Vapour Pressure	1.28 ×10^{-1} kPa at 20 °C	Exempt Information 12
Water Solubility	12 g/L at 25 °C	SDS

Property	*Value*	*Data Source/Justification*
Hydrolysis as a Function of pH	$T_{1/2}$ (Hr) 107 at pH 5	Measured (Exempt Information 4)
Partition Coefficient (n-octanol/water)	log Pow = 1.48 – 1.56	SDS
Adsorption/Desorption	log K_{oc} = 1.57	SDS
Dissociation Constant	Not determined	No dissociable groups present
Flash Point	-19 °C	Exempt Information 7
Flammability	Upper: 6% (v/v) Lower: 1% (v/v)	Exempt Information 7
Autoignition Temperature	310 °C	Exempt Information 7
Explosive Properties	Predicted negative	Based on chemical structure
Oxidising Properties	Predicted negative	Based on chemical structure

DISCUSSION OF PROPERTIES
For details of tests on explosive and oxidising properties, refer to Appendix A.

Reactivity
The notified chemical is expected to be stable under normal conditions of use.

Physical Hazard Classification
Based on the submitted physico-chemical data depicted in the above table, the notified chemical is recommended for physical hazard classification according to the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia. The recommended hazard classification is presented in the following table.

Hazard Classification	*Hazard Statement*
Flammable Liquids (Category 2)	H225 – Highly flammable liquid and vapour

5. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
The notified chemical will not be manufactured in Australia. It will be imported into Australia in finished racing fuels (ELF RACE 102) at < 30% concentration.

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

Year	*1*	*2*	*3*	*4*	*5*
Tonnes	< 100	< 100	< 100	< 100	< 100

PORT OF ENTRY
Melbourne

TRANSPORTATION AND PACKAGING
The product containing the notified chemical at < 30% concentration will be imported by sea in 24,000 L ISO tanks. These containers will be transported by road to the notifier's warehouse for repackaging into 200 L steel drums. Further repackaging from the 200 L steel drums into 50 L and 20 L steel drums may also occur. The repackaged products will be transported by road to motorsports racing events or to the warehouses of distributors.

USE
The notified chemical will be used as an additive in racing fuels at < 30% concentration.

OPERATION DESCRIPTION
The notified chemical will not be manufactured in Australia. It will be imported into Australia as a component of finished racing fuels at < 30% concentration for repackaging.

Repackaging
Repackaging from the 24,000 L ISO tank into 200 L, 50 L and 20 L steel drums will be carried out using a metered sealed pump that has been manually connected to the ISO tank. Steel drums containing the repackaged product will be sealed using a non-sparking wrench.

End-use
The product containing the notified chemical will be added into racing vehicle using a metered sealed pump that has been manually connected to the repackaged steel drum.

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)*
Stevedores	3	10-15
Transport and storage workers	4-6	260
Repackaging operators	6	260
End-use operators	6	260

EXPOSURE DETAILS

Transport and Storage
Transport and storage workers may come into contact with the notified chemical as an additive in racing fuels only in the unlikely event of accidental rupture of containers.

Repackaging
During repackaging, dermal, ocular and inhalation exposure of workers to the notified chemical (at < 30% concentration) may occur during connecting and disconnecting of pump and cleaning and maintenance of equipment. The notifier states that exposure is expected to be minimised through the use of personal protective equipment (PPE) such as protective clothing, gloves, safety glasses and respiratory protection where appropriate.

End-use
Dermal, ocular and inhalation exposure of personnel from the national and regional motorsports racing teams may be exposed to the notified chemical (at < 30% concentration) during connecting and disconnecting of pump and refuelling of the racing vehicle during motorsports racing events. Dermal, ocular and inhalation exposure of workers to the notified chemical may also occur during routine cleaning and maintenance of equipment and vehicles. The notifier states that exposure is expected to be minimised through the use of PPE such as protective clothing, gloves, safety glasses and respiratory protection where appropriate.

6.1.2. Public Exposure
The racing fuels containing the notified chemical at < 30% concentration will only be used in professional settings and will not be made available to the public.

6.2. Human Health Effects Assessment
No toxicological study reports were submitted for the notified chemical. The results from toxicological investigations conducted on the notified chemical available in literature are summarised below. For full details of the studies, refer to references.

Toxicokinetics, Metabolism and Distribution
Two studies on the kinetics and metabolism of inhaled notified chemical were conducted on human volunteers. In the first study, 8 male volunteers were exposed to the notified chemical for 2 hours during light exercise (Exempt Information 12). The net respiratory uptake of the notified chemical ranged from 32% to 34%, with average inhaled concentrations of 0.18, 0.9 and 1.8 mg/kg bw respectively and average blood concentrations (C_{max}) of 1.1, 5.4 and 10 µM respectively (Exempt Information 12). The kinetic profile in the blood appeared to have 4 phases of elimination with half-life ($T_{1/2}$) values of 2 min, 18 minutes, 1.7 hours and 8 hours and the primary metabolite

TBA had a single $T_{1/2}$ value of 12 hours for its elimination from the blood (Exempt Information 12). In urine, excretion of the notified chemical and the key metabolite, *tert*-butanol (TBA), was < 1% of the uptake of the chemical and there were two $T_{1/2}$ values (8 minutes and 8.6 hours) for the chemical and a single $T_{1/2}$ value (approximately 8 hours) for TBA for urine elimination (Exempt Information 12). Respiratory excretion was calculated as a percentage of the respiratory uptake of the notified chemical and ranged from 45-50% (Exempt Information 14).

In the second study, 3 men and 3 women were exposed to atmospheres containing 4.5 ± 0.6 ppm and 40.6 ± 3.0 ppm of the notified chemical for 4 hours and the average inhaled concentrations were 0.18 and 1.65 mg/kg bw, respectively (Exempt Information 12). Following the exposure, the mean C_{max} values in the blood were 1.3 ± 0.7 and 12.1 ± 4.0 µM respectively and elimination of the notified chemical from the blood was biphasic with $T_{1/2}$ values of 1.1 hours and 6.2 hours after the high dose, whereas TBA elimination was monophasic with a $T_{1/2}$ value of 8.2 ± 2.2 hours (after the low dose) and 9.8 ± 1.4 hours (after the high dose) (Exempt Information 12). Urine analysis found the levels of the notified chemical and its known metabolites increased following the exposure and the $T_{1/2}$ values for urinary excretion were 3.5, 11.2, 12.3 and 28.3 h for each chemical respectively after the high dose exposure (Exempt Information 12). Although the notified chemical can be extensively distributed in human tissues based on its measured tissue/air partition coefficient, the rapid exhalation of the chemical and rapid elimination of its metabolites from urine suggest that it is unlikely to accumulate in human tissues (Exempt Information 14).

Acute Toxicity
Based on studies conducted in rats (oral and inhalation) and rabbits (dermal), the notified chemical is reported to be of low acute oral (LD50 > 5000 mg/kg bw), dermal (LD50 > 2000 mg/kg bw) and inhalation (LC50 > 5.88 mg/L/4 hour) toxicity (Exempt Information 12).

Irritation
Based on a skin irritation study in rabbits using the notified chemical under occlusive conditions, the notified chemical was considered to be moderately irritating to the skin (Exempt Information 12). In two more recent studies conducted in rabbits (OECD TG not reported) using the notified chemical under semi-occlusive conditions, signs of skin irritation was not observed (Exempt Information 12).

Three eye irritation studies were also conducted in rabbits for the notified chemical (OECD TG not indicated). In one study, irritation effects included conjunctival redness and chemosis noted in all animals (n = 6) 24 hours after application of the diluted chemical (concentration not available) and resolved within 7 days. A minor iridial response noted in 1/6 animals on day 1 (Exempt Information 12). In two more recent studies, conjunctival redness was minimal with no iridial or corneal effects observed (Exempt Information 12).

As details of the studies are not available to verify the conflicting results reported in the eye and skin irritation study summaries of the notified chemical, eye/skin irritation cannot be ruled out.

Sensitisation
In a guinea pig maximisation test (OECD TG 406) using the notified chemical at 10% for intracutaneous induction and with an epicutaneous challenge concentration of 100%, no evidence of skin sensitisation was observed (Exempt Information 12, 19).

Repeated Dose Toxicity
In a subchronic 28-day oral immunotoxicity study (OECD TG not reported), female Sprague-Dawley (SD) rats (10 rats/dose) were administered the notified chemical (in corn oil) through oral gavage doses of 0, 250, 500 or 1000 mg/kg bw/day (Exempt Information 3). There were no mortalities or biologically relevant effects on the humoral immune component of the immune response in all test and recovery group animals. The No Observed Effect Level (NOEL) for immune system suppression was considered to be 1,000 mg/kg bw/day, the highest dose tested (Exempt Information 3).

In a sub-chronic 180-day oral toxicity study (OECD TG 452), SD rats (15 rats/sex/dose) were dosed with the notified chemical through oral gavage doses of 0, 5, 25, 100 and 400 mg/kg bw/day (Exempt Information 14). Oral exposure to the test substance did not produce significant clinical, neurological or clinical pathology abnormalities at up to 100 mg/kg bw/day. Increased relative liver weights and hypertrophy of centrilobular hepatocytes were noted in male and female animals treated at 400 mg/kg bw/day (Exempt Information 14). One male treated at 25 mg/kg bw/day and two males treated at 400 g/kg bw/day were found dead during the study; however, the mortality of male treated at 25 mg/kg bw/day was not considered by the study to be test substance-related and no

abnormalities were observed during necropsy of the dead animals treated at 400 mg/kg bw/day (Exempt Information 14). The No Observed Adverse Effect Level (NOAEL) of 100 mg/kg bw/day was established by the study authors (Exempt Information 14).

In a 28-day repeated dose inhalation toxicity study (OECD TG not reported), SD rats (10 rats/sex/dose) was exposed to vapours of the notified chemical at 0, 500, 2,000 and 4,000 ppm for 6 hours/day, 5 days a week for 4 weeks (Exempt Information 20). No mortalities or significant clinical, neurological or clinical pathology abnormalities were observed at up to 4,000 ppm (Exempt Information 20). Animals treated at 4,000 ppm appeared sedated and showed mild to moderate ataxia during exposure, but appeared to be normal 15 minutes after exposure ended (Exempt Information 20). There was also a significant trend in hind-limb splay and increased relative liver weights (without histopathology or functional changes) in both male and female animals treated at 2,000 ppm or 4,000 ppm. The NOAEL was established to be 500 mg/kg bw/day by the study authors, based on the effects observed in animals treated at 2,000 ppm or 4,000 ppm (Exempt Information 20).

In a 13-week repeated dose inhalation toxicity study (OECD TG not reported), Fischer 344 (F344) rats (n = 10-15 /sex/dose) and CD-1 mice (n = 10-15/sex/dose) were exposed to vapours of the notified chemical at 0, 500, 1,750 or 5,000 ppm for 6 hours/day, 5 days a week for 13 weeks (Exempt Information 13). Four mice (3 treated at 5,000 ppm and 1 control) were found dead but was not considered by the study authors to be test substance-related (Exempt Information 13). There were no mortalities in rats or major changes in clinical pathology parameters of either rats or mice, with the exception of a transient ataxia sometimes observed in male rats and male and female mice treated at 5000 ppm. Degenerative effects in the testicular seminiferous tubules were observed in male rats treated at 1,750 ppm or 5,000 ppm (Exempt Information 13). Increases in the incidences of regenerative foci, rates of renal cell proliferation and α_{2u}-globilin containing protein droplets were noted in the kidneys of all male rats that appeared to be time- and concentration-dependent (Exempt Information 13). The study authors considered that the effects in the kidney are associated with male rat specific syndrome of α_{2u}-globilin-mediated nephrotoxicity, which may be of no relevance to humans (Exempt Information 13). Increases in the incidences of centrilobular hypertrophy and rate of hepatocyte cell proliferation were noted in mice treated at 1,750 ppm or 5,000 ppm, which was considered by the authors to be consistent with a mitogenic response caused by the exposure to the test substance (Exempt Information 13). The NOAEL was established as 500 mg/kg bw/day by the study authors, based on the degeneration in the testes of male rats treated at 1,750 ppm or 5,000 ppm.

In a 90-day repeated dose inhalation toxicity study focusing on neurotoxicity (non-guideline study), F344 rats (12/sex/concentration) were exposed to the vapours of the notified chemical at 500, 1,750 or 5,000 ppm for 6 hours/day, 5 days a week for 13 weeks (Exempt Information 5). No mortalities or significant clinical, neurological or clinical pathology abnormalities were observed at up to 5,000 ppm. However, transient ataxia was immediately observed in male animals after exposure to 5,000 ppm until the 35th day of treatment and changes in grip strength and hindlimb splay were noted (including decreased mean hindlimb grip strength and a statistically significant increase in mean hindlimb splay in male animals following a single exposure to 500 ppm, a statistically significant increase in mean forelimb grip strength observed in male animals following 10 exposure days to 5000 ppm, a statistically significant decrease in mean forelimb grip strength observed in female animals following 65 exposures to 500 ppm), without showing a dose-response relationship or a consistent pattern of neurological dysfunction (Exempt Information 5). It was noted by the study authors that although ataxia was a common feature of acute neurotoxicity in rats for the notified chemical following high-dose exposure (Exempt Information 5).

The notified chemical is considered to cause acute neurotoxicity with inhalation exposure, warranting hazard classification as Specific Target Organ Toxicity – Single Exposure (Category 2) (H371 - May cause damage to organs (neurotoxicity)(inhalation), based on the available information including:
- In a 28-day inhalation study, SD rats exposed to vapours of the notified chemical at 4,000 ppm appeared sedated and showed mild to moderate ataxia during exposure, but appeared to be normal 15 minutes after exposure ended. There was also a significant trend in hind-limb splay in both males and females treated at 2,000 ppm or 4,000 ppm (Exempt Information 20).
- In a 13-week repeated dose inhalation study, F344 rats and CD-1 mice exposed to vapours of the notified chemical showed transient ataxia in male rats and male and female mice at 5000 ppm (Exempt Information 13).
- In a 90-day repeated dose inhalation study focusing on neurotoxicity, F344 male rats showed transient ataxia immediately after exposure to 5,000 ppm until the 35th day of treatment. Changes in grip strength and hindlimb splay were noted in male animals following a single exposure at 500 ppm (Exempt Information 5).

Mutagenicity/Genotoxicity
The notified chemical gave negative results in three bacterial reverse mutation tests (in *Salmonella typhimurium* and tested up to 500, ,5000 and 10,000 μg/plate, respectively), an *in vitro* gene mutation test (using Chinese hamster

V79 cells and tested up to 5,000 μg/mL), an *in vitro* chromosomal aberration test (using Chinese Hamster Ovary cells and tested up to 5,000 μg/mL) and two *in vivo* micronucleus formation tests (using CD-1 mouse bone marrow cells and tested up to 5,000 mg/kg bw and 5,000 ppm (21200 mg/m^3, 6 h/day for 5 days), respectively) (Exempt Information 12).

Genotoxicity of the notified chemical was investigated by a sub-chronic drinking water study (OECD TG 408) and inhalation exposure study in F344 rats (OECD TG 413). In an *in vivo* micronucleus formation test, F344 rats (10 /sex/dose for each study) were treated with the notified chemical in the drinking water at 0, 250, 640, 1,600, 4,000 and 10,000 ppm or exposed to vapour of the notified chemical at 0, 500, 1,500 and 5,000 ppm for 13 weeks (Exempt Information 15). Exposure through drinking water resulted in significantly decreased red blood cell counts and haemoglobin concentration in female rats treated at 640, 4,000 and 10,000 ppm. Exposure to vapour resulted in similar effects in male rats treated at 5,000 ppm. These systemic effects indicated that the test substance and/or its metabolites had reached the bone marrow (Exempt Information 15). The test substance did not increase the frequency of micronucleated polychromatic erythrocytes in the bone marrow in any of the treatment groups in both studies (Exempt Information 15).

Carcinogenicity
In a 2-year carcinogenicity study (OECD TG not reported), SD rats (60 rats/sex/dose, at 8 weeks of age) were administrated the notified chemical through oral gavage doses of 0, 250 or 1000 mg/kg bw/day for 4 days/week (Exempt Information 11). There was a dose-related increase in mortalities in male and female animals and the results showed that the test substance caused an increase in total malignant tumours and an increase in oncological pathologies of the mouth epithelium and forestomach, of malignant tumours of the uterus (mainly sarcomas) and of hemolymphoreticular neoplasms (mainly lymphoimmunoblastic lymphoma) from 250 mg/kg bw/day (Exempt Information 11). However, it was reported that several issues were identified with the study including that the study did not meet the requirements of the OECD TG 451: Carcinogenicity studies (1981). (Exempt Information 12).

In another 2-year carcinogenicity study (OECD TG 451), F344 rats (50 /sex/dose) were administrated the notified chemical in drinking water at the nominal concentrations of 0, 625, 2,500 or 10,000 ppm (actual concentrations were 28-542 mg/kg bw for males and 46 - 560 mg/kg bw for females) (Exempt Information 18). Survival rates were comparable to the control and there were no test substance-related changes in clinical signs, while rat-specific non-neoplastic lesions were noted in the kidneys including an increase in the severity of chronic progressive nephropathy (CPN) observed in male and female animals treated at 10,000 ppm and increased incidences of urothelial hyperplasia of the pelvis and mineral deposition in the renal papilla observed in male animals treated at 2,500 or 10,000 ppm (Exempt Information 18). There was no significant increase in the incidence of tumours in any organ of either sex at up to 10,000 ppm, the highest dose tested (Exempt Information 18).

In an inhalation carcinogenicity study (OECD TG 451), F344 rats (50/sex/dose) were exposed to vapours of the notified chemical at 0, 500, 1,500 or 5,000 ppm using a whole-body chamber for 6 h/day, 5 days/week for 104 weeks (Exempt Information 17). In comparison to the control, survival rates decreased significantly in the mid dose (60% compared to 76% in the control group in females) and high dose treatment groups (60% compared to 88% in the control group in males and 60% compared to 76% in the control group in females), which was attributed by the study authors to the presence of pituitary tumours (in females) and an increase in CPN (in males). Treatment-related effects included an increase in kidney weight, an increase in the incidences of hepatocellular adenomas (9/50), the formation of a hepatocellular carcinoma (1/50) and a significant increase in the incidences of eosinophilic cell foci (39/50) and basophilic cell foci (33/50) in male animals treated at 5,000 ppm. The NOEL for hepatotumorigenicity was reported as 1,500 ppm by the study authors, based on the incidence of liver tumours (Exempt Information 17). The study authors considered the relevance of hepatotumorigenicity observed in the study to humans as inconclusive as the chemical has no genotoxicity (Exempt Information 17).

In a 36-week two-stage urinary bladder carcinogenesis study on the notified chemical (non-guideline study), male F344 rats were initially administered an initiator, *N*-butyl-*N*-(4-hydroxybutyl)nitrosamine (BBN), through their drinking water at a concentration of 500 ppm for 4 weeks (Exempt Information 9). At week 6, the test substance was then administered (30 rats/dose) via oral gavage doses of 0, 100, 300, 500 or 1,000 mg/kg bw/day for 7 days/week until week 36 (Exempt Information 9). Statistically significant test substance-related effects included increases in relative liver weights in the 100, 300 and 1,000 mg/kg bw/day dose groups, increases in relative kidneys weights in all treatment groups and an increase in relative urinary bladder weights in the 1,000 mg/kg bw/day dose group (Exempt Information 9). In the 1,000 mg/kg bw/day dose group, it was observed that 4/30 (13%) animals had papillomatosis (extensive papillary hyperplasia) in the urinary bladder with 1/4 rats developing a carcinoma and 3/4 developing eosinophilic soft stones (Exempt Information 9). The study authors concluded

that the test substance does not have tumour promoting activity in the urinary bladder despite confirmation that rats exposed to the test substance at 1,000 mg/kg bw/day may develop papillomatosis in the urinary bladder (Exempt Information 9).

In a 23-week two-stage liver and kidney carcinogenesis bioassay study on the notified chemical (non-guideline study), male 6-week-old F344 rats were initially administered with the initiator, *N*-ethyl-*N*-(2-hydroxyethyl)nitrosamine (EHEN) through drinking water at a concentration of 500 ppm for 2 weeks (Exempt Information 10). The test substance was administered on week 4 (30 rats/dose) via oral gavage doses at 100, 300, 500 or 1,000 mg/kg bw/day for 7 days/week for 19 weeks (Exempt Information 10). No mortalities or significant clinical abnormalities were observed at up to 1,000 mg/kg bw/day; however, there were statistically significant increases in relative liver weights (in animals treated at 300, 500 or 1,000 ppm) and relative kidney weights (in all treatment groups) (Exempt Information 10). A statistically significant increase in incidences of hepatocellular adenomas and combined hepatocellular adenomas and carcinomas in animals treated at 1,000 mg/kg/day and a significant increase in the average numbers of lesions was also noted (Exempt Information 10). No significant differences in incidences and average numbers of renal tubule neoplasms were noted in any treatment group; however, the average numbers of atypical tubule hyperplasias (considered to be preneoplastic lesions) were significantly increased in animals treated at 1,000 mg/kg/day (Exempt Information 10). The NOEL for tumor-promoting effects was established as 500 mg/kg bw/day, based on the hepatic and renal adverse effects noted at 1,000 mg/kg bw/day. The study author stated that the tumour promoting effects of the test substance in the kidney were not relevant to humans as they are due to the rat-specific accumulation of α2u-globulin in renal tubules (Exempt Information 10).

Reproductive and Developmental Toxicity

Several studies on reproductive and developmental toxicity of the notified chemical administered to animals via oral gavage or inhalation have been summarised in a review (Exempt Information 16):

- Studies evaluating specifically for mating success and fertility of female and male rats reported no evidence of adverse effects on male or female gamete production and transport, female oestrous cycle, sexual behaviour, fertility, gestation length, or parturition at doses tested up to 1,000 mg/kg bw/day.
- Studies measured reproductive organ weights, sperm counts, motility and morphology, or oestrous cycle in rats and mice revealed no significant changes from controls.
- One study reported evidence of spermatocyte degeneration in F344 rats exposed by inhalation for 13 weeks at 1,750 and 5,000 ppm; however, testes were not preserved according to methods currently considered optimal. Follow-up studies using preferred preservation methods with a different route of exposure using both SD and F344 rats failed to confirm these findings.
- Two independent prenatal development studies conducted via oral gavage using SD rats reported the maternal NOEL as 1,000 mg/kg bw/day and 500 mg/kg bw/day (based on reduced maternal body weight gain in the 1,000 mg/kg bw/day group) respectively and the reproductive and developmental NOEL/NOAEL as 1,000 mg/kg bw/day (the highest dose tested).
- In two prenatal studies (one preliminary and one definitive) in rabbits, the maternal NOEL was 300 mg/kg bw/day (based on significantly lower body weight and food consumption in the 1,000 mg/kg bw/day group) and the embryofetal NOAEL was 1,000 mg/kg bw/day based on no significant test substance-related effects observed.
- A one-generation study involving treatment and observation of pups through sexual development reported a slight, non-statistically significant decline in pup survival on postnatal day (PND) 1–4. A two-generation study reported some statistically significant increases in pup mortality that were not seen at the highest dose in the F0 offspring and a statistically significant increase in pup mortality at the highest dose (only) in F1 offspring (could be attributed to a single total litter loss of 16 of the 20 pups). No other test substance-related effects on implantations, resorptions, numbers of offspring, foetal weights, physical malformations, postnatal developmental delays were observed in these studies in the absence of maternal toxicity. It was reported that the total litter losses could be associated with higher susceptibility of certain dams to maternal toxicity, maternal neglect during lactation, or possibly exposure through maternal milk and individual high susceptibility to other environmental factors (e.g., excessive noise).

In a more recent prenatal developmental toxicity study (OECD TG 414), New Zealand white rabbits (6 rabbits/dose) were administered the notified chemical via oral gavage from gestational day (GD) 6 to GD 27 at 0, 100, 300 or 1,000 mg/kg bw/day (Exempt Information 1). There were no mortalities or abortion in pregnant animals (Exempt Information 1). Slightly but statistically significant suppressed body-weight gain and transiently decreased maternal food consumption were reported for animals treated at 1,000 mg/kg/day, there were no clinical or macroscopic findings in dams at this dose level and no test substance-related effects observed in dams treated at 300 mg/kg bw/day or less (Exempt Information 1). There were no significant effects on the numbers of corpora

lutea, implantations, live foetuses, resorptions and dead foetuses, incidences of pre- and post-implantation loss, viability of foetuses, foetal body weight, sex ratio of foetuses, or weights of gravid uteri, no significant difference in the incidences of foetuses with malformations or variations when compared to the control, and no adverse effects on the progress of ossification noted in foetuses of dams treated with the test substance (Exempt Information 1). The NOAEL was established by the study authors as 300 mg/kg bw/day for maternal toxicity (based on the adverse effects on maternal body weight and food consumption) and 1,000 mg/kg bw/day for foetal toxicity (based on no adverse effects at up to the highest dose tested) (Exempt Information 1).

In more recent a prenatal developmental toxicity study (OECD TG 414), female SD rats (21-22/dose) were administrated daily with the notified chemical via oral gavage from day 5 to day 19 post-coitum at 0, 100, 300 or 1,000 mg/kg bw/day (Exempt Information 2). There were no mortalities or test substance-related toxicological effects on pregnant animals or their embryos and foetuses and therefore the maternal and developmental NOAEL was established by the study authors as 1,000 mg/kg bw/day (Exempt Information 2).

Health Hazard Classification
Based on the available information, the notified chemical is a hazardous chemical according to the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia. The hazard classification applicable to the notified chemical is presented in the following table.

Hazard Classification	*Hazard Statement*
Specific Target Organ Toxicity – Single Exposure (Category 2)	H371 - May cause damage to organs (neurotoxicity)(inhalation)

6.3. Human Health Risk Characterisation

6.3.1. Occupational Health and Safety
Based on the available toxicological information, the notified chemical is expected to be of low acute toxicity. The information available is not sufficient to rule out the potential for slight skin and eye irritation. Exposure to the chemical vapours may cause drowsiness or dizziness. Systemic toxicity effects after repeated exposure at high doses/concentrations cannot be ruled out.

Dermal, ocular and inhalation exposure of workers to the notified chemical at < 30% concentration may occur during repackaging (including connecting and disconnecting of pumps and cleaning and maintenance of equipment) and automotive refuelling. However, transfer of the fuel during repackaging and refuelling is reported to be through dedicated lines and sealed pumps therefore potential for skin contact is expected to be minimal. Exposure should be minimised through the use of control measures (such as enclosed, automated processes where possible and sufficient ventilation) and personal protective equipment (respiratory protection where appropriate). Adverse neurological effects are not expected at the exposure levels associated with automotive refuelling.

Provided that the recommended controls are being adhered to, under the conditions of the occupational settings described, the notified chemical is not considered to pose an unreasonable risk to the health of workers.

6.3.2. Public Health
The notified chemical is for industrial use only. The public will not come into contact with the notified chemical and therefore the risk to the public is not considered to be unreasonable.

7. ENVIRONMENTAL IMPLICATIONS
The notified chemical is a part of a class of chemicals, known as fuel oxygenates, which are used widely as a component of unleaded petrol in the European Economic Area and other jurisdictions. The United States, has mandated their use in some urban areas to help reduce atmospheric concentrations of carbon monoxide (CO) or ozone (O_3). The use of a fuel oxygenate similar to the notified chemical has led to detections in ground and drinking water in the United States, and some Member States of the EU. These have been largely attributed to point source contamination from leaking or overfilling underground storage tanks. Above ground storage is not considered to be a major source of water contamination, as controls are required to contain spills and leaks (e.g. bunding) and leaks are readily detected. Where a fuel oxygenate similar to the notified chemical is used widely, fugitive emissions have led to detections in urban run-off, ≤ 8.7 µg/L and in nearby urban creeks ≤ 0.76 µg/L (Exempt Information 8).

7.1. Environmental Exposure & Fate Assessment

7.1.1. Environmental Exposure

RELEASE OF CHEMICAL AT SITE

The notified chemical will be repackaged to smaller drums, for distribution (see Section 5). Repackaging to smaller drums will be completed using metered sealed pumps capable of collecting and recycling condensed vapours. Therefore release of the notified chemical to the environment during repackaging is expected to be limited to accidental minor spills, which will be absorbed with appropriate substrate and disposed of by incineration or disposal in accordance with local government regulations. There will be no underground storage of the notified chemical at the notifier's warehouse.

RELEASE OF CHEMICAL FROM USE

Use of the notified chemical will be restricted to site limited applications at racing events and will not be available to members of the general public. It is possible for the notified chemical to enter groundwater sources through above ground leaks or spills from storage areas, mechanical servicing areas and on the race tracks; contaminated stormwater runoff or inappropriate containment or disposal of solid waste and wastewater from mechanical servicing and washdown areas. The notifier has stated that losses from use are expected at rates of ≤ 0.2% (≤ 200 kg per annum). However, constructed racetracks are typically regulated by State and Territory environmental impact site assessments and compliance with these regulations will mitigate adverse effects to the aquatic environment.

The majority of the notified chemical is expected to be consumed through combustion during race events.

RELEASE OF CHEMICAL FROM DISPOSAL

It is expected that recycling of the steel drums will result in return of the drums to the notifier for disposal or reuse. Where it is not practical for the drums to be returned to the notifier it is expected that disposal will occur through a drum recycler or licensed waste disposal agent where the unused product containing the notified chemical will be pre-mixed with waste fuel and incinerated or used as a low grade fuel source (e.g. cement kilns). The notifier has indicated losses from unreturned drums are expected at the rate of 0.3% (≤ 300 kg per annum).

7.1.2. Environmental Fate

The bulk of the chemical is expected to be consumed through combustion in high performance motor vehicles producing oxides of carbon and water vapour. Emissions to air due to volatilization or incomplete combustion are likely to be minimal as racing competitiveness relies on optimal engine efficiency and fuel consumption. Emissions to air will rapidly degrade due to reaction with atmospheric hydroxyl radicals with half-lives less than 2 days (Exempt Information 7).

The biodegradability of the notified chemical in soil in aerobic and especially in anaerobic conditions are very slow and favourable conditions for degradation are difficult to attain (Exempt Information 6, 8).

Due to the solubility of the notified chemical in water in conjunction with low potential for binding to soils and sediments it may reach groundwater if it reaches the soil (Exempt Information 7).

The notified chemical is readily biodegradable (SDS), but only with adapted microorganisms. Generally it is not considered readily biodegradable (Exempt Information 6).

7.1.3. Predicted Environmental Concentration (PEC)

A PEC could not be reliably calculated due to variability in scale and number of racing sites, event days, and number of competitors using the fuel additive. However release is expected to be minimal due to the risk management of motorsport events through Federal, State and Territory guidelines.

7.2. Environmental Effects Assessment

The ecotoxicological endpoints for the notified chemical derived from the submitted SDS are presented below.

Endpoint	*Result*	*Assessment Conclusion*
Fish Toxicity	LC50 = 974.1 mg/L	not harmful to fish
Daphnia Toxicity	EC50 = 110 mg/L	not harmful to aquatic invertebrates
Algal Toxicity	EC50 = 110 mg/L	not harmful to algal growth

Based on the above ecotoxicological endpoints for the notified chemical, it is not expected to be harmful to aquatic organisms. Therefore, the notified chemical is not formally classified under the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS)* for acute and chronic toxicities (United Nations, 2009).

However, ground water and drinking water sources may undergo aesthetic water quality changes as a result of the notified chemical entering the aquatic compartment at concentrations exceeding the odour threshold of 13 µg/L volume or the taste threshold of 47 µg/L.

7.2.1. Predicted No-Effect Concentration

A Predicted No-Effect Concentration was calculated using the most sensitive endpoint (Algal growth EC50 = 110 mg/l) and a safety factor of 100 as at least three trophic endpoints were provided.

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
EC50 (Algal)	110	mg/L
Assessment Factor	100	
Mitigation Factor	1.00	
PNEC	1.1	mg/L

7.3. Environmental Risk Assessment

A risk quotient (RQ = PEC/PNEC) could not be determined, as a PEC could not be established. However, the notified chemical is not expected to be toxic to aquatic organisms but may cause aesthetic water quality changes. The use of the notified chemical will be restricted to site limited applications at racing events and will not be available to the general public. These uses will not involve underground storage which is regarded as the main source of contamination of the aquatic environment by fuel oxygenates, including the notified chemical. Other sources of aquatic contamination from racing events and fugitive emissions are expected to be minimal. Therefore on the basis of the reported use pattern, the notified chemical is not considered to pose an unreasonable risk to the environment.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Explosive Properties Predicted negative

Method	EC Council Regulation No 440/2008 A.14 Explosive Properties.
Remarks	Based on the chemical structure.
Test Facility	Chemicalia (2019)

Oxidizing Properties Predicted negative

Method	EC Council Regulation No 440/2008 A.21 Oxidizing Properties (Liquids)
Remarks	Based on the chemical structure.
Test Facility	Chemicalia (2019)

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