FOREOWRD INTRODUCTION

2-METHYL-2-BUTENE

CAS N°: 513-35-9

SIDS Initial Assessment Report

For

SIAM 19

Berlin, Germany, 19-22 October 2004

1. Chemical Name:	2-Methyl-2-butene
2. CAS Number:	513-35-9
3. Sponsor Country:	United States
4. Shared Partnership With:	American Chemistry Council (ACC), Olefins Panel
5. Roles/Responsibilities of the Partners:	
• Name of industry sponsor /consortium	ACC, Olefins Panel: Dr. Elizabeth Moran
• Process used	SIDS documents were drafted by ExxonMobil Biomedical Sciences, Inc. (EMBSI), Annandale, NJ, USA, then reviewed by industry toxicologists from the ACC, Olefins Panel and submitted to the United States (US) EPA for comment prior to their being posted on the chemical discussion group (CDG).
6. Sponsorship History	
• How was the chemical or category brought into the OECD HPV Chemicals Programme?	Industry committed to support 2-methyl-2-butene in the SIDS Program. Industry contacted the US EPA and requested their support as a sponsor for this chemical. Industry prepared draft SIDS documents intended for consideration at SIAM 19; initial drafts were submitted and reviewed by the US EPA.
7. Review Process Prior to the SIAM:	ACC, Olefins Panel industry toxicologists reviewed and commented on the first draft prepared by EMBSI. The second draft was submitted to the US EPA for review and comment. The submission documents were then updated and the US EPA posted all documents for review and comment within the CDG. CDG comments addressed 28 Sep 2004.
8. Quality Check Process:	**Industry Consortium:** Critical biological studies discussed in the SIAR were reviewed for quality by industry and assigned a reliability code, based on the review process guidance of Klimisch *et al*. (1999). Robust summaries of critical data were added to a SIDS dossier and key studies identified and flagged as "critical". The summary formats for selected endpoints were based on descriptions in the OECD Form and Guidance for preparing and submitting the SIDS

DOSSIER (INCLUDING ROBUST STUDY SUMMARIES), which is from the Manual for Investigation of HPV Chemicals.

US Competent Authority:
US EPA reviewed the SIDS documents and audited selected key studies to check the robust study summaries.

9. Date of Submission: July 23, 2004 revised 29 Sep 2004

10. Comments: None

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	513-35-9
Chemical Name	2-Methyl-2-butene (2M2B)
Structural Formula	CH3 | CH3-C=CH-CH3

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

No toxicokinetic studies have been conducted with 2-methyl-2-butene (2M2B). Mice are likely to be more sensitive to 2M2B compared to rats, consistent with data on the metabolism of other olefins. The oral LD_{50} of 2M2B is in the range of 1000 to 1700 mg/kg (1.6-2.5 mL/kg). Survivors showed reversible signs of intoxication. The dermal LD_{50} is >2 g/kg. The 4-hour LC_{50} is 61,000 ppm (174,500 mg/m^3). Inhalation of 2M2B can produce central nervous system depression, anesthesia and/or asphyxiation that are reversible following cessation of exposures. 2M2B is a mild skin irritant but does not produce eye irritation. 2M2B is not a skin sensitizer.

In a combined repeat dose/reproductive/developmental study (OECD 422), rats were exposed (whole body) via inhalation to 580, 2,000, and 7,000 ppm (1,660; 5,720; and 20,000 mg/m^3) 2M2B. For the repeated dose phase of the study the exposures were for 6 hr/day, 7 days/week for 28 days. There was a slightly lower bodyweight gain at 7,000 ppm, slightly longer clotting times at 2,000 ppm (prothrombin time for females) and 7,000 ppm (prothrombin times for both sexes and activated partial thromboplastin times for males). Cholesterol levels were increased among the females exposed to 7,000 ppm but in the absence of any further effects in the clinical chemistry parameters or the males this finding is of uncertain significance. Pathological changes were noted among the high-dose females in the liver, as evidenced by increased organ weight and minimal centrilobular hepatocyte hypertrophy. There was also a decreased incidence of extramedullary hematopoiesis in the spleen in the high dose animals and an increase in goblet cell hyperplasia in the nasal passages of the high dose males. In addition, a slight increase in severity of myocardial inflammatory heart lesions and in cortical/medullary tubular basophilia in the kidneys was observed in the high- and intermediate-dose males. Although some general systemic effects were observed in this study, these effects were slight and were most apparent in those animals exposed to the highest dose, 7,000 ppm, and to a lesser extent to those exposed to 2,000 ppm. Based on these observations, the No Observed Effect Level (NOEL) in this study was 580 ppm (1,660 mg/m^3).

2M2B is not mutagenic *in vitro*. It did not induce gene mutations in reverse mutation assays conducted in *Salmonella typhimurium* and *Escherichia coli* either in the presence or absence of metabolic activation. 2M2B did not produce revertant colonies in a gene conversion assay conducted in *Saccharomyces cerevisiae* and it did not induce chromosome damage in cultured rat liver cells.

2M2B was mutagenic at high exposure concentrations ($\geq$ 3,207 ppm ($\geq$ 9,199 mg/m^3)) when tested *in vivo* for its ability to induce micronuclei in bone marrow polychromatic erythrocytes in both mice and rats. However, the incidence was not considered statistically significant at 1,000 ppm (2,869 mg/m^3).

In the combined repeat dose/reproductive/developmental study (OECD 422), rats exposed to concentrations up to 7,000 ppm, 6 hr/day, 7days/week for two weeks prior to breeding, during breeding and through day 19 of gestation. No evidence of reproductive or developmental toxicity was seen. The estrus cycle was unaffected by exposure, and mating performance, fertility indices, and gestation length were similar in all groups. There were no adverse effects upon survival or growth of the offspring *in utero* or up to day 4 of lactation. Thus, the No Observed Effect Level (NOEL) for reproductive and developmental toxicity is 7,000 ppm (20,000 mg/m^3) (highest dose tested).

Environment

2M2B is a flammable liquid with a measured vapour pressure of 623.9 hPa (25 °C), water solubility of 193 mg/l (25 °C), log K_{ow} of 2.67boiling point of 38.5 °C, and density of 0.662 g/cm^3 (25 °C).

In the air, 2M2B has the potential to rapidly degrade through indirect photolytic processes mediated primarily by hydroxyl radicals and ozone with calculated degradation half-lives ranging from approximately 1 to 4 and 0.6 hours, respectively, depending on hydroxyl radical and ozone concentrations. Aqueous photolysis and hydrolysis will not contribute to the transformation of 2M2B in aquatic environments because it is either poorly or not susceptible to these reactions.

The photochemical ozone creation potential index for 2M2B has been reported to range from 77.1 to 84.2. Because of the relatively short half-life of 2M2B in the atmosphere and the low environmental concentrations typically found, its contribution to potential global warming can be considered minor. The ozone depletion potential of this substance is negligible as indicated by its net ability to form ozone in the atmosphere.

Results of Mackay Level I distribution modeling show that 2M2B will partition primarily to the air compartment (99.97%), with a negligible amount partitioning to water (0.02%) and soil (0.01%). Level III modeling indicates that at steady state, water is the dominant medium on a percentage basis. Level III modeling may not be representative of ultimate disposition of 2M2B because default emission data used in the model (1000 kg/h) is not a representative rate of chemical discharge. However, concentrations in water are most likely very low because 2M2B is quite volatile, and any volatilised substance will be quickly degraded in the atmosphere. When released primarily to the air compartment, the primary mode of removal would be via photodegradation based on the volatility of 2M2B. In spite of its water solubility, wet deposition of 2M2B is not likely to play a significant role in its atmospheric fate because of rapid photodegradation. Volatilisation to the air will contribute to the rapid loss of 2M2B from aqueous and terrestrial habitats.

2M2B is not readily biodegradable. Bioaccumulation of 2M2B is unlikely based on a low potential to bioconcentrate based on a BCF of 22.7. 2M2B is not expected to sorb significantly to organic matter in soil, sediment, and wastewater solids based on a log K_{oc} of 1.83.

Acute aquatic toxicity values for fish and invertebrates are 5.0 (96hr-LC50) and 3.8 (48hr-EC50) mg/L, respectively. For algae, the 96-hr EC_{50} values are 10.1 mg/L and 13.2 mg/L for biomass and growth rate, respectively, while the NOEC values are 3.61 mg/L and 7.22 mg/L for biomass and growth rate, respectively.

Measured chronic aquatic toxicity values for fish and invertebrates are not available. However, QSAR (Quantitative Structure-Activity Relationship) data include a fish 30-day chronic value of 1.75 mg/L and a 16-day daphnid chronic value of 0.94 mg/L.

Although there are no experimental terrestrial toxicity data available, a 14-day LC_{50} value of 268.3 mg/kg soil has been calculated for an earthworm.

Exposure

Production of 2M2B in the United States is between 5,000 and 23,000 metric tonnes annually. 2M2B is largely used as a chemical intermediate, primarily in the production of isoprene and hydrocarbon resins. It is also used as an intermediate in the production of tertiary pentyl alcohol and is a constituent of gasoline, typically at levels below 1%.
2M2B is a component of natural gas and crude oil. Although 2M2B has been identified in natural environments, this has traditionally been associated with losses from petrogenic sources resulting from off gassing or venting. Anthropogenic sources of 2M2B can result from combustion of fossil fuels and losses from gas plants and refineries.

Exposure to 2M2B may occur at workplaces where it is manufactured. Based on physical properties, inhalation and dermal contact would be the primary workplace routes of exposure. One company reports there are 228 workers potentially exposed to 2M2B during production at 6 sites in 5 countries (2 in the US, 3 in Europe, 1 in Asia-Pacific). Since 2M2B production occurs in closed systems, significant worker exposure would occur only during equipment maintenance or under upset conditions. An exposure assessment indicated that 2 of 228 workers (1%) were likely to be exposed to concentrations of 2M2B between 1 and 5 ppm. Slightly less than 10% (22/228) would be exposed to concentrations between 0.1 to 1 ppm, and approximately 90% of workers would have negligible exposures (below

the limit of detection, or < 0.1 ppm).Inhalation of 2M2B by consumers can occur and is the primary route of exposure at gas stations where gasoline-containing 2M2B is sold. Average 2M2B air concentrations at gas stations were reported as 0.11 ppm (0.3 mg/m^3) (air) based on data for six stations from three United States cities between October to November 1990. Mean 2M2B exposure levels for gas station attendants, transport drivers, and outside operators were reported as 1.986, 0.740, and 0.446 mg/m^3, respectively. Fueling at gas stations may result in air-borne concentrations of 1 to 3.5% in the vapor phase from those formulations containing 2M2B.

RECOMMENDATION AND RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

The chemical is currently of low priority for further work. The chemical possesses properties indicating a hazard for human health (mutagenic at high concentrations) and the environment (acute fish, aquatic invertebrates, and algae). Based on exposure data presented by the sponsor country (relating to production in one country which accounts for an unknown fraction of the global production and relating to the use pattern in one country), under normal manufacturing, formulation, industrial and consumer use, this chemical is a low priority for further work. Countries may wish to investigate any exposure scenarios that were not presented by the sponsor country.

SIDS Initial Assessment Report

1 IDENTITY

1.1 Identification of the Substance

CAS Number:	513-35-9
IUPAC Name:	2-methyl-2-butene (2M2B)
Molecular Formula:	C_5H_{10}
Structural Formula:	CH3 | CH3-C=CH-CH3
Molecular Weight:	70.14
Synonyms:	2-Methylbut-2-ene; 2-Butene-2-methyl; Methyl butene-2, 2-; Amylene; Amylene, tertiary; Isoamylene, beta; ß-Isoamylene; 1,1,2-Trimethyl ethylene; Trimethyl ethylene; n-Amylene

1.2 Purity/Impurities/Additives

2-Methyl-2-butene (2M2B) purity is greater than 99% w/w. Impurities in 2M2B may include 2M2B dimer at less than or equal to 0.5% w/w. 2M2B can contain 150 to 250 ppm p-tert-butyl catechol added as a stabiliser.

1.3 Physico-Chemical properties

Table 1. Summary of 2-methyl-2-butene physico-chemical properties.

Property	Value	Reference/Comment
Physical state	Liquid at 25°C	
Melting point (°C)	-133.7	Lide et al., 1997
Boiling point (°C @ 1,013 hPa)	38.5	Lide et al., 1997
Relative density (g/cm^3, @20°C)	0.662	Lide et al., 1997
Vapour pressure (hPa, @25°C)	623.9	Daubert and Danner, 1989
Water solubility (mg/L, @25°C)	193	Hine and Mookerjee, 1975
Partition coefficient n-octanol/water (log K_{ow} value)	2.67	Abraham et al., 1994
Henry's Law constant (HLC) ($Pa\text{-}m^3$/mole, @ 25°C)	11,145 (0.110 $atm\text{-}m^3$/mole)	Hine et al., 1975
Partition coefficient organic carbon/water (log K_{oc} value)	1.83	EPIWIN, 1999

2 GENERAL INFORMATION ON EXPOSURE

Exposure to 2M2B may occur at workplaces where it is manufactured. Based on physical properties, inhalation and dermal contact would be the primary workplace routes of exposure. Consumers may be exposed to 2M2B since it is present in gasoline at about 1 to 3.5% in the vapor phase. Inhalation of 2M2B by consumers can be the primary route of consumer exposure at gas stations where gasoline-containing 2M2B is sold (Sawyer, 1994; Conner, 1995).

2.1 Production Volumes and Use Pattern

2M2B is produced commercially by catalytic or thermal cracking of high boiling petroleum fractions or steam cracking of a mixture of saturated hydrocarbons. Isopentane is separated from the resultant product mixture of C5 hydrocarbons by extraction into 45 to 65% sulphuric acid with subsequent regeneration of 2M2B by steam stripping. Other processes that may be used to produce 2M2B include the dehydration of pentanols and the thermal dehydrogenation of pentanes (SRI, 1998; Kirk-Othmer, 2004).

Production of 2M2B in the United States is between 5,000 and 23,000 metric tonnes annually according to the 2002 USEPA Inventory Update Report.

2M2B is largely used as a chemical intermediate, primarily in the production of isoprene (SRI, 1998. It is also used as an intermediate in the production of hydrocarbon resins, tertiary pentyl alcohol, a stabilizer for chloroform, and is a constituent of gasoline, typically at levels below 2.5% (Kirk-Othmer, 2004).

2.2 Environmental Exposure and Fate

2.2.1 Sources of Environmental Exposure

2M2B is a component of natural gas and crude oil. Although 2M2B may be found in natural environments, offgassing or venting (e.g. underwater or near-shore oil seepage) from petrogenic sources is likely to have contributed to its presence. Trace levels of 2M2B may be identified in urban and suburban air arising from combustion of fossil fuels and losses from gas plants and refineries.

2.2.2 Photodegradation

The relatively high vapor pressure of 2M2B suggests that its environmental fate can occur predominantly in the atmosphere. Results from the Mackay Level I distribution model (Mackay, 1998) support this position and show that 2M2B will partition predominantly to the air compartment (Table 2). 2M2B has the potential to degrade to a significant extent in the atmosphere through indirect photolytic process mediated by OH^- and O_3. In spite of its water solubility, wet deposition of 2M2B is not likely to play a significant role in its atmospheric fate. In comparison, direct photolysis is not expected to contribute to the fate of 2M2B in the aqueous environment.

Indirect Photolysis

In air, a chemical can react with photosensitised oxygen in the form of OH^- and ozone O_3. These reactions can result in a degradative change in the parent chemical that can ultimately lead to its complete degradation.

2M2B can rapidly react with OH^- in air, which can be a predominant daylight atmospheric degradation process for this chemical. It can also react with O_3. 2M2B air half-lives of 4.4 and 0.63 hours have been reported based on reactions with OH^- (Atkinson, 1985) and O_3 (Atkinson and Carter, 1984), respectively. The OH- reaction half life was calculated using a rate constant of 8.69E-11 $cm^3mol^{-1}s^{-1}$ and an OH^- concentration of 5E5 OH^-/cm^3, while the O_3 reaction half life was calculated using a rate constant of 4.23E-16 $cm^3mol^{-1}s^{-1}$ and an O_3 concentration of 7.2E11 O_3/cm^3.

Potential OH^- reaction rate and atmospheric chemical half-life is calculated based on an average OH^- radical concentration. The atmospheric oxidation potential model (Meylan and Howard, 1993) uses a rate constant of 8.73E-11 $cm^3mol^{-1}s^{-1}$ to calculate an average 2M2B atmospheric half-life ($t_{½}$) of 1.47 hours or 0.12 days based on a 12-hour day (the 12-hour day half-life value normalizes degradation to a standard day light period during which hydroxyl radicals needed for degradation are generated). The atmospheric half-life was calculated using an average global OH^- concentration of 1.5E6 OH^-/cm^3 (EPIWIN, 1999).

These data indicate that indirect photodegradation can contribute significantly to the rapid degradation of 2M2B in the environment.

Direct Photolysis

Direct photochemical degradation in aqueous solution occurs through the absorbance of solar radiation by a chemical substance. If the absorbed energy is high enough, then the resultant excited state of the chemical may undergo a transformation. A prerequisite for direct photodegradation is the ability of one or more bonds within a chemical to absorb ultraviolet (UV)/visible light in the 290 to 750 nm range. Light wavelengths longer than 750 nm do not contain sufficient energy to

break chemical bonds, and wavelengths below 290 nm are shielded from the earth by the stratospheric ozone layer.

An approach to assessing the potential for a substance to undergo photochemical degradation is to assume that degradation will occur in proportion to the amount of light wavelengths >290 nm absorbed by constituent molecules (Zepp and Cline, 1977). 2M2B does not absorb light within a range of 290 to 750 nm, which indicates that photolysis will not significantly contribute to the degradation of 2M2B in the aquatic environment.

Conclusion

Data indicate that indirect photodegradation can contribute significantly to the rapid degradation of 2M2B in the environment. Direct photolysis, however, will not significantly contribute to the degradation of 2M2B in the aquatic environment.

2.2.3 Stability in Water

Results from an equilibrium distribution model (Mackay Level I) show that 2M2B will partition negligibly to the water compartment. However, the low levels of 2M2B that may occur in aquatic environments are unlikely to degrade by hydrolysis because this process requires specific chemical structures not present in 2M2B. The lack of a suitable leaving group renders a compound resistant to hydrolysis. Simple hydrocarbons such as 2M2B are resistant to hydrolysis because they lack a functional group that is hydrolytically reactive (Harris, 1982).

Conclusion

Hydrolysis will not contribute to the removal of 2M2B from the environment.

2.2.4 Transport between Environmental Compartments

Fugacity-based multimedia modeling provides basic information on the relative distribution of a chemical between selected environmental compartments (i.e., air, soil, water, sediment, suspended sediment, and biota). Widely used fugacity models are the EQC (Equilibrium Criterion) Level I and Level III models (Mackay, 1996). These models require the input of basic physicochemical parameters (i.e., molecular weight, melting point, vapor pressure, water solubility, log K_{ow}). The Level III model also requires the input of emission rate and half-life data.

Results of the Mackay Level I environmental distribution model (Table 2) show that 2M2B has the potential to partition primarily to air, with a negligible amount partitioning to water and soil. These results can be explained by 2M2B's high vapour pressure, 623.9 hPa at 25°C (Daubert and Danner, 1989). Whereas, Level III modeling (Table 3) indicates that 2M2B partitions mostly to the water compartment rather than air compartment when an equal emission rate (1000 kg/hr) to each compartment is assumed. When releases occur only to each of the air and water compartments, independent of one another, 2M2B is indicated in the modeling to partition primarily to those compartments, respectively. However, Level III modeling is unlikely to be representative of the ultimate disposition of 2M2B because a default emission rate was used in the model (1000 kg/hr) and is not representative of actual chemical discharge.

Table 2. Environmental distribution as calculated by the Mackay (1998) Level I fugacity model.

Environmental Compartment	Percent Distribution*
Air	99.97
Water	0.02
Soil	0.01
Sediment	0.00

* Physicochemical data used in the distribution calculation:

Molecular Weight	70.14
Temperature	25°C
Log K_{ow}	2.67
Water Solubility	193 g/m^3
Vapour Pressure	623.9 hPa (468 mmHg)
Melting Point	-133.7°C

Table 3. Environmental distribution as calculated by the Mackay (1998) Level III fugacity model.

Environmental Compartment	Percent Distribution* (equal emission rate to each compartment, 1000 kg/hr)	Percent Distribution* (releases only to the air compartment, 1000 kg/hr)	Percent Distribution* (releases only to the water compartment, 1000 kg/hr)
Air	2.01	100	0.52
Water	94.2	0	98.2
Soil	2.62	0	6.86E-5
Sediment	1.19	0	1.24

* Physicochemical data used in the distribution calculation:

Molecular Weight	70.14
Temperature	25°C
Log K_{ow}	2.67
Water Solubility	193 g/m^3
Vapour Pressure	623.9 hPa (468 mmHg)
Melting Point	-133.7°C

Furthermore, 2M2B has the potential to rapidly volatilize from surface waters, based on a Henry's Law constant (HLC) representing volatility of 11,145 Pa-m^3/mole (0.110 atm*m^3/mole). The HLC was calculated using a water solubility of 193 mg/L, a vapor pressure of 623.9 hPa, and a molecular weight of 70.14. The volatilization half-life of 2M2B from a model river and lake is estimated to be approximately 51 minutes and 3.32 days, respectively (EPIWIN, 1999). 2M2B is not expected to sorb significantly to organic matter in soil, sediment, and wastewater solids based on a log K_{oc} of 1.83 (EPIWIN, 1999).

Conclusion

Level I modeling indicates that at equilibrium, air is the dominant medium on a percentage basis. Level III modeling indicates that at steady state, water is the dominant medium on a percentage basis. However, Level III derived concentrations in water are unlikely to be realised because 2M2B is quite volatile.

2.2.5 Biodegradation

2M2B is not readily biodegradable based on unacclimated biodegradation data from a 28-day study (Huntingdon Life Sciences Ltd., 2003a). This study followed a stringent test guideline (OECD 301D, Closed Bottle Test) that requires a relatively low microbial inoculum loading, a low-test material concentration, and sacrifice of test systems on sampling days. These test conditions can cause a range of results as evidenced by the data. Replicate data for days 25 and 28 demonstrated a range of 4 to 15% biodegradation, while mean day 28 data was 7%, based on replicate results of 4 and 10%.

Conclusion

2M2B is not readily biodegradable.

2.2.6 Bioaccumulation

A log bioconcentration factor (log BCF) of 1.36 (BCF = 22.7) is calculated (EPIWIN, 1999). With respect to the log K_{ow} = 2.67, 2M2B in the aquatic environment is expected to demonstrate a low potential for bioaccumulation.

Conclusion

2M2B is not expected to be bioaccumulate.

2.2.7 Other Information on Environmental Fate

2M2B is volatile and will partition to the air from aquatic and terrestrial environments at an appreciable rate. Based on a Henry's Law constant of 1.1 E4 Pa*m^3/mole (0.224 atm*m^3/mole), the volatilization half-life of 2M2B in a model river and lake is estimated to be 51 minutes and 3.32 days, respectively.

The photochemical ozone creation potential (POCP) index for a chemical provides a relative measure of its reactivity or ozone forming potential. The POCP index can also provide a means of ranking volatile organic compounds (VOCs) by their ability to form ozone in the troposphere. Reported POCP indices for 2M2B in northwestern Europe range from 77.1 to 84.2 (Derwent *et al.*, 1996; Derwent *et al.*, 1998), in comparison with a POCP index of 100 for ethylene, the reference substance.

2M2B can react easily with hydroxyl radicals and ozone. The atmospheric life-time is approximately 1 day or less. 2M2B does not have Cl- or Br-atoms. Therefore, reactive Cl- or Br-substances, which can have an adverse impact on stratospheric ozone concentration, are not formed following photochemical degradation. The ozone depletion potential of this substance is negligible. When considered with 2M2B's relatively short atmospheric half-life, its contribution to global warming can be considered minor.

2.3 Human Exposure

2.3.1 Occupational Exposure

Manufacturing of 2M2B is done in a closed system. Potential for exposure is therefore generally limited to maintenance operations, product sampling and upset conditions. Exposure monitoring results obtained after a scheduled maintenance procedure indicated airborne concentrations of less than 0.1 ppm; thus, low exposure (< 0.1 ppm) would be expected during typical production operations (unpublished data, Exxon Biomedical Sciences, 1990). One manufacturer recommends an Occupational Exposure Limit of 10 ppm for isoamylenes (e.g., 2M2B, 2M1B) (ExxonMobil, 1999, updated 2004). Permission was obtained from the manufacturer to make available data from an unpublished qualitative exposure assessment for 2M2B conducted for its facilities to determine compliance with its revised Occupational Exposure Limit of 10 ppm. The manufacturer reported 228 workers potentially exposed to 2M2B during production at 6 sites in 5 countries (2 in the US, 3 in Europe, 1 in Asia-Pacific). The exposure assessment indicated that 2 of 228 workers (1%) were likely to be exposed to Long-Term Average (LTA) concentrations of 2M2B between 1 and 5 ppm. Both of these individuals were instrumentation technicians at one of the EU facilities. Slightly less than 10% (22/228) would be exposed to LTA concentrations between 0.1 to 1 ppm, and approximately 90% of workers would have negligible exposures (below the limit of detection, or < 0.1 ppm) for this material (unpublished data, ExxonMobil Biomedical Sciences, 2004).

2M2B air concentration at gas stations were reported as 0.11 ppm (0.3 mg/m^3) (air) based on data for six stations from three United States cities between October to November 1990 (API, 1991). Mean 2M2B exposure levels for gas station attendants, transport drivers, and outside operators were reported as 1.986, 0.740, and 0.446 mg/m^3, respectively (Rappaport, 1987).

2.3.2 Consumer Exposure

2M2B is present in gasoline vapor at levels of about 1-3.5%. Due to the nature of exposure during refueling of vehicles, consumer exposure would be expected to be well below that reported for gas station attendants.

3 HUMAN HEALTH HAZARDS

3.1 Effects on Human Health

3.1.1 Toxicokinetics, Metabolism and Distribution

Studies in Animals

No toxicokinetic studies have been conducted with 2M2B either *in vivo* or *in vitro*. Mice are likely to be more sensitive to 2M2B compared to rats, consistent with data on the metabolism of other olefins.

Studies in Humans

No toxicokinetic studies have been conducted with 2M2B in humans.

3.1.2 Acute Toxicity

Studies in Animals

Oral

In order to determine the acute oral LD50 of 2M2B two studies were performed: a range finding study in which two albino Wistar rats of each sex were dosed with 0.5, 1.0 and 5.0 ml/kg and a second study in which six albino Wistar rats of each sex were dosed. In both studies the dosing was by intraesophageal intubation using a ballpoint needle fitted to a syringe. Because the test material was so volatile, it was necessary to keep it on ice until it was dosed. Therefore, the animals received 2M2B at a temperature of approximately 24.5°C. After dosing the animals were given food and water ad libitum and observed for toxicological signs over the following 14 days. Body weights were recorded at 7 and 14 days. Based on the results of the range-finding study, the acute oral LD50 value was estimated to be between 1 and 5 ml/kg. To determine a more accurate LD50 value, groups of six males and six females were dosed with 1.0, 1.6, 2.5, 4.0, 6.3 and 10 ml/kg. In this study, the majority of deaths occurred within the first 3 days following dosing and most survivors had recovered from signs of intoxication by the third day. All but one of the survivors had gained weight at the conclusion of the 14-day observation period. The oral LD50 was estimated to be in the range of 1 to 4 ml/kg (i.e., 700 to 2600 mg/kg) (Dewar, 1980). However, inspection of the data indicate the LD50 is in the range of 1.6 to 2.5 ml/kg (1000 to 1700 mg/kg).

Dermal

The acute (24 hour) dermal toxicity of 2M2B was determined using a method based on that of Noakes and Sanderson (1969). Two tests were performed, a range finding test in which two albino Wistar rats of each sex were dosed with 0.5, 1.0 and 2.0 ml/kg and a second test in which six rats of each sex were dosed with 3.03 ml/kg. The calculated dose was applied to the shaven skin by syringe, the dose being altered by varying the volume of the material applied. It was necessary to apply the material at a temperature of approximately 5°C on account of its volatility. The test material was covered with aluminum foil held in place by a double overwrap of waterproof adhesive tape. The rats were individually housed for the next 24 hours, food being withheld but water given ad libitum. At the end of the 24 hours exposure period, the foil and dressing were removed and the skin washed with warm dilute detergent solution and then dried. The animals were returned to group housing and observed for signs of toxicity over the following 14 days. Initial, 7-day and 14-day body weights were recorded. In the range finding study, the acute dermal LD50 was estimated to be >2.0 ml/kg. In order to obtain a more accurate LD50, a group of six males and six females were dosed with 3.03 ml/kg, which is equivalent to a dose of 2 g/kg. No mortalities were recorded and there were no signs of systemic toxicity. All animals gained weight within one week of dosing. The mean erythema scores for abraded skin were 1.08, 1.42, 1.58, and 1.75 at 24 hrs, 48 hrs, 72 hrs, and 7 days, respectively. The mean erythema scores for non-abraded skin were 0.83, 1.17, 1.25 and 1.5 at 24 hrs, 48 hrs, 72 hrs, and 7 days, respectively. The mean edema scores for abraded skin were 0.58, 0.67, 0.67, and 0.83 at 24 hrs, 48 hrs, 72 hrs, and 7 days, respectively. The mean edema scores for non-abraded skin were 0.50, 0.58, 0.67, and 0.82 at 24 hrs, 48 hrs, 72 hrs, and 7 days, respectively. The primary irritation score calculated according to the method of Draize was 1.79. Eschar, necrosis, and scarring were not reported. Thus, the acute dermal LD50 value of 2M2B is >2 g/kg (Dewar, 1980).

Inhalation

In this study, groups of 5 male and 5 female albino Wistar rats were exposed for 4 hours to a test atmosphere containing 6.1 per cent (v/v) 2M2B. During the exposure the animals became narcotized, but revived within 30 minutes of cessation of exposure. There were no deaths and macroscopic and microscopic examination at necropsy of animals killed 14 days post-exposure

revealed no compound related effects. The acute 4 hours inhalation LC_{50} of 2M2B in rats is greater than 6.1 per cent (i.e., 61,000 ppm) (Blair, et al, 1982).

Studies in Humans

No human data exists.

Conclusion

2M2B has a low order of acute toxicity in animals by the oral, dermal and inhalation routes of exposure.

3.1.3 Irritation

Skin Irritation

Studies in Animals

An occlusive patch test based on the method of Draize (1975) was used to assess the primary skin irritation induced by 2M2B applied neat. Three male and three female New Zealand White rabbits were used. After 24 hours the intact and abraded test sites were examined and scored for erythema and edema on a graded scale (0 to 4) at 24, 48 and 72 hours and 7 days post-dosing. The mean erythema scores for abraded skin were 1.08, 1.42, 1.58, and 1.75 at 24 hrs, 48 hrs, 72 hrs, and 7 days, respectively. The mean erythema scores for non-abraded skin were 0.83, 1.17, 1.25, and 1.5 at 24 hrs, 48 hrs, 72 hrs, and 7 days, respectively. The mean edema scores for abraded skin were 0.58, 0.67, 0.67, and 0.83 at 24 hrs, 48 hrs, 72 hrs, and 7 days, respectively. The mean edema scores for non-abraded skin were 0.50, 0.58, 0.67, and 0.82 at 24 hrs, 48 hrs, 72 hrs, and 7 days, respectively. The primary irritation score calculated according to the method of Draize was 1.79. Eschar, necrosis or scarring were not reported.On the basis of this score 2M2B may be regarded as being mildly irritating to rabbit skin. The erythema and edema scores at 7 days were higher than those at 72 hours. However, at 7 days all the skin patches were beginning to dry out and flake and it is possible that a contributory factor to the slightly higher erythema scores was the animals scratching these areas (Dewar, 1980).

Studies in Humans

There are no skin irritation studies with 2M2B in humans.

Eye Irritation

Studies in Animals

The method of Draize (1963) was used to assess the eye irritancy of 2M2B. Six New Zealand White rabbits were used. The reactions of the animals were observed immediately after instillation and the initial pain response was graded on a scale of 1 to 6 with 6 being very severe initial pain. A visual assessment of eye irritancy was made at 1 hour, 1 day, 2 days, 3 days, and 7 days after instillation or until the irritancy was no longer discernible. The instillation of 2M2B into the eye resulted in a moderate initial pain response (grade 4) in all animals. The mean total scores for the responses of the conjunctiva, cornea and iris at 1 hour, 1, 2, 3, and 7 days were 0.5, 0, 0, 0, and 0, respectively. Based on these results, 2M2B should be considered as non-irritating to rabbit eyes (Dewar, 1980).

Studies in Humans

There are no human data.

Respiratory Tract Irritation

No studies on respiratory tract irritation have been conducted with 2M2B.

Conclusion

Based on the available data, 2M2B should be considered as mildly irritating to skin and non-irritating to eyes. The respiratory tract irritation potential of 2M2B is not known, as no data are available for this endpoint.

3.1.4 Sensitization

Studies in Animals

Skin

The skin sensitization potential of 2M2B was assessed using the guinea-pig maximization method of Magnusson and Kligman (1969). The test was accomplished in two stages, with a preliminary range finding study to determine the concentrations of 2M2B to be used for intradermal induction, topical induction and topical challenge, and the main study

The purpose of the preliminary study was to determine the concentrations of 2-methyl-2-butene to be used for intradermal induction, topical induction, and topical challenge. Trace levels of erythema, defined as "slight redness, edges not defined," or positive response defined as "pink/red squares with defined edges" were observed in all animals receiving intradermal injection. Trace levels of erythema were observed in 2 of 4 animals receiving undiluted, and 1 of 4 animals receiving a 50% dilution in corn oil, topically applied. No erythema was observed with 25% in corn oil, topically applied. On the basis of the range finding tests, the following concentrations of 2M2B were selected for use in the main skin sensitization test: 0.1% w/v in corn oil (intradermal induction), 50% w/v in corn oil (topical induction), and 25% w/v in corn oil (topical challenge). The erythema resulting from the topical challenge was scored on a four-point scale immediately on removal of the challenge patch and 24 and 48 hours later. Since none of the twenty test animals showed any positive reactions 24 or 48 hours after the removal of the challenge patch, it can be concluded that 2M2B is not a skin sensitizer in guinea pigs (Dewar, 1980).

Respiratory Tract

No respiratory sensitization tests have been conducted in animals.

Studies in Humans

No human data exist.

Conclusion

2M2B is not a skin sensitizer in animals.

3.1.5 Repeated Dose Toxicity

Studies in Animals

Inhalation

An OECD 422 combined general toxicity and reproduction/developmental toxicity screening study was conducted in Sprague-Dawley rats (Huntingdon Life Sciences, 2003e). In this study, groups of

12 male and 12 female rats were exposed (whole body exposure) by inhalation to 0, 580, 2000, or 7,000 ppm (approximately 1660, 5720, or 20,000 mg/m^3) 2M2B for approximately 6 hours/day, 7 days/week. In the main study, i.e., repeated-dose general toxicity study, the males and females were exposed for 28 days, respectively. Parameters measured during this study included clinical signs, a detailed functional observational battery, motor activity, bodyweight, food consumption, hematology, blood chemistry, organ weight and macroscopic and microscopic pathology.

The clinical signs observed during this study included half-closed eyes on day 1 in the groups exposed to 2000 and 7000 ppm. In addition, these animals exhibited a lower level of response to external stimuli. This latter finding was observed on one other occasion in the high dose animals. No signs were observed indicative of any general systemic effects either during routine clinical examination or during the functional observational battery. There was a slightly lower bodyweight gain at 7000 ppm, and slightly longer clotting times at 2000 ppm (prothrombin time for females) and 7000 ppm (prothrombin times for both sexes and activated partial thromboplastin times for males). Cholesterol levels were increased among the females exposed to 7000 ppm but in the absence of any further effects in the clinical chemistry parameters or the males this finding is of uncertain significance.

Pathological changes were noted among the high dose females in the liver, as evidenced by increased organ weight and minimal centrilobular hepatocyte hypertrophy. There was also a decreased incidence of extramedullary hematopoiesis in the spleen in the high dose animals and an increase in goblet cell hyperplasia in the nasal passages of the high dose males. In addition, a slight increase in severity of myocardial inflammatory heart lesions and in cortical/medullary tubular basophilia in the kidneys was observed in the high and intermediate dose males.

Although some general systemic effects were observed in this study, these effects were slight and were most apparent in those animals exposed to the highest dose, 7000 ppm, and to a lesser extent to those exposed to 2000 ppm. Based on these observations, the No Observed Effect Level in this study was 580 ppm (lowest dose tested).

Studies in Humans

There are no human data.

Conclusion

2M2B produced some general systemic effects in rats following repeated exposure. These effects were slight and were most apparent in the high dose animals and only to a small extent in the mid-dose animals. The No Observed Effect Level was 580 ppm (lowest dose tested).

3.1.6 Mutagenicity

2M2B (>95% and blends containing 2M2B) have been tested for mutagenic activity in both *in vitro* and *in vivo* test systems. The critical studies discussed below are from the studies containing primarily >95% 2M2B, as they are the most relevant.

In vitro Studies

2M2B was tested in an Ames assay in 5 strains of *Salmonella typhimurium* (i.e., TA1535, TA 1537, TA1538, TA 100, and TA98) and in 2 strains of *Escherichia coli* (i.e., WP_2 and WP_2uvrA) in the presence and absence of rat liver S-9 (Dean et al., 1985). Five dose levels were tested, with three plates per dose level using sealed containers. Concurrent positive and solvent controls were also tested with and without metabolic activation (rat liver S9). Two replicate assays were performed on different days to confirm the reproducibility of the results. 2M2B was not mutagenic in any of the

five strains of *Salmonella* or in the two strains of *E. coli* tested in the presence or absence of metabolic activation

2M2B was tested in a *Saccharomyces cerevisiae* gene conversion assay (Dean et al., 1985). In this assay liquid suspension cultures of S. cerevisiae in dilute growth medium were dosed with 0.2, 2, 10, 20, or 50 mg/ml of 2M2B in ethanol to give a final concentration of 0.01, 0.1, 0.5, 1.0, or 5.0 mg/ml. After 18 hours of incubation with shaking at 30°C either in the presence of absence of rat liver S9 fraction, the cultures were seeded onto the appropriate culture media for the selection of revertant colonies. After 3 days incubation at 30°C, the number of revertant colonies were counted. In this assay, a test material is considered to be mutagenic if the number of revertants per 10^6 survivor cells in the treated plates is greater than twice the control value. This did not occur with 2M2B at any of the concentrations tested either with or without metabolic activation. Thus, 2M2B was not mutagenic to yeast cells under the conditions of this assay.

In the cytogenetics assay, cultured rat liver cells (RL_4) (Dean et al., 1985) were incubated at 30°C for 24 hours to allow active growth to commence; freshly prepared solutions of 2M2B were then added at concentrations of 12.5, 25, or 50 µl/ml. These concentrations were selected on the basis of a previously conducted cytotoxicity test which determined the concentration producing 50% growth inhibition (i.e., 100 µl/ml) and appropriate dilutions of this concentration (i.e., 0.125, 0.25, and 0.5%). Positive control cultures using 1 µg/ml 7,12-dimethyl benzanthracene were run in parallel. The chromosome preparations were randomly coded and 100 cells from each culture were analysed microscopically for chromosome changes. Based on the results of the metaphase chromosome analysis, 2M2B did not induce chromosome damage in cultured rat liver cells (RL_4) exposed for 24 hours to concentrations of 12.5, 25.0, and 50 µl/ml. Thus, 2M2B was not genotoxic under the conditions of this assay.

In vivo Studies

2M2B was evaluated for its ability to induce micronuclei in bone marrow polychromatic erythrocytes (PCEs) in male $B_6C_3F_1$ mice (Exxon Biomedical Sciences, 1991a). Male mice (10/group) were exposed 6 hours a day for 2 consecutive days to 0, 1005, 3207 or 9956 ppm (0, 2883, 9200, and 28,561 mg/m^3) 2M2B, 99.2% purity, by inhalation. Another group of 10 male mice was exposed to 1000 ppm 1,3-butadiene and served as the positive control. On Day 1, all mice appeared normal. A few (i.e., 10 to 30%) of the animal in the high dose group (10,000 ppm) displayed decreased activity that started the second hour of exposure and continued for the remainder of the exposure. A few animals also exhibited labored breathing at the second hour of exposure and continued throughout the exposure. All of the mice in the positive control group (1000 ppm Bd) appeared normal during most of the exposure and a few animals displayed white ocular discharge during the sixth hour of exposure. On Day 2, all the mice in the air and positive control groups appeared normal. All the mice in the low and high dose group appeared normal for the first three hours of exposure. Few (i.e.,10 to 30%) to some (i.e., 40 to 60%) of the mid dose group animals displayed decreased activity at the second hour of exposure that continued for the remainder of the exposure. A few mice also exhibited labored breathing for the last three hours of the exposure. A few to most (i.e., 70 to 90%) of the high dose animals displayed decreased activity during the last three hours of exposure and a few to some also exhibited labored breathing during the last three hours of exposure. The mean micronucleated PCE values were 4.2, 16.6, and 36.1 at 1005, 3207, and 9956 ppm, compared to 3.4 micronucleated PCEs for the negative control. 2M2B induced statistically significant ($p<0.01$) and dose related increases in micronucleated PCEs at 3207 and 9956 ppm. A statistically significant ($p<0.01$) decrease in the %PCEs, which is a measure of hematotoxicity, was only observed at 9956 ppm. The positive control produced a statistically significant increase in micronucleated PCEs (29.7) and decrease in %PCEs (44.5%). Under the

conditions of this study, exposure to 2M2B ≥3207 ppm induced statistically significant increases in micronucleated polychromatic erythrocytes in male mice.

2M2B was evaluated for its ability to induce micronuclei in bone marrow polychromatic erythrocytes (PCEs) in male CrlCDBR rats (Exxon Biomedical Sciences, 1991b). Male rats (10/group) were exposed 6 hours a day for 2 consecutive days to 0, 1005, 3207, or 9956 ppm (0, 2883, 9200, and 28,561 mg/m^3) 2M2B, 99.2% purity, by inhalation. On Day 1, all the rats in the air control and low dose and most of the rats in the mid dose groups appeared normal. A few (i.e., 10 to 30%) of the rats in the mid dose group exhibited decreased activity at two hours into the exposure and continued for the remainder of the exposure. Most (i.e., 70 to 90%) of the high dose rats exhibited decreased activity throughout the exposure and a few (i.e., 10 to 30%) rats appeared normal. On Day 2, all the rats in the air control, low and mid dose groups appeared normal. Most (i.e., 70 to 90%) of the rats in the high dose group appeared normal for the first three hours of exposure, although a few (i.e. 10-30%) displayed decreased activity. During the last three hours of the exposure, some (i.e., 40-60%) of the rats appeared normal and some exhibited decreased activity. 2M2B induced statistically significant ($p<0.01$) and dose related increases in micronucleated PCEs at 3207 and 9956 ppm. The mean micronucleated PCE values were 2.2, 4.2, and 4.9 at 1005, 3207, and 9956 ppm, respectively, compared to 2.7 for the negative control (air). The mean %PCEs at 1005, 3207, and 9956 ppm (48.6, 51.0, and 49.8%, respectively) were slightly decreased from the negative control (54.9%), but they were not different from each other and did not show evidence of dose-response. Therefore, the biological significance of this observation is unclear. Under the conditions of this study, inhalation exposure to 2M2B ≥3207 ppm induced small but statistically significant increases in micronucleated polychromatic erythrocytes in male rats.

Two other micronucleus studies conducted to GLP in mice, one additional GLP study conducted in rats, and an older mouse study (not reviewed) conducted with concentrations of 2M2B from 85% to 92% are summarized in the IUCLID dossier. Results were consistent with the studies discussed above.

Conclusion

2M2B is not mutagenic *in vitro*. It did not induce gene mutations in a reverse mutation assays conducted in *Salmonella typhimurium* and *Escherichia coli* either in the presence or absence of metabolic activation. 2M2B did not produce revertant colonies in a gene conversion assay conducted in *Saccharomyces cerevisiae* and it did not induce chromosome damage in cultured rat liver cells.

2M2B was mutagenic at high exposure concentrations (at exposures greater than or equal to 3207 ppm (9199 mg/m^3)) when tested *in vivo* for its ability to induce micronuclei in bone marrow polychromatic erythrocytes (PCEs) in both mice and rats.

3.1.7 Carcinogenicity

No carcinogenicity studies have been conducted with 2M2B.

3.1.8 Toxicity for Reproduction

An OECD 422 combined repeated dose and reproduction/developmental toxicity study was conducted in Sprague Dawley rats (Huntingdon Life Sciences, 2003e). In this study a satellite group of 12 female rats was exposed to 0, 580, 2000, or 7,000 ppm (approximately 1660, 5720, or 20,000 mg/m^3) 2M2B by inhalation for approximately 6 hours/day, (7 days/week) for two weeks

prior to breeding, during breeding and through Day 19 of gestation. Males from the main study (discussed in section 3.1.5) were used to breed these females. The dams were allowed to deliver their litters, which were retained until lactation Day 4. During the study, clinical condition, bodyweight, food consumption, estrus cycles, mating performance, litter data, organ weights and macroscopic pathology were undertaken.

Exposure of female rats for 2 weeks prior to mating and up to Day 19 of gestation did not produce any evidence of reproductive or developmental toxicity. The estrus cycle was unaffected by exposure, and mating performance, fertility indices and gestation length were similar in all groups. There were no adverse effects upon survival or growth of the offspring in utero or up to Day 4 of lactation. Thus, the No Observed Adverse Effect Level (NOAEL) for reproductive/developmental toxicity was 7000 ppm (highest dose tested).

Conclusion

The No Observed Adverse Effect Level (NOAEL) for reproductive toxicity was 7000 ppm (highest dose tested).

3.1.9 Developmental Toxicity

As discussed above in Section 3.1.8, an OECD 422 combined repeated dose and reproduction/developmental toxicity study was conducted in Sprague Dawley rats (Huntingdon Life Sciences, 2003e). In this study a satellite group of 12 female rats was exposed to 0, 580, 2000, or 7000 ppm (approximately 1660, 5720, or 20,000 mg/m^3) 2M2B by inhalation for approximately 6 hours/day, 7 days/week for two weeks prior to breeding, during breeding and through Day 19 of gestation. Males from the main study (discussed in Section 3.1.5) were used to breed these females.

The dams were allowed to deliver their litters, which were retained until lactation Day 4. There were no adverse effects upon survival or growth of the offspring *in utero* or up until Day 4 of lactation. Thus, the No Observed Adverse Effect Level (NOAEL) for developmental toxicity in this study was 7000 ppm (i.e., the highest dose tested).

Conclusion

Teratogenic effects were not observed in the OECD TG 422 study. The No Observed Adverse Effect Level (NOAEL) for developmental toxicity in this study was 7000 ppm (i.e., the highest dose tested).

3.2 Initial Assessment for Human Health

The oral LD_{50} of 2M2B is in the range of 700 to 2600 mg/kg. Survivors indicated reversible signs of intoxication were observed. The dermal LD_{50} is >2 g/kg. The 4-hour LC_{50} is 61,000 ppm (174,500 mg/m^3). Inhalation of 2M2B can produce central nervous system depression, anesthesia and/or asphyxiation that are reversible following cessation of exposures. 2M2B is a mild skin irritant but does not produce eye irritation. 2M2B is not a skin sensitizer.

In a combined repeat dose/reproductive/developmental study (OECD 422), rats were exposed via inhalation, to 580, 2000 and 7,000 ppm (1660, 5720, and 20,000 mg/m^3) 2M2B. For the repeated dose phase of the study the exposures were for 6 hr/day, 7 d/week for 28 days. There was a slightly lower bodyweight gain at 7000 ppm, slightly longer clotting times at 2000 ppm (prothrombin time for females) and 7000 ppm (prothrombin times for both sexes and activated partial thromboplastin times for males). Cholesterol levels were increased among the females exposed to 7000 ppm but in

the absence of any further effects in the clinical chemistry parameters or the males this finding is of uncertain significance. Pathological changes were noted among the high-dose females in the liver, as evidenced by increased organ weight and minimal centrilobular hepatocyte hypertrophy. There was also a decreased incidence of extramedullary hematopoiesis in the spleen in the high dose animals and an increase in goblet cell hyperplasia in the nasal passages of the high dose males. In addition, a slight increase in severity of myocardial inflammatory heart lesions and in cortical/medullary tubular basophilia in the kidneys was observed in the high- and intermediate-dose males. Although some general systemic effects were observed in this study, these effects were slight and were most apparent in those animals exposed to the highest dose, 7000 ppm, and to a lesser extent to those exposed to 2000 ppm. Based on these observations, the No Observed Effect Level in this study was 580 ppm (1660 mg/m^3).

2M2B is not mutagenic *in vitro*. It did not induce gene mutations in reverse mutation assays conducted in *Salmonella typhimurium* and *Escherichia coli* either in the presence or absence of metabolic activation. 2M2B did not produce revertant colonies in a gene conversion assay conducted in *Saccharomyces cerevisiae* and it did not induce chromosome damage in cultured rat liver cells.

2M2B was mutagenic at high exposure concentrations ($\geq$ 3207 ppm, $\geq$ 9199 mg/m^3) when tested *in vivo* for its ability to induce micronuclei in bone marrow polychromatic erythrocytes (PCEs) in both mice and rats. However, the incidence was not considered statistically significant at 1000 ppm (2869 mg/m^3).

In the combined repeat dose/reproductive/developmental study (OECD 422), rats exposed to concentrations up to 7000 ppm, 6 hr/day, 7d/week for two weeks prior to breeding during, during breeding and thru day 19 of gestation. No evidence of reproductive or developmental toxicity was seen. The estrus cycle was unaffected by exposure, and mating performance, fertility indices and gestation length were similar in all groups. There were no adverse effects upon survival or growth of the offspring *in utero* or up to Day 4 of lactation. Thus, the No Observed Adverse Effect Level (NOAEL) for reproductive and developmental toxicity is 7000 ppm (highest dose tested).

4 HAZARDS TO THE ENVIRONMENT

Measured acute data are available for aquatic toxicity endpoints.

4.1 Aquatic Effects

Fish Acute Toxicity Test Results

The measured 2M2B freshwater fish (*Oncorhynchus mykiss*) 96-hour LC50 is 4.99 mg/L (Huntingdon Life Sciences Ltd., 2003b).

Ivertebrate Acute Toxicity Test Results

The measured invertebrate (*Daphnia magna*) 48-hour LC_{50} is 3.84 mg/L (Huntingdon Life Sciences Ltd., 2003c).

Alga Toxicity Test Results

The measured alga (*Pseudokirchneriella subcapitata*) 96-hour EC_{50} values are 10.1 and 13.2 mg/L based on biomass and growth rate, respectively, while the NOEC values are 3.61 mg/L and 7.22 mg/L for biomass and growth rate, respectively (Huntingdon Life Sciences Ltd., 2003d).

Chronic Toxicity Test Results

The measured alga (*Pseudokirchneriella subcapitata*) 96-hour NOEC for biomass is 3.61 mg/L, while the 96-hour NOEC for growth rate is 7.22 mg/L (Huntingdon Life Sciences Ltd., 2003d). Measured fish and invertebrate chronic data are not available.

Measured chronic aquatic toxicity values for fish and invertebrates are not available. However, QSAR (Quantitative Structure-Activity Relationship) data include a fish 30-day chronic value of 1.75 mg/L and a 16-day daphnid chronic value of 0.94 mg/L (ECOSAR/EPIWIN, 1999).

4.2 Terrestrial Effects

There are no experimental data available using standard testing procedures that can be used to assess the terrestrial hazard of 2M2B. However, there is a calculated earthworm 14-day LC_{50} value of 268.3 mg/kg soil (ECOSAR/EPIWIN, 1999). This value was calculated using a log K_{ow} = 2.67.

4.3 Other Environmental Effects

Toxicity to Microorganisms

There are no reliable data to assess the toxicity of 2M2B to micoorganisms.

4.4 Initial Assessment for the Environment

In the air, 2M2B has the potential to rapidly degrade through indirect photolytic processes mediated primarily by hydroxyl radicals and ozone with calculated degradation half-lives ranging from approximately 1 to 4 and 0.6 hours, respectively, depending on hydroxyl radical and ozone concentrations. Aqueous photolysis and hydrolysis will not contribute to the transformation of 2M2B in aquatic environments because it is either poorly or not susceptible to these reactions.

The photochemical ozone creation potential index for 2M2B has been reported to range from 77.1 to 84.2. Because of the relatively short half-life of 2M2B in the atmosphere and the low environmental concentrations typically found, its contribution to potential global warming can be considered minor. The ozone depletion potential of this substance is negligible as indicated by its net ability to form ozone in the atmosphere.

Results of Mackay Level I distribution modelling show that 2M2B will partition primarily to the air compartment (99.97%), with a negligible amount partitioning to water (0.02%) and soil (0.01%). Level III modelling indicates that at steady state, water is the dominant medium on a percentage basis. Level III modeling may not be representative of ultimate disposition of 2M2B because default emission data used in the model (1000 kg/h) is not a representative rate of chemical discharge. However, concentrations in water are most likely very low because 2M2B is quite volatile, and any volatilised substance will be quickly degraded in the atmosphere. When released primarily to the air compartment, the primary mode of removal would be via photodegradation based on the volatility of 2M2B. In spite of its water solubility, wet deposition of 2M2B is not likely to play a significant role in its atmospheric fate because of rapid photodegradation. Volatilisation to the air will contribute to the rapid loss of 2M2B from aqueous and terrestrial habitats.

2M2B is not readily biodegradable. Bioaccumulation of 2M2B is unlikely based on a low potential to bioconcentrate based on a BCF of 22.7. 2M2B is not expected to sorb significantly to organic matter in soil, sediment, and wastewater solids based on a log K_{oc} of 1.83.

Acute aquatic toxicity values for fish and invertebrates are 5.0 (96hr-LC_{50}) and 3.8 (48hr-EC_{50}) mg/L, respectively. For algae, the 96-hr EC_{50} values are 10.5 mg/L and 12.0 mg/L for biomass and growth rate, respectively, while the NOEC values are 3.61 mg/L and 7.22 mg/L for biomass and growth rate, respectively.

Measured chronic aquatic toxicity values for fish and invertebrates are not available. However, QSAR (Quantitative Structure-Activity Relationship) data include a fish 30-day chronic value of 1.75 mg/L and a 16-day daphnid chronic value of 0.94 mg/L.

Although there are no experimental terrestrial toxicity data available, a 14-day LC_{50} value of 268.3 mg/kg soil has been calculated for an earthworm.

5 RECOMMENDATIONS

The chemical is currently of low priority for further work.

The chemical possesses properties indicating a hazard for human health (mutagenic at high concentrations) and the environment (acute fish, aquatic invertebrates, and algae). Based on exposure data presented by the sponsor country (relating to production in one country which accounts for an unknown fraction of the global production and relating to the use pattern in one country), under normal manufacturing, formulation, industrial and consumer use, this chemical is a low priority for further work. Countries may wish to investigate any exposure scenarios that were not presented by the sponsor country.

6 REFERENCES

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ANNEX

A literature search was conducted on 8 October 2002 going back at least 10 years to update the IUCLID file. Search strategy included CAS number, chemical nomenclature, and key words relevant to the endpoints addressed in this SIAR. The databases searched included:

Aquire (1992-2002)
BIODEGRADATION DATA (BIODEG) (1992-2002)
BIODEGRADATION BIBLIOGRAPHIC REFERENCES (BIOLOG) (1992-2002)
Biological Abstracts - BIOSIS (1992-2002)
Cancerlit (1992-2002)
EMBASE (1992-2002)
EMBSINFO (formerly RBird) (1992-2002)
Engineering Index - Compendex (1992-2002)
Enviroline (1992-2002)
Environmental Bibliography (1992-2002)
Gene-Tox (1992-2002)
Medline (1992-2002)
National Technical Information Service - NTIS (1992-2002)
NIOSH (1992-1998)
PASCAL (1992-2002)
Pollution Abstracts (1992-2002)
TERRETOX (1992-2002)
TSCATS (1992-2002)
Toxfile (1992-2002)

S I D S

Dossier

Existing Chemical	:	ID: 513-35-9
CAS No.	:	513-35-9
Producer related part		
Company	:	ExxonMobil Biomedical Sciences Inc.
Creation date	:	13.10.2003
Substance related part		
Company	:	ExxonMobil Biomedical Sciences Inc.
Creation date	:	13.10.2003
Status	:	
Memo	:	EMBSI
Printing date	:	28.07.2005
Revision date	:	
Date of last update	:	28.07.2005
Number of pages	:	
Chapter (profile)	:	Chapter: 1, 2, 3, 4, 5, 6, 7, 8, 10
Reliability (profile)	:	Reliability: without reliability, 1, 2, 3, 4
Flags (profile)	:	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 APPLICANT AND COMPANY INFORMATION

Type	:	
Name	:	ExxonMobil Chemical Company
Contact person	:	
Date	:	
Street	:	13501 Katy Freeway
Town	:	77079-1398 Houston, TX
Country	:	United States
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	
Email	:	
Homepage	:	

05.08.2004

Type	:	
Name	:	Shell Nederland Chemie B.V.
Contact person	:	
Date	:	
Street	:	Vondelingenweg 601
Town	:	3196 KK Rotterdam
Country	:	Netherlands
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	
Email	:	
Homepage	:	

Source : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11.02.2000

1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR

1.0.3 IDENTITY OF RECIPIENTS

1.0.4 DETAILS ON CATEGORY/TEMPLATE

1.1.0 SUBSTANCE IDENTIFICATION

1.1.1 GENERAL SUBSTANCE INFORMATION

Purity type	:	
Substance type	:	organic
Physical status	:	liquid
Purity	:	> 99 % w/w
Colour	:	

Odour :

05.08.2004

Purity type :
Substance type : organic
Physical status : liquid
Purity :
Colour :
Odour :

Source : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11.02.2000

1.1.2 SPECTRA

1.2 SYNONYMS AND TRADENAMES

1,1,2-Trimethyl ethylene

Source : ExxonMobil Biomedical Sciences, Inc., Annandale, NJ, USA
27.10.2003

2-Butene-2-methyl

Source : ExxonMobil Biomedical Sciences, Inc., Annandale, NJ, USA
27.10.2003

2-Methyl-2-butene

Source : ExxonMobil Biomedical Sciences, Inc., Annandale, NJ, USA
27.10.2003

2-Methylbut-2-ene

Source : ExxonMobil Biomedical Sciences, Inc., Annandale, NJ, USA
27.10.2003

2-Methylbut-2-ene

Source : ExxonMobil Biomedical Sciences, Inc., Annandale, NJ, USA
27.10.2003

Amylene

Source : ExxonMobil Biomedical Sciences, Inc., Annandale, NJ, USA
27.10.2003

Amylene, tertiary

Source : Shell Nederland Chemie B.V. Rotterdam
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

22.03.1995

Isoamylene, beta

Source : Shell Nederland Chemie B.V. Rotterdam
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
22.03.1995

Methyl butene-2, 2-

Source : Shell Nederland Chemie B.V. Rotterdam
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
22.03.1995

n-Amylene

Source : ExxonMobil Biomedical Sciences, Inc., Annandale, NJ, USA
27.10.2003

Trimethyl ethylene

Source : Shell Nederland Chemie B.V. Rotterdam
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
22.03.1995

ß-Isoamylene

Source : ExxonMobil Biomedical Sciences, Inc., Annandale, NJ, USA
27.10.2003

1.3 IMPURITIES

Remark : Impurities may include 2M2B dimer at less than or equal to 0.5% w/w.
05.08.2004

1.4 ADDITIVES

Remark : 2M2B can contain 150 to 250 ppm p-tert-butyl catechol added as a stabiliser.
05.08.2004

1.5 TOTAL QUANTITY

Remark : Production of 2M2B in the United States is between 5,000 and 23,000 metric tonnes annually according to the USEPA IUR.
05.08.2004 (42)

1.6.1 LABELLING

1.6.2 CLASSIFICATION

1.6.3 PACKAGING

1.7 USE PATTERN

Remark : 2M2B is largely used as a chemical intermediate, primarily in the production of isoprene. It is also used as an intermediate in the production of tertiary pentyl alcohol, a stabilizer for chloroform, and is a constituent of gasoline, typically at levels below 2.5%.

09.08.2004 (28)

1.7.1 DETAILED USE PATTERN

Remark : 2M2B is largely used as a chemical intermediate, primarily in the production of isoprene (SRI, 1998. It is also used as an intermediate in the production of hydrocarbon resins, tertiary pentyl alcohol, a stabilizer for chloroform, and is a constituent of gasoline, typically at levels below 2.5%.

29.09.2004 (29)

1.7.2 METHODS OF MANUFACTURE

Remark : 2M2B is produced commercially by catalytic or thermal cracking of high boiling petroleum fractions or steam cracking of a mixture of saturated hydrocarbons. Isopentane is separated from the resultant product mixture of C5 hydrocarbons by extraction into 45 to 65% sulphuric acid with subsequent regeneration of 2M2B by steam stripping. Other processes that may be used to produce 2M2B include the dehydration of pentanols and the thermal dehydrogenation of pentanes.

09.08.2004 (28)

1.8 REGULATORY MEASURES

1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES

Remark : None established.
Source : Shell Nederland Chemie B.V. Rotterdam
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

02.06.1995

1.8.2 ACCEPTABLE RESIDUES LEVELS

1.8.3 WATER POLLUTION

1.8.4 MAJOR ACCIDENT HAZARDS

1.8.5 AIR POLLUTION

1.8.6 LISTINGS E.G. CHEMICAL INVENTORIES

1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS

1.9.2 COMPONENTS

1.10 SOURCE OF EXPOSURE

1.11 ADDITIONAL REMARKS

Remark : DISPOSAL OPTIONS

Dispose to licensed disposal contractor.
Recover or recycle if possible; otherwise incinerate in licensed waste incineration plant.

TRANSPORT INFORMATION

United Nations
UN Number : 2460
Class/Packing Group : 3/II
Proper Shipping Name: 2-METHYL-2-BUTENE

Sea (IMO)
UN Number : 2460
Class/Packing Group : 3.1/II
Symbol : Flammable liquid
Marine Pollutant : No
Proper Shipping Name: 2-METHYL-2-BUTENE

Rail/Road (RID/ADR)
Class/Item : 3/2(b)
Symbol : Flammable liquid
Kemler Plate : 33/2460
Proper Shipping Name: 2-METHYL BUTENE-2

Air (IATA/ICAO)
UN Number : 2460
Class/Packing Group : 3/II
Symbol : Flammable liquid
Proper Shipping Name: 2-METHYL-2-BUTENE

Source : Shell Nederland Chemie B.V. Rotterdam
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

02.06.1995

1.12 LAST LITERATURE SEARCH

1.13 REVIEWS

2.1 MELTING POINT

Value : = -133.7 °C
Sublimation :
Method : other: not specified
Year :
GLP : no data
Test substance : other TS: 2-methyl-2-butene

Test substance : 2-methyl-2-butene purity is unknown.
Reliability : (2) valid with restrictions
The CRC Handbook of Chemistry and Physics is a peer reviewed publication. This robust summary has a reliability rating of 2 because there is insufficient information available on the method and analytical procedure.
Flag : Critical study for SIDS endpoint
27.10.2003 (30)

Value : = -116.2 °C
Sublimation :
Method : other
Year :
GLP :
Test substance :

Method : The calculated value was determined using MPBPWIN version 1.40, a subroutine within the computer program EPIWIN version 3.04.
Melting Point estimations performed by MPBPWIN are based on the average result of the calculation methods of K. Joback and Gold and Ogle. Joback's Method is described in Joback, K.G. 1982. A Unified Approach to Physical Property Estimation Using Multivariate Statistical Techniques. In The Properties of Gases and Liquids. Fourth Edition. 1987. R.C. Reid, J.M. Prausnitz and B.E. Poling, Eds.
The Gold and Ogle Method simply uses the formula
Tm = 0.5839Tb, where Tm is the melting point in Kelvin and Tb is the boiling point in Kelvin.
Reliability : (2) valid with restrictions
The value was calculated based on chemical structure as modeled by EPIWIN. This robust summary has a reliability rating of 2 because the data are not measured.
27.10.2003 (15)

Value : ca. -134 °C
Decomposition : no, at °C
Sublimation : no
Method :
Year :
GLP :
Test substance :

Source : Shell Nederland Chemie B.V. Rotterdam
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance : 2-methyl-2-butene purity is unknown.
This robust summary has a reliability rating of 4 because the data were not reviewed.
01.06.1995 (35)

2.2 BOILING POINT

Value	:	= 38.5 °C at 1013 hPa
Decomposition	:	
Method	:	other: not specified
Year	:	
GLP	:	no data
Test substance	:	other TS: 2-methyl-2-butene
Test substance	:	2-methyl-2-butene purity is unknown.
Reliability	:	(2) valid with restrictions The CRC Handbook of Chemistry and Physics is a peer reviewed publication. This robust summary has a reliability rating of 2 because there is insufficient information available on the method and analytical procedure.
Flag	:	Critical study for SIDS endpoint

27.10.2003 (30)

Value	:	= 46.9 °C at 1013 hPa
Decomposition	:	
Method	:	other: calculated
Year	:	
GLP	:	
Test substance	:	other TS: 2-methyl-2-butene
Method	:	The calculated value was determined using MPBPWIN version 1.40, a subroutine within the computer program EPIWIN version 3.04. Boiling Point estimations performed by MPBPWIN are based on the calculation method of S. Stein and R. Brown in "Estimation of Normal Boiling Points from Group Contributions". 1994. J. Chem. Inf. Comput. Sci. 34: 581-587.
Reliability	:	(2) valid with restrictions The value was calculated based on chemical structure as modeled by EPIWIN. This robust summary has a reliability rating of 2 because the data are not measured.

27.10.2003 (15)

Value	:	35 - 38 °C at 1013 hPa
Decomposition	:	
Method	:	other
Year	:	
GLP	:	no data
Test substance	:	other TS: 2-methyl-2-butene
Source	:	Shell Nederland Chemie B.V. Rotterdam EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance	:	2-methyl-2-butene purity is unknown.
Reliability	:	(4) not assignable This robust summary has a reliability rating of 4 because the data were not reviewed.

27.10.2003 (35)

2.3 DENSITY

Type	:	density
Value	:	= .662 g/cm³ at 25 °C
Method	:	other: not specified
Year	:	

GLP : no data
Test substance : other TS: 2-methyl-2-butene

Test substance : 2-methyl-2-butene purity is unknown.
Reliability : (2) valid with restrictions
The CRC Handbook of Chemistry and Physics is a peer reviewed publication. This robust summary has a reliability rating of 2 because there is insufficient information available on the method and analytical procedure.
Flag : Critical study for SIDS endpoint
27.10.2003 (30)

Type : density
Value : ca. 662 kg/m3 at 20 °C
Method : other
Year :
GLP : no data
Test substance :

Source : Shell Nederland Chemie B.V. Rotterdam
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance : 2-methyl-2-butene purity is unknown.
This robust summary has a reliability rating of 4 because the data were not reviewed.
01.06.1995 (35)

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value : 623.94 hPa at 25 °C
Decomposition :
Method : other (calculated)
Year :
GLP :
Test substance : other TS: 2-methyl-2-butene

Reliability : (2) valid with restrictions
This robust summary has a reliability rating of 2 because the data retrieved and reviewed for quality, however, reference is from a peer-reviewed journal.
Flag : Critical study for SIDS endpoint
27.10.2003 (10) (30)

Value : ca. 613 hPa at 20 °C

Source : Shell Nederland Chemie B.V. Rotterdam
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance : 2-methyl-2-butene purity is unknown.
This robust summary has a reliability rating of 4 because the data were not reviewed.
01.06.1995 (40)

2.5 PARTITION COEFFICIENT

Partition coefficient :

Log pow : = 2.67 at °C
pH value :
Method :
Year :
GLP : no data
Test substance : other TS: 2-methyl-2-butene

Method : Peer reviewed/selected octanol-water partitioning data together with other organic-water systems were identifed and used to develop a general linear solvation energy equation with 1,353 solutes. The calculated log Pow value for 2-methyl-2-butene , 2.79, was in good agreement with the measured value, 2.67, from the training set.
Test substance : 2-methyl-2-butene purity is unknown.
Reliability : (2) valid with restrictions
This robust summary has a reliability rating of 2 because there is insufficient information available on the method and analytical procedure used to develop the cited value.

27.10.2003 (1)

Partition coefficient :
Log pow : = 2.64 at 25 °C
pH value :
Method : other (calculated)
Year :
GLP :
Test substance : other TS: 2-methyl-2-butene

Method : Calculated values using KOWWIN version 1.65, a subroutine of the computer program EPIWIN version 3.04
Octanol / Water Partition Coefficient estimations performed by KOWWIN are based on an atom/fragment contribution method of W. Meylan and P. Howard in "Atom/fragment contribution method for estimating octanol-water partition coefficients". 1995. J. Pharm. Sci. 84:83-92.
Reliability : (2) valid with restrictions
The value was calculated based on chemical structure as modeled by EPIWIN. This robust summary has a reliability rating of 2 because the data are not measured.

27.10.2003 (15)

Partition coefficient :
Log pow : 2.57 - 2.77 at °C
pH value :
Method : other (calculated)
Year : 1993
GLP : yes
Test substance :

Source : Shell Nederland Chemie B.V. Rotterdam
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (4) not assignable
This robust summary has a reliability rating of 4 because the data were not reviewed.

27.10.2003 (36)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in : Water
Value : 193 mg/l at 25 °C

pH value	:	
concentration	:	at °C
Temperature effects	:	
Examine different pol.	:	
PKa	:	at 25 °C
Description	:	
Stable	:	
Deg. product	:	
Method	:	other: no data
Year	:	
GLP	:	no data
Test substance	:	other TS: 2-methyl-2-butene

Method : The authors correlated values of log P, where P is the activity coefficient in the ideal gas phase relative to infinitely dilute aqueous solution. They identified 34 bond contributions obtained by least-squares treatment of data on 263 compounds. Values of log P calculated from the contributions differed from the experimental values with a standard deviaton of 0.41. The experimental water solubility value listed for 2-methyl-2-butene (at 25 °C) was -log Sw = 2.56 (moles/L).

Reliability : (2) valid with restrictions
This robust summary has a reliability rating of 2 because the data are not from the primary source, but rather from reviewed, acceptable data.

Flag : Critical study for SIDS endpoint

29.09.2004 (22)

Solubility in	:	Water
Value	:	= 206.3 mg/l at 25 °C
pH value	:	
concentration	:	at °C
Temperature effects	:	
Examine different pol.	:	
PKa	:	at 25 °C
Description	:	
Stable	:	
Deg. product	:	
Method	:	other: calculated
Year	:	
GLP	:	
Test substance	:	other TS: 2-methyl-2-butene

Method : Water solubility calculated by WSKOWWIN, a subroutine of the computer program EPIWIN version 3.04. that is based on a Kow correlation method described by W. Meylan, P. Howard and R. Boethling in "Improved method for estimating water solubility from octanol/water partition coefficient". Environ. Toxicol. Chem. 15:100-106. 1995.

Reliability : (2) valid with restrictions
The value was calculated based on chemical structure as modeled by EPIWIN. This robust summary has a reliability rating of 2 because the data are calculated and not measured.

15.07.2004 (15)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

Value : ca. -45 °C

Type : closed cup

Remark : Some references give a flash point of -18 degrees Centigrade.
Source : Shell Nederland Chemie B.V. Rotterdam
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance : 2-methyl-2-butene purity is unknown.
This robust summary has a reliability rating of 4 because the data were not reviewed.

01.06.1995 (35)

2.8 AUTO FLAMMABILITY

Value : ca. 240 °C at

Source : Shell Nederland Chemie B.V. Rotterdam
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance : 2-methyl-2-butene purity is unknown.
Reliability : (4) not assignable
This robust summary has a reliability rating of 4 because the data were not reviewed.

27.10.2003 (37)

2.9 FLAMMABILITY

Result : extremely flammable

Remark : Based on flash point
Source : Shell Nederland Chemie B.V. Rotterdam
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance : 2-methyl-2-butene purity is unknown.
Reliability : (4) not assignable
This robust summary has a reliability rating of 4 because the data were not reviewed.

27.10.2003

2.10 EXPLOSIVE PROPERTIES

Result : other

Remark : Upper explosion limit in air 7.7% v/v
Lower explosion limit in air 1.6% v/v
Source : Shell Nederland Chemie B.V. Rotterdam
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance : 2-methyl-2-butene purity is unknown.
Reliability : (4) not assignable
This robust summary has a reliability rating of 4 because the data were not reviewed.

27.10.2003 (37)

2.11 OXIDIZING PROPERTIES

Result : no oxidizing properties

Source : Shell Nederland Chemie B.V. Rotterdam
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Test substance : 2-methyl-2-butene purity is unknown.
This robust summary has a reliability rating of 4 because the data were not reviewed.

23.03.1995

2.12 DISSOCIATION CONSTANT

2.13 VISCOSITY

2.14 ADDITIONAL REMARKS

3.1.1 PHOTODEGRADATION

Type	:	air
Light source	:	
Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight
INDIRECT PHOTOLYSIS		
Sensitizer	:	OH
Conc. of sensitizer	:	1500000 molecule/cm³
Rate constant	:	= .000000000087308 cm³/(molecule*sec)
Degradation	:	= 50 % after 1.5 hour(s)
Deg. product	:	
Method	:	other (calculated): Calculated values using AOPWIN version 1.89, a subroutine of the computer program EPIWIN version 3.04
Year	:	
GLP	:	
Test substance	:	other TS: 2-methyl-2-butene
Method	:	Calculated values using AOPWIN version 1.89, a subroutine of the computer program EPIWIN version 3.04 Indirect photodegradation, or atmospheric oxidation potential, is based on the structure-activity relationship methods developed by R. Atkinson under the following conditions: Temperature 25°C Sensitizer OH- radical Concentration of Sensitizer 1.5E6 OH- radicals/cm3
Conclusion	:	The half-life of 2-metyl-2-butene, based on a 12-hour day, is 0.12 days. The half-life is normalized to a 12-hour day because atmospheric oxidation reactions only take place in the presence of sunlight.
Reliability	:	(2) valid with restrictions The value was calculated based on chemical structure as modeled by EPIWIN. This robust summary has a reliability rating of 2 because the data are not measured.
Flag	:	Critical study for SIDS endpoint

27.10.2003 (34)

Type	:	air
Light source	:	
Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight
INDIRECT PHOTOLYSIS		
Sensitizer	:	O3
Conc. of sensitizer	:	700000000000 molecule/cm³
Rate constant	:	.000000000000000423 cm³/(molecule*sec)
Degradation	:	50 % after 0 day(s)
Deg. product	:	
Method	:	other (calculated)
Year	:	
GLP	:	no data
Test substance	:	other TS: 2-methyl-2-butene
Remark	:	Reactions with nitrate radicals may be important.
Test condition	:	The author applied an unweight least-squares analysis of degradation rate constants for organic chemicals by O3 developed by the following investigators: Bufalini and Altshuller (1965); Cox and Penkett (1972); Japar et al. (1974); and Huie and Herron (1975). These data were used to derive

a recommended Arrhenius expression that yielded the following rate constant for 2-methyl-2-buene at 298K:
4.23E-16 cm3molecule-1sec-1.

Two experimental methods used to study the kinetics of OH- reactions with organic chemicals included absolute and relative rate constant techniques. The absolute methods include static/stopped flow and flow systems. The author characterized the relative rate constant techniques as invalid due to confounding secondary reactions and those data were not included in analyses.

Static/stopped flow systems monitor the rate of O3 decay in the presence of a known excess concentration of the test sample. In comparison, flow systems include flow-tubes where known concentrations of O3 and organic enter a reaction tube and final concentrations at the tube terminus are monitored, which can include a chemiluminescence analyzer for O3 and gas chromatography for organics.

Reliability : (2) valid with restrictions
This robust summary has a reliability rating of 2 because the data are calculated. Measured data from other investigators that were reviewed for reliability, were included in the development of rate constants.

Flag : Critical study for SIDS endpoint
29.09.2004 (4)

Type : air
Light source :
Light spectrum : nm
Relative intensity : based on intensity of sunlight
INDIRECT PHOTOLYSIS
Sensitizer : OH
Conc. of sensitizer : 500000 molecule/cm³
Rate constant : .0000000000869 cm³/(molecule*sec)
Degradation : 50 % after .2 day(s)
Deg. product :
Method : other (calculated)
Year :
GLP : no data
Test substance : other TS: 2-methyl-2-butene

Test condition : The author applied a unit -weight least-squares analysis of degradation rate constants for organic chemicals by OH- developed by the following investigators at temperatures less than or equal to 467K: Morris and Niki (1971); Atkinson et al. (1976); Atkinson and Pitts (1978); Atkinson et al. (1978); Atkinson et al. (1982); Ohta (1983); and Atkinson and Aschmann (1984). These data were used to derive a recommended Arrhenius expression that yielded the following rate constant for 2-methyl-2-buene at 298K:
8.69E-11 cm3molecule-1sec-1.

Two experimental methods used to study the kinetics of OH- reactions with organic chemicals included absolute and relative rate constant techniques. The absolute methods have involved primarily the discharge flow and flash photolysis techniques. Several relative rate methods are available.

Detection of OH- from an electric discharge in water using ultraviolet absorption was the first absolute method employed. A subsequent method involved an electric discharge in water vapor, which yielded a cleaner source of OH-. The flash photolysis method was adapted to monitor OH-, which were produced by photodissociation of H20 and H2O2 in vacuum- and far-ultraviolet, respectively. OH- concentrations were they monitored

by kinetic spectroscopy.

Numerous relative rate methods exist. However, the predominant method has involved monitoring the relative disappearance rates of two or more organic componds in systems containing OH-.

Conclusion : The half-life of 2-methyl-2-butene, based on a 12-hour day, is 0.37 days. The half-life is normalized to a 12-hour day because atmospheric oxidation reactions only take place in the presence of sunlight.

Reliability : (2) valid with restrictions
This robust summary has a reliability rating of 2 because the data are calculated. Measured data from other investigators that were reviewed for reliability, were included in the development of rate constants.

Flag : Critical study for SIDS endpoint

29.09.2004 (2) (3)

Type : air
Light source :
Light spectrum : nm
Relative intensity : based on intensity of sunlight
INDIRECT PHOTOLYSIS
Sensitizer : OH
Conc. of sensitizer : 1000000 molecule/cm³
Rate constant : .000000000087 cm³/(molecule*sec)
Degradation : 50 % after 2.2 hour(s)
Deg. product :
Method : OECD Guide-line draft "Photochemical Oxidative Degradation in the Atmosphere"
Year : 1991
GLP :
Test substance :

Remark : Calculated with the Atkinson method.
Source : Shell Nederland Chemie B.V. Rotterdam
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (4) not assignable
This robust summary has a reliability rating of 4 because the data were not reviewed.

27.10.2003

Type : air
Light source :
Light spectrum : nm
Relative intensity : based on intensity of sunlight

Remark : Estimated lifetime under photochemical smog conditions in S.E. England is 0.46 hour.
Source : Shell Nederland Chemie B.V. Rotterdam
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (4) not assignable
This robust summary has a reliability rating of 4 because the data were not reviewed.

12.11.2003 (7) (9)

3.1.2 STABILITY IN WATER

Type : abiotic
t1/2 Ph4 : at °C
t1/2 Ph7 : at °C

t1/2 pH9 : at °C

Remark : QSAR hydrolysis halflife = 1000 days.
Hydrolysis is not likely to be an important transformation mechanism for this chemical.

Source : Shell Nederland Chemie B.V. Rotterdam
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (4) not assignable
This robust summary has a reliability rating of 4 because the data were not reviewed.

04.01.2005 (39)

Type : abiotic
t1/2 Ph4 : at °C
t1/2 Ph7 : at °C
t1/2 pH9 : at °C
Deg. product :
Method :
Year :
GLP : no data
Test substance : other TS: 2-methyl-2-butene

Result : Hydrolysis of an organic molecule can occur when a molecule (R-X) reacts with water (H2O) to form a new carbon-oxygen bond after the carbon-X bond is cleaved. Mechanistically, this reaction is referred to as a nucleophilic substitution reaction, where X is the leaving group being replaced by the incoming nucleophilic oxygen from the water molecule. The leaving group, X, must be a molecule other than carbon because for hydrolysis to occur, the R-X bond cannot be a carbon-carbon bond. This reaction differs from other reactions with water such as hydration of carbonyls that can lead to the formation of an alcohol beginning with the transfer of a proton from the water to an alkene. However, water by itself is too weak an acid to transfer a proton in the absence of a strong acid, which could effect such an acid catalysed electrophilic addition.

Thus, hydrocarbons such as alkenes are not subject to hydrolysis under conditions typically found within the environment and therefore, this fate process will not contribute to the degradative loss of 2-methyl-2-butene from the environment.

Reliability : (2) valid with restrictions
This robust summary has a reliability rating of 2 because the data are not measured, but rather a technical discussion.

Flag : Critical study for SIDS endpoint

04.01.2005 (20) (21)

3.1.3 STABILITY IN SOIL

3.2.1 MONITORING DATA

3.2.2 FIELD STUDIES

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type :

Media : other: air - biota - sediment(s) - soil - water
Air : % (Fugacity Model Level I)
Water : % (Fugacity Model Level I)
Soil : % (Fugacity Model Level I)
Biota : % (Fugacity Model Level II/III)
Soil : % (Fugacity Model Level II/III)
Method : other: Calculation according Mackay, Level I
Year :

Remark : Physicochemical data used in the calculation:

Parameter	Value w/ Units
Molecular Weight	70.14
Temperature	25°C
Log Kow	2.67
Water Solubility	193 g/m3
Vapor Pressure	623.9 hPa
Melting Point	-133.7°C

Result : Using the Mackay Level I calculation, the following distribution is predicted for 2-methyl-2-butene:

% Distribution	Compartment
99.97	Air
0.02	Water
0.01	Soil
0.00	Sediment
0.00	Suspended Sediment
0.00	Biota

Test substance : 2-methyl-2-butene
Reliability : (2) valid with restrictions
This robust summary has a reliability rating of 2 because the partitioning data are modeled.
Flag : Critical study for SIDS endpoint
05.08.2004 (32)

Type :
Media : other: air - biota - sediment(s) - soil - water
Air : % (Fugacity Model Level I)
Water : % (Fugacity Model Level I)
Soil : % (Fugacity Model Level I)
Biota : % (Fugacity Model Level II/III)
Soil : % (Fugacity Model Level II/III)
Method : other: Calculation according Mackay, Level III
Year :

Remark : Physicochemical data used in the calculation:

Parameter	Value w/ Units
Molecular Weight	70.14
Temperature	25°C
Log Kow	2.67
Water Solubility	193 g/m3
Vapor Pressure	623.9 hPa
Melting Point	-133.7°C

Emissions rate parameters:
1000 kg/hr into air

1000 kg/hr into water
1000 kg/hr into soil

Degradation rate parameters:
Negligable in all compartments

Result : Using the Mackay Level III calculation, the following distribution is predicted for 2-methyl-2-butene:

% Distribution	Compartment
2.01	Air
94.18	Water
2.62	Soil
1.19	Sediment

Test substance : 2-methyl-2-butene
Reliability : (2) valid with restrictions
This robust summary has a reliability rating of 2 because the partitioning data are modeled.
Flag : Critical study for SIDS endpoint
05.08.2004 (33)

Type :
Media : other: air - biota - sediment(s) - soil - water
Air : % (Fugacity Model Level I)
Water : % (Fugacity Model Level I)
Soil : % (Fugacity Model Level I)
Biota : % (Fugacity Model Level II/III)
Soil : % (Fugacity Model Level II/III)
Method : other: Calculation according Mackay, Level III
Year :

Remark : Physicochemical data used in the calculation:

Parameter	Value w/ Units
Molecular Weight	70.14
Temperature	25°C
Log Kow	2.67
Water Solubility	193 g/m3
Vapor Pressure	623.9 hPa
Melting Point	-133.7°C

Emissions rate parameters:
1000 kg/hr into air
0 kg/hr into water
0 kg/hr into soil

Degradation rate parameters:
Negligable in all compartments

Result : Using the Mackay Level III calculation, the following distribution is predicted for 2-methyl-2-butene:

% Distribution	Compartment
100	Air
0	Water
0	Soil
0	Sediment

Test substance : 2-methyl-2-butene
Reliability : (2) valid with restrictions

This robust summary has a reliability rating of 2 because the partitioning data are modeled.

Flag : Critical study for SIDS endpoint
05.08.2004 (33)

Type :
Media : other: air - biota - sediment(s) - soil - water
Air : % (Fugacity Model Level I)
Water : % (Fugacity Model Level I)
Soil : % (Fugacity Model Level I)
Biota : % (Fugacity Model Level II/III)
Soil : % (Fugacity Model Level II/III)
Method : other: Calculation according Mackay, Level III
Year :

Remark : Physicochemical data used in the calculation:

Parameter	Value w/ Units
Molecular Weight	70.14
Temperature	25°C
Log Kow	2.67
Water Solubility	193 g/m3
Vapor Pressure	623.9 hPa
Melting Point	-133.7°C

Emissions rate parameters:
0 kg/hr into air
1000 kg/hr into water
0 kg/hr into soil

Degradation rate parameters:
Negligable in all compartments

Result : Using the Mackay Level III calculation, the following distribution is predicted for 2-methyl-2-butene:

% Distribution	Compartment
0.52	Air
98.2	Water
6.86E-5	Soil
1.24	Sediment

Test substance : 2-methyl-2-butene
Reliability : (2) valid with restrictions
This robust summary has a reliability rating of 2 because the partitioning data are modeled.
Flag : Critical study for SIDS endpoint
05.08.2004 (33)

Type :
Media : water - air
Air : % (Fugacity Model Level I)
Water : % (Fugacity Model Level I)
Soil : % (Fugacity Model Level I)
Biota : % (Fugacity Model Level II/III)
Soil : % (Fugacity Model Level II/III)
Method : other: Henry's Law constant calculation
Year :

Result : The Henry's Law constant (HLC) representing volatility for 2-methyl-2-

butene is 11,145 Pa-m3/mole (0.224 atm-m3/mole) at 25°C. The HLC was calculated using a water solubility of 193 mg/L (Hine and Mookejee, 1975), a vapour pressure of 623.94 hPa (Daubert et al, 1989), and a molecular weight of 70.14. Measured values for melting and boiling points of -133.7 and 38.5°C (Lide, 1997), respectively, were also used.

Test substance : other TS: 2-methyl-2-butene
Reliability : (2) valid with restrictions
This robust summary has a reliability rating of 2 because the data are calculated.
Flag : Critical study for SIDS endpoint
29.09.2004 (15) (30)

Type :
Media : water - air
Air : % (Fugacity Model Level I)
Water : % (Fugacity Model Level I)
Soil : % (Fugacity Model Level I)
Biota : % (Fugacity Model Level II/III)
Soil : % (Fugacity Model Level II/III)
Method : other: Calculation
Year :

Result : The volatilization half-life of 2-methyl-2-butene from a model river and lake is estimated to be approximately 51 minutes and 3.32 days, respectively.
Test substance : Other: 2-Methyl-2-Butene
Reliability : (2) valid with restrictions
The data were calculated based on chemical structure as modeled by EPIWIN. This robust summary has a reliability rating of 2 because the data are not measured.
Flag : Critical study for SIDS endpoint
05.08.2004 (15)

Type : volatility
Media : water - air
Air : % (Fugacity Model Level I)
Water : % (Fugacity Model Level I)
Soil : % (Fugacity Model Level I)
Biota : % (Fugacity Model Level II/III)
Soil : % (Fugacity Model Level II/III)
Method : other
Year :

Result : Based on the calculated Henry's Law constant (18.9 E3 Pa.m3/mole) the volatization halflife of the substance in a model river, depth 1 m, current 1 m/s and a windvelocity of 3 m/s is estimated to be 2.4 hours.
Source : Shell Nederland Chemie B.V. Rotterdam
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (4) not assignable
This robust summary has a reliability rating of 4 because the data were not reviewed.
05.08.2004 (31)

3.3.2 DISTRIBUTION

Media :
Method : other (calculation)
Year :

Method	:	The calculated value was determined using PCKOCWIN version 1.66, a subroutine within the computer program EPIWIN version 3.04.
Result	:	Koc = 67.7 Log Koc = 1.83
Test substance	:	other TS: 2-methyl-2-butene
Reliability	:	(2) valid with restrictions The value was calculated based on chemical structure as modeled by EPIWIN. This robust summary has a reliability rating of 2 because the data are not measured.

27.10.2003 (15)

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type	:	aerobic
Inoculum	:	other: filtered secondary effluent from the Canterbury Sewage Works
Concentration	:	2 mg/l related to Test substance related to
Contact time	:	
Degradation	:	5 (±) % after 5 day(s)
Result	:	other: not readily biodegradable
Kinetic of testsubst.	:	5 day(s) 5 % 15 day(s) 0 % 28 day(s) 0 % % %
Deg. product	:	
Method	:	other
Year	:	1984
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Method: EEC (1984), Part C: Methods for the determination of ecotoxicity, Official Journal of the european communities No, L251, 188-198, C.4-E. Temperature 20 deg C Inhibition of the micro-organisms at 2 mg/l. Therefore a negative aerobic biodegradation after: 15 day: -10% 28 day: -18% / -21 %
Source	:	Shell Nederland Chemie B.V. Rotterdam EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(4) not assignable This robust summary has a reliability rating of 4 because the data were not reviewed.

12.11.2003 (5)

Type	:	aerobic
Inoculum	:	other: domestic sewage effluent
Concentration	:	2.1 mg/l related to Test substance related to
Contact time	:	28 day(s)
Degradation	:	7 (±) % after 28 day(s)
Result	:	
Kinetic of testsubst.	:	5 day(s) 2 - 4 %

7 day(s) 1 - 2 %
11 day(s) 0 - 1 %
14 day(s) 2 - 2 %
18 day(s) 4 - 4 %

Control substance : Benzoic acid, sodium salt
Kinetic : 5 day(s) 67 - 68 %
28 day(s) 83 - 85 %
Deg. product :
Method : other: OECD Guideline 301D and EC Directive 92/69, C.4-E and EPA OPPTS 835.3110
Year : 2001
GLP : yes
Test substance : other TS: 2-methyl-2-butene (CAS No. 513-35-9)

Remark : Kinetic of test substance (cont'd.)
21 day(s) 2 and 6%
25 day(s) 12 and 15%
28 day(s) 4 and 10%

Result : A maximum of 15% biodegradation was measured (on Day 25) by the end of the Closed Bottle test.

The mean Total Viable Count of the sample of final sewage effluent in the main test was 1.0 x 10E5 Colony Forming Units (CFU) per ml and the mean count in inoculated MSM on Day 0 was 8.2 x 10E3 CFU/ml.

The presence of the test substance did not cause any inhibitory affect on the normal degradative activity of the microbial inoculum on the reference substance.

Test condition : Test inoculum preparation:
A sample of secondary effluent was collected on the day of the test from a trickling-filter plant, which treats predominantly domestic waste. It was maintained under aerobic conditions in the laboratory, then, immediately before use, filtered through glass wool and the filtrate used as the inoculum for the test (1 ml filtrate/litre test medium).

Study design:
Eighteen bottles were filled with a mineral salts medium, inoculated with unacclimated sewage effluent at a loading of 1ml/l, and the test substance at a nominal loading of 2.1 mg/l. The test substance was injected into modified BOD bottles using a microsyringe to establish the appropriate test concentrations. The dissolved oxygen (DO) concentration in replicate bottles was measured on Days 0, 5, 7, 11, 14, 18, 21, 25 and 28. Four bottles were established for a concurrent five-day microbial inhibition assay, in which the biodegradation of the readily biodegradable reference substance, sodium benzoate, was examined in the presence of the test substance. DO concentration was measured in replicate bottles on Days 0 and 5.
A further eighteen bottles were filled with mineral salts medium, inoculated with unacclimated sewage effluent at a loading of 1 ml/l, and the reference substance, sodium benzoate, at a nominal loading of 5 mg/l. DO concentrations in replicate bottles was measured on Days 0, 5, 7, 11, 14, 18, 21, 25 and 28.
All test systems were incubated at 22 +/- 2 degree C in darkness.
Theoretical oxygen demands for the test and reference substances were based on their empirical formulae and molecular weights. The study was initiated on 8 October 2001.

Test substance : 2-methyl-2-butene (CAS No. 513-35-9) purity was 98.0%.

The test substance was stable for the duration of all studies performed at the test house.

The carbon content of the test substance was determined before the start of the Closed Bottle test using a CEC Model 440 Elemental Analyser. The measured carbon content (85.47%) was equivalent to 99.8% of the theorectical value (85.63%), which was calculated using the empirical formula of 2-methyl-2-butene, which comprised 98.2% of the test substance.

Conclusion : 7% biodegradation after 28 days.
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
19.07.2004 (27)

Type : aerobic
Inoculum :

Remark : Based on this data: expected to be inherently biodegradable.
Waste water treatment:
6 h 0.1% ThOD
12 h 1.1% ThOD
24 h 0.9% ThOD
Source : Shell Nederland Chemie B.V. Rotterdam
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (4) not assignable
This robust summary has a reliability rating of 4 because the data were not reviewed.
12.11.2003 (19)

3.6 BOD5, COD OR BOD5/COD RATIO

BOD5
Method : other
Year : 1984
Concentration : 2 mg/l related to Test substance
BOD5 : mg/l
GLP : yes
RATIO BOD5 / COD
BOD5/COD : = .05

Remark : BOD5 = 0.18 mg O2/mg substance.
BOD5/ThOD = 0.053
calculated ThOD = 3.42 g O2/ g substance.
Source : Shell Nederland Chemie B.V. Rotterdam
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (4) not assignable
This robust summary has a reliability rating of 4 because the data were not reviewed.
12.11.2003 (5)

3.7 BIOACCUMULATION

Species : other: (see remark)
Exposure period : at °C
Concentration :
BCF : = 22.69
Elimination :
Method : other: calculation
Year :

GLP : no data
Test substance : other TS: 2-methyl-2-butene

Remark : A log BCF of 1.36 (BCF = 22.69) is calculated, based on a log Pow of 2.67. With respect to the log Pow = 2.67, bioaccumulation of 2-methyl-2-butene in the aquatic environment is expected to occur at low levels.
Reliability : (2) valid with restrictions
This robust summary has a reliability rating of 2 because the data are calculated.
Flag : Critical study for SIDS endpoint
28.10.2003 (15)

Remark : Based on a QSAR calculation (BCF = 50) and on a calculated (ClogP) log Pow (2.67), the substance is expected to have a low potential to bioaccumulate.
Source : Shell Nederland Chemie B.V. Rotterdam
Reliability : (2) valid with restrictions
This robust summary has a reliability rating of 2 because the data are calculated.
28.10.2003 (40)

3.8 ADDITIONAL REMARKS

Remark : The photochemical ozone creation potential (POCP) index for a chemical provides a relative measure of its reactivity or ozone forming potential. The POCP index can also provide a means of ranking volatile organic compounds (VOCs) by their ability to form ozone in the troposphere. Reported POCP indices for 2-methyl-2-butene in northwestern Europe range from 77.1 to 84.2, in comparison with an POCP index of 100 for ethylene, the reference substance.
Reliability : (2) valid with restrictions
The values were calculated. This robust summary has a reliability rating of 2 because the data are not measured.
12.11.2003 (12) (13)

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	semistatic
Species	:	Oncorhynchus mykiss (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC50	:	= 4.99 measured/nominal
Limit test	:	no
Analytical monitoring	:	yes
Method	:	other: OECD Guide-line 203 and EC Directive 92/96 C1
Year	:	2002
GLP	:	yes
Test substance	:	other TS: 2-methyl-2-butene (CAS No. 513-35-9)
Result	:	After 96 hours, the highest measured concentration at which no mortality had occurred was 2.93 mg/l and the lowest at which there was 100% mortality was 8.51 mg/l. Treatment-related effects were exhibited at 5.33 mg/l and higher concentrations. Based on these findings the following values have been estimated: 96-hour LC50 value = 4.99 mg/l (95% confidence limits of 2.93 and 8.51 mg/l).
Test condition	:	Study design: The study was conducted in completely filled (no headspace) and sealed vessels because of the volatility of 2-methyl-2-butene. At each concentration, the test medium was prepared by stirring the test substance in a sealed vessel for approximately 24 hours. After being allowed to stand for at least 30 minutes to obtain an equilibrium concentration of 2-methyl-2-butene, aliquots of medium were removed from the middle of the vessel and used to fill the test vessels at each concentration. Groups of ten juvenile fish were exposed for 96 hours to a control solution (dechlorinated tap water, ca. 150-200 mg/l as CaCO3) or to 2-methyl-2-butene at nominal concentration of 2.13, 4.70, 10.3, 22.7 and 50.0 mg/l. The exposure levels were monitored by measuring the concentrations of 2-methyl-2-butene in samples of the test media using a GLC method of analysis. Test temperature was 13.7 to 15.4 deg C, pH ranged from 7.3 to 8.1, and the dissolved oxygen in the new solutions were 97 to 101% of the air saturation value (ASV), while the dissolved oxygen in the old solutions ranged from 31 to 99% ASV. The measured concentrations of 2-methyl-2-butene ranged between 33% and 89% of their nominal values in samples of freshly prepared media and between 33 and 99% of their nominal values in samples of expired (24-hour-old) media (between 93 and 116% of their starting values). Based on an arithmetic mean, the overall mean measured levels of 2-methyl-2-butene were 1.67, 2.93, 5.33, 8.5l and 25.9 mg/l. Observations of the fish were made after 0.25, 2, 4, 24, 48, 72 and 96 hours of exposure. Statistical: LC50 values were estimated by non-linear interpolation between the two concentrations which bracket the 50% effect level using a computer program; the program uses the number of fish exposed and the number dead at each measured concentration.
Test substance	:	2-methyl-2-butene (CAS No. 513-35-9) also known as 2-methyl, 2-butene. Purity of 2-methyl-2-butene was 98.0%. The test substance was stable for the duration of all the studies performed

by the test house.

Conclusion : LC50 = 4.99 mg/l (measured concentration)
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
19.07.2004 (25)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type : static
Species : Daphnia magna (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
EC50 : = 3.84
Limit Test : no
Analytical monitoring : yes
Method : other: OECD Guide-line 202 and EC Directive 92/96 C2
Year : 2002
GLP : yes
Test substance : other TS: 2-methyl-2-butene (CAS No. 513-35-9)

Result : The mean measured concentrations of 2-methyl-2-butene at the start (between 30 and 49% of their nominal values) were adequately maintained during the test, giving measured levels of between 28 and 46% of nominal after 48 hours. Based on an arithmetic mean, the overall mean measured levels of isoprene were 0.691, 1.74, 2.95, 6.63 and 23.6 mg/l.
After 48 hours, the lowest measured concentration resulting in 100% immobility was 6.63 mg/l and the highest measured concentration at which immobilisation was </= 10% was 1.74 mg/l.

Test condition : Study design:
The study was conducted in completely filled (no headspace) and sealed vessels because of the volatility of 2-methyl-2-butene. The test media were prepared, either directly or by dilution, from an aqueous preparation in which the test substance was stirred in a sealed vessel in the dark for approximately 24 hours. After being allowed to stand for approximately 30 minutes to obtain an equilbrium concentration of 2-methyl-2butene, aliquots of medium were removed from the middle of the vessel and used to fill replicate vessels at each concentration.

Groups of twenty Daphnia, less than 24 hours old, were exposed for 48 hours to 2-methyl-2-butene, prepared in Elendt M4 medium at nominal concentrations of 2.13, 4.70, 10.3, 22.7 and 50.0 mg/l. The exposure levels were monitored by measuring the concentrations of 2-methyl-2-butene in samples of the test media using a GLC method of analysis. Test temperature ranged from 19.6 to 20.5 deg C, pH ranged from 7.5 to 7.9, and dissolved oxygen ranged from 97 to 100% of the air saturation value.

Observations of the Daphnia in each control and test vessel were made after 24 and 48 hours.

Statistical:
EC50 values were estimated either by the moving average method or by non-linear interpolation between the two concentrations which bracket the 50% effect level using a computer program; the program uses the number o Daphnia exposed and the number immobile at each nominal and measured concentration.

Test substance : 2-methyl-2-butene (CAS No. 513-35-9) purity was 98.0%.

The test substance was stable for the duration of all the studies performed by the test house.

Conclusion	:	48-hour EC50 value = 3.84 mg/l (95% confidence limits of 3.01 and 4.80 mg/l; measured concentration)
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

19.07.2004 (24)

Type	:	
Species	:	Daphnia magna (Crustacea)
Exposure period	:	48 hour(s)
Unit	:	mg/l
EC50	:	3
Analytical monitoring	:	no
Method	:	other
Year	:	1975
GLP	:	yes
Test substance	:	other TS: 2-methyl-2-butene
Remark	:	Method: APHA, Standard Methods for the Examination of Water and Waste Water, 14th edition, American Public Health Assoc., Washington, 1975. Temperature 20 deg C, pH= 8.0 - 8.3, Hardness = 210 - 230 mg CaCO3 /l, initial Dissolved Oxygen = 9.2-9.6 mg/l. In the open test system the Dissolved oxygen stays around 9.1 mg/l; in the closed test system the Dissolved oxygen the concentration fell to 4.6 - 6.2 mg/l. Daphnia's < 24 h old. The 48h EC50 in the open test system is > 100 mg/l for D. magna. The QSAR 96h LC50 = 11.14 mg/l.
Source	:	Shell Nederland Chemie B.V. Rotterdam EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance	:	2-methyl-2-butene purity is unknown.
Reliability	:	(4) not assignable This robust summary has a reliability rating of 4 because the data were not reviewed.

12.11.2003 (38)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species	:	other algae: Pseudokirchneriella subcapitata (formerly Selenastrum capricornutum)
Endpoint	:	growth rate
Exposure period	:	96 hour(s)
Unit	:	
Limit test	:	no
Analytical monitoring	:	yes
Method	:	other: OECD Guide-line 201, EC Directive 92/69 C3, US EPA TSCA 797.1050 & 797.1060
Year	:	2003
GLP	:	yes
Test substance	:	other TS: 2-methyl-2-butene (CAS No. 513-35-9)
Result	:	The measured concentrations of 2-methyl-2-butene ranged between 19 and 27% of their nominal values at the start of the test and between 22 and 29% of nominal after 96 hours. Based on an arithmetric mean, the overall mean measured levels of 2-methyl-2-butene were 0.689, 1.53, 3.61, 7.22 and 21.1 mg/l.

Area under the growth curve (measured concentrations):
EbC50 (72h): 10.5 mg/l (95% confidence limits,
9.55 & 11.7 mg/l)
EbC50 (96h): 10.1 mg/l (95% confidence limits,
9.21 & 11.1 mg/l)
No observed effect concentration (NOEC): 3.61 mg/l

Average specific growth rate (measured concentrations):
ErC50 (0-72h): 12.0 mg/l (95% confidence limits,
7.22 & 21.1 mg/l)
ErC50 (0-96h): 13.2 mg/l (95% confidence limits,
12.2 & 14.3 mg/l)
No observed effect concentration (NOEC): 7.22 mg/l

Observations:
After 96 hours of exposure, the majority of the cells at 21.1 mg/l were swollen and/or mis-shapen.

Test condition : Study design:
The study was conducted in completely filled (no headspace) and sealed vessels because of the volatility of 2-methyl-2-butene. The test media were prepared, either directly or by dillution, from an aqueous preparation in which the test substance was stirred in a sealed vessel for approximately 23 hours in the dark. After being allowed to stand for at least one hour to obtain an equilibrium concentration of 2-methyl-2-butene, aliquots of medium were removed from the middle of the vessel and after dilution and inoculated with alga cells, was used to fill the test vessels. The cultures were incubated in an orbital incubator under continuous illumination at temperatures ranging from 22.3 to 23.4 degree C for 96 hours. Replicate algal cultures, with an initial cell density of 1 x 10E4/ml, were exposed to 2-methyl-2-butene at nominal concentrations of 3.20, 7.04, 15.5, 34.1 and 75 mg/l.

The exposure levels were monitored by measuring the concentrations of isoprene in samples of the test media using a GLC method of analysis.

Cell densities were measured daily to monitor growth, and the test results are expressed in terms of the area under the growth curve and growth rate.

The hardness of the test soltions was not reported during the study. The pH ranged from 7.2 to 7.4 at test initiation. At termination, the pH in the high dose was 7.4, the pH in the remaining concentrations ranged from 10.3 to 10.7. The pH increase is believed to be associated with the high level of cell growth that occurred in all but the high dose.

Evaluation of data:
The area under the growth curve and the average specific growth rate are taken to be an index of growth and are calculated mathematically.

The EbC50 ("x" h) is the median effect concentration for inhibition of growth based on a comparison of areas under the growth curves after "x" hours. The EbC50 was calculated using the moving average method of a computer program (Stphan; 1977, 1982) which uses percentage effect and the nominal and measured test concentration in test samples.
The ErC50 ("x"-"y" h) is the median effect concentration for inhibition of growth based on a comparison of growth rates from "x" to "y" hours. The ErC50 was calculated by either the moving average method or by non-linear interpolation between the two concentrations which bracket the 50% effect level of a computer program (Stephan; 1977, 1982); the program uses percentage effect and the nominal and measured test concentration in test samples. The "no observed effect concentrations" (NOEC) was

		determined using Dunnett's multicomparison test to compare the percentage inhibition in the test group with that for the control cultures.
Test substance	:	2-methyl-2-butene (CAS No. 513-35-9) also known as 2-methyl, 2-butene. Purity of 2-methyl-2-butene was 98.0% The test substance was stable for the furation of all the studies performed by the test house.
Conclusion	:	After 72 and 96 hours of exposure to 2-methyl-2-butene, the EbC50 values were 10.5 and 13.2 mg/l respectively; the ErC50 values were 12.0 and 13.2 mg/l respectively. The "no observed effect concentration" (NOEC) for area under the growth curve and growth rate respectively, were 3.61 and 7.22 mg/l.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

29.09.2004 (26)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

Type	:	aquatic
Species	:	other bacteria: filtered secondary effluent from the Canterbury Sewage Works
Exposure period	:	28 day(s)
Unit	:	mg/l
EC50	:	2
Analytical monitoring	:	no
Method	:	other
Year	:	1984
GLP	:	yes
Test substance	:	other TS: 2-methyl-2-butene
Remark	:	Method: EEC (1984), Part C: Methods for the determination of ecotoxicity, Official Journal of the european communities No, L251, 188-198. Temperature = 20 deg C Effect is inhibition of oxygen uptake.
Source	:	Shell Nederland Chemie B.V. Rotterdam EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance	:	2-methyl-2-butene purity is unknown.
Reliability	:	(4) not assignable This robust summary has a reliability rating of 4 because the data were not reviewed.

12.11.2003 (5)

4.5.1 CHRONIC TOXICITY TO FISH

Species	:	other: fish
Endpoint	:	
Exposure period	:	30 day(s)
Unit	:	mg/l
ChV*	:	= 1.75 calculated
Method	:	other: ECOSAR Computer Model (in: EPIWIN)
Year	:	
GLP	:	
Test substance	:	other TS: 2-methyl-2-butene
Remark	:	Test Type: Chronic Fish Toxicty Calculation

Test condition	:	The chronic value (ChV) was calculated using ECOSAR, which is a structure-activity relationship model that can estimate chronic toxicity values for selected groups of aquatic organisms (i.e., fish Daphnids, algae) and specific exposure durations. The ChV for fish, Daphnid, and algae are for survival/growth, survival/reproduction, and growth, respectively. A log Kow (octanol/water partition coefficient) value and a chemical structure are needed to complete the calculation with this model, which can be used with chemicals like hydrocarbons whose mode of toxic action is non polar narcosis. The log Kow value used 2.67 (Abraham et al., 1994). The SMILES (Simplified Molecular Input Line Entry System) structure used with the model was: CC(C)=CC.
Reliability	:	(2) valid with restrictions This robust summary has a reliability rating of 2 because the data are not measured.
Flag	:	Critical study for SIDS endpoint

29.10.2003 (1) (15)

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

Species	:	other: Daphnid
Endpoint	:	
Exposure period	:	16 day(s)
Unit	:	mg/l
ChV*	:	= .94 calculated
Method	:	other: ECOSAR Computer Model (in: EPIWIN)
Year	:	
GLP	:	
Test substance	:	other TS: 2-methyl-2-butene
Remark	:	Test Type: Chronic Daphnid Toxicity Calculation
Test condition	:	The chronic value (ChV) was calculated using ECOSAR, which is a structure-activity relationship model that can estimate chronic toxicity values for selected groups of aquatic organisms (i.e., fish Daphnids, algae) and specific exposure durations. The ChV for fish, Daphnid, and algae are for survival/growth, survival/reproduction, and growth, respectively. A log Kow (octanol/water partition coefficient) value and a chemical structure are needed to complete the calculation with this model, which can be used with chemicals like hydrocarbons whose mode of toxic action is non polar narcosis. The log Kow value used was 2.67 (Abraham et al., 1994). The SMILES (Simplified Molecular Input Line Entry System) structure used with the model was: CC(C)=CC.
Reliability	:	(2) valid with restrictions This robust summary has a reliability rating of 2 because the data are not measured.
Flag	:	Critical study for SIDS endpoint

29.10.2003 (1) (15)

4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS

Species	:	other: earthworm
Endpoint	:	Mortality
Exposure period	:	14 other: day(s)
Unit	:	other: ppm
LC50	:	= 268.3 calculated
Method	:	other: ECOSAR Computer Model (in: EPIWIN)
Year	:	
GLP	:	

Test substance	:	other TS: 2-methyl-2-butene
Remark	:	Test Type: Earthworm Toxicity Calculation
Test condition	:	A log Kow (octanol/water partition coefficient) value and a chemical structure are needed to complete the calculation with this model, which can be used with chemicals like hydrocarbons whose mode of toxic action is non polar narcosis. The log Kow value used was 2.67 (Abraham et al., 1994). The SMILES (Simplified Molecular Input Line Entry System) structure used with the model was: CC(C)=CC.
Reliability	:	(2) valid with restrictions This robust summary has a reliability rating of 2 because the data are not measured.
Flag	:	Critical study for SIDS endpoint

29.10.2003 (1) (15)

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50
Value	:	ca. 700 - 2600 mg/kg bw
Species	:	rat
Strain	:	other: Albino Wistar
Sex	:	male/female
Number of animals	:	16
Vehicle	:	
Doses	:	Initial range-finding study: 0.5, 1.0 and 5.0 ml/kg; Final study: 1.0, 1.6, 2.5, 4.0, 6.3 and 10 ml/kg
Method	:	other
Year	:	1980
GLP	:	yes
Test substance	:	other TS: 2-methyl-2-butene (CAS No. 513-35-9)
Method	:	Statistical Methods: None
Result	:	In the range-finding study, the acute oral LD50 value was estimated to be between 1 and 5 ml/kg. Thus, a second study was done using additional doses, i.e., 1.0, 1.6, 2.5, 4.0, 6.3 and 10 ml/kg. Virtually all animals, even at the lowest doses had diarrhea, bleeding from the anus and piloerection on the day of dosing. Most animals were also lethargic. Most deaths occured within 3 days and most surviving animals had recovered from signs of intoxication by day 3. However, there were a few animals in which signs of intoxication persisted for up to a week after dosing. All but one of the survivors had gained weight at the conclusion of the fourteen-day observation period. The cumulative mortality over 14 days at each of the tested doses was as follows: 0/12 at 1.0 ml/kg; 6/12 at 1.6 ml/kg; 4/12 at 2.5 ml/kg; 9/12 at 4.0 ml/kg; 9/12 at 6.3 ml/kg; and 12/12 at 10.0 ml/kg.
Test condition	:	In an initial range-finding study, 2 rats of each sex were dosed with 0.5, 1.0 and 5.0 ml/kg. The dosing was done by intraesophageal intubation using a ballpoint needle fitted to a syringe. The material was kept on ice until it was dosed due to its volatility and it dosed at a temperature of 24.50C . After dosing the animals were given food and water ad libitum and observed for toxicological signs over the following 14 days. Body weights were recorded at 7 and 14 days. In the second study, 6 males and 6 females were dosed by intraesophageal intubation (same as above) with 1.0, 1.6, 2.5, 4.0, 6.3 and 10 ml/kg. The animals were again observed for toxicological signs over the next 14 days.
Test substance	:	2-methyl-2-butene (CAS No. 513-35-9) Indent No. 9200/9579.
Conclusion	:	Based on the above data, the oral LD50 was estimated to be in the range of 1.6 - 2.5 ml/kg (1000 - 1700 mg.kg) (Reviewer's comments).
Reliability	:	(1) valid without restriction GLP study.

29.09.2004 (14)

5.1.2 ACUTE INHALATION TOXICITY

Type	:	LC50
Value	:	> 61000 ppm
Species	:	rat

Strain	:	other: Albino Wistar
Sex	:	male/female
Number of animals	:	10
Vehicle	:	
Doses	:	6.1% (v/v)
Exposure time	:	4 hour(s)
Method	:	other
Year	:	1982
GLP	:	yes
Test substance	:	other TS: 2-methyl-2-butene (CAS No. 513-35-9)
Method	:	Statistical Methods: None
Result	:	During the exposure the animals became narcotized, but revived within 30 minutes of cessation of exposure. There were no deaths and macroscopic and microscopic examination at necropsy of animals killed 14 days after exposure was terminated revealed no compound related effects.
Test condition	:	In this study, 5 male and 5 female albino Wistar rats were exposed for 4 hours to a test atmosphere containing 6.1 per cent (v/v) 2-methyl 2-butene.
Test substance	:	2-methyl-2-butene (CAS No. 513-35-9) Batch No. Indent 9200/9315, 84.9% purity.
Conclusion	:	The acute 4-hour inhalation LC50 of 2-methyl 2-butene in rats is greater than 6.1% (v/v) or 61,000 ppm.
Reliability	:	(1) valid without restriction GLP study.

21.11.2003 (6)

5.1.3 ACUTE DERMAL TOXICITY

Type	:	LD50
Value	:	> 2000 mg/kg bw
Species	:	rat
Strain	:	other: Albino Wistar
Sex	:	male/female
Number of animals	:	10
Vehicle	:	
Doses	:	Range finding study: 0.5, 1.0 and 2.0 ml/kg; Final study: 3.03 ml/kg (equivalent to 2 g/kg)
Method	:	other
Year	:	1980
GLP	:	yes
Test substance	:	other TS: 2-methyl-2-butene (CAS No. 513-35-9)
Method	:	Statistical Methods: None
Result	:	In the range finding study, the acute dermal LD50 was estimated to be >2.0 ml/kg. In order to obtain a more accurate LD50 value, 6 males and 6 females were dosed with 3.03 ml/kg (equivalent to a dose of 2 g/kg). No mortalities were recorded and there were no signs of systemic toxicity. All animals gained weight within one week of dosing.
Test condition	:	The acute dermal toxicity of 2-methyl-2-butene was determined in albino Wistar rats using a method based on that of Noakes and Sanderson (1969). In an initial range finding study, 2 rats/sex/dose were treated with 0.5, 1.0 and 2.0 ml/kg. In the next study, 6 rats of each sex were dosed with 3.03 ml/kg. Twenty-four hours prior to each test, the animals were weighed and approximately 60% of the dorsal hair was closely shaven. The dose was applied to the shaven skin by syringe, the dose being altered by varying the volume of the material applied. Again, as for the other acute studies, it was necessary to apply the material at a temperature of approximately 5C on

account of its volatility. The test material was covered with a piece of aluminum foil and held in place by a double overwrap of waterproof adhesive tape. The animals were housed for the next 24 hours, food being withheld but water given ad libitum.
At the end of the 24-hour exposure period, the foil and dressing were removed and the skin washed with warm dilute detergent solution and then dried. The animals were returned to group housing and observed for signs of toxicity over the following 14 days. Initial, 7 day and 14 day body weights were recorded.

Test substance : 2-methyl-2-butene (CAS No. 513-35-9) Indent No. 9200/9579.
Conclusion : The acute dermal LD50 of 2-methyl2-butene is > 2 g/kg.
Reliability : (1) valid without restriction
GLP study.

28.07.2005 (14)

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.2.1 SKIN IRRITATION

Species : rabbit
Concentration : .5 other: ml
Exposure : Occlusive
Exposure time :
Number of animals : 6
Vehicle :
PDII : 1.79
Result : slightly irritating
Classification : irritating
Method : Draize Test
Year : 1980
GLP : yes
Test substance : other TS: 2-methyl-2-butene (CAS No. 513-35-9)

Method : Statistical Methods: None
Remark : Primary Skin Irritation Study (single application) performed on 3 male and 3 female New Zealand White rabbits.
Result : The mean erythema scores for abraded skin were 1.08, 1.42, 1.58 and 1.75 at 24 hrs, 48 hrs, 72 hrs and 7 days, respectively. The mean erythema scores for non-abraded skin were 0.83, 1.17, 1.25 and 1.5 at 24 hrs, 48 hrs, 72 hrs and 7 days, respectively. The mean edema scores for abraded skin were 0.58, 0.67, 0.67 and 0.83 at 24 hrs, 48 hrs, 72 hrs and 7 days, respectively. The mean edema scores for non-abraded skin were 0.50, 0.58, 0.67 and 0.82 at 24 hrs, 48 hrs, 72 hrs and 7 days, respectively. The primary irritation score calculated according to the method of Draize was 1.79. Eschar, necrosis or scarring were not reported.
Test condition : An occlusive patch test based on the method of Draize (1975) was used to assess the primary skin irritation induced by 2-methyl-2-butene applied neat. Three male and three female New Zealand White rabbits were used.

The dorsal hair between shoulders and hindquarters was closely shaven and two test sites approximately 10 cm apart located lateral to the midline were selected. One of the sites was abraded using a fine hypodermic needle giving injuries deep enough to disturb the stratum corneum without bleeding. To each test site, a 2 x 2 lint patch was applied and 0.5 ml of the test material applied. The patches were occluded by an impervious polythene sheet held in place by means of an elastic adhesive bandage.

After 24 hours, the wrappings and patches were removed. The intact and abraded test sites were examined and scored for erythema and edema on a graded scale of 0 to 4 at 24, 48, and 72 hours and 7 days post-dosing.

Test substance : 2-methyl-2-butene (CAS No. 513-35-9) Indent No. 9200/9579
Conclusion : Based on the Draize primary irritation score of 1.79, 2-methyl-2-butene may be regarded as mildly irritating to rabbit skin.
Reliability : (1) valid without restriction
GLP study.

11.08.2004 (14)

5.2.2 EYE IRRITATION

Species : rabbit
Concentration : .2 other: ml
Dose : .2 ml
Exposure time :
Comment : not rinsed
Number of animals : 6
Vehicle :
Result : not irritating
Classification : not irritating
Method : Draize Test
Year : 1980
GLP : yes
Test substance : other TS: 2-methyl-2-butene (CAS No. 513-35-9)

Method : Statistical Methods: None
Result : The instillation of 2-methyl-2-butene into the eye resulted in a moderate initial pain response (grade 4) in all animals. The mean total scores for the responses of the conjunctiva, cornea and iris at 1 hour, 1,2,3, and 7 days were 0.5, 0, 0, 0, and 0, respectively.
Test condition : The method of Draize (1963) was used to assess the eye irritancy of 2-methyl 2-butene. Six New Zealand White rabbits were used. A dose of 0.2 ml 2-methyl-2-butene was instilled into the lower conjunctival sac of one eye of each rabbit and the lids were held together for a few seconds to prevent loss of material. The eyes were not washed.

The reactions of the animals were observed immediately after instillation and the initial pain response was graded on a scale of 1 to 6 with 6 being very severe initial pain. A visual assessment of eye irritancy was made at 1 hour, 1 day, 2 days, 3 days and 7 days after instillation or until the irritancy was no longer discernible. Irritancy was scored for the cornea, iris and conjunctivae. Visualization of any corneal damage was aided by the instillation of one drop of 2% fluorescein solution.
Test substance : 2-methyl-2-butene (CAS No. 513-35-9) Indent No. 9200/9579
Conclusion : Based on these results, 2-methyl-2-butene should be considered as non-irritating to rabbit eyes.
Reliability : (1) valid without restriction
GLP study.

21.11.2003 (14)

5.3 SENSITIZATION

Type : Guinea pig maximization test
Species : guinea pig
Concentration : 1st: Induction .1 % other: s/v in corn oil
2nd: Induction 50 % other: s/v in corn oil

		3rd: Challenge 25 % other: w/v in corn oil
Number of animals	:	20
Vehicle	:	other: corn oil
Result	:	not sensitizing
Classification	:	not sensitizing
Method	:	other
Year	:	1982
GLP	:	yes
Test substance	:	other TS: 2-methyl-2-butene (CAS No. 513-35-9)
Method	:	Statistical Methods: None
Result	:	The erythema resulting from the topical challenge was scored on a four-point scale immediately on removal of the challenge patch and 24 and 48 hours later. None of the twenty test animals showed any positive reactions 24 or 48 hours after the removal of the challenge patch.
Test condition	:	The skin sensitization potential of 2-methyl-2-butene was assessed using the guinea pig maximization method of Magnusson and Kligman (1969). The test was accomplished in two stages: a preliminary range finding study, and the actual study. The purpose of the range finding study was to determine the concentrations of 2-methyl-2-butene to be used for intradermal induction, topical induction, and topical challenge. Trace levels of erythema, defined as "slight redness, edges not defined," or positive response defined as "pink/red squares with defined edges" were observed in all animals receiving intradermal injection. Trace levels of erythema were observed in 2 of 4 animals receiving undiluted, and 1 of 4 animlas receiving a 50% dilution in corn oil, topically applied. No erythema was observed with 25% in corn oil, topically applied. On the basis of the range finding tests, the following concentrations of 2-methyl-2-butene were selected for use in the skin sensitization test: 0.1% w/v in corn oil for intradermal induction; 50% w/v in corn oil for topical induction; 25% w/v in corn oil for topical challenge.
Test substance	:	2-methyl-2-butene (CAS No. 513-35-9) Indent No. 9200/9579
Conclusion	:	2-Methyl-2-Butene is not a skin sensitizer in guinea pigs.
Reliability	:	(1) valid without restriction GLP study.

29.09.2004 (14)

5.4 REPEATED DOSE TOXICITY

Type	:	Sub-chronic
Species	:	rat
Sex	:	male/female
Strain	:	other: Crl:CD (Sprague-Dawley) IGS BR
Route of admin.	:	other: inhalation: gas
Exposure period	:	28 days
Frequency of treatm.	:	6 hours/day, 7 days/week
Post exposure period	:	not applicable
Doses	:	0, 580, 2000, or 7000 ppm
Control group	:	other: yes--air only exposure
NOAEL	:	580 ppm
LOAEL	:	2000 ppm
Method	:	other: OECD 422
Year	:	2002
GLP	:	yes
Test substance	:	other TS: 2-methyl-2-butene (CAS No. 513-35-9)
Method	:	All statistical analyses were carried out separately for males and females.

Data relating to food consumption was analysed on a cage basis. For all other parameters, the analyses were carried out using the individual animal as the basic experimental unit. The following data tyoes were analysed at each timepoint separately:
Rearing and activity counts
Bodyweight (FOB) and body temperature
Grip strength, landing footsplay and motor activity.
Bodyweight, using gains over appropriate study periods.
Food consumption, over appropriate study periods, using cumulative cage totals.
Blood chemistry and haematology
Organ weights, absolute and/or adjusted for terminal bodyweight
Pathological findings, for the number of animals with and without each finding.
For categorical data, including rearing and activity counts and pathological findings, the proportion of animals was analysed using Fisher's Exact test (Fisher 1973) for each treated group versus the control.
For continuous data, Bartlett's test (Bartlett 1937) was first applied to test the homogeneity of variance between the groups. Using tests dependent on the outcome of Bartlett's test, treated groups were then compared with the Control group, incorporating adjustment for multiple comparisons where necessary.
The following sequence of statistical tests was used for bodyweight (FOB), body temperature, grip strength, landing toot splay and motor activity, bodyweight, food consumption, organ weight and clinical pathology data.
If 75% of the data (across all groups) were the same value, for example c, then a frequency analysis was applied. Treatment groups were compared using a Mantel test for a trend in proportions (Mantel 1963) and also pairwise Fisher's Exact tests (Fisher 1973) for each dose group against the control both for i) values <c versus values >=c, and for ii) values <=c versus values >c, as applicable.
If Bartlett's test for variance homogeneity (Bartlett 1937) was not significant at the 1% level, then parametric analysis was applied. If the F1 test for monotonicity of dose-response (Healey 1999) was not sinificant at the 1% level, Williams' test for a monotonic trend (Williams 1971, 1972) was applied. If the F1 test was significant, suggesting that the dose-response was not monotone, Dunnett's test (Dunnett 1955, 1964) was performed instead.
If Bartlett's test was significant at the 1% level, then logarithmic and square-root transformations were tried. If Bartlett's test was still significant, then non-parametric tests were applied. If the H1 test for monotonicity of dose-response (Healey 1999) was not significant at the 1% level, Shirley's test for a monotonic trend (Shirley 1977) was applied. If the H1 test was significant, suggesting that the dose-response was not monotone, Steel's test (Steel 1959) was performed instead.
For organ weight data, analysis of variance was initially performed using terminal bodyweight as covariate. If the within group relationship between organ weight and bodyweight was significant at the 10% level (Angervall and Carstrom, 1963), then the treatment comparisons were made on adjusted group means in order to allow for differences in bodyweight which might influence the organ weights.
Significant differences between Control and treated groups were expressed at the 5% ($p<0.05$) or 1% ($p<0.01$) or 0.1% ($p<0.001$) level. Williams test is denoted by '*'; t tests are denoted by '+', Dunnett's test is denoted by '*' and Shirley's test by '+'.

Remark : Test type: 4-week general toxicity and reproduction/developmental toxicity screening test by inhalation exposure to rats

Result : NOAEL (NOEL) 580 ppm; LOAEL (LOEL) not applicable.
The test atmospheres were analysed by GC and the analysed concentrations were in agreement with the target concentrations.

Toxicity Phase

Clinical signs during exposure included half-closed eyes on day 1 at 2000 and 7000 ppm, and a lower level of reponse to external stimuli. This latter finding also occurred on one further occasion at 7000 ppm. There were no signs considered reflective of a general systemic effect observed during routine clinical examination or during the functional observational battery. There was a slightly lower bodyweight gain at 7000 ppm, and slightly longer clotting times at 2000 ppm (prothrombin time for females) and 7000 ppm (prothrombin times for both sexes and activated partial thromboplastin time for males). Cholesterol levels were increased amongst females exposed to 7000 ppm but in the absence of any further effects in the clinical chemistry parameters or the males this is of uncertain significance. Pathological changes were noted amongst high dose females in the liver, evidence as an increased organ weight and minimal centrilobular hepatocyte hypertrophy. There was a decreased incidence of extramedullary haemopoiesis of the spleen of high dose animals, an increase in globlet cell hyperplasia in the nasal passages of high dose males, and, amongst high and intermediate dose males, a slight increase in severity of mycardial inflammatory heart lesions and cortical/medullary tubular basophila in the kidneys.

Test condition : Groups of 12 male and 12 female CD rats were exposed to the test material as a gas daily by inhalation for approximately six hours/day 7 days/week at exposure levels of 0, 580, 2000, or 7000 ppm. In this main study (repeated exposure general toxicity) males and females were exposed for 28 days, respectively. During the study, clinical condition, detailed functional observational battery, motor activity, bodyweight, food consumption, haematology, blood chemistry, organ weight and macroscopic and microscopic pathology investigations were undertaken. The study also contained reproductive/developmental toxicity satellite groups (summarized separately).

Test substance : 2-methyl-2-butene (CAS No. 513-35-9)

The test substance was stable for the duration of all studies performed at the test house.

Conclusion : Slight effects on general systemic toxicity due to the test substance were apparent amongst animals receving 7000 ppm, and to a lesser extent at 2000 ppm. The no effect level of the test substance for the general systemic toxicity to rats for 28 days inhalation administration was 580 ppm.

Reliability : (1) valid without restriction

11.08.2004 (23)

5.5 GENETIC TOXICITY 'IN VITRO'

Type	:	other: Escherichia coli/ salmonella typhimurium/bacterial reverse mutation test (pre-incubation assay)
System of testing	:	Bacterial
Test concentration	:	0, 0.2, 2, 20, 500, and 2000 ug/plate
Cycotoxic concentr.	:	
Metabolic activation	:	with and without
Result	:	negative
Method	:	OECD Guide-line 471
Year	:	1980
GLP	:	yes
Test substance	:	other TS: 2-Butene, 2-methyl (CAS No. 513-35-9)

Method : A positive response was defined as a minimum consistent doubling of the spontaneous reversion frequency, or if the number of induced revertants is

		less than twice the spontaneous rate then a reproducible, dose-related increase in any one strain/activation combination was interpreted as positive.
Remark	:	Species/Strain: Escherichia coli WP2 and WP7 uvrA and Salmonella typhimurium/TA98, TA100, TA1535, TA1537, TA1538 Species and cell type: Rat liver S9 fraction Quantity: 0.5 ml/plate Induced or not induced: Arochlor 1254-induced
Result	:	The test substance was not mutagenic in any of the five strains of Salmonella or in the 2 strains of E.coli tested in the presence or absence of metabolic activation (rat liver S9).
Test condition	:	Because of the low boiling point, it was necessary to carry out a pre-incubation of bacteria and test compound (diluted in absolute ethanol) with rat liver S9 fraction, as appropriate, using sealed containers before incorporating into the top agar. The preincubation modification of the Salmonella/mammalian microsome assay was tested in five different Salmonella strains and two different E.coli strains in the presence and absence of rat liver S-9. Five dose levels were tested, with three plates per dose level. Bacteria (0.5 ml) and S9 mix or pH 7.4 phosphate buffer (2.5 ml) were incubated at 37 degree C with the test substance in ethanol (0.1 ml) 30 minutes before incorporation of 0.5 ml of this mixture into 2 ml of top agar. Concurrent positive and solvent controls were also tested with an without metabolic activation. Two replicate assays were performed on different days to confirm the reproducibility of the results.
Test substance	:	2-Methyl-2-butene (CAS No. 513-35-9) Batch No. ID-9579 (7.3% 3-methyl-1-butene; 4.6% pentanes; 1.5% 1- and 2-pentene), 85% purity.
Conclusion	:	Solutions of 2M2B in absolute ethanol were considered to be stable for at least one working day. The test substance was not mutagenic in the Ames Salmonella or E.coli mutagenicity test.
Reliability	:	(1) valid without restriction
28.07.2005		(8) (11)

Type	:	other: Saccharomyces Gene Conversion Assay
System of testing	:	Suspension cultures of Saccharomyces cerevisiae
Test concentration	:	0.01, 0.1, 0.5, 1.0, and 5.0 mg/ml
Cycotoxic concentr.	:	
Metabolic activation	:	with and without
Result	:	
Method	:	other: none specified
Year	:	1980
GLP	:	yes
Test substance	:	other TS: 2-methyl 2-butene (CAS No. 513-35-9)
Remark	:	Species/Strain: S. cerevisiae Species and cell type: Rat liver S9 Quantity: 0.3 ml Induced or not induced: Aroclor-induced
Result	:	In this assay, a test material is considered to be mutagenic if the number of revertants per 106 survivor cells in the treated plates is greater than twice the control value. This did not occur with 2-Methyl 2-Butene at any of the concentrations tested (diluted in absolute ethanol) either with or without metabolic activation.
Test condition	:	Liquid suspension cultures of Saccharomyces cerevisiae in dilute growth medium were dosed with 0.2, 2, 10, 20 or 50 mg/ml of 2-methyl-2-butene in ethanol to give a final concentration of 0.01, 0.1, 0.5, 1.0 or 5.0 mg/ml. After 18 hours of incubation using sealed containers with shaking at 30°C either in the presence or in the absence of rat liver S9 fraction, the cultures were seeded onto the appropriate culture media for the selection of revertant colonies. After 3 days incubation at 30°C the number of revertant colonies were counted.

Test substance : 2-Methyl-2-butene (CAS No. 513-35-9) Batch No. ID-9579 (7.3% 3-methyl-1-butene; 4.6% pentanes; 1.5% 1- and 2-pentene), 85% purity.

Conclusion : Solutions of 2M2B in absolute ethanol were considered to be stable for at least one working day. 2-Methyl 2- Butene was not mutagenic to yeast cells under the conditions of this assay.

Reliability : (1) valid without restriction
GLP study comparable to guideline study.

28.07.2005 (8) (11)

Type : Cytogenetic assay
System of testing : Cultered rat liver cells (RL4)
Test concentration : 0.5, 0.25 and 0.125 of the 50% growth inhibition level corresponding to 12.5, 25.0 and 50 ml/ml, respectively.
Cycotoxic concentr. :
Metabolic activation : without
Result :
Method :
Year : 1980
GLP : yes
Test substance : other TS: 2-methyl 2-butene (CAS No. 513-35-9)

Method : No suitable statistical treatment for these types of data has been identified and results are judged on the reproducibility and dose-responsiveness of the aberration frequencies.

Remark :

COMPOUND	CONC uG/ML	NO. OF CELLS ANALYZED	% CELLS SHOWING Chromatid Aberrations	Chromosome Aberrations
2M2B	0	300	0	0
2M2B	12.5	300	0.33	0
2M2B	25.0	300	0	0.33
2M2B	50.0	231	0.43	0.43
DMBA	1.0	125	4.8	1.6

COMPOUND	CONC uG/ML	NO. OF CELLS ANALYZED	FREQUENCY PER CELL OF Chromatid Gaps	Chromatid Breaks	Chromatid Exchanges
2M2B	0	300	0.003	0	0
2M2B	12.5	300	0.036	0.007	0
2M2B	25.0	300	0.02	0	0
2M2B	50.0	231	0.03	0.004	0
DMBA	1.0	125	0.67	0.016	0.032

COMPOUND	CONC uG/ML	NO. OF CELLS ANALYZED	FREQUENCY PER CELL OF Chromosome Breaks	Chromosome Exchanges
2M2B	0	300	0	0
2M2B	12.5	300	0	0
2M2B	25.0	300	0.003	0

2M2B	50.0	231	0.004	0
DMBA	1.0	125	0.016	0

Result : The results of the metaphase chromosome analysis of RL4 cells after exposure to 2M2B or DMBA are shown in the table below. These results demonstrate that 2M2B did not induce chromosome damage in cultured rat liver cells (RL4) exposed for 24 hours to concentrations of 12.5, 25.0 and 50 ml/ml, respectively.

Test condition : The cultures of rat liver cells (RL4) were prepared in glass prescription bottles (200 ml) at an initial cell density of 10-6 cells using 25 ml of culture medium, (Minimum Essential medium + 10% fetal calf serum + 1% non-essential amino acids). The cultures were incubated at 30°C for 24 hours to allow active growth to commence; freshly prepared solutions of 2-Methyl 2-Butene (2M2B) were then added and the bottles sealed. The concentrations of 2M2B added were 12.5, 25.0 and 50 ml/ml, respectively. These concentrations were selected on the basis of a previously conducted cytotoxicity test. In this test, the concentration of 2M2B producing 50% growth inhibition (i.e., 100 ml/ml) was determined and appropriate dilutions of this concentration (i.e., 0.125, 0.25 and 0.5%) were used. Positive control cultures using 1 mg/ml 7,12-dimethyl benzanthracene (DMBA) were run in parallel.

After a further 24 hour incubation, Colcemid was added to each culture at a final concentration of 0.4 mg/ml and, 2 hours later, the cultures were harvested. The cells were dislodged from the surface of the glass by treatment with 4 ml trypsin-versene solution, and after the trypsin activity was neutralised by the addition of 0.5 ml fetal bovine serum, 8 ml of distilled water were added to produce a hypotonic solution. After 15 minutes hypotonic treatment, the suspension was centrifuged, the supernatant decanted and the cells fixed with three changes of methanol: acetic acid (3:1) solution. Chromosome preparations were made on microscope slides and stained with Giemsa stain diluted 1 in 10 with distilled water at pH 7.2. The chromosome preparations were randomly coded and 100 cells from each culture were analysed microscopically for chromosome changes.

Test substance : 2-Methyl-2-butene (CAS No. 513-35-9) Batch No. ID-9579 (7.3% 3-methyl-1-butene; 4.6% pentanes; 1.5% 1- and 2-pentene), 85% purity.

Conclusion : Solutions of 2M2B in absolute ethanol were considered to be stable for at least one working day. 2M2B was not genotoxic under the conditions of this assay.

Reliability : (1) valid without restriction
GLP study comparable to guideline study.

28.07.2005 (8) (11)

5.6 GENETIC TOXICITY 'IN VIVO'

Type : Micronucleus assay
Species : Syrian hamster
Sex : no data
Strain :
Route of admin. : inhalation
Exposure period : 6 hours/day, 2 days
Doses : 1000 ppm
Result : negative
Method : other
Year :
GLP : no data
Test substance :

Result	:	No significant haematotoxic effects were seen and only a marginal increase in bone marrow micronuclei were observed.
Source	:	Shell Nederland Chemie B.V. Rotterdam EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(4) not assignable This robust summary has a reliability rating of 4 because the data were not reviewed.
11.08.2004		(41)

Type	:	Micronucleus assay
Species	:	mouse
Sex	:	no data
Strain	:	B6C3F1
Route of admin.	:	inhalation
Exposure period	:	6hours/day for two days
Doses	:	1,000; 3,260; 10,000 ppm
Result	:	positive
Method	:	other
Year	:	
GLP	:	no data
Test substance	:	

Result	:	There was a dose related increase in numbers of micronuclei and a dose related decrease in the mean percent of polychromatic erythrocytes (a measure of toxicity). These effects were seen at 3,260 ppm and higher.
Source	:	Shell Nederland Chemie B.V. Rotterdam EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(4) not assignable This robust summary has a reliability rating of 4 because the data were not reviewed.
11.08.2004		(41)

Type	:	other: Mammalian erythrocyte micronucleus test
Species	:	mouse
Sex	:	male
Strain	:	B6C3F1
Route of admin.	:	inhalation
Exposure period	:	6 hours/day for 2 consecutive days
Doses	:	0, 1034, 3258 or 10,350 ppm (analytical mean concentration)
Result	:	positive
Method	:	OECD Guide-line 474 "Genetic Toxicology: Micronucleus Test"
Year	:	1990
GLP	:	yes
Test substance	:	other TS: 90% 2-methyl-2-butene; 10% 2-methyl-1-butene
Method	:	Means and standard deviations of micronuclei data. ANOVA to test for equality of group means followed by Duncan's Multiple Range Test if appropriate. Standard regression analysis to test for dose-related response. Wilk's Criterion for normality.
Remark	:	No. of animals per dose: 10 males/exposure level Control groups and treatment: 10 males exposed to air (negative control), 10 males exposed to 1000 ppm 1,3-butadiene (positive control)
Result	:	All mice in all groups appeared normal throughout the exposures. The test substance induced a statistically significant ($p<0.01$) and dose-related increase in micronucleated PCEs at 3258 and 10,350 ppm. The mean micronucleated PCE values were 15.7 and 31.5 at 3258 and 10,350 ppm, respectively, compared to 2.6 micronucleated PCEs for the negative

control and 4.6 at 1034 ppm. The positive control produced a statistically significant increase in micronucleated PCEs (29.1). Statistically sigificant ($p<0.01$) and dose-related decreases in the mean percent PCEs, which is a measure of hematotoxicity, were also observed at 3258 and 10,350 ppm. The %PCEs were 58.7, 59.6, 54.4, and 40.5% at 0, 1034, 3258, and 10,350 ppm. The %PCEs for the positive control was 42.0%.

Test condition : Ten male B6C3F1 mice (weighing 22-26 g, approximately 8-9 weeks old) per group were exposed for 2 consecutive days, 6 h/day to 0, 1034, 3258, or 10,350 ppm (analytical means) of the test substance by inhalation. Exposure concentrations were determined by on-line gas chromatography. Bone marrow smears were prepared and stained 24 hours after the last exposure. 1000 polychromatic erythrocytes (PCEs) per animal were scored for the incidence of micronucleated PCEs. The proportion of PCEs to normochromatic erythrocytes (NCEs) was determined by counting a total of 1000 erythrocytes per animal.

Conclusion : Under the conditions of this study, inhalation exposure to 3258 and 10,350 ppm of the test substance induced statistically sighificant increases in micronucleated polychromatic erythrocytes in male B6C3F1 mice.

Reliability : (1) valid without restriction

29.09.2004 (16)

Type : other: Mammalian erythrocyte micronucleus test
Species : mouse
Sex : male
Strain : B6C3F1
Route of admin. : inhalation
Exposure period : 6 hours/day for 2 consecutive days
Doses : 0, 1005, 3207, or 9956 ppm (analytical mean concentrations)
Result : positive
Method : OECD Guide-line 474 "Genetic Toxicology: Micronucleus Test"
Year : 1991
GLP : yes
Test substance : other TS: 2-Butene, 2-methyl (CAS No. 513-35-9)

Method : Means and standard deviations of micronuclei data. ANOVA to test for equality of group means followed by Duncan's Multiple Range Test if appropriate. Standard regression analysis to test for dose-related response. Wilk's Criterion for normality.

Remark : No. of animals per dose: 10 males/exposure level

Control groups and treatment: 10 males exposed to air (negative control), 10 males exposed to 1000 ppm 1,3-butadiene (positive control)

Result : On Day 1, all mice appeared normal. A few (i.e., 10-30%) of the animal in the high dose group (10,000 ppm) displayed decreased activity that started the second hour of exposure and continued for the remainder of the exposure. A few animals also exhibited labored breathing at the second hour of exposure and continued throughout the exposure. All of the mice in the positive control group (1000 ppm Bd) appeared normal during most of the exposure and a few animals displayed white ocular discharge during the sixth hour of exposure.

On Day 2, all the mice in the air and positive control groups appeared normal. All the mice in the low and high dose group appeared normal for the first three hours of exposure. Few (i.e.,10-30%) to some (i.e., 40-60%) of the mid dose group animals displayed decreased activity at the second hour of exposure that continued for the remainder of the exposure. A few mice also exhibited labored breathing for the last three hours of the exposure. A few to most (i.e., 70-90%) of the high dose animals displayed decreased activity during the last three hours of exposure and a few to some also exhibited labored breathing during the last three hours of

exposure.

The test substance induced statistically significant ($p<0.01$) and dose-related increases in micronucleated PCEs at 3207 and 9956 ppm. The mean micronucleated PCE values were 4.2, 16.6 and 36.1 at 1005, 3207 and 9956 ppm, compared to 3.4 micronucleated PCEs for the negative control. The positive control produced a statistically significant increase in micronucleated PCEs (29.7). A statistically significant ($p<0.01$) decrease in the %PCEs, which is a measure of hematotoxicity, was also observed at 9956 ppm. The %PCEs were 57.4, 57.4, 54.3, and 37.9% at 0, 1000, 3207, and 9956 ppm. The %PCEs for the positive control was 44.5%.

Test condition : Ten male B6C3F1 mice (weighing 24-28 g, approximately 6-7 weeks old) per group were exposed for 2 consecutive days, 6h/day to 0, 1005, 3207 or 9956 ppm (analytical mean) of the test substance by inhalation. Exposure concentrations were determined by on-line gas chromatography. Bone marrow smears were prepared and stained 24 hours after the last exposure. 1000 polychromatic erythrocytes (PCEs) per animal were scored for the incidence of micronucleated PCEs. The proportion of PCEs to normochromatic erythrocytes (NCEs) was determined by counting a total of 1000 erythrocytes per animal.

Test substance : 2-methyl-2-butene >99.2% purity

Conclusion : Under the conditions of this study, inhalation exposure to 3207 and 9956 ppm of the test substance induced statistically significant increases in micronucleated polychromatic erythrocytes in male B6C3F1 mice.

Reliability : (1) valid without restriction

29.09.2004 (17)

Type : other: Mammalian erythrocyte micronucleus test
Species : rat
Sex : male
Strain : other: CrlCDBR
Route of admin. : inhalation
Exposure period : 6 hours/day for 2 consecutive days
Doses : 0, 1005, 3207, or 9956 ppm (analytical mean concentration)
Result : positive
Method : OECD Guide-line 474 "Genetic Toxicology: Micronucleus Test"
Year : 1991
GLP : yes
Test substance : other TS: 2-Butene, 2-methyl (CAS No. 513-35-9)

Method : Means and standard deviations of micronuclei data. ANOVA to test for equality of group means followed by Duncan's Multiple Range Test if appropriate. Standard regression analysis to test for dose-related response. Wilk's Criterion for normality.

Remark : No. of animals per dose: 10 males/exposure level

Control groups and treatment: 10 males exposed to air (negative control)

Result : On Day 1, all the rats in the air control and low dose and most of the rats in the mid dose groups appeared normal. A few (i.e., 10-30%) of the rats in the mid dose group exhibited decreased activity at two hours into the exposure and continued for the remainder of the exposure. Most (i.e., 70-90%)of the high dose rats exhibited decreased activity throughout the exposure and a few (i.e., 10-30%) rats appeared normal.

On Day 2, all the rats in the air control, low and mid dose groups appeared normal. Most (i.e., 70-90%) of the rats in the high dose group appeared normal for the first three hours of exposure, although a few (i.e.,10-30%) displayed decreased activity. During the last three hours of the exposure, some (i.e., 40-60%) of the rats appeared normal and some exhibited decreased activity.

The test substance induced statistically significant ($p<0.01$) and dose-related increases in micronucleated PCEs at 3207 and 9956 ppm. The mean micronucleated PCE values were 4.2, 4.9 at 3207 and 9956 ppm, respectively, compared to 2.7 for the negative control (air) and 2.2 at 1005 ppm. Statistically significant decreases in the mean percent PCEs, which is indicative of hematotoxicity, were also observed at all three exposure levels. Although the mean PCE frequencies at 1005, 3207 and 9956 ppm (48.6, 51.0, 49.8%, respectively) were slightly decreased from the negative control (54.9%), they were not different from each other and did not show evidence of a dose-response. Therefore, the biological significance of this observation is unclear.

Test condition : Ten male CrlCDBR rats (weighing 295-345 g, approximately 9 weeks old) per group were exposed for 2 consecutive days, 6h/day to 0, 1005, 3207 or 9956 ppm (analytical means) of the test substance by inhalation. Exposure concentrations were determined by on-line gas chromatography. Bone marrow smears were prepared and stained 24 hours after the last exposure. 1000 polychromatic erythrocytes (PCEs) per animal were scored for the incidence of micronucleated PCEs. The proportion of PCEs to normochromatic erythrocytes (NCEs) was determined by counting a total of 1000 erythrocytes per animal.

Test substance : 2-methyl-2-butene >99.2% purity.

Conclusion : Under the conditions of this study, inhalation exposure to 3207 and 9956 ppm of the test substance induced small but statistically significant increases in micronucleated polychromatic erythrocytes in male rats.

Reliability : (1) valid without restriction

29.09.2004 (17)

Type : other: Mammalian erythrocyte micronucleus test

Species : mouse

Sex : male

Strain : B6C3F1

Route of admin. : inhalation

Exposure period : 6 hours/day for 2 consecutive days

Doses : 0, 1034, 3266 or 10,097 ppm (analytical mean concentrations)

Result : positive

Method : OECD Guide-line 474 "Genetic Toxicology: Micronucleus Test"

Year : 1991

GLP : yes

Test substance : other TS: ~92% 2-methyl-2-butene; ~7% 2-methyl-1-butene

Method : Means and standard deviations of micronuclei data. ANOVA to test for equality of group means followed by Duncan's Multiple Range Test if appropriate. Standard regression analysis to test for dose-related response. Wilk's Criterion for normality.

Remark : No. of animals per dose: 10 males/exposure level

Control groups and treatment: 10 males exposed to air (negative control), 10 males exposed to 1000 ppm 1,3-butadiene (positive control)

Result : On Day 1, all the mice in the air control, low, and mid dose groups appeared normal throughout exposure. All of the mice in the high dose group appeared normal for the first three hours of exposure; most (i.e., 70-90%) appeared normal and a few (i.e., 10-30%) animals displayed decreased activity during the last three hours of exposure. All of the mice in the positive control group (1000 ppm Bd) appeared normal during most of the exposure until the sixth hour of exposure when most appeared normal and a few animals displayed white ocular discharge.

On Day 2, all mice in the air and positive control groups appeared normal throughout the exposure. All of the mice in the low and mid dose groups

appeared normal for the first two hours of exposure, however, a few of the low dose and a few to some of the mid dose mice exhibited decreased activity during the last four hours of exposure. All of the animal in the high dose group (10,000 ppm) appeared normal for the first hour; a few (i.e., 10-30%) mice displayed decreased activity during the second hour with most (i.e., 70-90%) of the mice so affected during the last four hours of exposure.

The test substance induced statistically significant ($p<0.01$) and dose-related increases in micronucleated PCEs at 3266 and 10,097 ppm. The mean micronucleated PCE values were 3.7, 22.6 and 42.1 at 1034, 3266 and 10,097 ppm, compared to 2.5 micronucleated PCEs for the negative control. The positive control produced a statistically significant increase in micronucleated PCEs (39.5). Statistically significant ($p<0.01$) decreases in the mean percent PCEs, which is a measure of hematotoxicity, were also observed at 3266 and 10,097 ppm. The %PCEs were 58.2, 58.0, 51.4, and 34.6% at 0, 1034, 3266, and 10,097 ppm. The %PCEs for the positive control was 43.7%.

Test condition : Ten male B6C3F1 mice (weighing 24-30 g, approximately 8-9 weeks old) per group were exposed for 2 consecutive days, 6h/day to 0, 1034, 3266 or 10,097 ppm (analytical means) of the test substance by inhalation. Exposure concentrations were determined by on-line gas chromatography. Bone marrow smears were prepared and stained 24 hours after the last exposure. 1000 polychromatic erythrocytes (PCEs) per animal were scored for the incidence of micronucleated PCEs. The proportion of PCEs to normochromatic erythrocytes (NCEs) was determined by counting a total of 1000 erythrocytes per animal.

Conclusion : Under the conditions of this study, inhalation exposure to 3266 and 10,097 ppm of the test substance induced statistically significant increases in micronucleated polychromatic erythrocytes in male B6C3F1 mice.

Reliability : (1) valid without restriction

29.09.2004 (18)

Type : other: Mammalian erythrocyte micronucleus test
Species : rat
Sex : male
Strain : other: CrlCDBR
Route of admin. : inhalation
Exposure period : 6 hours/day for 2 consecutive days
Doses : 0, 1034, 3266 or 10,097 ppm (analytical mean concentrations)
Result : positive
Method : OECD Guide-line 474 "Genetic Toxicology: Micronucleus Test"
Year : 1991
GLP : yes
Test substance : other TS: ~92% 2-methyl-2-butene; ~7% 2-methyl-1-butene

Method : Means and standard deviations of micronuclei data. ANOVA to test for equality of group means followed by Duncan's Multiple Range Test if appropriate. Standard regression analysis to test for dose-related response. Wilk's Criterion for normality.

Remark : No. of animals per dose: 10 males/exposure level

Control groups and treatment: 10 males exposed to air (negative control)

Result : On Day 1, all the rats in the air control group appeared normal. All low dose rats appeared normal for the first five hours of exposure, although a few (i.e., 10-30%) displayed decreased activity during the sixth hour. All rats in the mid and high dose groups appeared normal during the first hour of exposure. A few (i.e., 10-30%) to some (i.e., 40-60%) of the rats in both groups exhibited decreased activity for the remaining five hours. A few of the high dose rats displayed dried red nasal discharge during the second,

third, and sixth hours of exposure.

On Day 2, all the rats in the air control appeared normal throughout exposure. All of the rats in the low and mid dose groups appeared normal for the first two hours of exposure, then some (i.e., 40-60%) of the rats in the both groups displayed decreased activity for the last four hours. All of the high dose rats appeared normal during the first hour; during the last five hours of the exposure, some (i.e., 40-60%) to most (i.e., 70-90%) of the rats exhibited decreased activity.

The test substance induced a statistically significant ($p<0.01$) increase in micronucleated PCEs at 10,097 ppm. The mean micronucleated PCE values were 3.4, 4.2 and 7.0 at 1034, 3266 and 10,097 ppm, compared to 3.3 micronucleated PCEs for the negative control. The slight increase in mean micronucleated PCEs (4.2) noted at 3266 ppm was slightly above the normal range for the negative control (0-4) although it was not statistically significant. The mean percent PCEs were within the normal range of the negative control for all exposed groups. The %PCEs were 48.3, 46.9, 46.1, and 45.3% at 0, 1034, 3266, and 10,097 ppm.

Test condition : Ten male CrlCDBR rats (weighing 348-447 g, approximately 11-12 weeks old) per group were exposed for 2 consecutive days, 6h/day to 0, 1034, 3266, or 10,097 ppm (actual mean exposures) of the test substance by inhalation. Exposure concentrations were determined by on-line gas chromatography. Bone marrow smears were prepared and stained 24 hours after the last exposure. 1000 polychromatic erythrocytes (PCEs) per animal were scored for the incidence of micronucleated PCEs. The proportion of PCEs to normochromatic erythrocytes (NCEs) was determined by counting a total of 1000 erythrocytes per animal.

Conclusion : Under the conditions of this study, inhalation exposure to 10,097 ppm of the test substance induced a statistically significant increase in micronucleated polychromatic erythrocytes in male rats.

Reliability : (1) valid without restriction

29.09.2004 (18)

5.7 CARCINOGENICITY

5.8.1 TOXICITY TO FERTILITY

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species	:	rat
Sex	:	female
Strain	:	other: Crl:CD (Sprague-Dawley) IGS BR
Route of admin.	:	other: inhalation: gas
Exposure period	:	
Frequency of treatm.	:	6 hours/day, 7 days/week
Duration of test	:	Two weeks prior to breeding, during breeding, and continuing through day 19 of gestation. The dams were then allowed to deliver their litters, which were retained until lactation day 4
Doses	:	0, 580, 2000, or 7000 ppm
Control group	:	other: yes--air-only exposure
NOAEL maternal tox.	:	= 7000 ppm
NOAEL teratogen.	:	= 7000 - ppm
Method	:	other: OECD 422
Year	:	2002
GLP	:	yes

Test substance : other TS: 2-methyl-2-butene (CAS No. 513-35-9)

Method : All statistical analyses were carried out separately for males and females. Data relating to food consumption was analysed on a cage basis. For all other parameters, the analyses were carried out using the individual animal as the basic experimental unit. The following data tyoes were analysed at each timepoint separately:
Rearing and activity counts
Bodyweight (FOB) and body temperature
Grip strength, landing footsplay and motor activity.
Bodyweight, using gains over appropriate study periods.
Food consumption, over appropriate study periods, using cumulative cage totals.
Blood chemistry and haematology
Organ weights, absolute and/or adjusted for terminal bodyweight
Pathological findings, for the number of animals with and without each finding.
For categorical data, including rearing and activity counts and pathological findings, the proportion of animals was analysed using Fisher's Exact test (Fisher 1973) for each treated group versus the control.
For continuous data, Bartlett's test (Bartlett 1937) was first applied to test the homogeneity of variance between the groups. Using tests dependent on the outcome of Bartlett's test, treated groups were then compared with the Control group, incorporating adjustment for multiple comparisons where necessary.
The following sequence of statistical tests was used for bodyweight (FOB), body temperature, grip strength, landing toot splay and motor activity, bodyweight, food consumption, organ weight and clinical pathology data.
If 75% of the data (across all groups) were the same value, for example c, then a frequency analysis was applied. Treatment groups were compared using a Mantel test for a trend in proportions (Mantel 1963) and also pairwise Fisher's Exact tests (Fisher 1973) for each dose group against the control both for i) values <c versus values >=c, and for ii) values <=c versus values >c, as applicable.
If Bartlett's test for variance homogeneity (Bartlett 1937) was not significant at the 1% level, then parametric analysis was applied. If the F1 test for monotonicity of dose-response (Healey 1999) was not sinificant at the 1% level, Williams' test for a monotonic trend (Williams 1971, 1972) was applied. If the F1 test was significant, suggesting that the dose-response was not monotone, Dunnett's test (Dunnett 1955, 1964) was performed instead.
If Bartlett's test was significant at the 1% level, then logarithmic and square-root transformations were tried. If Bartlett's test was still significant, then non-parametric tests were applied. If the H1 test for monotonicity of dose-response (Healey 1999) was not significant at the 1% level, Shirley's test for a monotonic trend (Shirley 1977) was applied. If the H1 test was significant, suggesting that the dose-response was not monotone, Steel's test (Steel 1959) was performed instead.
For organ weight data, analysis of variance was initially performed using terminal bodyweight as covariate. If the within group relationship between organ weight and bodyweight was significant at the 10% level (Angervall and Carstrom, 1963), then the treatment comparisons were made on adjusted group means in order to allow for differences in bodyweight which might influence the organ weights.
Significant differences between Control and treated groups were expressed at the 5% ($p<0.05$) or 1% ($p<0.01$) or 0.1% ($p<0.001$) level. Williams test is denoted by '*'; t tests are denoted by '+', Dunnett's test is denoted by '*' and Shirley's test by '+'.

Result : NOAEL (NOEL) 7000 ppm; LOAEL (LOEL) not applicable.
The test atmospheres were analysed by GC and the analysed

concentrations were in agreement with the target concentrations.

Developmental Phase

Exposure to female rats for 2 weeks prior to pairing, and up to Day 19 of gestation, did not produce any evidence of developmental toxicity or teratogenicity. There were no adverse effects upon survival or growth of the offspring in uterus or up to Day 4 of lactation.

Test condition : Satellite groups of 12 female Sprague Dawley rats were exposed to the test material as a gas daily by inhalation for approximately six hours/day at exposure levels of 0, 580, 2000, or 7000 ppm. The study design included a main study for repeated dose toxicity end points (summarized separately) and reproductive/developmental toxicity satellite groups of 12 females per exposure level. The reproductive/developmental toxicity satellite groups were exposed for two weeks prior to breeding, during breeding and continuing through day 19 of gestation. Males from the main study were used to breed these females. The dams were allowed to deliver their litters, which were retained until lacation day 4. During the study clinical condition, bodyweight, food consumption, oestrus cycles, mating performance, litter data, organ weights and macroscopic pathology were undertaken.

Test substance : 2-methyl-2-butene (CAS No. 513-35-9)

The test substance was stable for the duration of all studies performed at the test house.

Conclusion : Teratogenic effects were not observed in the OECD TG 422 study. The no effect level for developmental toxicity and teratogenicity was 7000 ppm.

Reliability : (1) valid without restriction

Flag : Critical study for SIDS endpoint

28.07.2005 (23)

5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

Type : other: 4-week general toxicity and reproduction/development toxicity screening test by inhalation exposure to rats

In vitro/in vivo : In vivo

Species : rat

Sex : female

Strain : other: Crl:CD (Sprague-Dawley) IGS BR

Route of admin. : other: inhalation: gas

Exposure period : per guideline

Frequency of treatm. : 6 hours/day, 7 days/week

Duration of test : Two weeks prior to breeding, during breeding, and continuing through day 19 of gestation. The dams were then allowed to deliver their litters, which were retained until lactation day 4

Doses : 0, 580, 2000, or 7000 ppm

Control group : other: yes--air-only exposure

Result : NOAEL (NOEL) 7000 ppm

Method : other: OECD 422

Year : 2002

GLP : yes

Test substance : other TS: 2-methyl-2-butene (CAS No. 513-35-9)

Method : All statistical analyses were carried out separately for males and females. Data relating to food consumption was analysed on a cage basis. For all other parameters, the analyses were carried out using the individual animal as the basic experimental unit. The following data tyoes were analysed at each timepoint separately:
Rearing and activity counts
Bodyweight (FOB) and body temperature

Grip strength, landing footsplay and motor activity.
Bodyweight, using gains over appropriate study periods.
Food consumption, over appropriate study periods, using cumulative cage totals.
Blood chemistry and haematology
Organ weights, absolute and/or adjusted for terminal bodyweight
Pathological findings, for the number of animals with and without each finding.
For categorical data, including rearing and activity counts and pathological findings, the proportion of animals was analysed using Fisher's Exact test (Fisher 1973) for each treated group versus the control.
For continuous data, Bartlett's test (Bartlett 1937) was first applied to test the homogeneity of variance between the groups. Using tests dependent on the outcome of Bartlett's test, treated groups were then compared with the Control group, incorporating adjustment for multiple comparisons where necessary.
The following sequence of statistical tests was used for bodyweight (FOB), body temperature, grip strength, landing toot splay and motor activity, bodyweight, food consumption, organ weight and clinical pathology data.
If 75% of the data (across all groups) were the same value, for example c, then a frequency analysis was applied. Treatment groups were compared using a Mantel test for a trend in proportions (Mantel 1963) and also pairwise Fisher's Exact tests (Fisher 1973) for each dose group against the control both for i) values <c versus values >=c, and for ii) values <=c versus values >c, as applicable.
If Bartlett's test for variance homogeneity (Bartlett 1937) was not significant at the 1% level, then parametric analysis was applied. If the F1 test for monotonicity of dose-response (Healey 1999) was not sinificant at the 1% level, Williams' test for a monotonic trend (Williams 1971, 1972) was applied. If the F1 test was significant, suggesting that the dose-response was not monotone, Dunnett's test (Dunnett 1955, 1964) was performed instead.
If Bartlett's test was significant at the 1% level, then logarithmic and square-root transformations were tried. If Bartlett's test was still significant, then non-parametric tests were applied. If the H1 test for monotonicity of dose-response (Healey 1999) was not significant at the 1% level, Shirley's test for a monotonic trend (Shirley 1977) was applied. If the H1 test was significant, suggesting that the dose-response was not monotone, Steel's test (Steel 1959) was performed instead.
For organ weight data, analysis of variance was initially performed using terminal bodyweight as covariate. If the within group relationship between organ weight and bodyweight was significant at the 10% level (Angervall and Carstrom, 1963), then the treatment comparisons were made on adjusted group means in order to allow for differences in bodyweight which might influence the organ weights.
Significant differences between Control and treated groups were expressed at the 5% ($p<0.05$) or 1% ($p<0.01$) or 0.1% ($p<0.001$) level. Williams test is denoted by '*'; t tests are denoted by '+', Dunnett's test is denoted by '*' and Shirley's test by '+'.

Result : NOAEL (NOEL) 7000 ppm; LOAEL (LOEL) not applicable.
The test atmospheres were analysed by GC and the analysed concentrations were in agreement with the target concentrations.

Reproductive Phase

Exposure to female rats for 2 weeks prior to pairing, and up to Day 19 of gestation, did not produce any evidence of reproductive toxicity or teratogenicity. The oestrus cycle was unaffected by exposure, and mating performance, fertility indices and gestation length were similar in all groups. There were no adverse effects upon survival or growth of the offspring in

uterus or up to Day 4 of lactation.

Test condition : Satellite groups of 12 female Sprague Dawley rats were exposed to the test material as a gas daily by inhalation for approximately six hours/day at exposure levels of 0, 580, 2000, or 7000 ppm. The study design included a main study for repeated dose toxicity end points (summarized separately) and reproductive/developmental toxicity satellite groups of 12 females per exposure level. The reproductive/developmental toxicity satellite groups were exposed for two weeks prior to breeding, during breeding and continuing through day 19 of gestation. Males from the main study were used to breed these females. The dams were allowed to deliver their litters, which were retained until lacation day 4. During the study clinical condition, bodyweight, food consumption, oestrus cycles, mating performance, litter data, organ weights and macroscopic pathology were undertaken.

Test substance : 2-methyl-2-butene (CAS No. 513-35-9)

The test substance was stable for the duration of all studies performed at the test house.

Conclusion : The no effect level for reproduction/developmental toxicity and teratogenicity was 7000 ppm.

Reliability : (1) valid without restriction

29.09.2004 (23)

5.9 SPECIFIC INVESTIGATIONS

5.10 EXPOSURE EXPERIENCE

5.11 ADDITIONAL REMARKS

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