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March 2013

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

Chemical in HiTEC 4898C Fuel Additive

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 Ageing, and conducts the risk assessment for public health and occupational health and safety. The assessment of environmental risk is conducted by the Department of Sustainability, Environment, Water, Population and Communities.

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
NICNAS

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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/1445	Afton Chemical Asia Pacific LLC	Chemical in HiTEC 4898C Fuel Additive	ND*	≤ 150 tonnes per annum	Diesel fuel additive

* 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
Provided the recommended control measures are in place, 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 engineering controls to minimise occupational exposure to the notified chemical as introduced in product:
  - Use closed and automated facilities when blending the notified chemical into diesel fuel

- 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 as introduced in product and in fuel:
  - Avoid direct skin and eye contact
  - Clean up spills or drips 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 as introduced in product:
  - Impervious gloves
  - Face shield, chemical glasses or goggles
  - Protective clothing

  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 being a fuel additive, or is likely to change significantly;
- the amount of chemical being introduced has increased from 150 tonnes per annum, 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.

No additional secondary notification conditions are stipulated.

(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.

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Afton Chemical Asia Pacific LLC (ABN: 99 109 644 288)
Level 9, 20 Berry Street
NORTH SYDNEY, NSW 2059

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

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

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed as follows: vapour pressure, hydrolysis as a function of pH, adsorption/desorption, dissociation constant, explosive properties, oxidising properties, acute oral toxicity, acute dermal toxicity, skin irritation, eye irritation, skin sensitisation, induction of point mutations, genotoxic damage *in vivo* and chromosome damage *in vitro*

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
Canada, 2010

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
HITEC® 4898C Fuel Additive (product containing the notified chemical > 80%)

MOLECULAR WEIGHT
< 500 Da

ANALYTICAL DATA
Reference IR spectrum was provided.

3. COMPOSITION

DEGREE OF PURITY > 80%

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: Dark brown liquid

Property	Value	Data Source/Justification
Pour Point[1]	-8 °C	Provided by the notifier
Initial Boiling Point[2]	239.4 °C	Measured
Density	940 kg/m^3	(M)SDS
Vapour Pressure[3]	< 8.83 × 10^{-3} kPa at 25°C	Estimated based on boiling point
Water Solubility	0.7–1.46 × 10^{-3} g/L at 24 °C	Analogue data
Hydrolysis as a Function of pH	Not determined	Not expected as the notified chemical does not contain readily hydrolysable functionalities and has limited solubility in water
Partition Coefficient (n-octanol/water)	log Pow 4.55 to > 6.50 at 35 °C	Measured (several peaks, majority was > 6.50)
Adsorption/Desorption	log Koc > 4.4	Estimated
Dissociation Constant	Not determined	Not expected to be ionised under environmental conditions
Flash Point	198 °C (closed cup)	Measured
Flammability Limits	Expected to be not flammable	Estimated based on flash point
Autoignition Temperature	Not determined	Expected to be high based on high flash point
Explosive Properties	Not determined	Contains no functional groups that would imply explosive properties

Oxidising Properties	Not determined	Contains no functional groups that would imply oxidative properties

[1] Pour point was provided in lieu of melting point as the notified chemical does not crystallize and therefore does not have a defined melting/freezing point.
[2] The notified chemical decomposes before starting to boil. According to American Society for Testing and Materials petroleum-analysis distillation procedures, initial boiling point is defined as the recorded temperature when the first drop of distilled vapour is liquefied and falls from the end of the condenser.
[3] Vapour pressure was calculated in accordance with Modified Watson Correlation based on the boiling point of the notified chemical.

DISCUSSION OF PROPERTIES
For full details of tests on physical and chemical properties that were not detailed in the Canada reports, refer to Appendix A.

Reactivity
The notified chemical is expected to be stable under normal conditions of use and to be combusted with diesel fuel in the engines at end-use.

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 not be manufactured in Australia. The notified chemical will be imported into Australia in a fuel additive product at > 80%.

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

Year	*1*	*2*	*3*	*4*	*5*
Tonnes	< 20	< 30	< 50	< 60	< 150

PORT OF ENTRY
Sydney, Melbourne, Brisbane and Perth

TRANSPORTATION AND PACKAGING
The product containing the notified chemical will be imported in carbon steel 24,000-L ISO tank containers and transported by road or railway to diesel fuel blending facilities.

USE
The product containing the notified chemical will be blended into diesel fuel. The diesel fuel containing < 0.05% of the notified chemical will be used in freight, construction, agriculture and transport vehicles including buses, trucks and some passenger cars. The majority of the blended fuel will be used for the operation of heavy-duty diesel equipment. The notified chemical will be combusted with the diesel fuel during the use.

OPERATION DESCRIPTION
Transport
The product containing the notified chemical at > 80% will be transported by road or railway from the ports of entry to diesel fuel blending facilities in original 24,000-L ISO tank containers. Blended fuel containing the notified chemical at concentration < 0.05% will be transported by road with 20,000-kg bulk tank trucks from storage tanks at the blending facilities to commercial/retail fuel outlets.

Storage
The product containing the notified chemical will be transferred from the original ISO tank containers into bulk storage tanks at diesel fuel blending facilities. Upon arrival, the ISO tank containers are expected to be in a contained area outside the blending facilities. Hose lines will be connected manually to the ISO tank containers and the product containing the notified chemical will be pumped into storage tanks using an air back flush system to prevent spilling automatically.

Blended diesel fuel containing the notified chemical at < 0.05% is expected to be stored in either above-ground or under-ground bulk storage tanks at commercial and fuel outlets.

Blending
At the fuel blending site, the product containing the notified chemical will be transferred from local storage tanks to the blending vessels using automated systems with hard piping and computer-controlled valves. The loading of the product to the blending vessels will take approximately 10 minutes. The blending process is typically automated and occurs in a closed system. Quality control sampling may occur immediately after blending.

Packaging
Once the blending is completed, the blended fuel will be transferred into bulk storage tanks. When the fuel is requested by commercial/retail fuel outlets, it will be transferred from bulk storage tanks to 20,000 kg bulk tank trucks for transport to the fuel outlets.

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)*
Workers analysing the notified chemical or finished fuel	0.5	16
Workers unloading ISO tank containers	0.5	16
Workers sampling finished fuel after blending	0.5	12
Workers filling containers with finished fuel	8	12
Maintenance workers	4	4
Commercial end users	4	220

EXPOSURE DETAILS
Transport and storage
During transport and storage, the potential for worker exposure to the fuel additive or the blended diesel containing the notified chemical is expected to be low, except in an accidental breach of the packaging. Workers are recommended to use coveralls, safety boots and gloves during these operations.

Blending and Tank filling
During the blending process, incidental dermal and ocular exposure to splashes, drips and spills of the product containing the notified chemical at > 80% may occur when connecting and disconnecting the lines used to load the blending vessels. The blending process will mainly be automated and occur in a closed system, reducing the likelihood of potential exposure to the notified chemical. However, dermal contact with surfaces contaminated with the fuel containing the notified chemical may occur. Workers involved in blending process will be required to wear PPE including coveralls, chemical gloves, protective glasses or goggles, safety boots and hard hats.

Maintenance
Workers involved in the cleaning and maintenance of the blending and filling equipment will have the potential for dermal and ocular exposure to the residues containing the notified chemical. Workers will be required to wear appropriate PPE during the process.

Laboratory Staff
Laboratory workers are expected to have the potential for dermal and ocular exposure to small amounts of the notified chemical and the blended diesel fuel containing the notified chemical during sampling and testing. Operators will be required to wear PPE including chemical gloves, lab coats and safety glasses during the processes.

End Users

End users of the finished fuel may have the potential for dermal and ocular exposure to diesel fuel containing the notified chemical at < 0.05% during filling or draining the fuel tanks, handling automotive components that have come into contact with the diesel fuel and during cleaning of equipment. Workers will usually be required to wear PPE including coveralls, safety boots, gloves and safety goggles or glasses when handling diesel fuel containing the notified chemical. The design of the fuel dispensing equipment at commercial/retail fuel outlets is expected to reduce the occurrence of accidental dermal and ocular exposure to the diesel fuel.

6.1.2. Public Exposure

The fuel additive containing the notified chemical will not be available to the public and will be blended into diesel fuel in well-controlled industrial facilities. As the diesel fuel containing the notified chemical will be distributed to retail fuel outlets for consumer use, the public may have potential for incidental dermal or ocular exposure to the notified chemical at concentration < 0.05% during refuelling processes. Due to the relatively low concentration of the notified chemical and the design of the refuelling equipment, the exposure to the notified chemical by the public is expected to be low and infrequent. After the blended diesel fuel is consumed, the notified chemical is expected to be combusted with the fuel and will not be bioavailable for further exposure.

6.2. Human Health Effects Assessment

6.2.1 Toxicological studies on the notified chemical

The results from toxicological investigations conducted on the notified chemical or the analogue are summarised in the following table.

Endpoint	*Tested Substance*	*Result and Assessment Conclusion*
Rat, acute oral toxicity	Analogue	LD50 > 14,430 mg/kg bw; low toxicity
Rabbit, acute dermal toxicity	Analogue	LD50 > 20,000 mg/kg bw; low toxicity
Rabbit, skin irritation	Analogue	Slightly irritating
Rabbit, eye irritation	Analogue	Slightly irritating
Guinea pig, skin sensitisation – adjuvant test	Analogue	No evidence of sensitisation
Rat, combined repeat dose oral and reproductive/developmental toxicity– 28 days	Notified Chemical	NOAEL = 200 mg/kg bw/day for adult toxicity NOAEL = 750 mg/kg bw/day for reproductive/developmental toxicity
Rat, repeat dose oral toxicity – 28 days	Analogue	NOAEL = 150 mg/kg bw/day
Mutagenicity – bacterial reverse mutation	Analogue	Non mutagenic
Genotoxicity – *in vivo* mouse micronucleus assay	Notified chemical	Non clastogenic
Genotoxicity – *in vitro* chromosomal aberration	Analogue	Non clastogenic

6.2.2 Summary of health effects

Toxicokinetics

The measured octanol-water partition coefficient of the notified chemical (with peaks ranging from log Pow 4.55 to > 6.50 at 35 °C) suggests that there may be some dermal absorption.

Acute toxicity

No data were available on acute oral, dermal or inhalation toxicity of the notified chemical.

An acute oral toxicity study on the analogue chemical was performed in male rats (10/dose). The test substance was administered once by oral gavage at doses of 5, 7.12, 10.14 and 14.43 g/kg bw. There were no mortalities during the 14 day observation period. Clinical signs included diarrhoea and lethargy which were present at all doses but was limited to the first couple of days at the lower two doses. At the upper two doses clinical signs persisted up to10 days. Other clinical signs observed, primarily at the two higher doses, included chromodacryorrhea, chromorhinorrhea, ptosis and body surface stains (greasy hair). All animals gained weight during the observation period and there were no gross abnormalities noted at necropsy. The notified substance has a low acute oral toxicity with an LD50 > 14.43 g/kg bw.

Two acute dermal toxicity studies were performed on the analogue chemical in New Zealand white rabbits. In

the first experiment the test substance was applied to the shaved intact and abraded ventral skin of the animals (2 animals/sex) at a dose of 20 g/kg bw and covered with an impervious material for a period of 24 hours. There were no mortalities during the 14 day observation period. Clinical signs included diarrhoea in one male and another which had yellow nasal discharge for the first 4 days. Both males also had a yellow nasal discharge on the last day of observation. Both females started showing clinical signs at day 9 which persisted until the end of the observation period. The most common clinical signs were diarrhoea, emaciation, few feces and lethargy. Dermal reactions included mild to moderate erythema in most animals which persisted throughout the 14 day observation period. Mild oedema was also present initially and persisted only in one animal.

In the second experiment, the analogue chemical was applied to the shaved intact and abraded ventral skin of the animals (4 males/dose) at doses of 16 and 20 g/kg bw and covered with an impervious material for a period of 24 hours. One male treated at 20 g/kg bw died on day 11 of the 14 day observation period. All surviving animals maintained their body weight or gained body weight during the observation period. All animals showed clinical signs throughout the 14 day observation period; the most common were lethargy (during the first 10 days), yellow material in the eye and face area, red ears and body stained with material. On day 1, all animals treated at 16 g/kg bw showed dermal erythema (score 1-2) and oedema (score 2) at the site of application. Three of 4 males treated at 20 g/kg bw showed dermal erythema (score 1) and the presence of large swollen veins at the site of application. No oedema was noted. Necropsy performed on animals treated at 20 g/kg bw showed congested and hemorrhagic lungs as well as a dilated heart. Two of the animals showed a decrease in thymus size and the animal which died also had body wasting, scaly skin at the site of treatment and a distended intestine due to gas. An observation noted that the rabbits were licking the material off each other, therefore, the clinical signs observed are likely the result of oral ingestion and not via a dermal exposure. Despite the presence of clinical signs in both experiments, the notified substance has a low acute dermal toxicity in rabbits with an LD50 > 20 g/kg bw.

In above two studies, clinical signs and dermal irritation were observed. One death was noted in the second study only. In this study, necropsy was performed on animals treated at the high dose showing congested and hemorrhagic lungs, a dilated heart, and decrease in thymus size. The effects were partially attributed to oral exposure.

Eye and skin irritation

A non-GLP acute eye irritation assay was performed on the analogue chemical in 2 male and 4 female New Zealand white rabbits. The test substance (0.1 mL) was administered into the conjunctival sac of one eye for each rabbit. There were no corneal or iridial reactions observed in any of the animals at any of the observation time points. Conjunctival redness (score 2) was present in all animals on days 1 and 2 and was reduced to a score of 1 on day 3. Conjunctival chemosis (score 1-2) was present in all animals on all 3 days of observation with the exception of 1 animal where it was not present until the third day. Conjunctival discharge (score of 1-2) was present in all animals on day 1 and 2 but was only present in 2 of 6 animals on day 3. The Maximum Average Score (MAS) on day 1 was 9 which classifies the notified substance as a mild eye irritant according the modified Kay and Calandra classification scheme.

A non-GLP acute skin irritation assay was performed on the analogue chemical in 2 male and 4 female New Zealand white rabbits. The test substance was applied to the intact, shaved dorsal skin of the animals, covered with gauze, held in place with tape. The trunk was then covered with an impervious material for a period of 4 hours. At 4 hours, erythema (score 1) was noted in 5 of 6 animals and oedema (score 1) in 2 of 6 animals. At 24 hours, erythema was noted in 2 animals with a score of 1 and in 4 animals with a score of 2. Oedema (score 1) was noted in 3 animals. At 48 hours, erythema (score 2) was noted on all animals and oedema (score 1 and 2) was noted on 2 animals. The primary irritation score, between 4-48 hours, is 1.94 which corresponds to slight dermal irritation according to the Draize classification scheme.

Skin sensitization

A skin sensitization assay (Magnusson-Kligman) was performed on the analogue chemical in Dunkin-Hartley Guinea pigs (10/dose/sex). Intradermal inductions were done with Freunds Complete Adjuvant (FCA) and 5% w/v of the test substance in olive oil on day 1. Topical inductions were done on day 7; a 5% w/v of the test material in olive oil was applied to the same area of the skin and covered by an occlusive dressing for 48 hours. On day 22, all animals were challenged by application of olive oil to the left flank and 1% of the test substance to the right flank under an occlusive dressing. A second challenge was carried out on day 29 with olive oil or 5% test substance.

In the primary irritation screen, slight erythematous responses were apparent at both sites of occluded topical applications of 5% and at the test site treated with 2.5%. During induction, intradermal administration of olive oil, FCA or 5% test substance elicited dermal responses and changes which did not exceed moderate erythema and discoloration. During the first challenge, with olive oil or 1% test substance in olive oil, the treatment elicited moderate erythema from both flanks of one test animal and slight erythema from both flanks of 2 test and one control animal. One control animal showed slight erythema on the left flank. During the second challenge, there were no responses in the control animals. One animal in the test group developed slight erythema to 5% test substance and one animal in the test group developed slight erythema to olive oil.

The notified substance is not a dermal sensitizer when tested in rabbits at concentrations up to 5% as the reactions present are most likely the result of irritation.

Repeated Dose / Reproductive / Developmental Toxicity

A combined 28-day repeated dose with a reproductive/developmental study was performed on the notified chemical in Wistar rats (10/sex/dose). The test substance was administered once daily to the animals by oral gavage at doses of 50, 200 and 750 mg/kg bw/day for approximately 54 days in males. Females were treated for a 2 week maturation period, pairing, gestation and the first 5 days of lactation. There were no mortalities in adult animals during the test period and there were no clinical signs of systemic toxicity, other than increased salivation at the mid and high dose and episodes of red/brown staining around the mouth and instances of generalized fur loss in high dose animals. There were no differences in behavioural or sensory reactivity assessments between control and treated animals. Males treated at 750 mg/kg bw/day showed a decrease in body weight as compared to controls but no differences in food consumption, food efficiency or water consumption between control and treated animals were noted. There were no differences in hematological parameters between control and treated animals. There was a reduction in alanine aminotransferase in males treated at 750 mg/kg bw/day and a reduction in alkaline phosphatase was observed in all treated males but not females. At day 4 postpartum, females treated at 750 mg/kg bw/day had a 2 fold increase in alanine aminotransferase levels. On day 42, males treated at 750 mg/kg bw/day showed increases in albumin/globulin ratio, a 2 fold increase in alanine aminotransferase level and a reduction in total protein, calcium and bilirubin levels.

Reproductive parameters did not present any treatment related effects detected in mating performance or fertility between control and treated animals. There were no treatment related changes in gestation length and no differences in litter size and offspring viability between control and treated animals. There were no differences in litter weights, or mean offspring body weights between control and treated animals. No clinical signs of systemic toxicity were detected.

At necropsy, there were no gross treatment related changes noted. Both males and females treated at 750 mg/kg bw/day showed an increase in liver weights. Histopathological examination revealed a centrilobular hepatocyte enlargement in males treated at 750 mg/kg bw/day. There was also an increase in follicular cell hypertrophy in the thyroid of males treated at 750 mg/kg bw/day and females treated at 750 mg/kg bw/day had higher grades of lymphoid atrophy of the thymus. In conclusion, the notified substance has a moderate toxicity in adults with a NOAEL of 200 mg/kg bw/day and a low reproductive/developmental toxicity with a NOAEL of 750 mg/kg bw/day.

A 28-day repeated dose assay was performed on the analogue chemical in Sprague-Dawley rats (5/sex/dose). The animals were dosed once daily by oral gavage for 28 consecutive days at doses of 25, 150 and 1,000 mg/kg bw/day (dose volume of 4 mL). An additional two groups, a control and high dose (1,000 mg/kg bw/day), were kept for an additional 14 days after termination of dosing as recovery groups. There were no mortalities noted during the test or observation period. There were no clinical signs of systemic toxicity noted during the test or observation period other than an increase in salivation immediately after dosing and red/brown staining around the mouth of some treated animals. There were no differences in behavioural assessments, functional performance tests and sensory reactivity tests between treated and control animals. There were no significant differences in body weights and body weight gains and no significant differences in food and water consumption between control and treated animals. There were no significant differences in haematological parameters. However, blood chemistry parameters demonstrated the following changes in males: the A/G ratio was elevated in both mid-dose (10%) and high dose males (13.4%), K+ was elevated (8.6%) and P was decreased (25%) at the high dose. ASAT was increased (18.8%) as well as ALAT (2.35 fold) at the high dose. Triglycerides were decreased by 43% and cholesterol was also decreased but did not reach statistical significance. In females, the γGT was elevated in all treated females and was statistically significant at the high dose with an 8 fold increase. ASAT was increased (23%), as well as ALAT (2.7 fold), at

the high dose. As with high dose males, triglycerides and cholesterol were decreased but did not reach statistical significance in females.

There were no differences in urinalysis parameters between control and treated animals.

The brain weight, both absolute and relative to body weight were increased 3- 4.8% in all treated males but was not dose related and is not considered biologically relevant. There was an increase in absolute and relative to body weights in liver weights (15-16%) in females treated with 1,000 mg/kg bw/day after 28 days of treatment and in males treated at 1,000 mg/kg bw/day at the end of the recovery period. The liver was also increased in recovery females but did not reach statistical significance. The epididymis weights were decreased (8.5%) in recovery animals but no change was present at the end of the treatment period. There were no test substance related macroscopic changes noted at necropsy between control and treated animals. Histopathological examination showed a centrilobular hepatocyte enlargement in 4 males treated at 1,000 mg/kg bw/day. Based on the effects on the liver and epididymis the NOAEL was lowered to 150 mg/kg bw/day, therefore the notified substance has a moderate subchronic toxicity in rats.

Genotoxicity
A bacterial reverse mutation assay was performed on the analogue chemical in Salmonella typhimurium strains TA 98, TA 100, TA 1535, TA 1537 and the Escherichia coli strain WP2uvrA at concentrations between 50 – 5,000 µg/plate in both the presence and absence of metabolic activation for 48 hours using the plate incorporation method. There was no visible reduction in the growth of the bacterial background lawn at any of the concentrations tested. A cream coloured particulate precipitate was observed at 1,500 µg/plate and above. The negative control gave the expected number of revertant colonies and all positive controls generated a significant increase in the number of revertant colonies in either the presence or absence of metabolic activation. The test substance did not generate any significant increases in the number of revertant colonies for any of the bacterial strains, in either the presence or absence of metabolic activation in either experiment, therefore the notified substance is not mutagenic *in vitro*.

A chromosomal aberration assay was performed on the analogue chemical using Chinese Hamster Lung (CHL) Cells. The cells were treated at concentrations of 16, 32, 64 and 96 µg/mL in the absence of metabolic activation and at concentrations of 64.38, 128.75, and 257.5 µg/mL in the presence of metabolic activation for an exposure time 6 hours and a harvest at 24 hours. The cells were also treated for a continuous 24 hours at concentrations of 2, 4, and 8 µg/mL in the absence of metabolic activation. A precipitate was observed at a concentration of 32 µg/mL but did not affect scoring of colonies. Negative controls gave the expected number of colonies and the positive controls, mytomycin C (-S9) and cyclophosphamide (+S9), generated significant increases in the number of colonies. The test substance did not induce any statistically significant increases in the number of mutant colonies in either the presence or absence of metabolic activation at any of the doses tested at either 24 or 48 hours; therefore, the notified substance is not clastogenic by the *in vitro* route.

An *in vivo* micronucleus assay was performed on the notified chemical using male CD-1 mice (7/dose). The animals were dosed once intraperitoneally at doses of 200, 400 and 800 mg/kg bw and sacrificed at 24 hours. Additional groups at 800 mg/kg bw and a vehicle control group were included and sacrificed at 48 hours. The positive controls using cyclophosphamide were sacrificed at 24 hours. After sacrifice, the bone marrow for the femur was harvested and the presence of polychromatic erythrocytes was determined as well as the ratio of polychromatic erythrocytes to normochromatic erythrocytes. There were no unscheduled mortalities during the test period. Clinical signs including hunched posture, ataxia and ptosis were observed at 400 and 800 mg/kg bw. The positive control group showed a marked increase in the incidence of micronucleated polychromatic erythrocytes. A statistically significant decrease in the PCE/NCE ratio was observed at 24 and 48 hour for the 800 mg/kg bw test material dose group as compared to the corresponding controls showing that the target organ had been reached. The test substance did not generate a significant increase in the incidence of micronucleated polychromatic erythrocytes at any of the doses tested; therefore, the test substance is not genotoxic/clastogenic when tested in an *in vivo* assay.

Health hazard classification
The data available in the non-Guideline studies submitted are not sufficient to determine fully if hazard classification for skin and eye irritation applies. However the initial irritation scores suggest that the classification would not be warranted.

Based on the available information, 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 or the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004).

6.3. Human Health Risk Characterisation

6.3.1. Occupational Health and Safety

The notified chemical is a mild irritant to the eyes and skin and has a moderate repeated dose toxicity. Workers with the highest potential for exposure are operators and laboratory staff handling the product containing the notified chemical at > 80% during the blending processes. Exposure would be reduced by the closed blending processes, safe work practices and use of personal protective equipment. Once incorporated into fuel, potential worker exposure is much reduced, as the concentration of the notified chemical in fuel is low (< 0.05%). The notified chemical is expected to be combusted as part of the diesel fuel and will then not be available for further exposure.

Based on the available information on toxicity and the occupational use scenarios and controls in place, the notified chemical is not expected to pose an unreasonable risk to workers.

6.3.2. Public Health

The public may have potential for incidental dermal or ocular exposure to the fuel containing the notified chemical at concentration < 0.05% during refuelling processes. Based on the available information on toxicity and the expected low frequency and extent of exposure of the public, the notified chemical is not expected to pose an unreasonable risk to the public.

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 for use as an additive in diesel fuel. No significant release of the notified chemical is expected from transportation and storage.

Blending of the additive containing the notified chemical into diesel fuels will occur in well-controlled industrial facilities. Minimal release of the notified chemical to the environment is expected as blending occurs in fully enclosed automated systems. Accidental spills and leaks during normal blending and packaging procedures, which account for up to 0.5% of the total annual import volume, will be contained and collected for appropriate disposal.

RELEASE OF CHEMICAL FROM USE

When used as an additive in diesel fuel, the majority of the notified chemical will be consumed during the combustion of the fuel by vehicles or machinery.

RELEASE OF CHEMICAL FROM DISPOSAL

Waste water from the cleaning of the import containers and storage vessels is expected to be collected for disposal by an approved waste management company. Release of the notified chemical to surface water is expected to be negligible.

7.1.2. Environmental Fate

Most of the notified chemical in diesel fuel will be consumed and decomposed during use.

Minor amounts of the notified chemical are expected to be disposed of to landfill as residues in containers or collected waste. Given the estimated high soil adsorption-desorption coefficient (log Koc > 4.4) and low water solubility (approximately 1 mg/L based on experimental analogue data), the notified chemical sent to landfill is expected to be immobile. The notified chemical is expected to associate strongly with the organic compartment in soil according to it high log Koc and its potential to partition to organic phases (log Pow 4.55 to ≥ 6.50). The notified chemical is not readily biodegradable based on experimental analogue data (26% by measuring biochemical oxygen demand (BOD) and 36% by measuring the concentration of the residual test substance over 28 days, OECD TG 301C). However, bioaccumulation of the notified chemical is not expected given the low experimental analogue data for the bioconcentration factor (BCF = 258 - 492).

The notified chemical is expected to degrade by biotic and abiotic processes in landfill, or by thermal decomposition, to form water and oxides of carbon and nitrogen. For the details of the environmental fate study please refer to Appendix C.

7.1.3. Predicted Environmental Concentration (PEC)

The predicted environmental concentration (PEC) has not been calculated since no significant release of the notified chemical to the aquatic environment is expected from the reported use pattern.

7.2. Environmental Effects Assessment

No ecotoxicity data were submitted for the notified chemical. However, ecotoxicological investigations conducted on the analogue have been provided for fish, daphnia and algae and the results are summarised in the table below.

Endpoint	*Result*	*Test method*	*Assessment Conclusion*
Fish Toxicity	96 h LL50 > 100 mg/L (WAF)	OECD 203	Not harmful to fish
Daphnia Toxicity	48 h EL50 > 100 mg/L (WAF)	OECD 202	Not harmful to aquatic invertebrate life
Algal Toxicity	72 h EL50 > 100 mg/L (WAF)	OECD 201	Not harmful to algae

All three ecotoxicity studies used a water accommodated fraction (WAF) of the test substance as the exposure medium. WAF test solutions were prepared by adding an excess of the test substance to dechlorinated tap water and stirring for 23 hours, then allowing the mixture to stand for 1 hour. The test solution was obtained by siphoning from mid-depth of the mixing vessel. Microscopic observation of the WAF showed no microdispersions or undissolved material to be present. The dissolved test substance may be one or several components of the test substance. Given that toxicity cannot be attributed to a single component or a mixture of components but to the test material as a whole, the results are based on nominal loading rate only.

The analogue and the notified chemical have the same functional group of concern. They differ from each other only in the length of their carbon chains. Based on their structural similarity, it is expected that the analogue exhibits a similar toxicological profile to the notified chemical.

None of the tests showed any adverse effects of any kind to the test organisms for the analogue and, by inference, for the notified chemical. These results are supported by the estimated ecotoxicological endpoints for representative species of the notified chemical using ECOlogical Structure-Activity Relationships [ECOSAR 1.0, EPI Suite 4.1 (US EPA 2011)], which predicts that the notified chemical is not harmful to aquatic organism up to the limit of its water solubility for acute and long-term endpoints.

Based on both the experimental analogue data and modelling data for the representative species of the notified chemical, it is concluded that the notified chemical is not expected to be harmful to aquatic life up to the limit of its water solubility. Therefore, the notified chemical is not formally classified for acute or long-term hazard under the *Globally Harmonised System of Classification and Labelling of Chemicals* (GHS, United Nations, 2009).

7.2.1. Predicted No-Effect Concentration

Given the expected low hazard and low potential for release of the notified chemical to the aquatic environment, the calculation of the predicted no-effect concentration is not considered necessary.

7.3. Environmental Risk Assessment

Calculation of the Risk Quotient (PEC/PNEC) is not possible since neither the PEC nor the PNEC is available. The notified chemical is not considered to pose an unreasonable risk to the aquatic environment based on its low hazard to aquatic species and assessed use pattern indicating low potential for release to the aquatic environment.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Water Solubility 0.76 - 1.46 × 10^{-3} g/L at 24 °C

Method In house shake flask method (analogue)
Remarks The shake flask method was employed with LC-MS for the analytical detection of the analogue. Six peaks were detected having solubilities ranging from 0.76 - 1.46 mg/L. Since the analogue contains slightly longer carbon chains than the notified chemical, it is estimated that the notified chemical would be slightly more soluble in water than the analogue. The MSDS for the notified chemical states that it is insoluble in cold water.
Test Facility Mitsubishi (2007)

Partition Coefficient (n-octanol/water) log Pow 4.55 to > 6.50 at 35 °C

Method OECD TG 117 Partition Coefficient (n-octanol/water)
Remarks The HPLC method with UV detection was used to determine the octanol water partition coefficient for the notified chemical. Twenty substance peaks eluted having log Pow values ranging from 4.55 to > 6.50. Based on peak area percentage, the majority (85.3%) of the test substance has a log Pow > 6.50.
Test Facility Harlan (2009)

Adsorption/Desorption log Koc > 4.4

Method Güsten and Sabljic Quantitative Structure-Activity Relationship (QSAR)
Remarks The adsorption of the substance was estimated using a QSAR developed for non-hydrophobic chemicals based on their octanol-water partition coefficients where: log Koc = 0.52 × (log Kow) + 1.02. The QSAR model was developed using data from 390 chemicals including some heterocyclic nitrogen compounds. The adsorption coefficient for the substance was calculated using the experimentally derived log Pow value of > 6.50 for the majority of the substance where: log Koc = 0.52 × 6.5 + 1.02 = 4.4. This value is reported rather than the one provided by the notifier (log Koc > 3.4) since it represents the predominant components.
Test Facility Gusten and Sabljic (1995)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

C.1.1. Bioaccumulation

TEST SUBSTANCE	The analogue
METHOD	Bioconcentration test of chemical substances in fish and shellfish, (latest revision, November 2006)
Species	Carp (*Cyprinus carpio*)
Exposure Period	Exposure: 60 days
Auxiliary Solvent	HCO-40, 0.2 mg/L; Tetrahydrofuran, 25 ppm (v/v)
Concentration Range	Nominal: 0.02 mg/L Actual: 0.022 mg/L
Analytical Monitoring	Liquid Chromatography- Mass Spectrametry (LC-MS)
Remarks - Method	In addition to a control with 44 fish, a group of 28 carp were exposed to the test substance. During the exposure period, the concentration of the test substance in water and fish was measured periodically. There was no depuration period. The bioconcentration factor (BCF) was determined by comparing the concentration of the test substance in the fish to the mean concentration of test substance in the test water. Test conditions were: 24 ± 2 °C, pH 6.0 - 8.5 and ≥ 5 mg O_2/L.
RESULTS	
Bioconcentration Factor	BCF = 258 - 492
CT50	Not determined
Remarks - Results	As the test substance is a mixture, many peaks were detected in LC/MS chromatograms. Five quantifiable components (peak A-E) were measured in the determination of BCF. For peak A, B, C and D, the variation of mean BCF determined at the last three measurements fell within 20% and it is considered to reach the steady state. The BCF of peaks A, B, C and D was determined to be 492, 450 455 and 258, respectively. At the peak E the variation of mean BCF determined at the last three measurements could not be confirmed to fall within 20%. Therefore, the steady state BCF was not calculated and the BCF value was indicated to be less than 290. The lipid content of the fish ranged from 2.7 % (n = 3, 2.1 - 3.6%) at the beginning of the test to 4.4% (n = 3, 3.6 - 4.9%) at the end of the test. During the exposure period of 60 days, the mortalities in both control and treated fish were less than 10% at the end of the test. There were no abnormality in shape of the body or in swimming and eating behaviour during the test period. The test is considered reliable.
CONCLUSION	The analogue and, by inference, the notified chemical have a low potential to bioaccumulate in fish.
TEST FACILITY	MSI (2007)

BIBLIOGRAPHY

Gusten H & Sabljic A (1995) In: EC. Overview of Structure-Activity Relationships for Environmental Endpoints: Part 1: General Outline and Procedures: Report fo the EU-DG-XII project QSAR for Prediciton of Fate and Effects of Chemicals in the Environment. QSARS fro Soil Sorption. Belgium, European commission (EC), pp. 6-13, 25-27.EV5V-CT92-0211

Harlan (2009) Determination of partiiton coefficient (Study No. 1491/0095R, March, 2007). Derbyshire, UK, Harlan laboratories Ltd, Afton Chemical corporation (Unpublished report submitted by the notifier)

Mitsubishi (2007) Water solubility (Study No. A060454, March 2007). Yokohama, Japan, Mitsubishi Chemical Safety Institute Ltd. (Unpublished report submitted by the notifier)

MSI (2007) Bioconcentration study of R04-5135 with carp-the thrid concentration level (Study No. A060454). Yokohama, Japan, Mitsubishi Chemical Safety Institute Ltd (MSI), Media Services, Ltd (Unpublished report submitted by the notifier)

NOHSC (2004) Approved Criteria for Classifying Hazardous Substances, 3rd edition [NOHSC:1008(2004)]. National Occupational Health and Safety Commission, Canberra, AusInfo.

NTC (National Transport Commission) 2007 Australian Code for the Transport of Dangerous Goods by Road and Rail (ADG code), 7th Edition, Commonwealth of Australia

Southwest Research Institute (2012) Flammability Evaluation in Accordance with ASTM D93-11, Standard Test Methods for Flash Point by Pensky-Martens Closed Cup Tester, and in General Accordance with U/N. Manual of Tests and Criteria, Section 32.5.2 - Test L.2: Sustained Combustibility Test, of HiTEC 4897 Petroleum Fuel Additive (SwRI Project No.: 01.16919.01.304, April 2012). San Antonio, USA, Southwest Research Institute (Unpublished report submitted by the notifier)

United Nations (2009) Globally Harmonised System of Classification and Labelling of Chemicals (GHS), 3rd revised edition. United Nations Economic Commission for Europe (UN/ECE), <http://www.unece.org/trans/danger/publi/ghs/ghs_rev03/03files_e.html>.

US EPA (2011) Estimation Programs Interface (EPI) Suite™ for Microsoft® Windows, v 4.10. United States Environment Protection Agency, Washington, D.C., USA. Website: http://www.epa.gov/oppt/exposure/pubs/episuite.htm. Accessed on 6 February 2013