IUCLID

Data Set

Existing Chemical	:	ID: 4223-03-4
EINECS Name	:	2-Propenamide, *N*-(1,1,3,3-tetramethylbutyl)-
EC No.	:	224-169-7
Molecular Formula	:	C11H21NO
Producer related part		
Company	:	National Starch and Chemical Company
Creation date	:	17.10.2002
Substance related part		
Company	:	National Starch and Chemical Company
Creation date	:	17.10.2002
Status	:	
Memo	:	High Production Volume Challenge Program
Printing date	:	16.12.2002
Revision date	:	
Date of last update	:	16.12.2002
Number of pages	:	12
Chapter (profile)	:	Chapter: 2.1, 2.2, 2.4, 2.5, 2.6.1, 3.1.1, 3.1.2, 3.3.1, 3.5, 4.1, 4.2, 4.3, 5.1.1, 5.1.2, 5.1.3, 5.1.4, 5.4, 5.5, 5.6, 5.8.1, 5.8.2
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

2.1 MELTING POINT

Value	:	55 - 60 °C
Sublimation	:	
Method	:	other
Year	:	
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	No other details are available.
Reliability	:	(4) not assignable

05.11.2002 (2)

2.2 BOILING POINT

2.4 VAPOUR PRESSURE

2.5 PARTITION COEFFICIENT

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in	:	Water
Value	:	< .1 g/l at °C
pH value	:	
concentration	:	at °C
Temperature effects	:	
Examine different pol.	:	
pKa	:	at 25 °C
Description	:	
Stable	:	
Deg. product	:	
Method	:	other
Year	:	
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	No other details are available.
Reliability	:	(4) not assignable

13.12.2002 (2)

3.1.1 PHOTODEGRADATION

DIRECT PHOTOLYSIS

Halflife t1/2	:	7.6 hour(s)
Degradation	:	% after
Quantum yield	:	
Deg. product	:	
Method	:	other (calculated): AOPWIN v 1.90
Year	:	2002
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	The photodegradation was estimated using the AOPWIN module of EPIWIN v 3.10 as 7.6 hours assuming a 12 hour day and a hydroxyl concentration of 1.5xE6/cm3.

05.11.2002 (1)

3.1.2 STABILITY IN WATER

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

3.5 BIODEGRADATION

4.1 ACUTE/PROLONGED TOXICITY TO FISH

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

Robust Summary *in-vitro* dermal absorption of 2-Propenamide, *N*-(1,1,3,3,-tetramethylbutyl)- through Human and Rat Epidermis

Test substance	2-Propenamide, *N*-(1,1,3,3,-tetramethylbutyl). As prescribed by 1.1 - 1.4
Remarks	Purity 99.73% w/w
Method	Draft OECD dermal absorption 1996
Test type	in-vitro dermal absorption
GLP	Yes
Year	1998
Method	A static glass diffusion assay design, using male rat epidermis and female human abdominal epidermis based on the then current draft OECD protocol was used. Both rat and human epidermal membranes had their subcutaneous fat removed and were frozen before use. The integrity of the epidermal membranes was confirmed by measurement of their electrical resistance. 50% aqueous ethanol was used as the receptor fluid and was analysed by GLC. (LOQ 3 µg/mL).
Test Conditions	
Species	Rat, Human
Strain	Human: Not applicable. Rat: Wistar
Sex	Human: Female Rat: Male
Cell type	Epidermal membrane (whole tissue)
Age	Human: Not stated Rat: 28 days
Number of animals/donors	6 samples (3 donors, each in duplicate) for each species
Route	Dermal, unoccluded
Vehicle	None, applied directly
Doses	10 mg/cm^2, equivalent to 24.4 mg
Statistical Method	Not applicable
Results	The concentration of test chemical in the 50% aqueous ethanol receptor fluid was sampled at 6, 8, 10 and 24 hours after dosing and determined by gas-liquid chromatography. For human epidermis, the amounts absorbed at less than ten hours were at or below the limit of quantification (5 µg/cm^2) increasing to a maximum of 9.4 µg/cm^2 at 24 hours. Over the 6-24 hour exposure period, the mean absorption rate was 0.522 µg/cm^2/hr. The mass balance mean percentage recovered was 90%. Most of the dose, 85.7% (mean percentage) was recovered by mild skin washing, whereas 0.1% was detected in the epidermal membrane. For rat epidermis, the mean absorption rate was 1.386 µg/cm^2/hr. The mass balance mean percentage recovered was 90.6%. Again, most of the dose, 90.6% (mean percentage) was recovered by mild skin washing but no chemical was recovered from the epidermal membrane. 2-Propenamide, *N*-(1,1,3,3-tetramethylbutyl)- is considered to have a low rate of dermal penetration.
Conclusions	The dermal absorption of 2-Propenamide, *N*-(1,1,3,3-tetramethylbutyl)- is low.
Reliability	(1) valid without restriction

5.1.1 ACUTE ORAL TOXICITY

5.1.2 ACUTE INHALATION TOXICITY

5.1.3 ACUTE DERMAL TOXICITY

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.4 REPEATED DOSE TOXICITY

5.5 GENETIC TOXICITY 'IN VITRO'

Robust Summary
in-vitro genetic toxicity test with 2-Propenamide, *N*-(1,1,3,3,-tetramethylbutyl) –

Salmonella-Escherichia Coli Mammalian-Microsome Reverse Mutation Assay with a confirmatory assay.

Test substance	2-Propenamide, *N*-(1,1,3,3,-tetramethylbutyl)- As prescribed by 1.1 - 1.4
Remarks	Off-white, fluffy crystalline solid.
Guideline	OECD 471
Test type	Salmonella-Escherichia Coli Mammalian-Microsome Reverse Mutation Assay with a confirmatory assay.
System of testing	Salmonella typhimurium TA98, TA100, TA1535, TA1537, E. coli WP2urvA (Only TA100 and E. coli WP2*uvr*A were used in the rangefinding study)
GLP	Yes
Year	1998
Metabolic activation	With and without an exogenous metabolic activation system of mammalian microsomal enzymes derived from Aroclor™-induced rat liver (S9)
Test concentrations	Rangefinding study – ten doses of test article ranging from 5,000 to 6.67 µg/plate, both in presence and absence of S9 mix. Main study - 0, 33.3, 100, 333, 1000, 3330, 5000 µg/plate, in presence and absence of S9 mix.
Cytotoxic concentration	5000 µg/plate
Statistical Methods	Mean number of revertants per plate and standard deviations were calculated for each treatment and control group. Individual plate counts were also taken. Various criteria were used to determine a valid assay. A positive response was indicated by a 2-3 fold increase in mean revertant number dependent on the bacterial tester strain. The increase in mean number of revertants per plate had to be accompanied by a dose response to increasing concentrations of the test article.
Method	The assay was performed using tester strains TA98, TA100, TA1535, TA1537 and WP2*uvr*A. Six doses of test article in both the presence and absence of S9 mix were tested, along with concurrent vehicle and positive controls, using three plates per dose. The doses of test article

	were selected based on the results of the dose rangefinding study. The results of the initial mutagenicity assay were confirmed in an individual experiment. The tester strains were exposed to test article via the plate incorporation methodology described by Ames et al (1975)[1] and Maron and Ames (1983)[2]. The test article, the tester strain and the S9 mix (where appropriate) were combined in molten agar which was overlaid onto a minimal agar plate. The S9 mix and dilutions of the test article were prepared immediately prior to their use. When S9 mix was not required, 100µL of tester strain and 50 µL of vehicle or test article dose were added to 2.5 mL of molten agar. When S9 mix was required, 500µL of S9 mix, 100µL of tester strain and 50 µL of vehicle or test article dose were added to 2.0 mL of molten agar. Following incubation at 37±2°C for 52±4 hours, the condition of the bacterial background lawn was evaluated for evidence of cytotoxicity and test article precipitate and revertant colonies were counted. All doses of the test article, the vehicle controls and the positive controls were plated in triplicate. Combinations of positive controls, activation condition and tester strains were plated concurrently with the assay. The positive controls used were: Benzo[a]pyrene, 2-aminoanthracene, 2-nitrofluorene, sodium azide, 2-aminoanthracene, ICR-191, and 4-nitroquinoline-N-oxide). DMSO was used as a vehicle control.
Results	2-Propenamide, *N*-(1,1,3,3-tetramethylbutyl)- did not cause a positive increase in the number or revertants per plate of any of the tester strains either in the presence or absence of microsomal enzymes prepared from Aroclor™-induced rat liver (S9).
Conclusions	2-Propenamide, *N*-(1,1,3,3-tetramethylbutyl)- is not mutagenic in the tested species.
Reliability	(1) valid without restriction
Reference	National Starch and Chemical Company. Unpublished. Mutagenicity test with N-tert-Octylacrylamide in the Salmonella – Escherichia Coli/Mammalian-Microsome Reverse Mutation Assay with a Confirmatory Assay. T.E. Lawlor. Covance Laboratories Inc. Study No 19301-0-409OECD (1998). 1. Ames, B.N., McCann, J. and Yamasaki, E. Methods for detecting carcinogens and mutagens with the Salmonella/Mammalian-Microsome Mutagenicity Test. Mutation Research 31. pp 347-364 (1975). 2. Maron, D.M. and Ames, B.N. Revised methods for the Salmonella Mutagenicity Test. Mutation Research 113. pp173-215 (1983)

Robust Summary
in-vitro genetic toxicity test with 2-Propenamide, *N*-(1,1,3,3,-tetramethylbutyl) –

L5178Y TK +/- Mouse Lymphoma Forward Mutation Assay with a confirmatory assay.

Test substance	2-Propenamide, *N*-(1,1,3,3,-tetramethylbutyl)- As prescribed by 1.1 - 1.4
Remarks	Off-white, fluffy crystalline solid. Purity 99.7%.

Guideline	OECD 476
Test type	Mammalian Cell Gene Mutation Assay with a confirmatory assay.
System of testing	L5178Y mouse lymphoma cells
GLP	Yes
Year	1998
Metabolic activation	With and without a metabolic activation system comprised rat liver enzymes (S9 fraction) and an energy producing system (CORE) comprised nicotinamide adenine dinucleotide phosphate (NADP, sodium salt) and isocitrate.
Test concentrations	For the confirmatory trials- With metabolic activation: 0, 50, 100, 200, 300, 400, 450, 500, 550 µg/mL. Without metabolic activation: 0, 50, 100, 200, 300, 400, 450, 500 µg/mL
Cytotoxic concentration	Approximately 500 µg/mL
Statistical Methods	Various assay acceptance criteria were used. A positive response was considered if a dose-dependent increase of 2-fold or greater in mutant frequency was obtained over the concurrent background mutant frequency. The dose-dependence would be waived if a large increase in mutant frequency of 4-fold or higher was obtained for a single dose at or near the highest testable toxicity. Any increases would need to have been seen in both trials to evaluate the test material as positive in the assay.
Method	The assay procedure used was based on that reported by Clive and Spector (1975)[1], Clive *et al.* (1979)[2], Amacher *et al.* (1980)[3] and Clive *et al.* (1978)[4]. Two independent tests in the absence in the presence of exogenous metabolic activation (Arochlor induced rat liver S-9) were carried out. The test material dissolved in DMSO was tested without metabolic activation at 7 concentrations of 50 to 600 µg/ml (initial trial) and 50 to 500 µg/ml (confirmatory trial) and with metabolic activation at 7 concentrations of 25 to 500 µg/l (initial trial) and 50 to 550 µg/ml. Treatment was into cell cultures containing $6x10^6$ cells suspended in culture medium. The test article remained in solution in culture medium up to 915 µg/mL. Positive controls were carried out in the absence of metabolic activation with methyl methanesulfonate (MMS) at 5 nL/mL and in the presence of metabolic activation with methylcholanthrene (MCA) at 2 µg/ml and 4 µg/ml. Cells were incubated with test substance for about 4 hours, washed twice, resuspended in culture medium and incubated for an additional 48 hours. Growth in suspension was monitored at 24 and 48 hours after treatment. Cells were then cloned in soft agar and after 10-14 days the colonies were counted using an automated colony counter. The measurement of cytotoxicity of each treatment was the relative suspension growth of the cells over the two-day expression period multiplied by the relative cloning efficiency at the time of selection.
Results	2-Propenamide, *N*-(1,1,3,3-tetramethylbutyl)- was negative with and without S9 metabolic activation in the L5178Y TK +/- Mouse Lymphoma Forward Mutation Assay.
Conclusions	2-Propenamide, *N*-(1,1,3,3-tetramethylbutyl)- does not induce gene mutations in the cultured mammalian cells used.
Reliability	(1) valid without restriction
Reference	National Starch and Chemical Company. Unpublished. Mutagenicity

	test on N-tert-Octylacrylamide in the L5178Y TK +/- Mouse Lymphoma Forward Mutation Assay with a Confirmatory Assay. M.A. Cifone. Covance Laboratories Inc. Study No 19301-0-431OECD (1998). 2. Clive, D., Johnson, K.O., Spector, J.F.S., Batson, A.G., and Brown, M.M.M. Validation and characterization of the L5178Y TK+/- mouse lymphoma mutagen assay system. Mutation Res. 59. pp 61-108 (1979) 3. Amacher, D.E., Paillet, S.C., Turner, G.N., Ray, V.A., and Salsburg, D.S. Point mutations at the thymidine kinase locus in L5178Y mouse lymphoma cells II. Test validation and interpretation. Mutation Res. 72 pp 447-474 (1980) 4. Clive, D., Caspary, W., Kirkby, P.E., Krehl, R., Moore, M., Mayo, J., and Oberly, T.J. Guide for performing the mouse lymphoma assay for mammalian cell mutagenicity. Mutation res. 189. pp 143-156 (1987)

5.6 GENETIC TOXICITY 'IN VIVO'

Robust Summary
in-vivo genetic toxicity test with 2-Propenamide, *N*-(1,1,3,3,-tetramethylbutyl) –

In Vivo Mouse Micronucleus Assay.

Test substance	2-Propenamide, *N*-(1,1,3,3,-tetramethylbutyl)- As prescribed by 1.1 - 1.4
Remarks	Off-white, fluffy crystalline solid. Purity 99.7%.
Guideline	OECD 474
Test type	Micronucleus Assay
Species	Mouse
Sex	Males and females in the range-finding studies Males only in the micronucleus study (as there were no observed differences in toxicity between sexes)
Strain	Crl:CD-1®(ICR)BR
Route of admin.	Oral, gavage
Exposure period	24 hours
Doses	Dose range finding study No 1 – 200, 500, 800, 1500 and 2000 mg/kg Dose range finding study No 2 – 600 and 700 mg/kg Micronucleus study -175, 350, 700 mg/kg
GLP	Yes
Year	1998
Statistical Methods	Statistical methods: Assay data analysis by ANOVA. Statistically significant ($p<0.05$) differences were investigated using a Dunnett's t-test. Analyses were performed separately for each sampling time. The criteria for a positive response were the detection of a statistically significant positive response for at least 1 dose level and a statistically significant dose-related response.

Method	The age and weight of the animals in the test were: Dose range finding study No.1 – 29 animals, approx. 8 weeks old at time of dosing with a weight range of 28.8-35.8g (males) and 21.6-25.0g (females) Dose range finding study No.2 – 12 animals, approx. 9 weeks old at time of dosing with a weight range of 34.1-35.5g (males) and 22.8-27.8g (females) Micronucleus study – 48 animals, approx. 8 weeks old at time of dosing with a weight range of 31.4-38.4g (males) In the micronucleus study the test article was suspended in corn oil and dosed by oral gavage to 6 males per dose level/harvest timepoint. The animals were dosed at 175, 350 and 700 mg/kg. The first surviving animals dosed at the 175 and 350 mg/kg dose levels and with the positive control were euthanized ca. 24 hours after dosing for extraction of bone marrow. The first surviving animals dosed at the 700 mg/kg dose level and with the vehicle control were euthanized ca. 24 and 48 hours after dosing for extraction of the bone marrow. The positive control was cyclophosphamide solubilized in sterile deionized water. The slides from the first surviving five animals in each treatment and control group were scored for micronuclei and the polychromatic erythrocyte (PCE) to normochromatic erythrocyte (NCE) cell ratio. The micronucleus frequency was determined by analysing the number of micronucleated PCEs from at least 2000 PCEs per animal. The frequency of the PCE:NCE ratio was determined by scoring the number of PCEs and NCEs observed in the optic fields while scoring at least the first 200 erythrocytes on the slide. The criteria for identification of micronuclei were those of Schmid (1976).[1] All animals were observed at least daily. All animals in the vehicle and positive control groups and in the 175 mg/kg dose level, appeared normal after dosing and remained healthy until the appropriate harvest timepoint. At the 350 mg/kg dose level, all animals appeared slightly hypoactive immediately after dosing with one animal showing hunched posture and urine stains one hour after dosing. The other animals appeared normal one hour after dosing. At the 700 mg/kg dose level, all animals were hypoactive immediately after dosing, with some showing gait and co-ordination disturbances. All animals continued to show signs of toxicity (hypoactivity, hunched posture etc) at the 1 hour observation, however were observed to be normal 1 day after dosing.
Results	In the first dose range-finding study there was no mortality at 500 mg/kg and high mortality at 800 mg/kg. The maximum tolerated dose was not determined so additional doses between these two levels were tested in the second dose range finding study. In the second rage finding study there was no mortality at 600 mg/kg, with one mortality (female) at 700 mg/kg. Given the high level of mortality at 800 mg/kg in the previous test, the maximum tolerated dose was estimated to be 700 mg/kg. 2-Propenamide, *N*-(1,1,3,3-tetramethylbutyl)- induced signs of clinical toxicity in the treated animals and was cytotoxic to bone marrow (i.e., a statistically significant decrease in the PCE:NCE ratio) at 700 mg/kg. It did not induce a statistically significant increase in

	micronuclei in bone marrow polychromatic erythrocytes and is therefore considered negative in the mouse bone marrow micronucleus test.
Conclusions	2-Propenamide, *N*-(1,1,3,3-tetramethylbutyl)- does not produce micronuclei in the immature erythrocytes of the mouse.
Reliability	(1) valid without restriction
Reference	National Starch and Chemical Company. Unpublished. Mutagenicity test on N-tert-Octylacrylamide in the In Vivo Mouse Micronucleus Assay. P.T. Curry. Covance Laboratories Inc. Study No 19301-0-455OECD (1998). 1. Schmid, W. The micronucleus test. Mutation Res. 31. pp 9-15 (1976)

5.6 GENETIC TOXICITY 'IN VIVO'

5.8.1 TOXICITY TO FERTILITY

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

(1) Atmospheric Oxidation Potential for Windows (AOPWIN v 1.90). U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics, Washington, D.C., (2000)

(2) National Starch and Chemical Company

(3) National Starch and Chemical Company. Unpublished Report. Mutagenicity test on N-tert-Octylacrylamide in the in-vivo mouse micronucleus assay. Covance Inc, Study No.:19301-0-455OECD, (1998)

(4) National Starch and Chemical Company. Unpublished Report. Mutagenicity test on N-tert-Octylacrylamide in the L5178Y TK +/- Mouse Lymphoma Forward Mutation Assay with a confirmatory Assay. Covance Inc, Study No.:19301-0-431OECD, (1998)

(5) National Starch and Chemical Company. Unpublished Report. Mutagenicity test with N-tert-Octylacrylamide in the Salmonella-Esherichia Coli/Mammalian-Microsome Reverse Mutation Assay with a confirmatory Assay. Covance Inc, Study No.:19301-0-409OECD, (1998)

(6) National Starch and Chemical Company. Unpublished. In-Vitro Absorption of N-tert-Octylacrylamide through Human and Rat Epidermis. Central Toxicology Laboratory. Report No CTL/P/5922. (1998)