201-14355

NCIC HPV
Sent by: Mary-Beth Weaver

03/20/2003 01:29 PM

To: NCIC HPV@EPA, Peter Wendolkowski/DC/USEPA/US@EPA
cc: Mary-Beth Weaver/DC/USEPA/US@EPA, Vanessa Williams/DC/USEPA/US@EPA, Karen Boswell/DC/USEPA/US@EPA, Ralph Northrop/DC/USEPA/US@EPA
cc: Mary-Beth Weaver/DC/USEPA/US@EPA, Vanessa Williams/DC/USEPA/US@EPA, Karen Boswell/DC/USEPA/US@EPA, Ralph Northrop/DC/USEPA/US@EPA
Subject: FW: Request

"Nitschke, Kenneth (KD)" <kdnitsch@dow.com> on 12/16/2002 10:35:59 AM

To: Rtk Chem/DC/USEPA/US@EPA
cc: "Burgert, Linda (LC)" <lburgert@dow.com>, "Bollmeier, Allen (AF)" <AFBollmeier@dow.com>
Subject: FW: Request

Sir: Enclosed are the HPV documents for 2-(hydroxymethyl)-2-nitro-1,3-propanediol and 2-methyl-2-nitro-1-propanol which we wish to have posted on the EPA website for HPV chemicals. It is our intent to have these materials be considered as analogs, thus a test plan and two IUCLID documents are enclosed. This information has been added to the US HPV Chemical Tracking System at http://www.hpvchallenge.com. Please let us know if you have any questions. Thanks.

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> > <<Nitro Alcohol HPV edited1PDF.PDF>> > > <<2-Methyl-2-nitro-1-propanol.pdf>> > > <<2-(hydroxymethyl)-2-notro.pdf>>
>

- Nitro Alcohol HPV edited1PDF.PDF
- 2-Methyl-2-nitro-1-propanol.pdf
- 2-(hydroxymethyl)-2-notro.pdf

HIGH PRODUCTION VOLUME (HPV) CHEMICAL CHALLENGE PROGRAM TEST PLAN

For

2-(hydroxymethyl)-2-nitro-1,3-propanediol
and
2-methyl-2-nitro-1-propanol

Prepared by:
The Dow Chemical Company

December 16, 2002

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I. INTRODUCTION

ANGUS Chemical Company (ANGUS) committed to provide screening level human health effects, environmental effects and fate, and physiochemical test data on 2-methyl-2-nitro-1-propanol and 2-(hydroxymethyl)-2-nitro-1,3-propandiol under the Environmental Protection Agency's (EPA's) High Production Volume (HPV) Challenge Program (Program). After this commitment was made ANGUS was bought by the Dow Chemical Company (DOW) and is now a wholly owned subsidiary of DOW.

This plan details how both substances can be placed in a single category, nitro alcohols, and identifies existing data of adequate quality for those substances.

II. DESCRIPTION OF THE NITRO ALCOHOL CATEGORY

ANGUS Chemical Company is the largest producer of nitroparaffins in the world. Indeed, of those it manufactures, nitromethane, nitroethane, 1-nitropropane, and 2-nitromethane, only nitromethane is available from another producer. One use for these substances is the production of **nitro alcohols,** which are obtained by the reaction of the nitroparaffin with formaldehyde in the presence of base as a catalyst. The nitro alcohols obtained from each of the nitroparaffins are displayed in Table I.

Table I. Nitro Alcohols from the Niroparaffins*

NITROPARAFFIN Precursor	formaldehydes added	NITRO ALCOHOL Obtained
Nitromethane 75-52-5	2	2-nitro-1,3-propanediol
	3	**2-(hydroxymethyl)-2-nitro-1,3-propanediol**
Nitroethane 79-24-3	2	2-methyl-2-nitro-1,3-propanediol
1-Nitropropane 108-03-2	1	2-nitro-1-butanol
	2	2-ethyl-2-nitro-1,3-propanediol
2-Nitropropane 79-46-9	1	**2-methyl-2-nitro-1-propanol**

- Substances in bold are HPV substances

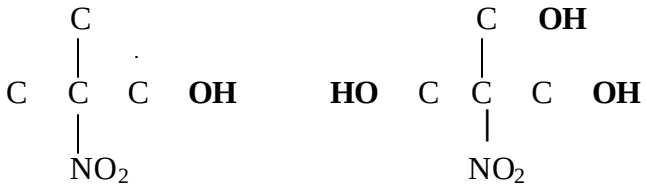
Of these substances only the following are High Production Volume chemicals:

	CAS Reg. No.
2-methyl-2-nitro-1-propanol (MNP)	76-39-1
2-(hydroxymethyl)-2-nitro-1,3-propandiol (TN)	126-11-4

Both are non-volatile crystalline solids. The major use of all nitroalcohols is as closed-system intermediates in the production of alkanolamines. These two, MNP and TN are used to produce 2-amino-2-methyl-1-propanol and 2-amino-2-(hydroxymethyl)-1,3-propanediol. Thus exposure to MNP and TN is only expected to occur under upset

conditions in this application. Suitable protective equipment would be worn during any operation where worker exposure is expected.

In addition, TN is used as a biocide and as a cross-linker in the production of plywood but this represents a relatively small portion of the total amount of TN produced. TN is used as an antimicrobial agent for the control of bacteria in industrial processes such as cooling towers and metalworking fluids. Efficacy as a biocide is obtained by the slow release of formaldehyde from TN in a alkaline environment. A Reregistration Eligibility Decision was published by EPA in 1993. In the case of plywood, TN is used in the resin curing operation releasing formaldehyde and is consumed during the curing process. During plywood production, limited dermal exposure could occur to workers handling the adhesive containing TN. Consumer exposure would be expected to be nil.



MNP (HPV) TN (HPV)

III. TEST PLAN RATIONALE

A. Overview

Due to its use as a biocide, TN is registered under the Federal Insecticide Fungicide and Rodenticide Act (FIFRA). Subsequently, a Reregistration Eligibility Decision (RED) document was published by EPA in 1993. Thus a complete HPV battery of tests are already available.

Only acute data are available for **MNP**; however, it currently is used only as a closed-system intermediate for the production of 2-amino-2-methyl-1-propanol. In the past it did find use as an adhesion promoter in tire production, a use in which the substance is consumed, however, this technology has been replaced and no further production for this use is planned.

At basic pH and/or when exposed to heat, all these nitro alcohols readily hydrolyze to yield formaldehyde and their parent nitroparaffin. The nitroparaffins involved and formaldehyde are all HPV substances which are subject to separate submission.

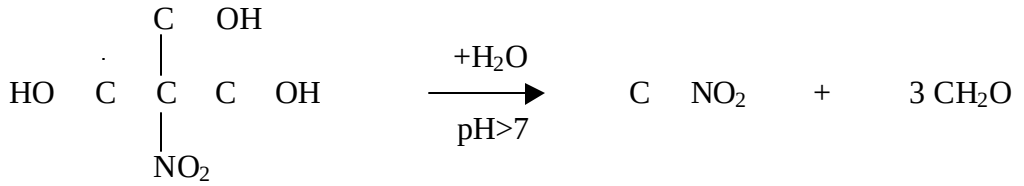
As **TN** is the only nitro alcohol for which there is any appreciable human and environmental exposures, it is the surrogate of choice for all of the nitro alcohols.

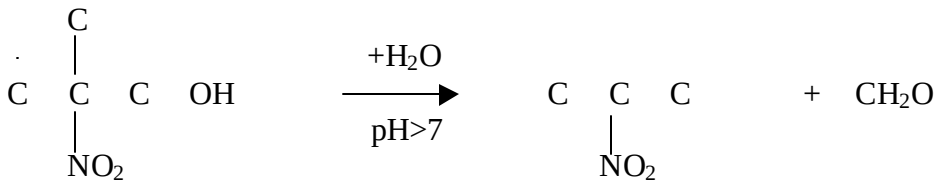
B. Physicochemical Properties

Extensive data already exist for all HPV endpoints (Table 2). All members of this category are crystalline solids at room temperature, and all decompose with a significant release of energy at temperatures only slightly above their melting points. Thus it is very difficult to measure vapor pressure of either material. The vapor pressure is expected to <1.3 hPa for both materials.

C. Environmental Fate

The estimated half-life of photodegradation of TN was 5.6 days and that of MNP was 14 days (AOPWIN model) (Table 2). The nitro alcohols all undergo hydrolysis at pH greater than 7 to yield formaldehyde and the nitroparaffin parent compound as follows:





Level I and level III fugacity-based models were used to evaluate the distribution of TN and MNP between environmental compartments. Based on the level III calculation, 77% of TN and 39.4% of MNP emissions will reside in water and 16.5% of TN and 43.4% of MNP will reside in the soil. Almost none of either substance will migrate to the air. TN was only 13.4% degraded in a ready biodegradation test (OECD 301F).

D. Ecotoxicity

Data on TN are available for all three aquatic toxicity endpoints in the HPV program (Table 2). MNP is site-limited and therefore does not get released to waters. The LC_{50} of TN in the fathead minnow (pimephales promelas) was determined to be 280 mg/L using OTS protocol 797.1400. Using the procedure of OPP 72-2, the 48-hour EC_{50} for daphnia magna was 80 mg/L. An EC_{50} of only

0.656 mg/L for TN was obtained using the OECD 201 "Algae Growth Inhibition Test".

E. Animal Toxicity Testing

A complete battery of HPV animal toxicity studies already are available for TN (Table 2). Only acute toxicological data and an AMES test are available on MNP. The oral LD_{50} for TN is 990-1000 mg/kg bw and that for MNP is 845-1480 mg/kg bw. These data do not indicate that there are differences in toxicity for the nitro alcohols which are great enough to warrant further testing of MNP.

The primary route of exposure to TN is the dermal route. Therefore, the 90-day repeat dose study was done via the dermal route. At 1000 mg/kg/day, a slight yellow discoloration of the skin was observed at the application site which was attributed to repeated application of an impurity. There were no systemic effects evident from the histopathological examination of the rat organs including the gonads. Further, in oral teratology studies in rats and rabbits, no significant effects in fetal mortality, developmental anomalies, malformations, or litter numbers were noted at doses below those which induced maternal toxicological effects.

Neither TN nor MNP were mutagenic in the Ames test either with or without S9 activation. Further negative results were obtained for TN in the Chinese Hamster Ovary (CHO) test and the *in vitro* Unscheduled DNA Synthesis test.

IV. TEST PLAN SUMMARY

Due to the closed system intermediate use for MNP, the use of protective equipment whenever worker exposure could occur to MNP and the lack of any effect observed in the 90-day dermal study with TN, additional studies are not considered to be necessary for MNP. A complete data set exists for TN. Thus no additional studies are needed. All data required for the HPV program are summarized in the IUCLID data sets which accompany this report. The two teratology studies conducted on TN and the 90-day dermal study suffice to satisfy the reproductive toxicity requirement.

Robust summaries for the nitro alcohol data as required for the HPV program as well as for addition studies follow in the IUCLID data sets. The references for the cited studies are found in them.

Table 2
Test Plan for 2-(hydroxymethyl)-2-nitro-1,3-propanediol
and 2-methyl-2-nitro-1-propanol

	2-Methyl-2-nitro-1-propanol CAS Reg. No. 76-39-1	**2-(Hydroxymethyl)-2-nitro-1,3-propanediol CAS Reg. No. 126-11-4**
Melting Point	D 90 C	D 175 C
Boiling Point	D 94 C @ 19.5hPa	D decomposes at mp
Vapor Pressure	D nil at normal pres.	D nil
Partition Coefficient	Estimate	D 1.06
Water Solubility	D 350g/100 mL water	D 220g/100g water
Stability in Water	CA	D 2.4 day @25 C
Photodegradation	$t_{1/2}$=14 days (Estimate)	$t_{1/2}$=5.6 days (Estimate)
Fugacity Level III 1000 kg/hr each to air, water and soil	39.4% water 43.4% soil 17.1% sediment <0.1% air	77% water 16.5% soil 6.5% sediment <0.1% air
Biodegradation	CA	D 13.4% in 28 days
Acute Toxicity - Fish	CA	D 96 hr LC50=280mg/L
Acute Toxicity - Daphnia	CA	D 48 hr EC50=80 mg/L
Acute Toxicity - Algae	CA	D 96 hr EC50=0.656 mg/L
Acute Toxicity - Mammalian	D LD50 rat, 845-1480mg/kg	D LD50 rat, 990-1000 mg/kg
Mutagenicity - invitro	D negative Ames	D negative Ames
Mutagenicity - invitro	CA	D negative CHO chrom aberr.
Repeat Dose Toxicity	CA	D NOAEL >1000mg/kg in dermal study with rats
Reproductive Toxicity	CA	Data available from exam of reproductive organs in 13 week repeated dose toxicitystudy.
Developmental Toxicity	Not Required	D Data avilable from studies in two mammalian species

CA - Analog
D - Data

I U C L I D

Data Set

Existing Chemical	:	ID: 76-39-1
CAS No.	:	76-39-1
TSCA Name	:	2-methyl-2-nitro-1-propanol
EINECS No.	:	200-957-6

Producer Related Part

Company	:	The Dow Chemical Company
Creation date	:	09.08.2001

Substance Related Part

Company	:	The Dow Chemical Company
Creation date	:	09.08.2001
Memo	:	
Printing date	:	16.12.2002
Revision date	:	
Date of last Update	:	13.12.2002
Number of Pages	:	4
Chapter (profile)	:	
Reliability (profile)	:	
Flags (profile)	:	???

1.0.1 OECD AND COMPANY INFORMATION

Type	:	cooperating company
Name	:	The Dow Chemical company
Partner	:	
Date	:	
Street	:	2020 Dow Center
Town	:	48674 Midland, Michigan
Country	:	United States
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	
Reliability	:	(1) valid without restriction

14.08.2001

1.0.2 LOCATION OF PRODUCTION SITE

Name of Plant	:	Angus Chemical Company
Street	:	Louisiana Highway 2
Town	:	71280 Sterlington, LA
Country	:	United States
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	

14.08.2001

1.0.3 IDENTITY OF RECIPIENTS

1.1 GENERAL SUBSTANCE INFORMATION

Substance type	:	organic
Physical status	:	solid
Purity	:	> 99 % w/w
Remark	:	This substance, when isolated is solid and crystalline at normal ambient temperatures. It is not, however, nomally isolated but is used in an aqueous solution for synthesis on a site limited basis.
Reliability	:	(1) valid without restriction

09.08.2001

1.1.0 DETAILS ON TEMPLATE

Comment		One of two HPV chemicals which are defined as the category, nitro alcohols.

07.12.2001

1.1.1 SPECTRA

1.2 SYNONYMS

1.3 IMPURITIES

1.4 ADDITIVES

1.5 QUANTITY

1.6.1 LABELLING

1.6.2 CLASSIFICATION

1.7 USE PATTERN

Type	:	industrial
Category	:	Chemical industry: used in synthesis
Remark	:	Virtually all of this substance being manufactured today is used as a site limited intermediate for the synthesis of 2-amino-2-methyl-1-propanol.
Reliability	:	(1) valid without restriction

14.08.2001

1.7.1 TECHNOLOGY PRODUCTION/USE

1.8 OCCUPATIONAL EXPOSURE LIMIT VALUES

1.9 SOURCE OF EXPOSURE

1.10.1 RECOMMENDATIONS/PRECAUTIONARY MEASURES

1.10.2 EMERGENCY MEASURES

1.11 PACKAGING

1.12 POSSIB. OF RENDERING SUBST. HARMLESS

1.13 STATEMENTS CONCERNING WASTE

1.14.1 WATER POLLUTION

1.14.2 MAJOR ACCIDENT HAZARDS

1.14.3 AIR POLLUTION

1.15 ADDITIONAL REMARKS

1.16 LAST LITERATURE SEARCH

1.17 REVIEWS

1.18 LISTINGS E.G. CHEMICAL INVENTORIES

2.1 MELTING POINT

Value : = 90 ° C
Reliability : (2) valid with restrictions
14.08.2001 (1)

2.2 BOILING POINT

Value : = 94 ° C at 19.5 hPa
Reliability : (2) valid with restrictions
14.08.2001 (1)

2.3 DENSITY

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Remark : 2-Methyl-2-nitro-1-propanol is essentially nonvolatile. Its vapor pressure at 94 degrees centigrade is only 19.5 hPa. Even this pressure may be the off-gassing of formaldehyde due to decompostion of the molecule.
Reliability : (2) valid with restrictions
26.11.2002 (2)

2.5 PARTITION COEFFICIENT

2.6.1 WATER SOLUBILITY

Value : = 350 other: g per 100 mL water at 25 ° C
Qualitative :
Pka : at 25 ° C
PH : at and ° C
Reliability : (2) valid with restrictions
22.10.2002 (1)

2.6.2 SURFACE TENSION

Remark : Not applicable to this solid material.
Reliability : (1) valid without restriction
14.08.2001

2.7 FLASH POINT

Remark : Not applicable to this solid material.
Reliability : (1) valid without restriction
14.08.2001

2.8 AUTO FLAMMABILITY

Remark : Not applicable to this solid material.
Reliability : (2) valid with restrictions
14.08.2001

2.9 FLAMMABILITY

2.10 EXPLOSIVE PROPERTIES

2.11 OXIDIZING PROPERTIES

2.12 ADDITIONAL REMARKS

3.1.1 PHOTODEGRADATION

Type	:	air
Light source	:	
Light spect.	:	nm
Rel. intensity	:	based on Intensity of Sunlight
Deg. Product	:	
Method	:	other (calculated): Atmospheric Oxidation Program (AOPWIN)
Year	:	2002
GLP	:	no
Test substance	:	
Method	:	The estimated atmospheric half-life based on hydroxyl radical attack was obtained using the AOPWIN version 1.90 computer program assuming 12-hour days.
Result	:	The atmospheric half-life was estimted to be 14 days.

27.11.2002

3.1.2 STABILITY IN WATER

Remark	:	While no definitive study has been conducted on this substance it is known, based on experience with tris(hydroxymethyl)nitromethane that the nitro alcohols all hydrolyze at basic pH to yield formaldehyde and nitroparaffins. In the case of 2-methyl-2-nitro-1-propanol the nitroparaffin formed is 2-nitropropane.
Reliability	:	(1) valid without restriction

14.08.2001

3.1.3 STABILITY IN SOIL

3.2 MONITORING DATA

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type	:	fugacity model level I
Media	:	
Air (level I)	:	
Water (level I)	:	99.9
Soil (level I)	:	.1
Biota (level II / III)	:	
Soil (level II / III)	:	43.4
Method	:	other
Year	:	2002
Remark	:	Regardless of the media to which MNP is released, a large majority at steady state is in the soil and water phases.
Result	:	Using the default emmissions of equal amounts to soil, air, water and sediment (1000 kg/hr for each) the Level III model predicts that the distribution of MNP will be 43.4% in soil, 39.4% in water, 17.1 % in sediment, and <0.1% in air.

13.12.2002 (3)

3.3.2 DISTRIBUTION

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

3.6 BOD5, COD OR BOD5/COD RATIO

3.7 BIOACCUMULATION

3.8 ADDITIONAL REMARKS

4.1 ACUTE/PROLONGED TOXICITY TO FISH

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

4.6.1 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO OTHER NON-MAMM. TERRESTRIAL SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50
Species	:	rat
Strain	:	other: Cox-SD
Sex	:	male/female
Number of animals	:	130
Vehicle	:	water
Value	:	= 845 - 1480 mg/kg bw
Method	:	other: IMC Toxicity Laboratory Protocol
Year	:	1980
GLP	:	no
Test substance	:	other TS: 99.6 % pure
Method	:	Cox-SD albino rats weighing 200 +/-25 g were dosed by gavage with test material in sterile deionized water. Groups of ten males were dosed at 0, 402, 570, 800, 1100, 1600, and 2300 mg/kg bw. Groups of ten females were dosed at 0, 800, 1100, 1310, 1600, and 2300 mg/kg bw. All animals were observed frequently on the day of compound administration and at least once a day thereafter for 14 days. All animals that died during this period were necropsied on the day of death or the day after death for rats that died overnight. After 14 days all surviving rats were weighed, sacrificed, and examined for gross pathology.
Result	:	Male rats exhibited signs of toxicity at all dose levels. At 800 mg/kg, the rats were lethargic and ataxic 30 minutes after dosing. At higher doses, the rats were prostrate and breathing slowly after 30 minutes. One rat each in the 800, 1100, and 1600 mg/kg groups showed mottled livers at necropsy. Female rats were more resistant to the compound and showed fewer signs of toxicity. With the 1600mg/kg group only, the rats were prostrate 24 hours after dosing and 7/10 exhibited mild hematuria. At necropsy, all organs were grossly normal. Deaths in all groups occurred within the first three days following dosing. The LD50 for males was calculated to be 845 (710-1150) mg/kg. For females the LD50 was 1480 (1370- 1598) mg/kg.
Reliability	:	(2) valid with restrictions

26.11.2002 (4)

5.1.2 ACUTE INHALATION TOXICITY

5.1.3 ACUTE DERMAL TOXICITY

Type	:	other: Dermal toxicity limit test
Species	:	rabbit
Strain	:	New Zealand white
Sex	:	male/female
Number of animals	:	10
Vehicle	:	water
Value	:	> - 2000 mg/kg bw
Method	:	other: IMC Toxicity Laboratory Protocol
Year	:	1980
GLP	:	no
Test substance	:	other TS: 99.6 % pure
Method	:	Ten New Zealand White rabbits weighing 2.9 +/-0.5 kg were placed in two groups. The abdomens of the rabbits were shaved free of hair. The abdomens of 3 males and 2 females were abraded without bleeding with a blunt hypodermic needle. All animals then were treated with 2000 mg/kg

bw of the test compound which dissolved readily in moisture present on the skin. The exposed skin was covered with gauze and impervious rubber cloth. After 24 hours, this cover was removed and the exposed skin was evaluated for irritancy. The rabbits were then observed for 14 days prior to sacrifice and pathological examination.

Result : No rabbits died during the test period and no signs of toxicity were observed. There was no irritation of the skin, and at necropsy, all organs examined were grossly normal.

Reliability : (2) valid with restrictions

07.12.2001 (4)

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.2.1 SKIN IRRITATION

Species : rabbit
Concentration : undiluted
Exposure : Occlusive
Exposure time : 24 hour(s)
Number of animals : 6
PDII : .13
Result : not irritating
EC classification : not irritating
Method : other: IMC Toxicology Laboratory Protocol
Year : 1980
GLP : no
Test substance : other TS: 99.6 % pure
Method : The backs of 6 New Zealand White rabbits weighing 3.0 +/- 0.5 kg were clipped free of hair. The skin area on the left side of the mid dorsal line was left intact while that to the right was abraded in a tic-tac-toe patern with a blunt hypodermic needle. Both sides of the backs of the animals received 0.5 g of test compound which readily dissolved in the moisture present on the skin. The animals backs were then covered with a gauze pad and occlusive cloth for 24 hours. After exposure, the treated sites were cleaned and scored for skin reaction. They were also scored at 72 hours (48 hours after the first scoring).
Result : Only three rabbits (one at the abraded site) exhibited minimal erythema at 24 hours. No irritation was observed at 72 hours. The primary irritation index was 0.13.
Reliability : (2) valid with restrictions

10.08.2001 (4)

5.2.2 EYE IRRITATION

Species : rabbit
Concentration : undiluted
Dose : .1 other: gram
Exposure Time : 24 hour(s)
Comment : not rinsed
Number of animals : 6
Result : highly irritating
EC classification : risk of serious damage to eyes
Method : other: IMC Toxicology Laboratory Protocol
Year : 1980
GLP : no
Test substance : other TS: 99.6 % pure
Method : The test compound was ground to a fine powder and 0.1 g was instilled

into the lower conjunctival sac of the right eye of each of 6 New Zealand White rabbits. The eye was held closed for two seconds to prevent loss of material. The eyes were then examined at 24, 48, and 72 hours post treatment. At 72 hours and on the 7th day, a drop of sodium fluorescein (0.24%) was placed in the eye and the excess washed from the eye with sterile saline. The eyes were then examined under UV light for corneal lesions.

Result : The compound affected the cornea, iris, and conjunctiva of all rabbits. At 72 hours, the eyes of all 6 rabbits showed corneal scaring. When re-examined after 7 days, very little if any recovery was evident. The average score for the study ranged from 36.5-37.7. The compound is a severe eye irritant.

Reliability : (2) valid with restrictions
07.12.2001 (4)

5.3 SENSITIZATION

Type : Buehler Test
Species : guinea pig
Concentration : Induction 25 % active substance occlusive epicutaneous
Challenge 25 % active substance occlusive epicutaneous

Number of animals : 30
Vehicle : water
Result : not sensitizing
Classification : not sensitizing
Method : other: IMC Toxicology Laboratory protocol
Year : 1980
GLP : no
Test substance : other TS: 99.6 % pure
Method : The backs and flanks of 30 female guinea pigs weighing 250-300 g were shaved free of hair. One group of ten animals was treated topically with 0.5 mL of 25 % test compound. A second group was treated with 0.5 mL of 5% formaldehyde, and a third group recieved 0.5 mL of 1% carboxymethyl cellulose (CMC) in water. After 24 hours under occlusive cover the sites were cleaned. This procedure was repeated once a week for three weeks after which the animals were allowed to rest for two weeks. On the first day of the third week each group of animals was challenged topically as follows:

Group 1 received 5, 10, and 25% test compound
Group 2 received 2% formaldehyde
Group 3 received all the above as well as 1% CMC

Result : Only 6 of the 10 animals in Group 2 reacted. All other animals did not react.

Reliability : (2) valid with restrictions
07.12.2001 (4)

5.4 REPEATED DOSE TOXICITY

5.5 GENETIC TOXICITY 'IN VITRO'

Type : Ames test
System of testing : Tested in Salmonalla typhimurium strains TA98, TA100, TA1537, and TA1538.
Concentration : 0, 0.1, 0.5, 2.5, 5.0, and 10 micro liter/plate
Cycotoxic conc. : There was no significant effect of the test substance on viability of the bacteria.

Metabolic activation	:	with and without
Result	:	negative
Method	:	other: EG&G Mason Protocol
Year	:	1980
GLP	:	no
Test substance	:	other TS: 60.1% active in MeOH/water
Reliability	:	(2) valid with restrictions

10.08.2001 (5)

5.6 GENETIC TOXICITY 'IN VIVO'

5.7 CARCINOGENITY

5.8 TOXICITY TO REPRODUCTION

5.9 DEVELOPMENTAL TOXICITY/TERATOGENICITY

5.10 OTHER RELEVANT INFORMATION

5.11 EXPERIENCE WITH HUMAN EXPOSURE

(1) Bollmeier, A.F., (1981), "Nitro Alcohols" in Kirk Othmer Encyclopedia of Chemical Technology, Vol. 15, Third Edition.

(2) ANGUS Chemical Company Unpublished Data

(3) Witt, M.E., (October 3, 2002), "Evaluation of the Environmental Distribution and Transport of Methylnitropropanol (MNP) Using the Level I and Level III Fugacity Models", The Dow Chemical Company Study 020156.

(4) Parekh, C., (March 6, 1980), "Acute Toxicity Profile of P-184 (2-nitro-2-methyl-1-propanol)", IMC Pharmacology Laboratories PLR-81.

(5) Haworth, S.R., (December 22, 1980), "Salmonella/Mammalian-Microsome Plate Incorporation Mutagenesis Assay", EG&G Mason Research Institute Report Number 049-314-568-1.

7.1 END POINT SUMMARY

7.2 HAZARD SUMMARY

7.3 RISK ASSESSMENT

I U C L I D

Data Set

Existing Chemical	:	ID: 126-11-4
CAS No.	:	126-11-4
CAS Name	:	2-(hydroxymethyl)-2-nitro-1,3-propanediol
EINECS No.	:	204-769-5
Molecular Formula	:	C4H9NO5

Producer Related Part

Company	:	The Dow Chemical Company
Creation date	:	11.06.2001

Substance Related Part

Company	:	The Dow Chemical Company
Creation date	:	11.06.2001
Memo	:	
Printing date	:	16.12.2002
Revision date	:	
Date of last Update	:	13.12.2002
Number of Pages	:	4
Chapter (profile)	:	
Reliability (profile)	:	
Flags (profile)	:	???

1.0.1 OECD AND COMPANY INFORMATION

Type	:	cooperating company
Name	:	ANGUS Chemical Company
Partner	:	
Date	:	
Street	:	1500 East Lake Cook Road
Town	:	60089 Buffalo Grove, IL
Country	:	United States
Phone	:	847-808-3554
Telefax	:	847-808-3710
Telex	:	
Cedex	:	
Remark	:	A wholly owned subsidiary of The Dow Chemical Company.

28.03.2002

1.0.2 LOCATION OF PRODUCTION SITE

Name of Plant	:	ANGUS Chemical Company
Street	:	Louisiana Highway 2
Town	:	71280 Sterlington, LA
Country	:	United States
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	
Remark	:	A subsidiary of The Dow Chemical Company

13.08.2001

1.0.3 IDENTITY OF RECIPIENTS

1.1 GENERAL SUBSTANCE INFORMATION

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

20.06.2002

1.1.0 DETAILS ON TEMPLATE

Comment	This is the most commercially important member of the category, "nitro alcohols".
Remark	Molecular Formula: C4H9NO5 Structural Formula: HOCH2C(CH2OH)(NO2)CH2OH

13.08.2001

1.1.1 SPECTRA

1.2 SYNONYMS

Tris(hydroxymethyl)nitromethane
20.06.2002

1.3 IMPURITIES

CAS-No	:	7732-18-5
EINECS-No	:	
EINECS-Name	:	water
Contents	:	< .2 % w/w

26.11.2002

1.4 ADDITIVES

1.5 QUANTITY

1.6.1 LABELLING

Labelling	:	as in Directive 67/548/EEC
Symbols	:	Xn
Nota	:	
Specific limits	:	no
R-Phrases	:	(20/22) Harmful by inhalation and if swallowed (43) May cause sensitization by skin contact
S-Phrases	:	(24) Avoid contact with skin (37) Wear suitable gloves

28.03.2002

1.6.2 CLASSIFICATION

Classification	:	as in Directive 67/548/EEC
Class of danger	:	harmful
R-Phrases	:	(20/22) Harmful by inhalation and if swallowed (43) May cause sensitization by skin contact

28.03.2002

1.7 USE PATTERN

1.7.1 TECHNOLOGY PRODUCTION/USE

1.8 OCCUPATIONAL EXPOSURE LIMIT VALUES

1.9 SOURCE OF EXPOSURE

1.10.1 RECOMMENDATIONS/PRECAUTIONARY MEASURES

1.10.2 EMERGENCY MEASURES

1.11 PACKAGING

1.12 POSSIB. OF RENDERING SUBST. HARMLESS

1.13 STATEMENTS CONCERNING WASTE

1.14.1 WATER POLLUTION

1.14.2 MAJOR ACCIDENT HAZARDS

1.14.3 AIR POLLUTION

1.15 ADDITIONAL REMARKS

1.16 LAST LITERATURE SEARCH

1.17 REVIEWS

1.18 LISTINGS E.G. CHEMICAL INVENTORIES

2.1 MELTING POINT

Decomposition	:	yes at ca. 175 ° C
Sublimation	:	no
Method	:	
Year	:	
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	The decompositon of solid TRIS NITRO takes place with the release of significant heat and evolution of gas which can be hazardous.
Reliability	:	(2) valid with restrictions

06.12.2002 (1)

2.2 BOILING POINT

Decomposition	:	yes
Method	:	
Year	:	
GLP	:	
Test substance	:	
Remark	:	Not applicable. This substance decomposes at "melting point".
Reliability	:	(1) valid without restriction

07.05.2002

2.3 DENSITY

Type	:	relative density
Value	:	ca. 2 at ° C
Method	:	
Year	:	
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	The specific gravity of solid TRIS NITRO as a single crystal is about 2.0; however, current product of "solid" TRIS NITRO is obtained by freeze drying. This form of the product varies widely in density. This substance as manufactured is obtained as a solution in water at 50 +/- 3%.

06.12.2002 (2)

2.3.1 GRANULOMETRY

Remark	:	The solid substance is obtained by "freeze-drying" the 50% solution; it therefore is availble commercially in a form of flake.
Reliability	:	(1) valid without restriction

06.12.2002 (1)

2.4 VAPOUR PRESSURE

Remark	:	No appreciable vapors are generated by the substance itself, exclusive of the vapors formed by decomposition.
Reliability	:	(1) valid without restriction

06.12.2002 (1)

2.5 PARTITION COEFFICIENT

Log pow	:	= 1.06 at 25° C
Method		other (measured): US 40CFR 796.1570
Year	:	1991
GLP	:	yes
Test substance	:	other TS: 99.69% pure
Method	:	The sample was analyzed by reverse phase-high pressure liquid chromatography using a C-18 column and an ultraviolet detector. The retention time of any substance on the column is a function of the hydrophobicity of the substance. The retention time of the sample was compared to a curve of the log of the retention time vs. the log of the partition coefficient of substances with known partition coefficients.
Reliability	:	(1) valid without restriction

07.12.2001 (3)

2.6.1 WATER SOLUBILITY

Value	:	other at ° C
Qualitative	:	of high solubility
Pka	:	at 25 ° C
PH	:	at and ° C
Method	:	other
Year	:	
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Solubility in water is 220 g/100g of water at 20 degrees C. The 50% aqueous solution precipitates when cooled below 50 degrees F.

11.06.2001 (4)

2.6.2 SURFACE TENSION

Remark	:	Not applicable for a solid.
Reliability	:	(1) valid without restriction

13.08.2001

2.7 FLASH POINT

Value	:	> 94 ° C
Type	:	closed cup
Method	:	other
Year	:	
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Not applicable for materials which are solids under normal ambient conditions (see melting point). 50% Aqueous solutions did not flash when tested up to 200 degrees F by Tag Closed Cup procedure.

11.06.2001

2.8 AUTO FLAMMABILITY

Remark	:	No data
Reliability	:	(1) valid without restriction

13.08.2001

2.9 FLAMMABILITY

Remark : Not applicable.
Reliability : (1) valid without restriction
13.08.2001

2.10 EXPLOSIVE PROPERTIES

Result : not explosive
Method : other
Year : 2000
GLP : no
Test substance : as prescribed by 1.1 - 1.4
Remark : Solid product was was subjected to a battery of three tests in order to assess the possibilty of explosion.
Result : In the Koenen test, as prescibed by the Transport of Dangerous Goods 1(b)(i), no change in the tube was observed in three trials with the 1 mm orifice.
The GAP test for solids and liquids was performed according to the procedure of Test 2 a (iii) of the UN Transport of Dangerous Goods Regulations. In two trials, only a slight warping of the witness plate was observed. 2-(Hydroxymethyl)-2-nitro-1,3-propanediol was judged to be insensitive to detonative shock.
The TIME/PRESSURE test was conducted accordung to the procedure of Test 2 a (i) of the UN Transort of Dangerous Goods Regulations. In three trials, the test samples failed to reach 300 psig, the pressure which must be reached for any positive finding.
Conclusion : Based on the results of these three tests 2-(hydroxymethyl)-2-nitro-1,3-propanediol is not regarded as an explosive (Class 1) according to transportation regulations.

26.11.2002 (5)

2.11 OXIDIZING PROPERTIES

Result : no oxidizing properties
Remark : Based upon the chemical structure of this substance it is not an oxidizing agent.

06.08.2001

2.12 ADDITIONAL REMARKS

Memo : The decomposition which begins at ca. 150 degrees C becomes exothermic and can lead to a deflagration when under confinement.

04.03.2002

3.1.1 PHOTODEGRADATION

Type	:	air
Light source	:	
Light spect.	:	nm
Rel. intensity	:	based on Intensity of Sunlight
Deg. Product	:	
Method	:	other (calculated): Atmospheric Oxidation Program(AOPWIN)
Year	:	2002
GLP	:	no
Test substance	:	
Method	:	The estimated atmospheric half-life based on hydroxyl radical attack was obtained using the AOPWIN version 1.90 computer program assuming 12-hour days.
Result	:	The estimated atmospheric half life was estimated as 5.6 days.

27.11.2002

3.1.2 STABILITY IN WATER

Type	:	abiotic
t1/2 pH4	:	at degree C
t1/2 pH7	:	= 3.4 day at 25 degree C
t1/2 pH9	:	= 2.4 day at 25 degree C
t1/2 pH 5	:	> 999 day at 25 degree C
Deg. Product	:	yes
Method	:	EPA OTS 796.3500
Year	:	1993
GLP	:	yes
Test substance	:	other TS: 99.69% pure
Method	:	Solutions of TRIS NITRO of concentration 0.001 M were prepared in buffer solutions that were adjusted to pH 5 (0.01 M phthalate), pH 7 (0.01 M phosphate), or pH 9 (0.0025 M borate). Aliquots of the solutions were transferred into 2 mL glass autosampler vials which were then maintained in a darkened incubator for up to 32 days at 25 degrees centigrade. Individual samples were analyzed at various times post-preparation as follows: 1. TRIS NITRO was determined by HPLC using an Alltech C-18 column eluted with water:methanol equiped with a UV (254 nm) spectrophotometric detector. 2. The pH 7 and 9 solutions were analyzed for formaldehyde using GC equipped with flame-ionization detection. To determine the effect of formaldehyde on the hydrolytic degradation of TRIS NITRO, a mixture of TRIS NITRO and formaldehyde was added at 0.00035 M:0.002 M to pH 9 solutions and 0.000648 M:0.000983 M to pH 7 buffer solutions. These were then incubated and analyzed as previously described over a period of up to 10 days.
Result	:	TRIS NITRO did not degrade at pH 5. At pH 7 a half life of 3.42 days was determined and at pH 9 the half life was 2.43 days. However, the presense of formaldehyde in closed vials was shown to stabilize TRIS NITRO. This was expected based on the fact that TRIS NITRO is synthesized by a reversible reaction of three moles of formaldehyde with one mole of nitromethane. Stabilization of the TRIS NITRO often was assured in the past by the addition of an acid to adjust the pH of aqueous TRIS NITRO to <2.
Reliability	:	(1) valid without restriction

07.12.2001 (6)

07.09.2001

3.1.3 STABILITY IN SOIL

3.2 MONITORING DATA

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type	:	fugacity model level I
Media	:	
Air (level I)	:	0
Water (level I)	:	99.998
Soil (level I)	:	.0019
Biota (level II / III)	:	
Soil (level II / III)	:	16.5
Method	:	other: calculation
Year	:	2002
Remark	:	Regardless of the media to which the TN is released, most of the TN at steady state is in the water phase.
Result	:	Using the default emmissions of equal amounts to soil, air, water and sediment (1000 kg/hr for each) the Level III model predicts that the distribution of TN will be 16.5% in soil, 77% in water, 6.5 % in sediment, and <0.1% in air.
Reliability	:	(1) valid without restriction

13.12.2002 (7)

Type	:	adsorption
Media	:	water - soil
Air (level I)	:	
Water (level I)	:	
Soil (level I)	:	
Biota (level II / III)	:	
Soil (level II / III)	:	
Method	:	other: OECD 121
Year	:	2002
Method	:	HPLC is used to estimate the Adsorption Coefficient of a test material by comparison of the retention time to those of a group of reference compounds. The reference compounds utilized were: acetanilide, phenol, 3-nitrobenzamide, methyl benzoate, naphthalene, 1,2,3-trichlorobenzene, and phenanthrene.
Result	:	The estimated log Koc for TRIS NITRO is 0.6.
Reliability	:	(1) valid without restriction

07.05.2002 (8)

07.05.2002

3.3.2 DISTRIBUTION

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type	:	aerobic
Inoculum	:	activated sludge, domestic
Concentration	:	1960mg/l related to related to
Contact time	:	
Degradation	:	= 13.4 % after 28 day
Result	:	inherently biodegradable
Control substance	:	Benzoic acid, sodium salt
Kinetic	:	**%** **%**
Deg. Product	:	
Method	:	OECD Guide-line 301 F "Ready Biodegradability: Manometric Respirometry Test"
Year	:	2002
GLP	:	yes
Test substance	:	other TS: 99.69% pure

26.11.2002 (9)

3.6 BOD5, COD OR BOD5/COD RATIO

3.7 BIOACCUMULATION

3.8 ADDITIONAL REMARKS

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	flow through
Species	:	Cyprinodon variegatus (Fish, estuary, marine)
Exposure period	:	96 hour(s)
Unit	:	mg/l
Analytical monitoring	:	yes
NOEC	:	m = 501
LC50	:	m > 501
Method	:	other: EPA FIFRA Guideline 72-3 (a)
Year	:	1993
GLP	:	yes
Test substance	:	other TS: 99.69% pure
Method	:	Sheepshead minnows ~14 weeks old were maintained in filtered saltwater with a salinity of ~22% at a temperature of 22+/-2 degrees C. Based upon a static range-finding study, test concentrations of nominal(measured) values were chosen for the study as follows: 77.8(64), 130(123), 216(190), 360(356), and 600(501) mg/L. About 1400 mL of each test solution was placed in test chambers and 20 fish were distributed to each test tank. Survival of the fish were then monitored daily and abnormalities of behavior or appearance were noted.
Result	:	There were no deaths at any test concentration during the 96 hours of the test.
Reliability	:	(1) valid without restriction

07.08.2001 (10)

Type	:	static
Species	:	Pimephales promelas (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no
NOEC	:	m = 180
LC50	:	c = 280
Method	:	EPA OTS 797.1400
Year	:	1989
GLP	:	yes
Test substance	:	other TS:99.69%
Method	:	Nominal concentrations of 0, 100, 180, 320, 560, and 1000 mg/L were prepared by dissolving the appropriate amount of test substance into 5 gallons of "soft blended" water. The study was conducted in duplicate with ten fish per tank for a total of twenty fish per concentration. Water quality parameters of temperature, dissolved oxygen, and pH were monitored and were within acceptable limits during the test.
Result	:	All exposed fish died at 560 and 1000 mg/L within 24 hours. No fish died at 100 and 180 mg/L. At 320mg/L ten fish died in the first 24 hours, and by 96 hours 14 had died. Only two fish at 320mg/L appeared normal at the end of the test. The LC50 was calculated to be 280 mg/L and the NOEC was 180 mg/L.
Reliability	:	(1) valid without restriction

04.03.2002 (11)

Type	:	static
Species	:	Oncorhynchus mykiss (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no
LC50	:	c = 410
Method	:	other
Year	:	1973

GLP : no
Test substance : no data
Reliability : (2) valid with restrictions
26.11.2002 (12)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type : static
Species : Daphnia magna (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
Analytical monitoring : no
NOEC : m = 56
EC50 : c = 80
Method : EPA OPP 72-2
Year : 1989
GLP : yes
Test substance : other TS:99.69% pure
Method : This static study was conducted in 250 mL glass beakers containing 200 mL of daphnid culture/test water. All test vessels were covered loosely with petri dishes to minimize evaporation. Solutions of 0, 10, 18, 32, 56, 100, and 180 mg/L were prepared in duplicate by weighing the appropriate amount of test article into test vessels. Ten daphnia (first instar <24 hours old) were placed in each vessel to give a total of 20 test organisms per concentration.
Result : Immobility was observed only at 100 and 180 mg/L. The 48-hour EC50 was calculated to be 80 mg/L.
Reliability : (1) valid without restriction
07.12.2001 (13)

Type : flow through
Species : Mysidopsis bahia (Crustacea)
Exposure period : 96 hour(s)
Unit : mg/l
Analytical monitoring : yes
EC0 : m = 95.5
Method : EPA OPP 72-3
Year : 1991
GLP : yes
Test substance : other TS: 99.69% pure
Method : Saltwater mysids were exposed to a geometric series of 5 test concentrations, a solvent control, and a negative (salt water) control. Nominal test concentrations used in the study were 13.0, 21.6, 36.0, 60.0, and 100 mg of TRIS NITRO per liter based on the results of a range-finding study. Based on the analyses of each dosage level at the beginning and end of the exposure period the mean measured test concentrations were 11.9, 22.6, 35.8, 54.3, and 95.5 mg/L. Ten shimp were placed in each chamber. Two chambers at each concentration were utilized so that a total of 20 shrimp were exposed at each dose. Observation of mortality, as well as treatment related effects were made at 17, 24, 48, 72, and 96 hours. The LC50 was calculated based on mortalities observed at various intervals of time.
Result : No mortality was observed in this study. The 96-hour EC50 is >95.5 mg/L, which is also an EC0 for this study.
Reliability : (1) valid without restriction
26.11.2002 (14)

Type : flow through
Species : other aquatic mollusc: Crassostrea virginica
Exposure period : 96 hour(s)

Unit	:	mg/l
Analytical monitoring	:	yes
NOEC	:	m = 1.3
EC50	:	m = 27.8
Method	:	EPA OTS 797.1800
Year	:	1991
GLP	:	yes
Test substance	:	other TS: 99.69% pure
Method	:	Oysters were exposed to a geometric series of five test concentrations, a negative (unfiltered saltwater) control, and a solvent control for a period of 96 hours. Nominal test concentrations selected for the study were 1.3, 3.2, 8.0, 20, and 50 mg of TRIS NITRO/L. The two lowest concentrations were below the limit of detection of the analytical method. However, the mean measured concentrations for the other test solutions were 9.2, 18.6, and 52.4 mg/L which were in close agreement to the nominal concentrations. Immediately prior to test initiation, 2-3 mm of the shell periphery were removed from each oyster using a motorized grinder. Twenty oysters were placed in chambers containing each test concentration. The flow of unfiltered salt water into each chamber was approximately 1 L per oyster per hour. Algal cells were provided to the solutions to maximize growth during the test. Measurement of shell deposition for each oyster was made at 96 hours and used to calculate the EC50 for inhibition of shell deposition.
Result	:	Shell deposition was inhibited at all TRIS NITRO concentrations except 1.3 mg/L. Shell deposition for the negative and sovent controls was ca. 4 mm in 96 hours. Inhibition in deposition varied from 6% at 3.2 mg/L to 71.4 % at 50 mg/L. The 96-hour EC50 was calculated to be 27.8 mg/L.
Reliability	:	(1) valid without restriction

07.12.2001 (15)

10.08.2001

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species	:	Selenastrum capricornutum (Algae)
Endpoint	:	growth rate
Exposure period	:	96 hour(s)
Unit	:	mg/l
Analytical monitoring	:	yes
NOEC	:	c = .269
EC50	:	c = .656
Method	:	OECD Guide-line 201 "Algae, Growth Inhibition Test"
Year	:	2002
GLP	:	yes
Test substance	:	other TS: 9.69% pure
Method	:	Tris Nitro was added to 250 mL erlenmeyer flasks containing approximately 10,000 cells/mL of Selenastrum capricornutum. The measured levels of TRIS NITRO in the flasks was 0, 0.017, 0.042, 0.109, 0.269, 0.654, 1.61, and 4.50 mg/L. After 96 hours of exposure at 23.9 C, algal cell densities were determined by electron particle counting using a Coulter Multisizer.
Result	:	The 3- and 4-day growth rate EC50 values, based on mean analyzed concentrations, were both greater than 4.50 mg/L. The 3- and 4-day percent inhibition EC50 values, based on mean analyzed concentrations, were 0.479 mg/L and 0.566 mg/L respectively The 3- and 4-day cell density EC25 values, based on mean analyzed concentrations, were 0.127 mg/L and 0.177 mg/L respectively. The 3- and 4-day cell density EC50 values, based on mean analyzed concentrations, were 0.468 mg/L and 0.651 mg/L respectively. The statistically derived 3- and 4-day no-observed-effect concentrations (alpha=0.05), based on mean analyzed concentrations, were both 0.269

mg/L.

Reliability : (1) valid without restriction
20.06.2002 (16)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

4.6.1 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO OTHER NON-MAMM. TERRESTRIAL SPECIES

Species	:	Anas platyrhynchas (avian)
Endpoint	:	mortality
Exposure period	:	5 day
Unit	:	ppm
Method	:	
Year	:	1978
GLP	:	no
Test substance	:	other TS: 50% in water
Method	:	Eight ducklings, 15 days old, were placed randomly into each of 9 separate pens. Groups 1,2, and 3 were control animals. Group 4 received a diet containing 80,000 ppm of TRIS NITRO 50%. The diets of the remaining groups contained the following levels of TRIS NITRO 50%: Group 5--40,000; Group 6--20,000; Group 7--10,000; Group 8--5,000;Group 9--2500 ppm. Following feeding for 5 days ad libitum with the treated feed, all animals were placed on the standard diet for a 3-day post treatment period. Weights were measured at initiation, after 5 days, and at termination (8 days). Feed consumption was monitored throughout the study and each pen was observed daily for signs of toxic effects and mortality.
Result	:	No mortality attributable to the test substance was observed during the initial 8 day feeding period. Within 24 hours of placement on the treated diets, all ducks at 80,000 and 40,000 ppm had a lack of coordination with difficulty in walking and the heads swinging from side to side. Occasionally, the duck's heads would refect backward until its skull would be resting on the back and the duck would walk backwards. At 20,000 ppm, these same symptoms appeared 96 hours after start in three ducks only. All ducks were normal at all other dosages. Because of the above symptoms, the study was extended for twelve additional days. By day 15 only 3 ducks at 80,000 ppm and one at 40,000 ppm were still affected. All ducks at 20,000 ppm appreared normal on day 14. Histopathological examination of the brains of those animals still affected showed focal loss of Purkinje cells of the cerebellum and edema in in cerebellum. The 8-day dietary LC50 was greater than 80,000 ppm in the diet.
Reliability	:	(2) valid with restrictions

26.11.2002 (17)

Species	:	Colinnus virginianus (avian)
Endpoint	:	mortality
Exposure period	:	
Unit	:	
Method	:	
Year	:	1978
GLP	:	no
Test substance	:	other TS: 50% in water
Method	:	Bobwhite quail, 10 days old, were placed randomly into 5 separate pens of 10 birds each. Groups 1,and 2 were control animals. Group 3 received a diet containing 5,000 ppm of TRIS NITRO 50%. The diets of the remaining groups contained the following levels of TRIS NITRO 50%: Group 4--2500 ppm; Group 5--1250 ppm. Following a 5 day ad libitum period with the treated feed, all animals were placed on the standard diet for a 3-day post treatment period. Weights were measured at initiation, after 5 days, and at termination (8 days). Feed consumption was monitored throughout the study and each pen was observed daily for signs of toxic effects and mortality.
Result	:	No mortality occurred during this study. Feed consumption and body weight gain were normal for all groups. No signs of toxicity or symptoms suggestive of toxicity were observed. The dietary LC50 was greater than 5000 ppm in the diet.
Reliability	:	(2) valid with restrictions

07.12.2001 (18)

13.08.2001

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50
Species	:	rat
Strain	:	other: Cox SD
Sex	:	male/female
Number of animals	:	
Vehicle	:	water
Value	:	= 990 - 1000 mg/kg bw
Method	:	other: IMC Toxicology Laboratory Protocol
Year	:	1979
GLP	:	no
Test substance	:	other TS
Method	:	This study was conducted using the IMC Toxicology Laboratory Standard protocol which is similar to EPA guidelines. Ten male and ten female rats were used at each dose level. Doses were at 0, 700, 900, 1300, 1600, and 2200 mg/kg body weight. The animals were weighed on days 1, 7, and 14 of the study. After 14 days the surviving rats were sacrificed and examined for gross pathology.
Result	:	One male rat in the 900 mg/kg group and two male rats in the 1300 mg/kg group died. Almost equal numbers of both sexes died in the 1600 mg/kg (5 total) and 2200 mg/kg (14 total) groups. The weight gain for all dosed animals was the same as was that of the controls except for that of the high dose males. At 1300 mg/kg and higher, dosed animals developed tremors within 24 hours and survivors returned to normal within 2 to 6 days. Animals that died had pale livers and spleens.
Test substance	:	53.1% in water
Conclusion	:	The LD50 for this substance in solution was 1860 to 1890 mg/kg body weight. Based on the concentration of this aqueous form of the test article the LD50 of the active ingredient is 990 to 1000 mg/kg body weight.
Reliability	:	(2) valid with restrictions

04.03.2002 (19)

5.1.2 ACUTE INHALATION TOXICITY

Type	:	LC50
Species	:	rat
Strain	:	Sprague-Dawley
Sex	:	male/female
Number of animals	:	10
Vehicle	:	other: none
Exposure time	:	4 hour(s)
Value	:	> 2.12 mg/l
Method	:	EPA OPP 81-3
Year	:	1995
GLP	:	yes
Test substance	:	other TS: >99.6%
Remark	:	Exposure was to a dust of test article ground to a fine particle size. The gravimetric chamber concentration was 2.12 mg/L. The mass median aerodynamic diameter was estimated to be 3.8 microns based on graphic analysis of the particle size distribution as measured with an Anderson Cascade Impactor. After whole-body exposure the rats were observed for 14 days prior to terminal sacrifice and necropsy.
Result	:	One male and one female died within four days of exposure. During the first hour of exposure, irregular respiration, hunched posture, and hypoactivity were noted. Within several days of the exposure, facial staining, piloerection, red nasal discharge and reduced feed consumption

and fecal volume were observed. All surviving rats recovered from the above conditions by day 6 and gained weight over the 14-day observation period. Gross necropsy of the decedents revealed discoloration of the lungs, liver, gastro-intestinal tract, gaseous distention of the stomach and rigor mortis. Gross necropsy findings at terminal sacrifice were unremarkable.

Reliability : (1) valid without restriction
26.11.2002 (20)

Type	:	LC50
Species	:	rat
Strain	:	Sprague-Dawley
Sex	:	male/female
Number of animals	:	10
Vehicle	:	other: none
Exposure time	:	4 hour(s)
Value	:	2.4 mg/l
Method	:	EPA OPP 81-3
Year	:	1980
GLP	:	yes
Test substance	:	other TS: 54.82% in water
Method	:	Groups of Sprague-Dawley rats (5 males and 5 females in each) were exposed for 4 hours to TRIS NITRO concentrate at actual measured concentrations of 4.7, 2.7, 1.9, 1.8, 0.67, and 0 mg/L. The aerosol had an equivalent aerodynamic diameter of 2.4 micro meters with a geometric standard deviation of 2.0. After exposure, the rats were observed for 14 days prior to sacrifice and necropsy.
Result	:	Mortality for the various groups was as follows: 4.7 mg/L - 80%; 2.7 mg/L - 70%; 1.9 mg/L - 50%; 1.8 mg/L - 20%; 0.67 mg/L and controls - 0. Mortality in the various dose groups occurred within the first 6 days post-exposure. During exposure nasal discharge was observed in almost all rats dosed at 2.7 mg/L or greater. At 1.8 mg/L, half of the animals exhibited nasal discharge; this effect seemed to be compound related. Four animals at 4.7 mg/L, two at 2.7 mg/L, and 3 at 0.67 mg/L exhibited dyspnea. During the post-exposure period, the following clinical signs were noted in both males and females exposed: dyspnea, red matter on the face, ataxia, and death. The incidence of these findings began with the 1.9 mg/L group and increased with dose. The only compound related finding in the histopathalogical examination were in the kidneys. All treatment groups except for low dose group (0.67 mg/L) were found to exhibit tubular nephrosis. Very slight to moderate nephritis, nephrolithiasis, papillitis, and pyelitis were found in all treatment groups. The severity of these effects was slightest for the low dose group.

Reliability : (1) valid without restriction
26.11.2002 (21)

5.1.3 ACUTE DERMAL TOXICITY

Type	:	LD0
Species	:	rat
Strain	:	Sprague-Dawley
Sex	:	male/female
Number of animals	:	10
Vehicle	:	water
Value	:	> 5000 mg/kg bw
Method	:	EPA OPP 81-2

Year	:	1998
GLP	:	yes
Test substance	:	other TS: >99.6%
Method	:	Five thousand milligrams of test substance per kilogram body weight was moistened to a dry paste with distilled water and applied to the skin of 10 healthy rats for 24 hours. The treated areas were covered with a gauze pad during exposure after which residual material was removed with a damp towel. The animals were observed for signs of gross toxicty and behavioral changes at least once a day for 14 days. Bodyweights were recorded prior to exposure and on days 7 and 14. Necropsies were performed on all animals at terminal sacrifice.
Result	:	All animals survived, gained weight, and appeared active and healthy. There were no signs of gross toxicity, skin irritation, adverse clinical effects. Gross necropsy findings at terminal sacrifice were generally unremarkable.
Reliability	:	(1) valid without restriction

26.11.2002 (22)

Type	:	LD0
Species	:	rabbit
Strain	:	New Zealand white
Sex	:	male/female
Number of animals	:	10
Vehicle	:	physiol. saline
Value	:	> 2000 mg/kg bw
Method	:	other: IMC Toxicology Protocol No. 5
Year	:	1981
GLP	:	no
Test substance	:	other TS: >99%
Method	:	Abdomens of ten rabbits (5 of each sex) were shaved and then abraded with a blunt syringe. The prepared area was then spread with enough finely ground test article to provide a dose of 2000 mg/kg bodyweight. The test article was wet with saline to form a paste which was then covered and left on the skin for 24 hours after which the cover and test material were removed. Animals were then held for 14 days before sacrifice and necropsy.
Result	:	There were no deaths, all rabbits gained weight normally, and exhibited no effects attributable to treatment.
Reliability	:	(2) valid with restrictions

19.07.2001 (23)

20.07.2001

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.2.1 SKIN IRRITATION

Species	:	rabbit
Concentration	:	undiluted
Exposure	:	Semiocclusive
Exposure time	:	4 hour(s)
Number of animals	:	6
PDII	:	0
Result	:	slightly irritating
EC classification	:	not irritating
Method	:	EPA OPP 81-5
Year	:	1998
GLP	:	yes
Test substance	:	other TS: >99.6%

Method	:	Five-tenths of a gram of test substance was moistened to a dry paste with distilled water and applied to the skin of 6 healthy rabbits (3 of each sex) for 4 hours. Following exposure, dermal irritation was evaluated by the method of Draize et al at 1, 24, 48, and 72 hours.
Result	:	Draize scores at all observation times were zero. Thus the material was not irritating to the skin.
Reliability	:	(1) valid without restriction

26.11.2002 (24)

5.2.2 EYE IRRITATION

Species	:	rabbit
Concentration	:	undiluted
Dose	:	.1 other: gm
Exposure Time	:	24 hour(s)
Comment	:	other: Six rabbits treated and left alone; six others had eye rinsed after 20-30 seconds.
Number of animals	:	12
Result	:	not irritating
EC classification	:	not irritating
Method	:	other: IMC Toxicity Laboratory protocol No. 2
Year	:	1982
GLP	:	no
Test substance	:	other TS: > 95%
Method	:	One-tenth of a gram of finely ground test material was placed in the left eye of 12 rabbits. The eyes of 6 rabbits were left untreated and the eyes of the other 6 were irrigated with lukewarm tap water after 20-30 seconds. At 24 hours and on the 7th day, a drop of sodium fluorescein was placed on the cornea of each treated eye and excess was flushed away with sterile saline. Eyes were examined at 24, 48, 72 hours and at 7 days.
Result	:	No lesions were observed following fluorescein treatment. At 24 hours, the average score for the unwashed eyes was 2.0 (redness of the conjuctivae). At 48 hours the average score had dropped to 0.3. Scores at 72 hours and later were zero. Washed eyes exhibited even lower scores: 1.3 at 24 hours and zero thereafter.
Reliability	:	(2) valid with restrictions

04.03.2002 (25)

5.3 SENSITIZATION

Type	:	Guinea pig maximization test
Species	:	guinea pig
Concentration	:	Induction 50 % active substance intracutaneous Induction 25 % active substance occlusive epicutaneous Challenge 25 % active substance occlusive epicutaneous
Number of animals	:	24
Vehicle	:	water
Result	:	not sensitizing
Classification	:	not sensitizing
Method	:	OECD Guide-line 406 "Skin Sensitization"
Year	:	1997
GLP	:	yes
Test substance	:	other TS: 99.69% pure
Method	:	The application sites of 24 Guinea pigs were prepared by clipping a 5 x 7 cm area of skin on the shoulder area free of hair (on days 0 and 7). On day 23, a 4 x 4 cm area on the flank was so clipped. Irritancy was determined in 5 animals total. Intradermal treatment caused

irritation at 50% concentration and topical treatment caused irritation at 70% (but not at 50%).

Induction thus was conducted intradermally on day 0 with:
1. 0.1mL Freund's Complete Adjuvant (FCA) 1:1 w water
2. 0.1mL test article
3. 0.1mL test article 1:1 w FCa

The test article was 50% TRIS NITRO or 0.1% DNCB (dinitrochlorobenzene) in 95% EtOH as the positive control. Water was the negative control. On day 7 the induction phase continued with a topical application of these same solutions which was left in place for 48 hours.

Challenge was conducted on day 23 with either 25% TRIS NITRO, water, or 0.1% DNCB in EtOH under occlusive patch. After 24 hours exposure the patches were removed and the treated area were scored for erythema and edema after 24 , 48 and 72 hours.

Result : There were no clinical signs of toxicity during the test and test animals gained weight in a manner comparable to that of the controls. The scores for all ten animals exposed to TRIS NITRO and the five the negative control (water) animals were zero for both erythema and edema at all evaluations times. All the animals exposed to DNCB exhibited irritation at all evaluations.

TRIS NITRO was nonsensitizing under conditions of this test.

Reliability : (1) valid without restriction
04.03.2002 (26)

Type : other: Intradermal method of Landsteiner and Jacobs
Species : guinea pig
Number of animals : 10
Vehicle : water
Result : not sensitizing
Classification : not sensitizing
Method : other: see J. Exper. Med., Vol.61:643-656 (1935).
Year : 1980
GLP : no
Test substance : other TS: 56.78% in water
Method : Thirty male guinea pigs weighing 250-300 g were divided into three groups of 10 each. The animals backs and flanks were shaved free of hair. Group I was intradermally injected with 0.05 mL of 0.5% solution of active TRIS NITRO in distilled water. Group II (positive control) was similarly injected with 0.05 mL of 0.3% DNCB alcoholic solution (4%). Group III (negative control) was injected with 0.05 mL of saline. After 24 hours the injected sites were scored for erythema and edema. At 48 hours, the intradermal injection procedure was repeated for each group with 0.1 mL of each solution 3 times a week for 3 weeks until a total of 10 injections had been made.

After the last injection, the animals were allowed to rest for 2 weeks. On the first day of the following week, animals in each group were challenged intradermally with 0.1 mL of their respective solution. In addition, Group III animals also were challenged with the TRIS NITRO and DNCB solutions. At the end of 24 and 48 hours, the injected sites were scored for inflammatory skin reactions according to the system of Draize.

Result : During the induction phase or at the challenge, none of the treated (Group I) or the control animals (Group III) showed any skin reactions. The Group II animals showed mild to severe skin reactions during the induction phase and at the challenge.

Reliability : (2) valid with restrictions
08.08.2001 (27)

Type	:	Guinea pig maximization test
Species	:	guinea pig
Concentration	:	Induction 10 % intracutaneous Induction undiluted occlusive epicutaneous Challenge undiluted occlusive epicutaneous
Number of animals	:	24
Vehicle	:	water
Result	:	sensitizing
Classification	:	sensitizing
Method	:	OECD Guide-line 406 "Skin Sensitization"
Year	:	1998
GLP	:	yes
Test substance	:	other TS: 40% in water as manufactured
Method	:	Method followed was the same as described previously except that no concurrent positive control animals were utilized. Intradermal induction was conducted with 0.1 mL of test article diluted 1:9 with water. Topical induction was with undiluted test article and challenge was conducted with undiluted test article and with 75% test article. Topical application was by a 40 mm x 20 mm filter paper saturated with solution.
Remark	:	The positive result in this test was a result of the 0.7% of free formaldehyde present in this product as manufactured in Europe. Unlike the crystalline, pure grade of TRIS NITRO, 40% TRIS NITRO contains more than 0.2% of free formaldehyde. Also, the degree of reaction was not unlike that observed in the topical induction phase of the where undiluted test material caused similar reactions at 24 hours post-exposure.
Result	:	The test material produced an 80% sensitization rate and was classified as a strong sensitizer.
Reliability	:	(2) valid with restrictions

06.12.2002 (28)

5.4 REPEATED DOSE TOXICITY

Species	:	rat
Sex	:	male/female
Strain	:	other: Crl:CD BR
Route of admin.	:	dermal
Exposure period	:	Six hours per day, five days per week for 13 weeks.
Frequency of treatment	:	Daily except weekends
Post obs. period	:	None
Doses	:	0, 250, 500, and 1000 mg/kg/day
Control group	:	yes, concurrent vehicle
NOAEL	:	> 1000 mg/kg bw
Method	:	EPA OPP 82-2
Year	:	1989
GLP	:	yes
Test substance	:	other TS:99.69% pure
Method	:	An area of approximately 20-25% of the surface area of the rats was clipped free of hair 24 hours before the first application to the skin. The test material was applied as a paste wet with water (0.05, 0.1, and0.2 mL for the 250, 500, and 1000 mg/kg/day groups respectively). The test material was spread over 6% of the body area with the 250 mg/kg group and over 9% of the body area with the 500 and 1000 mg/kg groups. The control group received deionized water spread over 9-10% of the body area. Animals were dosed daily and the exposed areas covered with a gauze binder secured with tape. After six hours the gauze was removed and the exposed areas washed. All rats wore Elizabethan collars to prevent ingestion of the test material.

Animals were inspected at least twice daily for mortality and overt signs of toxicity. Individual body weights and food consumption were measured weekly beginning one week before initiation of dosing. Ophthalmological examinations were conducted and hematology and clinical chemistry were checked prior to intiation of dosing and just prior to terminal sacrifice. Urinalysis was conducted on all rats during week 12 of the study. All animals were subject to gross and microscopic pathological examination at termination of the study.

Remark : Reproductive Toxicity:
Males- At sacrifice, there was no significant difference in the weight of the testes of the high dose rats in comparison to the weight of the testes of the controls; neither was there significant difference in their relative weight versus body weight. Histopathologic findings for all animals examined (i.e. controls and high dose rats) were that the testes of all animals were "within normal limits".

Females- Again, the weights (absolute and relative) of the ovaries of all animals were not significantly different. The only histopathologic finding was a minimal cyst in the ovary of one high-dose rat.

Result : The only mortality during the course of the study was for one control female which died in week 4. This death was attributed to an injury sustained several weeks prior to death.
No clinical signs of toxicity were observed. Although the application sites were discolored yellow throughout the study, microscopic examination of skin samples from the control and high dose group animals did not reveal any adverse effects related to exposure. The test material was essentially nonirritating. No compound related adverse effects were noted on body weights or body weight gain, food consumption, hematology or serum chemistry parameters, urinalysis parameters, absolute or relative organ weights, ophthalmoscopic findings, lesions at gross necropsy, or nonneoplastic histologic lesions.

Reliability : (1) valid without restriction
04.03.2002 (29)

5.5 GENETIC TOXICITY 'IN VITRO'

Type : Ames test
System of testing : Tested in Salmonella typhimurium, TA98, TA100, TA1535, TA1537, and TA1538.
Concentration : 0.1, 0.2, 0.3, 0.5, and 1 mg/plate
Cycotoxic conc. : 2 mg/plate
Metabolic activation : with and without
Result : negative
Method : EPA OTS 798.5265
Year : 1988
GLP : yes
Test substance : other TS: >99.6%
Reliability : (1) valid without restriction
31.07.2001 (30)

Type : Chromosomal aberration test
System of testing : Chinese Hamster Ovary
Concentration : 0.125, 0.25, 0.5, 1.0, and 2.0 mg/mL
Cycotoxic conc. : 0.1 mg/mL without S9 and 1 mg/mL with S9
Metabolic activation : with and without
Result : negative
Method : EPA OTS 798.5375
Year : 1991
GLP : yes
Test substance : other TS: 99.69%

Reliability	:	(1) valid without restriction
06.08.2001		(31)
Type	:	Unscheduled DNA synthesis
System of testing	:	
Concentration	:	Tested at 10, 50, 100, and 500 micrograms per mL as well as 1 and 10 mg/mL.
Cycotoxic conc.	:	In the preliminary test, there was no apparent cytotoxicity at any dosage up to 10 mg/mL.
Metabolic activation	:	no data
Result	:	negative
Method	:	EPA OTS 798.5500
Year	:	1991
GLP	:	yes
Test substance	:	other TS: >99.6%
Reliability	:	(1) valid without restriction
31.07.2001		(32)
Type	:	Mouse lymphoma assay
System of testing	:	Forward mutation of the TK+/- strain of L5178Y mouse lymphoma cells exposed to various concentrations of the test substance.
Concentration	:	5 to 80 micrograms/mL without S9 and 5 to 160 micrograms/mL with S9
Cycotoxic conc.	:	47.2 micrograms/mL withoyt S9 and 188.8 micrograms/mL with S9
Metabolic activation	:	with and without
Result	:	positive
Method	:	OECD Guide-line 476 "Genetic Toxicology: In vitro Mammalian Cell Gene Mutation Tests"
Year	:	2002
GLP	:	yes
Test substance	:	other TS: 99.69% pure
Reliability	:	(1) valid without restriction
20.06.2002		(33)

20.07.2001

5.6 GENETIC TOXICITY ‘IN VIVO‘

Type	:	Unscheduled DNA synthesis
Species	:	rat
Sex	:	male/female
Strain	:	Fischer 344
Route of admin.	:	gavage
Exposure period	:	2 to 4 or 14 to 16 hours after dosing
Doses	:	800 to 1200 mg/kg bw in water
Result	:	negative
Method	:	other: OECD Guideline 486
Year	:	2002
GLP	:	yes
Test substance	:	other TS:99.69% pure
Reliability	:	(1) valid without restriction
20.06.2002		(34)
Type	:	Micronucleus assay
Species	:	mouse
Sex	:	male/female
Strain	:	CD-1
Route of admin.	:	gavage
Exposure period	:	single gavage doses were given on two consecutive days and animals were sacrificed 24 hours after the second dose

Doses	:	0, 500, 1000, and 2000 mg/kg bw for males and 0, 500, 1000, and 1500 mg/kg bw for females
Result	:	negative
Method	:	OECD Guide-line 474 "Genetic Toxicology: Micronucleus Test"
Year	:	2002
GLP	:	yes
Test substance	:	other TS: 99.69% pure
Reliability	:	(1) valid without restriction

20.06.2002 (35)

5.7 CARCINOGENITY

Species	:	
Sex	:	
Strain	:	
Route of admin.	:	
Exposure period	:	
Frequency of treatment	:	
Post. obs. period	:	
Doses	:	
Result	:	
Control group	:	
Method	:	
Year	:	
GLP	:	
Test substance	:	no data

11.06.2001

5.8 TOXICITY TO REPRODUCTION

5.9 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species	:	rat
Sex	:	female
Strain	:	Sprague-Dawley
Route of admin.	:	gavage
Exposure period	:	Days 6 through 15 of the gestation period.
Frequency of treatment	:	Single dose daily.
Duration of test	:	
Doses	:	0, 50, 375, and 750 mg/kg/day in 10 mL/kg of water
Control group	:	yes, concurrent vehicle
NOAEL Maternalt.	:	= 375 mg/kg bw
NOAEL Teratogen	:	= 50 mg/kg bw
LOAEL Maternal Toxicity	:	= 750 mg/kg bw
LOAEL Teratogenicity	:	= 375 mg/kg bw
Method	:	EPA OPP 83-3
Year	:	1989
GLP	:	yes
Test substance	:	other TS: 99.69% pure
Method	:	Twenty-five females were mated 1:1 with males of the same strain and source. The presence of a copulatory plug was positive evidence of mating, and the day it was found was designated day 0 of gestation. All doses were in a volume of 10 m/kg bw/day as a single dose by gavage

based on the most recent recorded body weight. Dosing was conducted on days 6 through 15 of gestation. Dosing solutions were analyzed to confirm concentrations.

The dams were checked for mortality and clinical signs of toxicity at least twice a day. Maternal body weights were recorded days 0, 6, 9, 12, 16, and 20 of gestation. On day 20 of gestation, all surviving dams were sacrificed, and litters were delivered by cesarean section.

The females were examined for a number of parameters related to pregnancy including the number corpora lutea, live and dead fetuses, and early and late resorptions. The fetuses were weighed and sexed and examined for external abnormalities. Visceral abnormalities from one-half of the fetuses were determined and skeletal abnormalities were determined for the other half of the litters.

Result : Maternal Toxicity:
High mortality(7 of 25 dams died between days 9 and 11 of gestation), reduced body weight gain during dosing, and clinical signs (e.g. tremors and head bobbing) were observed at 750 mg/kg/day. Similar effects were not observed at lower doses.

Developmental Toxicity:

Deaths/resorptions - A significant, compound related, increase in the number of resorptions/dam was observed at 375 mg/kg/day. No fetal mortality was observed.

Altered growth - A statistically significant reduction in fetal body weight was observed at 750 mg/kg/day.

Developmental Anomalies - A nonsignificant increase in the incidence of 7th cervical rib was observed at 375 mg/kg/day. All other observations were within the range of historical findings.

Malformations - A nonsignificant increase in the incidence of omphalocele was observed at 750 mg/kg/day. All other observed incidences were within the range of historical controls. Therefore, TRIS NITRO was not teratogenic in rats.

Reliability : (1) valid without restriction
06.12.2002 (36)

Species : rabbit
Sex : female
Strain : New Zealand white
Route of admin. : gavage
Exposure period : Days 7 through 19 of gestation.
Frequency of treatment : Once each day of the exposure period.
Duration of test : Twenty-nine days
Doses : 10, 30, and 75 mg/kg/day in a volume of 1 mL/kg bw.
Control group : yes, concurrent vehicle
NOAEL Maternalt. : = 30 mg/kg bw
NOAEL Teratogen : = 75 mg/kg bw
Method : EPA OPP 83-3
Year : 1992
GLP : yes
Test substance : other TS: 99.69% pure
Method : Three groups of twenty artficially inseminated New Zealand white Rabbits were dosed by gavage once daily with 1 mL/kg bw of deionized water containing TRIS NITRO at levels of 10, 30, and 75 mg/kg bw. Dosing was conducted on days 7 through 19 of gestation. A concurrent control group of 20 rabbits received water only. All females were observed at least twice

daily for mortality, appearance, and behavior. Body weights were recorded at appropriate intervals and food consumption was recorded daily (gestation days 0-29). On gestation day 29 the rabbits were euthanized and subjected to Cesarean section. Mean gravid uterine weights and net body weight changes were calculated for each group. The fetuses were weighed, sexed, and examined for external, skeletal, soft tissue malformations, and developmental variations.

Result : At a dose level of 75 mg/kg/day, a group mean body weight loss was observed during gestation days 7-10 (statistically significant at $p<0.05$) and mean body weight gain was inhibited during the overall treatment period (gestation days 7-19). In this same group, food consumption was inhibited throughout the treatment period. Body weight gain and food consumption were not adversely affected in the 10 and 30 mg/kg/day groups.

Fetal numbers, intrauterine growth, and survival were unaffected at all dose levels. No treatment-related fetal malformations or variations were observed. No teratogenic effect was observed in this study.

Reliability : (1) valid without restriction
07.12.2001 (37)

Species : rat
Sex : female
Strain : Sprague-Dawley
Route of admin. : gavage
Exposure period : Days 6 trough 15 of gestation
Frequency of treatment : once daily
Duration of test :
Doses : 250, 500, 750, 1000, and 1500 mg/kg/day
Control group : yes, concurrent vehicle
NOAEL Maternalt. : = 500 mg/kg bw
NOAEL Teratogen : = 750 mg/kg bw
Method : EPA OPP 83-3
Year : 1988
GLP : yes
Test substance : other TS: 99.69% pure
Method : Five groups of five bred rats were used at each dose in this range-finding study.

Result : One dam died in the 1000 mg/kg group and 3 dams died in the 1500 mg/kg group during treatment. Decreased body weight was observed at the 750 mg/kg dose. No indication of prenatal toxicity was apparent upon evaluation of the gestation day 20 uterine examination data.

Reliability : (1) valid without restriction
06.12.2002 (38)

Species : rabbit
Sex : female
Strain : New Zealand white
Route of admin. : gavage
Exposure period : days 7 though 19 of gestation
Frequency of treatment : daily during gestation
Duration of test :
Doses : 5, 10, 20, 40, and 80 mg/kg/day
Control group : yes, concurrent vehicle
NOAEL Maternalt. : = 40 mg/kg bw
NOAEL Teratogen : = 80 - mg/kg bw
Method : EPA OPP 83-3
Year : 1992
GLP : yes
Test substance : other TS: 99.69% pure
Method : Six groups of seven artificially inseminated rabbits were used at each dose.

Result	:	No dams died in any of the groups. Maternal body weight gain and food consumption were depressed at the 80 mg/kg/day dose level. No effects on the intrauterine growth and survival were observed at any dose level. Neither were any external malformations or variations noted in fetuses.
Reliability	:	(1) valid without restriction

06.12.2002 (39)

5.10 OTHER RELEVANT INFORMATION

5.11 EXPERIENCE WITH HUMAN EXPOSURE

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7.1 END POINT SUMMARY

7.2 HAZARD SUMMARY

7.3 RISK ASSESSMENT