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HIGH PRODUCTION VOLUME (HPV)

CHALLENGE PROGRAM

FINAL SUBMISSION

For

Nitric Acid, 2-Ethylhexyl Ester

Prepared by
The American Chemistry Council
Petroleum Additives Panel
Health, Environmental, and Regulatory Task Group

October 2006

LIST OF MEMBER COMPANIES IN THE
HEALTH, ENVIRONMENTAL AND REGULATORY TASK GROUP

The Health, Environmental, and Regulatory Task Group (HERTG) of the American Chemistry Council Petroleum Additives Panel include the following member companies:

Chevron Oronite Company, LLC

Afton Chemical Company (formerly Ethyl Corporation)

Groupe SNPE

Infineum

The Lubrizol Corporation

SI Group (formerly Schenectady International Inc)

1.0 INTRODUCTION

In March 1999, the American Chemistry Council (formerly the Chemical Manufacturers Association) Petroleum Additives Panel Health, Environmental, and Regulatory Task Group (HERTG), and its participating member companies committed to address certain chemicals listed under the Environmental Protection Agency (EPA) High Production Volume (HPV) Chemical Challenge Program. This test plan follows up on that commitment. Specifically, the test plan set forth how the HERTG intended to address testing information for the following substance: Nitric Acid, 2-Ethylhexyl Ester (2-EHN) (CAS No.: 27247-96-7).

In preparing the test plan the following steps were undertaken:

Step 1: A review of the literature and confidential company data was conducted on the physicochemical properties, mammalian toxicity endpoints, and environmental fate and effects for 2-EHN, using its CAS number, CAS name, and synonyms. Searches included the following sources: MEDLINE, BIOSIS, CANCERLIT, CAPLUS, CHEMLIST, EMBASE, HSDB, RTECS, EMIC, and TOXLINE databases; the TSCATS database for relevant unpublished studies on these chemicals; and standard handbooks and databases (e.g., Sax, CRC Handbook on Chemicals, IUCLID, Merck Index, and other references) for physicochemical properties.

Step 2: The compiled data was evaluated for adequacy in accordance with the EPA guidance documentation.

This report summarizes the results of the test plan.

2.0 GENERAL SUBSTANCE INFORMATION

The substance that is the subject of this test plan is used as a fuel additive in diesel fuels. The chemical name, CAS Registry Number, molecular weight and chemical structure for this substance are presented below.

Chemical Name: Nitric acid, 2-ethylhexyl ester (2-EHN)

Chemical Abstract Service Registry Number: 27247-96-7

Molecular Weight: 175.2 g/mol

Chemical Structure:

$$\begin{array}{c} CH_2\text{-}O\text{-}NO_2 \\ | \\ CH_3CH_2\text{-}CH\text{-}CH_2CH_2CH_2CH_3 \end{array}$$

3.0 EXPOSURE INFORMATION

3.1 Manufacture

A 50/50 mixture of undiluted Nitric and Sulfuric Acids is fed to a reaction tank along with a stoichiometric amount of 2-Ethylhexanol. The formation of the 2-EHN is almost instantaneous.

The reaction equation is as follows:

C8H17OH + HNO3 + (H2SO4) ------> C8H17NO3 + H2O +(H2SO4) + H = 12 kcal/g mole

Any residual water is removed by passing the material through alumina bead dryers. The final 2-EHN product is then filtered and sent to storage.

3.2 Use

2-EHN is used as an ignition improver additive in diesel fuels to raise the cetane number.

4.0 PHYSICOCHEMICAL PROPERTIES

Chemical and physical properties for 2-EHN are listed below:

Flash point	>70°C (closed cup)
Freezing point	<-45ºC
Boiling point	>100ºC (decomposes)
Vapor pressure	27 Pa @ 20ºC
Vapor pressure	40-53 Pa @ 40ºC
Vapor pressure	1.33 kPa @ 82ºC
Density	0.96 g/ml @ 20ºC
Solubility in water	12.6 mg/L @ 20ºC
Lower explosive Limit	0.25% v/v in air (literature value)
Decomposition temperature	>100°C
Log_{10} K_{ow}	5.24

Note: 2-EHN is a liquid at ambient temperatures (thus melting point is not-applicable). This substance undergoes a self-accelerating decomposition reaction if heated above

100°C. This exothermic reaction can become extremely violent and can ultimately end in an explosion. Therefore, the boiling point of this substance is not applicable.

5.0 ENVIRONMENTAL FATE DATA

5.1 Biodegradability

A ready biodegradability, CO2 Headspace Test was conducted which showed that the test substance was not considered readily biodegradable under the criteria that requires 60% biodegradation within 28 days, achieved within 10 days of reaching 10% biodegradation. The CO_2 production from the reference chemical exceeded the 60% of theoretical necessary to consider the test valid. The degradation for the toxicity control was 34% as of day 28 therefore the test substance was not considered to be inhibitory at the concentration tested. The water solubility of this test material is relatively low and coupled with the volatile nature of the test material, this may have resulted in the majority of the test material being present in the headspace and not proportionally dissolving in the test media. The test material may not have been bioavailable and this may have contributed to the lack of biodegradation.

5.2 Hydrolysis

2-EHN was shown to hydrolyze in each of the pH conditions tested (pH 4, 7 and 9 at 25 and 50°C). The mean half-life of the compound and water reaction at 25°C ranged from 370 hours (pH 4.0) to 108 hours (pH 9.0)

5.3 Photodegradation

The test substance was found to have a molar absorption coefficient of 6.07 $dm^3cm^{-1}mol^{-1}$ and an absorbance of 0.0096113 at 290 nm. The concentration of the test substance was 1.581 x 10^{-3} mol/dm^3. It was clear from the absorption spectrum that the test material did not exhibit any significant absorbance at wavelengths greater than 250 nm. In order to assess if a photochemical degradation study is required the test substance must have significant absorbance at wavelengths greater than 290 nm. The critical value for the study to be performed requires a molar absorption coefficient to be >10 at 290 nm. This test substance had a molar absorption coefficient of <10 at 290 nm. Therefore no photochemical degradation study was required.

5.4 Fugacity Modeling

The relative distribution of 2-EHN among environmental compartments was evaluated using EQC (v 2.02) Level I Fugacity model. Water solubility (20 °C), vapor pressure (20 ºC), and octanol-water coefficient (see Physical Chemical Properties) were inputs in the EQC Level I model.

The modeled data are shown below. The modeled fugacity results for this compound indicate that these compounds will most likely distribute to soil and air. Much lesser amounts are found in water, sediment, suspended particles, and fish.

Medium	Amount % of total released
Air	32.7
Water	0.425
Soil	65.4
Sediment	1.45
Suspended particles	0.0454
Fish	0.00369

6.0 ECOTOXICOLOGY DATA

6.1 Aquatic Ecotoxicity Testing

6.1.1 Acute Toxicity to Fish

The 24, 48, 72 and 96 hour LC50s were all >12.6 mg/L.

6.1.2 Acute Toxicity to Daphnia

The 24 and 48 hour EC50s were >12.6 mg/L. The 24 and 48 hour NOECs were >10 mg/L.

6.1.3 Acute Toxicity to Algae

The 72-hour NOEC, based on growth rate and growth inhibition, was 12.6 mg/L.

7.0 MAMMALIAN TOXICOLOGY DATA

7.1 Acute Mammalian Toxicity

Acute oral and dermal toxicity studies are available for 2-EHN. In these studies, the LD_{50} was greater than 10 mL/kg by the oral route and greater than 5 mL/kg by the dermal route indicating very low acute toxicity.

7.1.1 Acute Oral Toxicity

LD50 (rat) >10 mL/kg (males and females)

7.1.2 Acute Dermal Toxicity

LD50 (rabbit) > 5 mL/kg

7.2. Genetic Toxicity

7.2.1 Bacterial Reverse Mutation Assay

The test substance was not mutagenic in this assay with or without metabolic activation.

7.2.2 In Vitro Chromosomal Aberration Assay

The test material was negative for the induction of structural and numerical chromosome aberrations in human peripheral blood lymphocytes in the presence and absence of a liver metabolizing system at dose levels that induced acceptable levels of toxicity.

7.3 Repeated-dose, Reproductive and Developmental Toxicity

7.3.1 14-day Inhalation Toxicity Studies in Rats (2 week recovery periods)

Male rats were exposed to the test article via inhalation at concentrations of 0, 14, 42, and 150 ppm. Exposure at 14 ppm or higher resulted in an elevation of mean liver weights. Lipid like cytoplasmic inclusions were found in hepatocytes at all concentrations tested. However since unrestrained, nonfasted rats did not exhibit a similar finding the inclusion bodies were considered a physiological response to restraint and were not considered related to the test article. Eosinophilic cytoplasmic inclusions in cells of the renal proximal tubule were also noted at 14 ppm and higher. This was considered to represent the male rat hydrocarbon nephropathy, a common finding in male CD rats and not relevant for hazard assessment for humans. This finding was less severe after recovery and was not considered biologically significant at concentrations of 42 ppm or less. A treatment related polycythemia was observed at 150 ppm. The NOAEL was 42 ppm.

7.3.2 21-day Dermal Toxicity Study in Rabbits

Animals were dosed at 0, 50, 500 mg/kg. Based upon the lack of systemic toxicity at any dose tested, a NOAEL of >500 mg/kg was established for this study.

7.3.3 28-day Oral Toxicity Study in Rats

Animals were dosed daily with 0, 20, 100, or 500 mg/kg/day for 28 days.

A statistically significant decrease was observed in the mean body weight of the high dose females during the last week of treatment and during the first week of recovery. A statistically significant decrease was observed in the mean food consumption of the high dose females during the last week of treatment but not during recovery.

Following 28 days of treatment the high dose males exhibited a statistically significant increase in mean platelet number. No other treatment related changes were observed in the hematology data. The high dose females exhibited a significant increase in urea nitrogen and a significant decrease in chloride following 28 days of treatment but not following recovery.

A number of alterations were observed in the urinalysis data of mid and high dose 28 day sacrifice animals, these included: a significantly acidic urinary pH in high dose males and females; a significant increase in protein, ketone bodies, urobilinogen, volume, potassium and chloride in high dose males and females; a significant increase in ketone bodies in the mid dose females; and a significant increase of epithelial cells in the urine sediment of the mid and high dose females. In the high dose recovery females significant decreases in sodium, potassium and chloride were observed.

Significant increases were observed in the absolute and relative liver and kidney weights of the high dose males and in the relative liver and kidney weights of the high dose females. Elevated kidney weights persisted in the high dose males throughout the recovery period. Increased relative adrenal weights were also observed in the high dose females.

At the 28 day necropsy enlarged livers were observed in the mid dose males and high dose males and females. Enlargement of the kidneys was observed in the high dose males. Following recovery enlarged kidney was observed in one high dose male.

Microscopic changes observed in the kidney of the mid and high dose males included the appearance of hyaline droplets in the proximal tubular epithelium and regenerative changes of the renal tubules. The regenerative change was also observed in one high dose recovery male. None of these effects were observed in the females.

The NOAEL was 20 mg/kg/day based on the appearance of effects in the liver and kidneys, as well as changes in clinical chemistry parameters at higher doses.

7.3.4 Developmental Toxicity

Male and female Sprague-Dawley rats were gavaged with the test article, from before mating, during mating, gestation and until day 5 *post-partum*, at dose-levels of 20, 100 or 500 mg/kg/day.

Systemic toxicity was observed at all dose-levels, as evidenced by reduced body weight gain during, at least, the premating period (at least 13% less weight gained than the controls during the first 2 weeks of treatment, statistically significant at 500 mg/kg/day). As body weight gains which are reduced by more than 10% are considered biologically significant, all groups had biologically significantly reduced body weight gains. Clinical signs of hypoactivity and half-closed eyes were also observed at 100 and 500 mg/kg/day and food consumption was lower than the controls' for females given 500 mg/kg/day. Clinical signs were also observed at 100 and 500 mg/kg/day and food consumption was lower than controls' for females given 500 mg/kg/day.

There were no effects of treatment on pairing. As pup survival was higher in the control group than the 500 mg/kg/day group, a relationship between development of the fetuses and pups and treatment cannot be excluded. At this high dose one female showed only implantation scars and a single dead fetus in the uterine horns whereas another female delivered a litter of small pups that subsequently died on day 3 *post-partum*.

Mean pup body weight at 500 mg/kg/day was less than that of the controls on day 1 *post-partum* and pup body weight gain was reduced at 100 and 500 mg/kg/day.

There were no treatment-related findings observed at macroscopic or microscopic examination of F0 animals and no effects on organ weights.

The No Observed Adverse Effect Level (NOAEL) for parental toxicity was considered to be 20 mg/kg/day, and the NOAEL for toxic effect on reproductive performance and on progeny was 100 mg/kg/day.

TABLE 1

SUMMARY OF DATA

	Study Results
Physical/Chemical Characteristics	
Melting Point	Not Applicable
Boiling Point	Not Applicable (violently decomposes)
Vapor Pressure	27 Pa @ 20ºC
Water Solubility	12.6 mg/L @ 20ºC
Partition Coefficient	Log_{10} K_{ow} = 5.24 Partition Coefficient: 1.73 x 10^5
Environmental Fate	
Biodegradation	Not considered readily biodegradable
Hydrolysis	Hydrolysis occurred under all conditions evaluated.
Photodegradation	This test substance had a molar absorption coefficient of <10 at 290 nm. Therefore no photochemical degradation study was required.
Fugacity	The modeled fugacity results for this compound indicate that these compounds will most likely distribute to soil and air. Much lesser amounts are found in water, sediment, suspended particles, and fish. Medium — Amount % of total released Air — 32.7 Water — 0.425 Soil — 65.4 Sediment — 1.45 Suspended particles — 0.0454 Fish — 0.00369
Ecotoxicity	
Acute Toxicity to Fish	24, 48, 72 and 96 hour LC50s: >12.6 mg/L
Acute Toxicity to Invertebrates	24 and 48 hour EC50s: >12.6 mg/L 24 and 48 hour NOEC: >10 mg/L
Acute Toxicity to Algae	72 hour NOEC: 12.6 mg/L

Mammalian Toxicity	
Acute Toxicity	Oral LD50: >10 mL/kg (rat) Dermal LD50: >5 mL/kg (rabbit)
Repeated Dose Toxicity	14 Day Inhalation NOEL: 42 ppm 21 Day Dermal NOEL: >500 mg/kg (systemic) 28 Day Oral NOEL: 20 mg/kg/day
Developmental Toxicity	NOAEL for parental toxicity = 20 mg/kg/day NOAEL for toxic effect on reproductive performance and progeny =100 mg/kg/day
Reproductive Toxicity	NOAEL for parental toxicity = 20 mg/kg/day NOAEL for toxic effect on reproductive performance and progeny =100 mg/kg/day
Genotoxicity	
Gene Mutation	Negative
Chromosomal Aberration	Negative for the induction of structural and numerical chromosome aberrations in human peripheral blood lymphocytes