201-14881

ARCADIS

Infrastructure, buildings, environment, communications

ARCADIS G&M, Inc.
4915 Prospectus Drive
Suite F
Durham
North Carolina 27713
Tel 919 544 4535
Fax 919 544 5690
www.arcadis-us.com

RISK & ASSSOCIATED SERVICES

Mr. Michael Leavitt
U.S. Environmental Protection Agency
P.O. Box 1473
Merrifield, VA 22116

Attn: Chemical Right-to-Know Program

Subject:
Submission of Quadrol (CAS No. 102-60-3) Documents via Electronic Submission to oppt.ncic@epa.gov

Date:
December 8, 2003

Dear Administrator Leavitt:

On behalf of BASF Corporation, we are submitting the attached test plan and robust summaries for Quadrol (CAS No. 102-60-3); Registration Number . This submission, made under the U.S. EPA's High Production Volume Chemical Challenge Program, consists of a test plan for Quadrol and robust summaries for both Quadrol and a surrogate compound, triisopropanolamine.

The documents are being submitted in electronic format (Adobe Acrobat pdf files). If you have difficulty with the electronic submission or require additional information, please contact me, as BASF's representative, by phone (919-544-4535) or e-mail (jstaveley@arcadis-us.com).

Sincerely,

ARCADIS G&M, Inc.

Contact:
Jane Staveley

Phone:
919-544-4535

Email:
jstaveley@arcadis-us.com

Our ref:
RN006015.0001

Jane P. Staveley
Principal Environmental Scientist

Attachments:
Test Plan
Robust Summaries – Quadrol
Robust Summaries - Triisopropanolamine

Copies:
Dr. Christopher Bradlee, BASF Corp.

201-14881

High Production Volume Chemical Challenge Program

Robust Summaries and Test Plan for Quadrol (CAS No. 102-60-3)

Submitted by:

ARCADIS G&M, Inc.
4915 Prospectus Drive
Durham, NC 27713

On behalf of:

BASF Corporation
3000 Continental Drive
Mt. Olive, NJ 07828-1234

Date:

December 8, 2003

Table of Contents

1.0 Executive Summary

Quadrol (CAS No. 102-60-3) is a 14-carbon symmetrically substituted ethylenediamine. It is a white viscous liquid with a mild fishy odor and low volatility. It is miscible with water and highly soluble in other polar organic solvents. Quadrol is used as an intermediate and catalyst in chemical reactions, as a complexing and chelating agent, and as a humectant, plasticizer, surfactant solubilizer, and viscosity control agent.

The available data for Quadrol (measured, estimated, and from references) were supplemented with data on a structurally-related surrogate compound, triisopropanolamine (CAS No. 122-20-3). In the environment, Quadrol is expected to react rapidly with atmospheric hydroxyl radicals, while hydrolysis is not an important fate process. Due to its low octanol-water partition coefficient, Quadrol is not expected to bioaccumulate. Rather, partitioning would be primarily to water and soil compartments. Quadrol is expected to be biodegradable, based upon estimations as well as the available data for triisopropanolamine.

The available pharmacokinetics data indicate that Quadrol is very poorly absorbed in rats following oral dosing (<2%), is distributed according to a one-compartment model, and is rapidly eliminated by a first order process. After oral dosing, the small fraction of Quadrol that is absorbed is rapidly excreted in the urine almost entirely (92-96%) unchanged.

The toxicity of Quadrol to aquatic species is measured or estimated to be low (for fish and invertebrates) to moderate (for algae). Toxicity to mammals is low based upon the oral LD50 for rats (11,200 mg/kg b.w.) and the NOAEL for repeated dose toxicity of 600 – 900 mg/kg/day in a three month feeding study. *In vitro* tests have not demonstrated any mutagenicity of Quadrol, and it is not expected to be clastogenic based upon *in vivo* tests with triisopropanolamine. Triisopropanolamine was not embryotoxic, fetotoxic, or teratogenic at maternal doses up to 1,000 mg/kg b.w./day; these data indicate that Quadrol is not expected to have developmental effects either. Data from a 2-year study on triisopropanolamine indicate that reproductive organs were not affected.

The overall conclusions and recommendations are that information is adequate for all HPV data elements and that no additional testing is required. This information is summarized in Table 1.

Table 1. Summary of Test Plan for Quadrol

SIDS Level I Endpoint	Quadrol (102-60-3)	Triisopropanolamine (122-20-3)
Physicochemical Properties		
Melting point	A	A
Boiling point	A	A
Vapor pressure	A	A
Partition coefficient	A	A
Water Solubility	A	A
Environmental Fate		
Photodegradation	A	A
Hydrolysis	NA	NA
Fugacity	A	A
Biodegradability	R	A
Ecotoxicity		
Acute Fish	A	A
Acute Daphnia	R	A
Algal Inhibition	R	A
Health Effects		
Acute	A	A
Repeated Dose	A	A
Gene Tox – Mutagenicity	A	A
Gene Tox – Clastogenicity	R	A
Developmental	R	A
Reproductive	R	A

A = Adequate Data Exists, R = Read Across, T = Testing Proposed, NA = Not Applicable

2.0 Introduction

2.1 Overview

ARCADIS G&M, Inc., on behalf of BASF Corporation, hereby submits for review and public comment the robust summaries and test plan for Quadrol [CAS No. 102-60-3; N,N,N',N'-tetrakis(2-hyroxypropyl) ethylenediamine)], under the United States Environmental Protection Agency's (U.S. EPA) High Production Volume (HPV) Chemical Challenge Program. This document addresses a single HPV sponsored chemical; however, data for a structurally related non-HPV chemical (triisopropanolamine; CAS No. 122-20-3) have been used to support the dataset for Quadrol through a read-across approach. Data read-across occurs when physicochemical and toxicological data from one chemical are used for another chemical, and is done only when the two chemicals are deemed sufficiently similar in structure that they are likely to have similar chemical and toxicological properties. The use of structural analogs is consistent with EPA guidance for use of structure-activity relationships (SAR) in the HPV Chemical Challenge Program (EPA, 1999).

The purpose of this plan is to develop physicochemical data, environmental fate and effects data, and mammalian health effects data for Quadrol consistent with the Screening Information Data Set (SIDS). Therefore, this plan summarizes the existing SIDS data for Quadrol and triisopropanolamine and evaluates the need for testing to fill any data gaps in the SIDS endpoints.

2.2 Methods for Data Review

A review of the scientific literature and BASF Corporation's company data was conducted on the physicochemical properties, environmental fate and effects, and mammalian toxicity endpoints for Quadrol and the structurally related triisopropanolamine. Searches were conducted using CAS numbers and chemical names using the following databases: EFDB, ECOTOX, TOXLINE, MEDLINE, and CHEMID. In addition, a comprehensive literature search service (NERAC) was used to search the published literature. Standard handbooks and databases (e.g., CRC Handbook on Chemicals, IUCLID, Merck Index, etc.) were consulted for physicochemical properties. A variety of individual studies, reports and other data sources were reviewed in development of this test plan, and the literature citations for all of these sources are included in Appendix A.

In accordance with U.S. EPA guidance, in those instances where measured physicochemical parameters and environmental fate data were not available, these properties were developed using EPIWIN (version 3.11) modeling. EPIWIN is an acronym for the Estimation Programs Interface for Microsoft Windows (June 1998), and is a package of computer programs developed by the U.S. EPA Office of Pollution Prevention and Toxics (OPPTS) that uses computational methods and structure-activity relationships (SAR) in estimating chemical properties, environmental fate and aquatic toxicity of

organic chemicals. Due to the inherent limitations of SAR approaches, EPIWIN modeling may produce non-realistic estimates; therefore, EPIWIN data are evaluated for reasonableness prior to use.

Lastly, robust summaries were prepared for studies as to provide a detailed summary of the test methods and results. Though several studies may have been evaluated for a particular SIDS endpoint, robust summaries were prepared only for the critical study that represented the best available data. Selection of the critical study was based on a review of all studies using the ranking system developed by Klimisch et al (1997), as well as the criteria outlined in the U.S. EPA's methods for determining the adequacy of existing data.

3.0 Substance Information for Quadrol

Quadrol (CAS No. 102-60-3) is a 14-carbon symmetrically substituted ethylenediamine (Fig. 1). At room temperature it is a white viscous liquid with a mild fishy odor. It has a low volatility and is miscible with water. It is also highly soluble in other polar organic solvents such as ethanol, methanol and ethylene glycol.

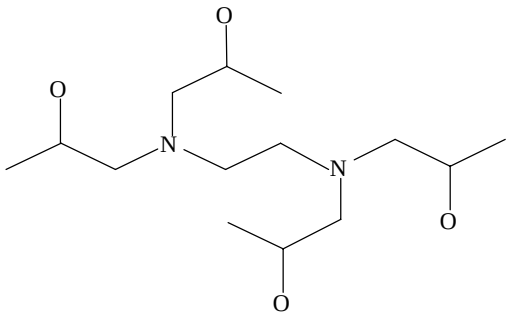


Figure 1. Structure of Quadrol

Quadrol is used as an intermediate (e.g., cross-linking agent) and catalyst in chemical reactions. Other major uses include as a complexing and chelating agent, humectant, plasticizer, surfactant solubilizer, and viscosity control agent.

Synonyms and trade names include:

- 2-propanol, 1,1',1'',1'''-(1,2-ethanediyldinitrilo)tetrakis-
- 1,1',1'',1'''-(1,2-ethanediyldinitrilo)tetrakis-2-propanol
- N,N,N',N'-tetrakis(2-hydroxypropyl) ethylenediamine
- Ethylenediamine N,N,N',N'-tetra-2-propanol
- Entrol

- Neutrol
- RTECS UB5604000

4.0 Triisopropanolamine as an Analog for Quadrol

4.1 EPA Guidance for Use of Analogs

In its SAR guidance for the HPV Chemical Challenge Program, the U.S. EPA states that the most likely analogs for an HPV chemical are those that resemble the candidate chemical in terms of the following:

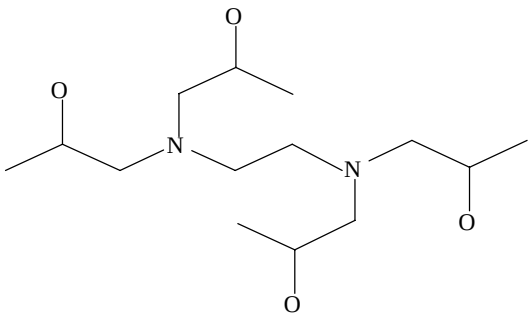
1. molecule structure/size;
2. some substructure that may play a critical functional role;
3. some molecular property (e.g., lipophilicity, electronic and steric parameters); and/or
4. some precursor, metabolite, or breakdown product.

In general, valid analogs should have close structural similarity and the same functional groups as the HPV chemical. In addition, a high correlation is desired between the HPV chemical and the putative analog for the following parameters:

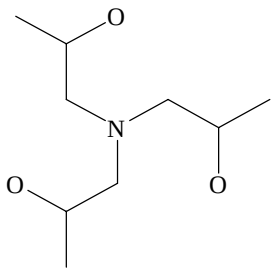
- Ø Physicochemical properties (e.g., physical state, molecular weight, log Kow, water solubility);
- Ø Absorption potential;
- Ø Mechanism of action of biological activity; and
- Ø Metabolic pathways/kinetics of metabolism.

4.2 Structural Similarity and Comparison of Data for Quadrol and Triisopropanolamine

The analog selected for Quadrol, triisopropanolamine, closely resembles the HPV chemical and is believed to possess most of the desired properties for an analog as described in U.S. EPA guidance. The structures of the two chemicals are shown in Figure 2. They are highly similar and have the same functional groups. According to ChemIDplus (http://chem.sis.nlm.nih.gov/chemidplus), the structural similarity of triisopropanolamine to Quadrol is 82.39%. Both chemicals are tertiary amines and act as bases. Each also has the chemical properties of both amines and alcohols, and both are expected to behave similarly in terms of chemical reactivity. For example, both compounds are capable of forming metal complexes and both react with long-chain fatty acids to from soaps (BUA, 1993; HSDB). Both are also used as cross-linking and curing agents in polymer formulations.



Quadrol



Triisopropanolamine

Figure 2. Comparison of structures of Quadrol and triisopropanolamine

Table 2 compares the properties of Quadrol and triisopropanolamine. The source of the information is classified as “measured”, “reference”, or “estimated.” Measured data were obtained through experimental procedures, while estimated data were obtained through structure-activity correlations. The designation of reference means that the values were obtained from handbooks (such as the Merck Index), from material safety data sheets, or from other literature. Complete information on the sources of information for each data element is provided in the Robust Summaries submitted with this Test Plan.

Table 2. Comparison of physico-chemical properties of Quadrol and triisopropanolamine

Substance Information and Properties	Quadrol (102-60-3)	Triisopropanolamine (122-20-3)
Synonym	2-propanol, 1,1’,1”,1’”-(1,2-ethanediyldinitrilo)tetrakis-	2-propanol, 1,1’1”-nitrilotri-
Molecular Formula	$C_{14}H_{32}N_2O_4$	$C_9H_{21}NO_3$
Molecular weight	292.42	191.27
Melting point	<25ºC (reference)	50ºC (reference)
Boiling point	190ºC at 1.3332 hPa (reference)	134.2ºC at 1.25 hPa (measured)
Vapor pressure	1.2 x 10^{-8} hPa (estimated)	1.808 x 10^{-8} hPa (measured)
Water solubility	• 1000 g/L (reference)	> 1000 g/L (reference)
pKa	4.30 and 8.99 (reference)	7.86 (reference)
Partition coefficient (log Kow)	- 2.08 (estimated)	-0.015 (measured)

Although Quadrol has a higher molecular weight than triisopropanolamine, both are highly soluble in water because of their polar amine and alcohol groups. Both also have low (negative) octanol/water partition coefficients when expressed as a log value. Therefore, the absorption and uptake kinetics of the two compounds is expected to be similar. In addition, because both compounds are tertiary amines with identical side chains, the metabolism of the two compounds is expected to be very similar. In general, tertiary amines can be metabolized to secondary amines by monaminooxidases, the reaction yielding the corresponding secondary amine, an aldehyde, and hydrogen peroxide (Beard and Noe, 1981) as per the following equation:

$$2\ RCH_2NR'R'' + O_2 + H_2O \longrightarrow 2\ RCHO + 2\ NH_2R'R'' + H_2O_2$$

Although amines are generally well absorbed from the gut and respiratory tract (Beard and Noe, 1981), the available pharmacokinetics data indicate that Quadrol is very poorly absorbed in rats following oral dosing (<2%), is distributed according to a one-compartment model, and is rapidly eliminated by a first order process (Dunphy, 1991). After oral dosing, the small fraction of Quadrol that is absorbed is rapidly excreted in the urine primarily (92-96%) unchanged. The half-life for elimination is 82 minutes in non-diabetic rats (Dunphy, 1991). Comparable pharmacokinetic data is not available for triisopropanolamine, but is expected to show a similar trend due to structural similarity.

The mechanism of biological activity of the two chemicals is unknown, although in the presence of nitrosating agents such as nitrites or nitrous oxides, triispropanolamine may be dealkylated under certain reaction conditions (i.e., low pH) to yield nitrosamines, including one known to be carcinogenic (BUA, 1993; Yamamoto, 1991). However, *in vitro* and *in vivo* studies, including a long-term carcinogenicity study, have not confirmed either the mutagenicity or carcinogenicity of triisopropanolamine (Yamamoto, 1991).

Available comparative mammalian toxicity data for both compounds support the contention that triisopropanolamine is a good analog for Quadrol. As shown in Table 3, the acute oral toxicity of the two chemicals to rats is similar (11,200 versus 6,500 mg/kg b.w.), with Quadrol being the less toxic of the two. Data from repeated dose studies also confirm that both compounds have a similar magnitude of toxicity. In addition, both compounds produced negative results in bacterial mutation assays with *Salmonella typhimurium*.

Both compounds are of a low order of toxicity to fish. The acute 96-h LC50 for Quadrol in a test with the fathead minnow was greater than the highest test concentration (>1,000 mg/L). This data is consistent with that for triisopropanolamine, which had a 96-h LC50 between 2,150 and 4,650 mg/L in studies with the golden orfe (BASF, 1987).

Table 3. Comparison of toxicity of Quadrol and triisopropanolamine

Endpoint	Quadrol (102-60-3)	Triisopropanolamine (122-20-3)
Acute Oral LD50 (mg/kg b.w.)	11,200 (neutralized solution)	6,500
Repeated dose NOAEL (mg/kg/d)	600 – 900 (90 d feeding study)	~1216 (2-yr feeding study)
Mutagenicity (*Salmonella typhimurium* assay)	Negative	Negative
Acute toxicity to fish (LC50, mg/L)	> 1,000	2,150 – 4,560

Based on the weight of evidence it is concluded that triisopropanolamine is a valid analog for Quadrol and that the uptake, metabolism, ecotoxicology and health effects of the two compounds is expected to be very similar. Therefore, data read-across is used for those instances where valid and reliable data is available for triisopropanolamine but not for Quadrol.

5.0 Data Analysis and Proposed Testing

A summary of proposed testing for this group is shown in Table 1 (in Section 1) and a completed SIDS data matrix is provided in Section 6. The SIDS endpoints for triisopropanolamine are largely covered by reliable experimental data. Therefore, data for the endpoints for Quadrol can be covered by data read-across from triisopropanolamine, where data for Quadrol itself are not available. Additional mammalian toxicity studies, aquatic toxicity studies and EPIWIN estimates for physicochemical data support data read-across.

5.1 Physico-chemical Properties

As previously presented in Table 2, measured data for boiling point, vapor pressure and partition coefficient are available for triisopropanolamine. A literature reference provided the water solubility data, and the melting point was obtained from a company Material Safety Data Sheet (MSDS). The melting point for Quadrol was obtained from the Merck Index, while the values for boiling point and water solubility were obtained from MSDSs and the vapor pressure and partition coefficient were predicted with EPIWIN modeling. For the needs of the HPV Program, reference data and estimation provide sufficiently reliable information and no further physicochemical testing is recommended for Quadrol.

5.2 Environmental Fate and Pathways

Environmental fate data for Quadrol was developed using EPIWIN model results. These estimated data are supported by the available data (estimated and measured) for triisopropanolamine. The environmental fate data are summarized in Table 4, below, along with identification of the sources of information

(reference, measured, or estimated). Detailed information is tabulated in Section 6 and more fully described in the Robust Summaries submitted concurrently with this Test Plan.

Indirect photodegradation in air was calculated for both Quadrol and triisopropanolamine using AOPWIN v1.91. The half-life for Quadrol was 0.6 h, compared to the half-life for triisopropanolamine of 2.1 h. Hydrolysis is not expected to be an important fate process for either substance based upon their structures. Based on the EQC Level III model, it is predicted that Quadrol will be distributed to soil (50.1%) and water (49.8%) under conditions of equal emission to water, soil and air. This is similar to the predictions for triisopropanolamine (54.6% distributed to soil and 45.3% to water). Modeling results (BIOWIN v.401) predict that the timeframe for ultimate biodegradation is weeks to months for Quadrol. The results of an inherent biodegradation study (OECD 302B) indicate that the degradation of triisopropanolamine is less than 10% after 28 days. However, other available information (Davis and Carpenter, 1997) indicates that biodegradation of triisopropanolamine increases from a 5-day BOD value of less than 5% using an unacclimated inoculum to 40-50% using an acclimated inoculum. In a simulation test with dilute activated sludge, diisopropanolamine was completely degraded within 72 – 120 hours; since this compound is a major metabolite of the aerobic biodegradation of triisopropanolamine, similar results would be expected with triisopropanolamine (Davis and Carpenter, 1997).

With the exception of the biodegradation endpoint, the available estimations fulfill the other endpoints for Quadrol, and are supported by the data for triisopropanolamine. Estimations are not considered acceptable in lieu of measured data for biodegradation. Therefore, this endpoint is fulfilled by read-across from triisopropanolamine.

Table 4. Environmental Fate & Pathways Information for Quadrol and Triisopropanolamine

Environmental Fate Endpoint	Quadrol (102-60-3)	Triisopropanolamine (122-20-3)
Photodegradation half-life	0.6 h (estimated)	2.1 h (estimated)
Hydrolysis	Expected to be stable to hydrolysis	Expected to be stable to hydrolysis
Fugacity (percent distribution over time assuming equal emissions to air, water and soil)	Air: <0.01; Water: 49.8; Soil: 50.1; Sediment: 0.1 (estimated)	Air: <0.01; Water: 45.3; Soil: 54.6; Sediment: 0.1 (estimated)
Biodegradation	Weeks – months for ultimate biodegradation (estimated)	<10% biodegradation after 28 days in Zahn-Wellens test (measured); 40-50% biodegradation with acclimated inoculum (measured) and complete degradation likely in activated sludge (reference)

5.3 Ecotoxicity

An acute toxicity test was conducted with Quadrol using the fathead minnow, resulting in a 96-h LC50 of greater than 1,000 mg/L, indicating low toxicity. There are no measured data available for Quadrol for invertebrates or algae. Acute fish, daphnia and algae inhibition studies were conducted for triisopropanolamine. Triisopropanolamine also had low toxicity to fish, with a reported 96-h LC50 between 2,150 and 4,640 mg/L. Additional measured results for triisopropanolamine include a 48-h EC50 for *Daphnia magna* of > 500 mg/L (low toxicity) and a 72-h EC50 (based upon biomass) for *Scenedesmus subspicatus* of 69 mg/L (moderate toxicity). In the absence of data for aquatic invertebrates and aquatic plants for Quadrol, ECOSAR predictions were made; these indicate low acute toxicity for Quadrol. The estimations are strengthened by the comparability to the triisopropanolamine data, including the pattern seen for both substances wherein the algae are the most sensitive, the invertebrates have intermediate sensitivity and the fish are the least sensitive. Additional supportive information is derived from the ECOSAR predictions for triisopropanolamine. These data are summarized in Table 5 below and are more fully described in Section 6 and the Robust Summaries. The measured and estimated data for Quadrol, as supported by both the measured and estimated data for triisopropanolamine, adequately cover the SIDS ecotoxicity endpoints and no further testing is warranted for Quadrol.

Table 5. Ecotoxicity Information for Quadrol and Triisopropanolamine

Ecotoxicity Endpoint	Quadrol (102-60-3)	Triisopropanolamine (122-20-3)
Acute fish LC50, 96-h (mg/L)	> 1,000 for fathead minnow (measured); 32,900 for fish (estimated)	2,150-4,640 for golden orfe (measured); 6,060 for fish (estimated)
Acute invertebrate EC50, 48-h (mg/L)	1,435 for daphnid (estimated)	> 500 for *Daphnia magna* (measured); 295 for daphnid (estimated)
Algal inhibition EC50 (mg/L)	662 for green algae, 96-h EC50 (estimated)	69 for *Scenedesmus subspicatus,* 72-h EbC50 (measured); 183 for green algae, 96-h EC50 (estimated)

5.4 Health Effects

5.4.1 Absorption, Distribution, and Excretion

The pharmacokinetic profile of Quadrol has been studied in male Sprague-Dawley rats after being given a single oral dose by gastric gavage at 50, 100, or 200 mg/kg b.w. (Dunphy, 1991). Peak plasma levels of Quadrol at 40 to 60 minutes after dosing were proportional to the oral dose. Pharmacokinetic calculations indicated that Quadrol was very poorly absorbed and eliminated by a first order process at all dose levels administered. These results were consistent with what was expected based upon Quadrol's polarity and lack of appreciable lipid solubility. The calculated oral bioavailability factor (F=0.018) indicated that less than 2% of the orally administered Quadrol was absorbed through the stomach and intestines. Protein and erythrocyte binding studies confirmed that Quadrol has a very low affinity for both bovine and human albumin, as well as rat erythrocytes, with less than 2% bound or partitioned. Therefore, Quadrol would be expected to exist almost exclusively as a "free drug" in the plasma. The half-life for urinary elimination of absorbed Quadrol was rapid (108 min) indicating that it would be virtually 100% eliminated from the bloodstream within 24 hours following a single dose. The kinetics of absorbed Quadrol conformed to a one-compartment model of distribution and indicated minimal tissue distribution (Vd = approx. 4 mL/kg b.w.) and metabolism. Approximately 92 –96% of the absorbed compound was excreted in the urine unchanged and none of the hypothetical metabolites such as keto- or N-dealkylated derivatives were detected.

5.4.2 Acute Toxicity

The results of an acceptable acute oral toxicity test with rats (Hilltop Research, 1956a) on Quadrol indicate an LD50 of 11,200 mg/kg b.w. when the test substance solution was neutralized to pH 7. Toxicity was increased (3,900 mg/kg b.w.) when the pH of the Quadrol test solution was at its initial value of 10.9, but still of a low order of magnitude. The difference in toxicity is believed to be due to the fact that Quadrol exists as a monocation at a pH of 7 (with low lipid solubility), while it is largely uncharged and more lipophilic at the higher pH[1]. The comparable study for triisopropanolamine does not provide details about any neutralization of the test substance, but indicates an oral LD50 for rats of 6,500 mg/kg b.w. (Smythe et al., 1941). Other reported oral LD50 values for the rat range from 4,000 to 9,000 mg/kg b.w. (BUA, 1993).

[1] Quadrol is a base with pKa values of 4.30 and 8.99, respectively, for the two amine groups (McMahon et al., 1986). Thus, one of the amine groups will exist largely as a cation at a pH of 7, while the other will be neutral (uncharged). Above the upper pKa (8.99), both amines will donate protons and be in the neutral form.

5.4.3 Repeated Dose Toxicity

A three-month feeding study on Quadrol with rats (Hilltop Research, 1956b) was conducted at dose levels of 0.1%, 0.3%, 1%, 3% and 5%; these dose levels were equivalent to average daily intakes (over the course of the study) of 70, 210, 720, 2,170 and 3,750 mg/kg/day. The effects observed at the two highest dosages included temporary decreased food consumption, loss of body weight, and interference with growth rate. The study authors express the NOAEL, presumably based upon the intakes during the first month of the study when the food consumption was affected, as 600 – 900 mg/kg/day. Two studies are used to provide information about repeated dose toxicity of triisopropanolamine. A feeding study with rats lasting 102 weeks was designed to examine carcinogenic effects of endogenously synthesized N-nitrosobis(2-hydroxypropylamine) from triisopropanolamine in the presence of sodium nitrite (Yamamoto, 1991). Data from this study using one dose level of triisopropanolamine in the absence of sodium nitrite indicates that approximately 1,216 mg/kg/day did not cause any significant increases in tumor incidence in a variety of organs. Another study, a 30-day drinking water exposure for rats, provides a NOAEL of triisopropanolamine of 140 mg/kg/day (Smythe and Carpenter, 1948). The LOAEL in this study, 260 mg/kg/day, is based upon micropathological lesions of the liver, kidney, spleen or testis.

5.4.4 Genetic Toxicity

Quadrol is not expected to be genotoxic. An Ames test on Quadrol using four strains of *S. typhimurium* (TA97, TA98, TA100, and TA102) and one strain of *E. coli*, both with and without activation, was negative. Both *in vitro* and *in vivo* studies are available for triisopropanolamine, which showed no mutagenic effects in the Ames test and no clastogenic effects in the mouse micronucleus test.

5.4.5 Developmental and Reproductive Toxicity

No information on developmental or reproductive toxicity is available for Quadrol. However, data on triisopropanolamine are available from a prenatal toxicity (teratogenicity) study conducted with Wistar rats according to OECD Guideline 414 (BASF, 1995). Doses in this study were 100, 400, and 1,000 mg/kg b.w. per day. Doses were administered to 23-25 pregnant female rats on days 6-15 post coitum (p.c.) by gavage as an aqueous solution. A control group of 25 dams was dosed with the vehicle only (double distilled water). On day 20 p.c., all females were sacrificed and assessed for gross pathology. The uterus and ovaries were removed, examined, and gestational data recorded (e.g., number of corpora lutea, dead implantations, resorptions, live and dead fetuses). The fetuses were removed from the uterus, sexed, weighed and further examined for any external, soft tissue and/or skeletal findings.

For animals in the high dose group (1,000 mg/kg b.w./d), feed intake, body weight gain, and corrected body weight gain were significantly decreased compared to the control group. Despite signs of overt maternal toxicity at this dose, no effects on fetuses or gestational parameters (e.g., conception rate, number of resorptions, number of viable fetuses) were observed. At the two lower doses, no treatment-related effects were observed on the dams, gestational parameters or fetuses. Overall, the NOAEL for teratogenic effects was >1,000 mg/kg b.w., while the NOAEL for maternal effects was 400 mg/kg b.w., based on reduced feed consumption and reduced body weight gain. No treatment-related effects upon gestational parameters or the fetuses were observed with any of the administered doses and it is concluded that triisopropanolamine is not embryotoxic, fetotoxic, or teratogenic with maternal doses up to 1,000 mg/kg b.w./d.

A long-term carcinogenic study by Yamamoto (1991) provides some additional information on reproductive effects of triisopropanolamine. After an exposure of 102 weeks to approximately 1,216 mg/kg/day, there were no significant increases in tumors of reproductive organs, including the testis, mammary gland, and pituitary gland.

5.4.6 Summary of Health Effects Data

The available data for Quadrol fulfill the endpoints for acute toxicity, repeated dose toxicity, and *in vivo* genotoxic effects (mutagenicity). There is no information available on Quadrol for clastogenic effects, developmental or reproductive toxicity. Using the read-across approach, the data from a mouse micronucleus test with triisopropanolamine is adequate to characterize clastogenic effects of Quadrol. Similarly, a teratogenicity study on triisopropanolamine is used to satisfy the developmental toxicity endpoint for Quadrol. Data from this study and a 2-year carcinogenicity study on triisopropanolamine provide information about reproductive effects, satisfying the reproductive toxicity endpoint for Quadrol.

The SIDS endpoints relative to health effects for Quadrol and triisopropanolamine are summarized in Table 6, with more detailed information provided in Section 6 (SIDS Data Matrix) and in the Robust Summaries submitted with this Test Plan.

Table 6. Health Effects Information for Quadrol and Triisopropanolamine

Toxicity Endpoint	Quadrol (102-60-3)	Triisopropanolamine (122-20-3)
Acute oral LD50 (mg/kg b.w.)	11,200 for rats, neutralized solution	6,500 for rats
Repeated dose toxicity, NOAEL (mg/kg/day)	600 – 900 in 3-month feeding study with rats	1,216 in 102-week feeding study with rats; 140 in 30-day drinking water study with rats
Mutagenicity	Negative in *S. typhimurium* and *E. coli* tests	Negative in *S. typhimurium* test
Clastogenicity		Negative in mouse micronucleus test
Developmental and reproductive toxicity		NOAEL 400 mg/kg b.w. for maternal effects and >1,000 mg/kg b.w. for embryo-fetotoxicity and teratogenic effects. NOAEL 1,216 mg/kg/d based upon no evidence of tumors in reproductive organs in 102-week feeding study with rats

Note: all data are based upon measured values.

5.5 Test Plan Summary

The majority of the SIDS Level I endpoints for Quadrol are filled by a combination of measured and estimated data for the compound, as listed in Table 7. The adequacy of this information is further supported by comparable data for triisopropanolamine. The structural similarity and comparability of physico-chemical and toxicological properties between the two chemicals makes triisopropanolamine a suitable surrogate for Quadrol. Where data are not available for Quadrol (e.g., biodegradability, acute daphnia toxicity, algal inhibition, clastogenic effects, and developmental and reproductive effects), information on triisopropanolamine is used in a read-across manner to fill these data gaps. Adequate data for triisopropanolamine were available for all of these remaining endpoints. Therefore, no additional testing on Quadrol is recommended.

Table 7: Summary of Data Gap Analysis for Quadrol

SIDS Level I Endpoint	Quadrol (102-60-3)	Triisopropanolamine (122-20-3)
Physicochemical Properties		
Melting point	A	A
Boiling point	A	A
Vapor pressure	A	A
Partition coefficient	A	A
Water Solubility	A	A
Environmental Fate		
Photodegradation	A	A
Hydrolysis	NA	NA
Fugacity	A	A
Biodegradability	R	A
Ecotoxicity		
Acute Fish	A	A
Acute Daphnia	R	A
Algal Inhibition	R	A
Health Effects		
Acute	A	A
Repeated Dose	A	A
Gene Tox – Mutagenicity	A	A
Gene Tox – Clastogenicity	R	A
Developmental	R	A
Reproductive	R	A

A = Adequate Data Exists, R = Read Across, T = Testing Proposed, NA = Not Applicable

6.0 SIDS Data Matrix

SIDS Endpoint	Quadrol (102-60-3)		Triisopropanolamine (122-20-3)	
	Value	**Comment**	**Value**	**Comment**
Physicochemical				
Melting point (°C)	< 25	Merck Index	50	MSDS
Boiling point (°C)	190 at 1.33 hPa	MSDS	134 at 1.25 hPa	BASF, 1972
Vapor pressure (hPa)	1.2×10^{-8}	EPIWIN	1.8×10^{-8} at 25ºC	BASF, 1972 (from linear regression based upon measured data)
Partition coefficient (Log Kow)	-2.08	EPIWIN	-0.015	BASF, 1987a
Water Solubility (g/L)	• 1,000	Merck Index	> 1,000	Dow, cited in Davis and Carpenter, 1997.
Environmental fate				
Photodegradation (t1/2 days)	0.6 h	EPIWIN	2.1 h	EPIWIN
Hydrolysis	Stable		Stable	
Fugacity	49.8% water, 50.1% soil	EQC Level III	45.3% water, 54.6% soil	EQC Level III
Biodegradability	Weeks – months (ultimate)	EPIWIN	< 10% in 28 day test (inherent); 40%-50% degradation with acclimated inoculum; degradable with activated sludge	BASF, 1981a; Davis and Carpenter, 1997
Ecotoxicity				
Acute Fish – LC50 (mg/L)	> 1,000 for fathead minnow	Industrial Biotest, 1976	2,150-4,640 for golden orfe	BASF, 1987b
Acute Invertebrate – EC50 (mg/L)	1,435 for daphnid	ECOSAR	> 500 for Daphnia magna	BASF, 1987c
Algal Inhibition – EC50 (mg/L)	662 for green algae (96-h)	ECOSAR	69 for *Scenedesmus subspicatus* (72-h)	BASF, 1988; BASF, 2003
Toxicity				
Acute – Oral LD50 (mg/kg)	11,200 for rats	Hilltop Research, 1956a	6,500 for rats	Smythe et al., 1941
Repeated Dose, NOAEL (mg/kg/d)	600- 900 for rats	Hilltop Research, 1956b. 3-month feeding study	1,216 in feed, for rats (102 weeks); 140 in drinking water, for rats (30 days)	Yamamoto, 1991; Smythe and Carpenter, 1948
Gene Tox – Mutagenic	Negative in Ames assay	Hachiya and Takizawa, 1994	Negative in Ames assay	Haworth, 1983
Gene Tox – In-vivo Cytogenetic			Negative in mouse micronucleus test	BASF, 1995a
Developmental – Rat Oral NOAEL (mg/kg bw)			Maternal: 400 Teratogenicity: >1000	BASF, 1995b
Reproductive			~ 1,216 mg/kg/d caused no tumors in reproductive organs over 102 week exposure	Yamamoto, 1991

7.0 References

This list of references is for studies as cited in Sections 1- 5, while a complete list of all data sources reviewed in the development of Robust Summaries and Test Plan for Quadrol is attached as Appendix A.

BASF AG, 1987. Department of Toxicology; unpublished results (87/271), 02.12.87.

BASF AG, 1995. Study of the Prenatal Toxicity of Triisopropanolamine in Wistar Rats after Oral Administration (Gavage). Department of Toxicology, unpublished data, Project No. 30R0013/93029, 07/14/1995.

Beard, R.R., and Noe, J.T., 1981. Aliphatic and cyclic amines. In: Clayton, G.D. and Clayton, F.E. (ed.) Patty's Industrial Hygiene and Toxicology, 3rd revised edition, Vol. 2B Toxicology, John Wiley & Sons< New York, pp. 3135-3173.

BUA, 1993. Triisopropanolamine, BUA Report 148. German Chemical Society (GDCh) – Advisory Committee on Existing Chemicals of Environmental Relevance (BUA).

Davis, J.W. and Carpenter, C.L., 1997. Environmental assessment of the alkanolamines. Reviews of Environmental Contamination and Toxicology, Vo. 149, pp. 87-137.

Dunphy, M.J. 1991. Quadrol, N,N,N',N'-(2-hydroxypropyl)ethylenediamine: Pharmacokinetics and assessment of acute toxicity in rats. Ph.D. Dissertation, University of Akron. 159 p.

EPA, 1999. The use of structure-activity relationships (SAR) in the High Production Volume Chemicals Challenge Program. At http://www.epa.gov/chemrtk/sarfinl1.htm

HSDB (Hazardous Substances Data Base), http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?hsdbb.htm

Hill Top Research Institute, 1956a. Acute Oral Toxicity of Quadrol, March 7, 1956.

Hill Top Research Institute, 1956b. Subacute Oral Toxicity of Quadrol, March 1, 1956. Project 151.

Klimisch, H.J., Andreae, M. And Tillmann, U., 1997. A systematic approach for evaluating the quality of experimental toxicological and ecotoxicological data. Regulatory Toxicol. and Pharmacol. 25:1-5.

McMahon, R., M. Brennan, and J.D. Glennon. 1986. The pKa values of N,N,N',N'-(2-hydroxypropyl)ethylenediamine. Talanta, 33(11): 927.

Smythe, H.F., Jr., and Carpenter, C.P., 1948. Further experience with the range finding test in the industrial laboratory. J. Ind. Hyg. Toxicol. 30, 63-68.

Smythe, H.F., Jr., Seaton, J. and Fischer, L. 1941. The single dose toxicity of some glycols and derivatives. J. Ind. Hyg. Toxicol. 25:259-268.

Yamamoto, K., 1991. Endogenously synthesized N-nitrosobis(2-hydroxypropyl)amine and its carcinogenic potential in rats. J. Nara. Med. Ass. 42:134-152.

Appendix A

This appendix contains the complete list of all data sources reviewed in the development of the Robust Summaries and Test Plan for Quadrol. Reference numbers in bold indicate studies for which robust summaries have been prepared.

(1) BASF AG, 1972. Verfahrenstechnik, unpublished results, report no. 172.096.1, April 6, 1972

(2) BASF AG, 1981a. Labor Oekologie; unveroeffentlichte Untersuchung, No. 7, 1981

(3) BASF AG, 1981b. Department of Ecology, unpublished study, 11.03.1981

(4) BASF AG, 1987a. Analytisches Labor: unveroeffentlichte Untersuchung, BRU 87.262, 18.12.1987

(5) BASF AG; 1987b. Department of Toxicology; unpublished results (87/271), 02.12.87

(6) BASF AG, 1987c. Labor Oekologie; unveroeffentlichte Untersuchung, 1133/87, 27.01.1987

(7) BASF AG, 1988. Analytisches Labor; unveroeffentlichte Untersuchung, 307371, 28.04.1988

(8) BASF AG, 1990. Department of Ecology, unpublished study, 1090/88, 19.12.1990

(9) BASF AG, 1991. Sicherheitsdatenblatt TRIISOPROPANOLAMIN (4/91)

(10) BASF AG, 1995a. Dept. of toxicology, unpublished data (26M0013/9[C196), 02/23/1995

(11) BASF AG, 1995b. Study of the Prenatal Toxicity of Triisopropanolamine in Wistar Rats after Oral Administration (Gavage). Department of Toxicology, unpublished data, Project No. 30R0013/93029, 07/14/1995.

(12) BASF AG, 1999. Safety Data Sheet, Triisopropanolamine, 09.11.1999

(13) BASF Corp., 2002. Material Safety Data Sheet, Quadrol. 17 SEP 2002

(14) BASF AG, 2003. Department of Product Safety, unpublished calculation, 04.09.2003

(15) BUA, 1993. Triisopropanolamine, BUA Report 148. German Chemical Society (GDCh) – Advisory Committee on Existing Chemicals of Environmental Relevance (BUA).

(16) BUA, 1998. Triisopropanolamine, Supplementary Report. BUA Report 219. German Chemical Society (GDCh) – Advisory Committee on Existing Chemicals of Environmental Relevance (BUA).

(17) Budavari, S., ed., The Merck Index: an encyclopedia of chemicals, drugs and biologicals. 12th ed., Merck and Co., New Jersey, 1996.

(18) Davis, J.W. and Carpenter, C.L., 1997. Environmental assessment of the alkanolamines. Reviews of Environmental Contamination and Toxicology, Vo. 149, pp. 87-137.

(19) Dunphy, M.J. 1991. Quadrol, N,N,N',N'-(2-hydroxypropyl)ethylenediamine: Pharmacokinetics and assessment of acute toxicity in rats. Ph.D. Dissertation, University of Akron. 159 p.

(20) The Dow Chemical Company, 1988. Physical properties of the alkanolamines. Form No. 111-1227-88. The Dow Chemical Company, Midland MI. Cited in Davis, J.W. and Carpenter, C.L., 1997, Environmental assessment of the alkanolamines, Reviews of Environmental Contamination and Toxicology 149:87-137.

(21) Hachiya, N. and Takizawa, Y., Mutagenicity of Plastic Additives, Hen'igensei Shiken 3(3):147-154 (1994). Cited at http://toxnet.nlm.nih.gov, CCRIS Record number 8275, last updated 02/12/2001.

(22) Hill Top Research Institute, 1956a. Acute Oral Toxicity of Quadrol, March 7, 1956

(23) Hill Top Research Institute, 1956b. Subacute Oral Toxicity of Quadrol, March 1, 1956, Project 151.

(24) Industrial Bio-Test Laboratories, Report No. 8560-08828, Four-Day Static Aquatic Toxicity Study with Quadrol in Fathead Minnows, May 4, 1976.

(25) McMahon, R., M. Brennan, and J.D. Glennon. 1986. The pKa values of N,N,N',N'-(2-hydroxypropyl)ethylenediamine. Talanta, 33(11): 927.

(26) MDL Information Systems, Material Safety Data Sheet, Quadrol, 11 DEC 2001

(27) MDL Information Systems, Material Safety Data Sheet, Quadrol, 22 MAR 2001

(28) Smyth, H.F., Jr., Seaton, J. and Fischer, L., 1941. The single dose toxicity of some glycols and derivatives. J. Ind. Hyg. Toxicol. 25:259-268.

(29) Smyth, H.F. and Carpenter C.P., 1948. Further experience with the range finding test in the industrial laboratory.J. Ind. Hyg. Toxicol. 30, 63-68

(30) Toropkov, V.V.: 1980. Tr. Leningr. San.-gigien Med.In-ta 130, 29 (1980), cited in: BIBRA Toxicity Profile "Triisopropanolamine"(1990)

(31) Yamamoto, K., 1991. Endogenously synthesized N-nitrosobis(2-hydroxypropyl)amine and its carcinogenic potential in rats. J. Nara. Med. Ass. 42:134-152

(32) Zeiger, E. et al.: Environ. Mutagen. 9, Suppl. 9, 1-18 (1987)

IUCLID

Data Set

Existing Chemical	:	ID: 102-60-3
CAS No.	:	102-60-3
Common name	:	Quadrol
Molecular Formula	:	C14 H32 N2 O4
Molecular Weight	:	292.42
Synonym	:	N,N,N',N'-tetrakis(2-hydroxypropyl)ethlyenediamine

Producer related part

Company	:	Arcadis
Creation date	:	20.09.2003

Substance related part

Company	:	Arcadis
Creation date	:	20.09.2003
Status	:	
Memo	:	
Printing date	:	01.12.2003
Revision date	:	
Date of last update	:	01.12.2003
Number of pages	:	13
Chapter (profile)	:	Chapter: 1.0.1, 1.1.0, 1.1.1, 1.2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6.1, 3.1.1, 3.3.2, 3.5, 4.1, 4.2, 4.3, 5.1.1, 5.4, 5.5
Reliability (profile)	:	Reliability: without reliability, 1, 2, 3, 4
Flags (profile)	:	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 APPLICANT AND COMPANY INFORMATION

Type	:	other
Name	:	Arcadis
Contact person	:	Jane Staveley
Date	:	
Street	:	4915 Prospectus Drive, Suite F
Town	:	27713 Durham, NC
Country	:	United States
Phone	:	919-544-4535
Telefax	:	
Telex	:	
Cedex	:	
Email	:	jstaveley@arcadis-us.com
Homepage	:	www.arcadis-us.com

Remark : This document has been prepared on behalf of BASF Corporation
16.10.2003

1.1.0 SUBSTANCE IDENTIFICATION

IUPAC Name	:	
Smiles Code	:	
Molecular formula	:	C14 H32 N2 O4
Molecular weight	:	292.42
Petrol class	:	

29.09.2003

1.1.1 GENERAL SUBSTANCE INFORMATION

Purity type	:	
Substance type	:	organic
Physical status	:	liquid
Purity	:	= 100 % w/w
Colour	:	white
Odour	:	mild polyol

02.10.2003 (1)

1.2 SYNONYMS AND TRADENAMES

1,1',1",1"'-(1,2-ethanediyldinitrilo)tetrakis-2-propanol

01.10.2003 (2)

2-propanol, 1,1',1",1"'-(1,2-ethanediyldinitrilo)tetrakis-

01.10.2003 (2)

Edetol

29.09.2003 (3)

Entprol

01.10.2003 (2)

N,N,N',N'- tetrakis(2-hydroxylpropyl)ethylenediamine

01.10.2003 (1)

Tetrahydroxypropyl Ethylenediamine

02.10.2003 (1)

2.1 MELTING POINT

Value : < 25 °C

Reliability : (2) valid with restrictions
Handbook data are assigned a reliability of 2

14.10.2003 (4)

2.2 BOILING POINT

Value : = 190 °C at 1.3332 hPa

01.10.2003 (2)

2.3 DENSITY

Type : relative density
Value : = 1.013 at °C

29.09.2003 (2)

2.4 VAPOUR PRESSURE

Value : = .000000012 hPa at °C
Decomposition :
Method : other (calculated): Modified Grain Method
Year :
GLP :
Test substance :

Method : MPBPWIN v1.41 (EPIWIN v3.11)
Remark : Calculated in mm Hg, converted to hPa
Reliability : (1) valid without restriction
calculated using scientifically acceptable method

14.10.2003

2.5 PARTITION COEFFICIENT

Partition coefficient : octanol-water
Log pow : = -2.08 at °C
pH value :
Method : other (calculated)
Year :
GLP :
Test substance :

Method : KOWWIN v1.67 (EPIWIN v.3.11)
Reliability : (1) valid without restriction
calculated using scientifically acceptable method

13.10.2003

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in	:	Water
Value	:	>= 1000 g/l at 25 °C
pH value	:	
concentration	:	at °C
Temperature effects	:	
Examine different pol.	:	
pKa	:	at 25 °C
Description	:	
Stable	:	
Remark	:	Quadrol is a base with pKa values of 4.30 and 8.99, respectively, for the two amine groups (McMahon, R., Brennan, M., and Glennon, J.D., Talanta 33(11):927 (1986).
Reliability	:	(2) valid with restrictions Handbook data are assigned a reliability of 2

01.12.2003 (4)

3.1.1 PHOTODEGRADATION

Type	:	air
Light source	:	
Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight
INDIRECT PHOTOLYSIS		
Sensitizer	:	OH
Conc. of sensitizer	:	
Rate constant	:	= .0000000002307401 cm³/(molecule*sec)
Degradation	:	= 50 % after .6 hour(s)
Deg. product	:	
Method	:	other (calculated)
Year	:	
GLP	:	
Test substance	:	

Method : AOPWIN v1.91 (EPIWIN v3.11)
Result :

AOP Program (v1.91) Results:
==========
SMILES : OC(C)CN(CCN(CC(O)C)CC(O)C)CC(O)C
CHEM : 2-Propanol, 1,1',1",1'"-(1,2-ethanediyldinitrilo)tetrakis-
MOL FOR: C14 H32 N2 O4
MOL WT : 292.42
---------- SUMMARY (AOP v1.91): HYDROXYL RADICALS ----------
Hydrogen Abstraction = 98.1801 E-12 cm3/molecule-sec
Reaction with N, S and -OH = 132.5600 E-12 cm3/molecule-sec
Addition to Triple Bonds = 0.0000 E-12 cm3/molecule-sec
Addition to Olefinic Bonds = 0.0000 E-12 cm3/molecule-sec
Addition to Aromatic Rings = 0.0000 E-12 cm3/molecule-sec
Addition to Fused Rings = 0.0000 E-12 cm3/molecule-sec

OVERALL OH Rate Constant = 230.7401 E-12 cm3/molecule-sec
HALF-LIFE = 0.046 Days (12-hr day; 1.5E6 OH/cm3)
HALF-LIFE = 0.556 Hrs
---------- SUMMARY (AOP v1.91): OZONE REACTION ----------

****** NO OZONE REACTION ESTIMATION ******
(ONLY Olefins and Acetylenes are Estimated)

Experimental Database: NO Structure Matches

Reliability : (1) valid without restriction
calculated using scientifically acceptable method

14.10.2003

3.3.2 DISTRIBUTION

Media	:	air - biota - sediment(s) - soil - water
Method	:	Calculation according Mackay, Level III
Year	:	

Method : EPIWIN v3.11
Result :

Level III Fugacity Model (Full-Output):
==========

Chem Name : 2-Propanol, 1,1',1",1"'-(1,2-ethanediyldinitrilo)tetrakis-
Molecular Wt: 292.42
Henry's LC : 4.15e-016 atm-m3/mole (Henrywin program)
Vapor Press : 8.69e-009 mm Hg (Mpbpwin program)
Liquid VP : 1.62e-007 mm Hg (super-cooled)
Melting Pt : 154 deg C (Mpbpwin program)
Log Kow : -2.08 (Kowwin program)
Soil Koc : 0.00341 (calc by model)

	Mass Amount (percent)	Half-Life (hr)	Emissions (kg/hr)
Air	4.7e-008	1.11	1000
Water	49.8	900	1000
Soil	50.1	900	1000
Sediment	0.0918	3.6e+003	0

	Fugacity (atm)	Reaction (kg/hr)	Advection (kg/hr)	Reaction (percent)	Advection (percent)
Air	1.42e-019	0.000693	1.11e-005	2.31e-005	3.71e-007
Water	8.37e-021	908	1.18e+003	30.3	39.3
Soil	3.11e-019	913	0	30.4	0
Sediment	7.71e-021	0.418	0.0435	0.0139	0.00145

Persistence Time: 789 hr
Reaction Time: 1.3e+003 hr
Advection Time: 2.01e+003 hr
Percent Reacted: 60.7
Percent Advected: 39.3

Half-Lives (hr), (based upon Biowin (Ultimate) and Aopwin):
Air: 1.113
Water: 900
Soil: 900
Sediment: 3600
Biowin estimate: 2.683 (weeks-months)

Advection Times (hr):
Air: 100
Water: 1000
Sediment: 5e+004

Reliability : (1) valid without restriction
calculated using scientifically acceptable method

13.10.2003

3.5 BIODEGRADATION

Contact time :
Degradation : (±) % after
Result : other: not readily biodegradable
Deg. product :
Method : other: calculated
Year :
GLP :
Test substance :

Method : BIOWIN v4.01 (EPIWIN v3.11)
Remark :

BIOWIN (v4.01) Program Results:
==========
SMILES : OC(C)CN(CCN(CC(O)C)CC(O)C)CC(O)C
CHEM : 2-Propanol, 1,1',1",1'"-(1,2-ethanediyldinitrilo)tetrakis-
MOL FOR: C14 H32 N2 O4
MOL WT : 292.42
---------- BIOWIN v4.01 Results ----------

Linear Model Prediction : Biodegrades Fast
Non-Linear Model Prediction: Does Not Biodegrade Fast
Ultimate Biodegradation Timeframe: Weeks-Months
Primary Biodegradation Timeframe: Days-Weeks
MITI Linear Model Prediction : Does Not Biodegrade Fast
MITI Non-Linear Model Prediction: Does Not Biodegrade Fast

Result : Summary output shown
Reliability : (1) valid without restriction
calculated using scientifically acceptable method

14.10.2003

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	static
Species	:	Pimephales promelas (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
TLm	:	> 1000
TL1	:	> 1000
TL99	:	> 1000
Limit test	:	
Analytical monitoring	:	no
Method	:	
Year	:	1976
GLP	:	no
Test substance	:	
Method	:	Fathead minnows (35-50 mm length) were exposed to nominal concentrations of 0, 1.0, 10, 100 and 1000 ppm Quadrol using 10 fish per test concentration.
Result	:	No mortality was observed in any control or test concentration at any time during the study. No unusual behavioral reactions were noted among the exposed fish.
Test condition	:	Tests were conducted in reconstituted water with pH 7.2-7.6, hardness 40-48 ppm calcium carbonate, and alkalinity of 30-35 ppm calcium carbonate. Dissolved oxygen and pH was measured in the control every 24 hours and in all test concentrations and control at 96 hours. A reference toxicant test was performed on the same lot of fish using p,p-DDT.
Reliability	:	(2) valid with restrictions Study pre-dates standardized methods and GLP. Basic data provided but test conditions not completely described.

14.10.2003 (5)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type	:	other: calculated
Species	:	Daphnia sp. (Crustacea)
Exposure period	:	48 hour(s)
Unit	:	mg/l
EC50	:	= 1435 calculated
Method	:	other: calculated
Year	:	
GLP	:	
Test substance	:	
Method	:	ECOSAR v0.99g (EPWIN v3.11)
Result	:	Class: aliphatic amines
Reliability	:	(1) valid without restriction calculated using scientifically acceptable method

14.10.2003

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species	:	other algae: green algae
Endpoint	:	
Exposure period	:	96 hour(s)
Unit	:	mg/l

EC50	:	= 662 calculated
Method	:	other: calculated
Year	:	
GLP	:	
Test substance	:	
Method	:	ECOSAR v0.99g (EPIWIN v3.11)
Result	:	Class: aliphatic amines
Reliability	:	(1) valid without restriction calculated using scientifically acceptable method

14.10.2003

5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50
Value	:	= 11200 mg/kg bw
Species	:	rat
Strain	:	
Sex	:	male
Number of animals	:	10
Vehicle	:	water
Doses	:	4400, 5600, 7500, 9750, 12600, 16500 mg Quadrol/kg
Method	:	other: study pre-dates standardized methods
Year	:	1956
GLP	:	no
Test substance	:	
Method	:	Doses prepared as 20% solution of Quadrol in water, neutralized to pH 7. Administered by stomach tube to male albino rats weighing approximately 100 grams. Animals observed for approximately one week following administration.
Reliability	:	(2) valid with restrictions Study pre-dates GLPs and standardized methods. Basic documentation provided, details of methods lacking

14.10.2003 (6)

5.4 REPEATED DOSE TOXICITY

Type	:	Sub-acute
Species	:	rat
Sex	:	male/female
Strain	:	other: Harlan albino
Route of admin.	:	oral feed
Exposure period	:	three months
Frequency of treatm.	:	ad libitum
Post exposure period	:	no post-exposure observation period
Doses	:	Doses were equivalent to average daily intakes of 70, 210, 720, 2170 and 3750 mg/kg bw
Control group	:	yes, concurrent no treatment
NOAEL	:	ca. 600 - 900 mg/kg
Method	:	
Year	:	1956
GLP	:	no
Test substance	:	
Method	:	10 males and 10 females were used in each group (5 doses and untreated control). Doses were administered as 0.1%, 0.3%, 1%, 3% and 5% Quadrol in the feed. Body weight and feed consumption were determined weekly. Hematology parameters (hemoglobin concentration, erythrocyte counts, total white cell counts, and differential white cell counts) were determined at the initiation and termination of exposure. At termination, prothrombin time and organ weights (lungs, liver, spleen, kidneys, adrenal glands, gonads and pancreas), as well as liver fat, were determined.
Result	:	Animals in the two highest dose groups exhibited temporary decreased food consumption, loss of body weight, and interference with growth rate. After the first month, however, food intake and rate of growth was similar in all groups. Rats fed Quadrol at levels up to 1% of the diet (representing a dosage of 600 - 900 mg/kg/d) exhibited no signs of toxicity. Rats fed Quadrol at levels of 3% and 5% of the diet (reaching a maximum daily dose

of 3300 mg/kg in the first week) suffered some failure to gain weight in the early weeks of the experiment, possibly due to unpalatability of the diet. In these higher dose groups no other evidence of toxicity was seen, except for a slightly greater incidence of borderline abnormalities of the liver, which were of questionable significance.

Reliability : (2) valid with restrictions
Study pre-dates GLPs and standardized methods. Basic documentation provided, details of methods lacking.

14.10.2003 (7)

5.5 GENETIC TOXICITY 'IN VITRO'

Type	:	Ames test
System of testing	:	Salmonella typhimurium TA97, TA98, TA100, TA 102; E. coli WP2(PKM101)
Test concentration	:	200 - 10000 ug/plate (test material solvent: DMSO)
Cycotoxic concentr.	:	
Metabolic activation	:	with and without
Result	:	negative
Method	:	other: only referred to as "standard plate"
Year	:	1994
GLP	:	no data
Test substance	:	no data

Reliability : (4) not assignable
secondary reference (from CCRIS in TOXNET)

14.10.2003 (8)

(1) MSDS, BASF Corp., 17 SEP 2002

(2) MSDS, MDL Information Systems, 11 DEC 2001

(3) MSDS, MDL Information Systems, 22 MAR 2001

(4) Budavari, S., ed., The Merck Index: an encyclopedia of chemicals, drugs and biologicals. 12th ed., Merck and Co., New Jersey, 1996.

(5) Industrial Bio-Test Laboratories, Report No. 8560-08828, Four-Day Static Aquatic Toxicity Study with Quadrol in Fathead Minnows, May 4, 1976.

(6) Hill Top Research Institute, Acute Oral Toxicity of Quadrol, March 7, 1956

(7) Hill Top Research Institute, Subacute Oral Toxicity of Quadrol, March 1, 1956, Project 151.

(8) Hachiya, N. and Takizawa, Y., Mutagenicity of Plastic Additives, Hen'igensei Shiken 3(3):147-154 (1994). Cited at http://toxnet.nlm.nih.gov, CCRIS Record number 8275, last updated 02/12/2001.

I U C L I D

Data Set

Existing Chemical	:	ID: 122-20-3
CAS No.	:	122-20-3
EINECS Name	:	1,1',1''-nitrilotripropan-2-ol
Common Name		triisopropanolamine
EC No.	:	204-528-4
TSCA Name	:	2-Propanol, 1,1',1''-nitrilotris-
Molecular Formula	:	C9H21NO3

Producer related part

Company	:	Arcadis
Creation date	:	02.10.2003

Substance related part

Company	:	Arcadis
Creation date	:	02.10.2003
Status	:	
Memo	:	
Printing date	:	01.12.2003
Revision date	:	
Date of last update	:	01.12.2003
Number of pages	:	16
Chapter (profile)	:	Chapter: 1.0.1, 1.1.0, 1.1.1, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6.1, 2.7, 2.14, 3.1.1, 3.3.2, 3.5, 3.6, 4.1, 4.2, 4.3, 4.4, 4.9, 5.1.1, 5.4, 5.5, 5.6, 5.8.1, 5.8.2, 5.8.3
Reliability (profile)	:	Reliability: without reliability, 1, 2, 3, 4
Flags (profile)	:	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 APPLICANT AND COMPANY INFORMATION

Type	:	other
Name	:	Arcadis
Contact person	:	Jane Staveley
Date	:	
Street	:	4915 Prospectus Drive, Suite F
Town	:	27713 Durham, NC
Country	:	United States
Phone	:	919-544-4535
Telefax	:	919-544-5690
Telex	:	
Cedex	:	
Email	:	jstaveley@arcadis-us.com
Homepage	:	www.arcadis-us.com

Remark This document has been prepared on behalf of BASF Corporation

15.10.2003

1.1.0 SUBSTANCE IDENTIFICATION

IUPAC Name	:	
Smiles Code	:	
Molecular formula	:	C9 H21 NO3
Molecular weight	:	191.27
Petrol class	:	

07.10.2003

1.1.1 GENERAL SUBSTANCE INFORMATION

Purity type	:	
Substance type	:	organic
Physical status	:	
Purity	:	>= 97 % w/w
Colour	:	
Odour	:	

Method : GC
02.10.2003 (1)

2.1 MELTING POINT

Value : ca. 50 °C

Source : BASF AG Ludwigshafen
02.12.1992 (2)

2.2 BOILING POINT

Value : = 134.2 °C at 1.25 hPa
Decomposition :
Method : other: vapour pressure measurement
Year : 1972
GLP : no
Test substance :

Method : Dynamic method
Result : measured values:

temperature (°C)	vapour pressure (torr)	vapour pressure (hPa)
134.2	0.94	1.25
144.7	1.74	2.31
155.7	3.18	4.24
165.3	5.30	7.07
175.9	8.88	11.84
186.2	14.3	19.07
198.8	24.9	33.20
199.8	25.5	34.00
214.4	45.3	60.40
228.3	80.1	106.80
244.8	140.0	186.65
263.6	240.0	319.97
267.5	320.2	426.90
270.4	338.1	450.76
272.6	329.8	439.70
277.0	355.5	473.96
287.5	530.0	706.61
301.1	760.0	1013.25

The regression of the results leads with a mean deviation of 3.18 % to the following equation:

P.VL(T) = EXP(A + B/T + C*LN(T) + D*T**E)

A = 838.1367
B = -42064.89
C = -130.1468
D = 0.1279836
E = 1

Source : BASF AG Ludwigshafen
Test substance : Triisopropanolamine, no further data
Reliability : (2) valid with restrictions
Acceptable study, meets basic scientific principles
22.10.2003 (3)

2.3 DENSITY

Type : density
Value : = 1.01 g/cm³ at 60 °C

Remark : DIN 51757
Source : BASF AG Ludwigshafen
02.12.1992 (2)

2.4 VAPOUR PRESSURE

Value : = .000000018084 hPa at 25 °C
Decomposition :
Method : other (measured)
Year : 1972
GLP : no
Test substance :

Method : Dynamic method
Result : measured values:

temperature (°C)	vapour pressure (torr)	vapour pressure (hPa)
134.2	0.94	1.25
144.7	1.74	2.31
155.7	3.18	4.24
165.3	5.30	7.07
175.9	8.88	11.84
186.2	14.3	19.07
198.8	24.9	33.20
199.8	25.5	34.00
214.4	45.3	60.40
228.3	80.1	106.80
244.8	140.0	186.65
263.6	240.0	319.97
267.5	320.2	426.90
270.4	338.1	450.76
272.6	329.8	439.70
277.0	355.5	473.96
287.5	530.0	706.61
301.1	760.0	1013.25

The regression of the results leads with a mean deviation of 3.18 % to the following equation:

P.VL(T) = EXP(A + B/T + C*LN(T) + D*T**E)

A = 838.1367
B = -42064.89
C = -130.1468
D = 0.1279836
E = 1

The Vapour Pressure at 20 °C, 25 °C and 50 °C was calculated from the regression equation:

temperature (°C)	vapour pressure (hPa)
20	7.7665E-09
25	1.8084E-08

50 6.8550E-07

Source : BASF AG Ludwigshafen
Test substance : Triisopropanolamine, no further data
Reliability : (2) valid with restrictions
Acceptable study, meets basic scientific principles

22.10.2003 (3)

2.5 PARTITION COEFFICIENT

Partition coefficient :
Log pow : = -.015 at °C
pH value :
Method : OECD Guide-line 107 "Partition Coefficient (n-octanol/water), Flask-shaking Method"
Year : 1987
GLP :
Test substance :

Source : BASF AG Ludwigshafen
16.10.2003 (4)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in : Water
Value : > 1000 g/l at 20 °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : 7.86 at 25 °C
Description :
Stable :

01.12.2003 (5) (6)

2.7 FLASH POINT

Value : = 160 °C
Type : closed cup
Method : other: DIN 51758
Year :
GLP :
Test substance :

Source : BASF AG Ludwigshafen
02.12.1992 (2)

2.14 ADDITIONAL REMARKS

Remark : Explosionsgrenzen in Luft: 0.8 - 5.8 Vol. %
Zuendtemperatur: 275 Grad C (DIN 51794)
Gefaehrliche Reaktionen: exotherme Reaktion mit Saeuren
Source : BASF AG Ludwigshafen
02.12.1992 (2)

3.1.1 PHOTODEGRADATION

Type : air
Light source :
Light spectrum : nm
Relative intensity : based on intensity of sunlight
INDIRECT PHOTOLYSIS
Sensitizer : OH
Conc. of sensitizer :
Rate constant : = .000000000124029 cm³/(molecule*sec)
Degradation : 50 % after .1 day(s)

Method : APOWIN v1.91 (EPIWIN v3.11)
Remark : assumed data: 1.5E6 OH/cm3; 12-h day
Result :

AOP Program (v1.91) Results:
==========
SMILES : OC(C)CN(CC(O)C)CC(O)C
CHEM : 2-Propanol, 1,1',1''-nitrilotris-
MOL FOR: C9 H21 N1 O3
MOL WT : 191.27
---------- SUMMARY (AOP v1.91): HYDROXYL RADICALS --------
Hydrogen Abstraction = 57.6090 E-12 cm3/molecule-sec
Reaction with N, S and -OH = 66.4200 E-12 cm3/molecule-sec
Addition to Triple Bonds = 0.0000 E-12 cm3/molecule-sec
Addition to Olefinic Bonds = 0.0000 E-12 cm3/molecule-sec
Addition to Aromatic Rings = 0.0000 E-12 cm3/molecule-sec
Addition to Fused Rings = 0.0000 E-12 cm3/molecule-sec

OVERALL OH Rate Constant = 124.0290 E-12 cm3/molecule-sec
HALF-LIFE = 0.086 Days (12-hr day; 1.5E6 OH/cm3)
HALF-LIFE = 1.035 Hrs
---------- SUMMARY (AOP v1.91): OZONE REACTION ----------

****** NO OZONE REACTION ESTIMATION ******
(ONLY Olefins and Acetylenes are Estimated)

Experimental Database: NO Structure Matches
Reliability : (1) valid without restriction
calculated using scientifically acceptable method

15.10.2003

3.3.2 DISTRIBUTION

Media : air - biota - sediment(s) - soil - water
Method : Calculation according Mackay, Level III
Year :

Method : EPIWIN v3.11
Result :

Level III Fugacity Model (Full-Output):
==========
Chem Name : 2-Propanol, 1,1',1''-nitrilotris-
Molecular Wt: 191.27
Henry's LC : 9.77e-012 atm-m3/mole (Henrywin program)
Vapor Press : 1.86e-005 mm Hg (Mpbpwin program)
Liquid VP : 6.31e-005 mm Hg (super-cooled)
Melting Pt : 78.6 deg C (Mpbpwin program)

Log Kow : -1.22 (Kowwin program)
Soil Koc : 0.0247 (calc by model)

	Mass Amount (percent)	Half-Life (hr)	Emissions (kg/hr)
Air	0.000321	2.07	1000
Water	45.3	360	1000
Soil	54.6	360	1000
Sediment	0.0755	1.44e+003	0

	Fugacity (atm)	Reaction (kg/hr)	Advection (kg/hr)	Reaction (percent)	Advection (percent)
Air	5.1e-015	1.36	0.0405	0.0452	0.00135
Water	1.46e-016	1.1e+003	572	36.7	19.1
Soil	6.5e-015	1.33e+003	0	44.2	0
Sediment	1.22e-016	0.459	0.0191	0.0153	0.000635

Persistence Time: 420 hr
Reaction Time: 519 hr
Advection Time: 2.21e+003 hr
Percent Reacted: 80.9
Percent Advected: 19.1

Half-Lives (hr), (based upon Biowin (Ultimate) and Aopwin):
Air: 2.07
Water: 360
Soil: 360
Sediment: 1440
Biowin estimate: 3.002 (weeks)

Advection Times (hr):
Air: 100
Water: 1000
Sediment: 5e+004

Reliability : (1) valid without restriction
calculated using scientifically acceptable method

16.10.2003

3.5 BIODEGRADATION

Type :
Inoculum : activated sludge, industrial
Concentration : 400 mg/l related to
related to
Contact time :
Degradation : < 10 (±) % after 28 day(s)
Result : other: poorly eliminated from water
Deg. product :
Method : OECD Guide-line 302 B "Inherent biodegradability: Modified Zahn-Wellens Test"
Year :
GLP : no
Test substance :

Remark : Other information (Davis and Carpenter, 1997) indicates that biodegradation of triisopropanolamine increases from a 5-day BOD value of <5% using an unacclimated inoculum to 40-50% using an acclimated

inoculum. In a simulation test with dilute activated sludge, diisopropanolamine was completely degraded within 72-120 hours; since this compound is a major metabolite of the aerobic biodegradation of triisopropanolamine, similar results would be expected for triisopropanolamine (Davis,J.W. and Carpenter, C.L., 1997. Environmental assessment of the alkanolamines. Reviews of Environmental Contamination and Toxicology, Vol. 149, pp. 87-137).

Source : BASF AG Ludwigshafen
24.11.2003 (7)

3.6 BOD5, COD OR BOD5/COD RATIO

Method : DIN 38409 T51
DIN 38409 T41

Remark : inoculum:
effluent of an industrial waste water treatment plant

Result : COD: 1963 mg/g
BOD5: <2 mg/g
TOC: 556 mg/g
BOD5*100/COD: 0 % (no degradation)

Source : BASF AG Ludwigshafen

Reliability : (2) valid with restrictions
test according to National Standard with restriction
03.09.2003 (8)

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	static
Species	:	Leuciscus idus (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC50	:	> 2150 - 4640
Limit test	:	
Analytical monitoring	:	no
Method	:	other: German Industrial Standard DIN 38412, Part 15
Year	:	1987
GLP	:	no
Test substance	:	other TS: triisopropanolamine, purity: >99 %
Method	:	Test concentrations of 1000, 2150, 4650 and 10000 mg/L were prepared in reconstituted fresh water, hardness 2.5 mmol/L, pH approx. 8.0.
Result	:	The 96-h LC50 was between 2200 and 4600 mg/L, with no effects at the former value and 100% mortality at the latter value.
Source	:	BASF AG Ludwigshafen
Reliability	:	(1) valid without restriction Test conducted according to standard procedure and with appropriate documentation.

15.10.2003 (9)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type	:	static
Species	:	other aquatic arthropod: Daphnia magna Straus
Exposure period	:	48 hour(s)
Unit	:	mg/l
EC0	:	= 250
EC50	:	> 500
EC100	:	> 500
Analytical monitoring	:	no
Method	:	other: Directive 79/831/EEC, Annex V, Part C
Year	:	1988
GLP	:	no
Test substance	:	other TS: triisopropanolamine
Result	:	effect values after 24 h (related to nominal concentrations): EC0 (24 h): =250 mg/L EC50 (24 h): >500 mg/L EC100 (24 h): >500 mg/L
Source	:	BASF AG Ludwigshafen
Reliability	:	(1) valid without restriction Test conducted according to standard procedure and with appropriate documentation.

15.10.2003 (10)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species	:	Scenedesmus subspicatus (Algae)
Endpoint	:	biomass
Exposure period	:	72 hour(s)
Unit	:	mg/l
EC10	:	= 8.84

EC50	:	= 68.93
EC90	:	> 100
Limit test	:	
Analytical monitoring	:	no
Method	:	other: German Industrial Standard DIN 38412, Part 9
Year	:	
GLP	:	no
Test substance	:	other TS: triisopropanolamine, purity: >98 %
Remark	:	Effect values were originally reported based upon inhibition of fluorescence at 72 h. These results were: EC20 = 11 mg/L EC50 = 35 mg/L EC90 > 100 mg/L Effect values were recalculated according to OECD Guideline 201 for growth rate and biomass using linear regression analysis considering fluorescence values mentioned in the report (BASF AG, Department of Ecology, unpublished data, 1090/88, 19.12.1990). This recalculation yielded 72 h growth rate values of: ErC10 = 16.1 mg/L ErC50 > 100 mg/L ErC90 > 100 mg/L and biomass values of: EbC10 = 8.84 mg/L EbC50 = 68.93 mg/L EbC90 > 100.0 mg/L The most sensitive results are those based upon biomass.
Result	:	effect values related to nominal concentration of the test substance.
Source	:	BASF AG Ludwigshafen
Reliability	:	(1) valid without restriction test procedure according to National Standard (German Industrial Standard DIN)

15.10.2003 (11) (12)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

Type	:	aquatic
Species	:	activated sludge, industrial
Exposure period	:	30 minute(s)
Unit	:	mg/l
EC20	:	> 1995
Analytical monitoring	:	no
Method	:	other
Year	:	
GLP	:	no
Test substance	:	
Remark	:	Bei sachgemaesser Einleitung in adaptierte biologische Klaer- anlagen sind keine Stoerungen der Abbauaktivitaet des Belebt- schlamms zu erwarten. Hoechste getestete Konzentration: 1995 mg/l; foerdernde Wirkung.
Source	:	BASF AG Ludwigshafen

03.09.2003 (7)

Type	:	aquatic
Species	:	Pseudomonas putida (Bacteria)
Exposure period	:	18 hour(s)
Unit	:	mg/l
TGK	:	= 20000
Analytical monitoring	:	no
Method	:	other: following DIN 38 412, Part 8
Year	:	
GLP	:	no
Test substance	:	
Method	:	test substance tested after neutralization
Source	:	BASF AG Ludwigshafen
Reliability	:	(4) not assignable original reference not available

03.09.2003 (13)

4.9 ADDITIONAL REMARKS

Memo	:	Further information can be taken from the BUA report No. 148 (Triisopropanolamin).
Source	:	BASF AG Ludwigshafen

22.12.1999

5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50
Value	:	= 6500 mg/kg bw
Species	:	rat
Strain	:	Wistar
Sex	:	male
Number of animals	:	10
Vehicle	:	water
Doses	:	Minimum: 140 mg/kg. Maximum: 1350 mg/kg.
Method	:	other
Year	:	1941
GLP	:	no
Test substance	:	
Method	:	Animals were dosed via gastric tube to the test substance diluted in water.
Remark	:	The results of this study are supported by other reported oral LD50 values for the rat ranging from 4000 to 9000 mg/kg bw (BUA Report 148, Triisopropanolamine, German Chemical Society Advisory Committee on Existing Chemicals of Environmental Relevance, December, 1993).
Result	:	The maximum dose having no effect was 140 mg/kg bw.
Reliability	:	(2) valid with restrictions Study pre-dates standarized methods and GLP. Test conditions not fully described.

22.10.2003 (14)

5.4 REPEATED DOSE TOXICITY

Type	:	
Species	:	rat
Sex	:	male
Strain	:	Wistar
Route of admin.	:	oral feed
Exposure period	:	102 weeks
Frequency of treatm.	:	
Post exposure period	:	
Doses	:	Single dose, approximately equal to 1216 mg/kg bw/day
Control group	:	yes, concurrent no treatment
NOAEL	:	> 1216 mg/kg bw
Method	:	other
Year	:	1991
GLP	:	no data
Test substance	:	
Method	:	The 2% dose was reported as equal to 324 mg/day per animal. Based upon the reported average initial and final body weights, this dose was calculated to be approximately equal to 1216 mg/kg bw/day
Result	:	This study, designed to examine carcinogenic effects, used a single group of 19 rats exposed to 2% triisopropanolamine and 17 controls. None of 19 exposed rats demonstrated tumors in the nasal cavity, lung, esophagus, liver, urinary bladder, thryroid, kidney, stomach, pancreas, or mammary gland. Pheochromocytoma (adrenal gland) and Leydig cell tumors (testis) were observed but at similar or lower percentages than observed in the controls. There was a 5% incidence (1 animal of 19) of pituitary gland adenomas in the treated rats versus none in the controls and an 11% incidence (2 animals of 19) of "other" tumors versus 18% in the controls; neither of these effects was statistically significant.
Test condition	:	Test conditions not described in English

Reliability	:	(4) not assignable Insufficient documentation

22.10.2003 (15)

Type	:	
Species	:	rat
Sex	:	male/female
Strain	:	no data
Route of admin.	:	drinking water
Exposure period	:	30 days
Frequency of treatm.	:	continuously in the drinking water
Post exposure period	:	no data
Doses	:	140 mg/kg - 1350 mg/kg
Control group	:	yes, concurrent no treatment
NOAEL	:	140 mg/kg
Method	:	other
Year	:	
GLP	:	no
Test substance	:	
Method	:	Animals (5 per dose) were exposed to triisopropanolamine in the drinking water for 30 days.
Result	:	The highest dose level reduced food intake and growth. 260 mg/kg still caused micropathological lesions of liver, kidney, spleen or testes (scope of examinations or kind of lesions are not mentioned). No treatment-related deaths occured during the study.
Reliability	:	(2) valid with restrictions Study pre-dates standardized methods and GLP. Test conditions not fully described.

01.12.2003 (16)

5.5 GENETIC TOXICITY 'IN VITRO'

Type	:	Ames test
System of testing	:	Salmonella typhimurium TA98, TA100, TA1535, TA1537
Test concentration	:	up to 10 mg/plate
Cycotoxic concentr.	:	
Metabolic activation	:	with and without
Result	:	negative
Method	:	other: according to Haworth, S. et al.: Environ. Mutagen. 5, Suppl. 1, 3-142
Year	:	1983
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Source	:	BASF AG Ludwigshafen

05.12.1993 (17)

5.6 GENETIC TOXICITY 'IN VIVO'

Type	:	Micronucleus assay
Species	:	mouse
Sex	:	male/female
Strain	:	NMRI
Route of admin.	:	gavage
Exposure period	:	
Doses	:	500, 1000, 2000 mg/kg bw in a volume of 10ml/kg bw
Result	:	

Method	:	OECD Guide-line 474 "Genetic Toxicology: Micronucleus Test"
Year	:	
GLP	:	yes
Test substance	:	other TS
Remark	:	According to the results of the present study, the single oral administration of Triisopropanolamin did not lead to any increase in the number of polychromatic erythrocytes containing either small or large micronuclei. No inhibition of erythropoiesis determined from the ratio of polychromatic to normochromatic erythrocytes was detected. Triisopropanolamin does not have any chromosome-damaging effect, and there were no indications of any impairment of chromosome distribution in the course of mitosis.
Source	:	BASF AG Ludwigshafen
Test substance	:	degree of purity: 92.0%

21.06.1996 (18)

5.8.1 TOXICITY TO FERTILITY

Type	:	other: no data
Species	:	rat
Sex	:	female
Strain	:	no data
Route of admin.	:	other: no data (presumably orally)
Exposure period	:	throughout pregnancy (no further data)
Frequency of treatm.	:	no data
Premating exposure period		
Male	:	
Female	:	
Duration of test	:	no data
No. of generation studies	:	
Doses	:	0.063 mg/kg/d
Control group	:	no data specified
Method	:	other: no data
Year	:	
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	no malformations, no adverse effects on reproductive parameters; original source not available
Source	:	BASF AG Ludwigshafen

05.12.1993 (19)

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species	:	rat
Sex	:	female
Strain	:	Wistar
Route of admin.	:	gavage
Exposure period	:	on day 6 through day 15 p.c.
Frequency of treatm.	:	daily
Duration of test	:	until day 20 p.c.
Doses	:	100; 400; 1000 mg/kg
Control group	:	yes
NOAEL maternal tox.	:	400 mg/kg bw

NOAEL teratogen.	:	>= 1000 mg/kg bw
Method	:	OECD Guide-line 414 "Teratogenicity"
Year	:	
GLP	:	yes
Test substance	:	other TS
Result	:	The test substance was administered as an aqueous solution to 23-25 pregnant rats/group. In the 1000 mg/kg dose group statistically significantly decreased food consumption at the beginning of the treatment period and significantly reduced body weight gain were observed. There were no effects on gestational parameters or fetuses. No substance-related effects on dams or fetuses were found in the other groups.
Source	:	BASF AG Ludwigshafen
Test substance	:	Triisopropanolamine, purity 92 %

22.10.2003 (20)

5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

Type	:	
In vitro/in vivo	:	In vivo
Species	:	rat
Sex	:	male
Strain	:	Wistar
Route of admin.	:	oral feed
Exposure period	:	102 weeks
Frequency of treatm.	:	
Duration of test	:	102 weeks
Doses	:	Single dose, approximately equal to 1216 mg/kg bw/day
Control group	:	yes, concurrent no treatment
Method	:	other: study was designed to examine carcinogenic effects
Year	:	1991
GLP	:	no data
Test substance	:	
Method	:	The 2% dose was reported as equal to 324 mg/day per animal. Based upon the reported average initial and final body weights, this dose was calculated to be approximately equal to 1216 mg/kg bw/day.
Result	:	This study, designed to examine carcinogenic effects, used a single group of 19 rats exposed to 2% triisopropanolamine and 17 controls. None of 19 exposed rats demonstrated a significant increase in tumors of reproductive organs relative to the controls. This included the testis, mammary gland and pituitary gland.
Test condition	:	Test conditions not described in English
Reliability	:	(4) not assignable Insufficient documentation

16.10.2003 (15)

(1) BASF AG, Safety data sheet, TRIISOPROPANOLAMINE, 09.11.1999

(2) BASF AG, Sicherheitsdatenblatt TRIISOPROPANOLAMIN (4/91)

(3) BASF AG, Verfahrenstechnik, unpublished results, report no. 172.096.1, April 6, 1972

(4) BASF AG, Analytisches Labor; unveroeffentlichte Untersuchung, BRU 87.262, 18.12.1987

(5) BUA, Triisopropanolamine, BUA Report 148. German Chemical Society (GDCh) - Advisory Committee on Existing Chemicals of Environmental Relevance (BUA). (1993)

(6) The Dow Chemical Company, 1988. Physical properties of the alkanolamines. Form No. 111-1227-88. The Dow Chemical Company, Midland MI. Cited in Davis, J.W. and Carpenter, C.L., 1997, Environmental assessment of the alkanolamines, Reviews of Environmental Contamination and Toxicology 149:87-137.

(7) BASF AG, Labor Oekologie; unveroeffentlichte Untersuchung, No. 7, 1981

(8) BASF AG, Department of Ecology, unpublished study, 11.03.1981

(9) BASF AG; Department of Toxicology; unpublished results (87/271), 02.12.87

(10) BASF AG, Labor Oekologie; unveroeffentlichte Untersuchung, 1133/87, 27.01.1987

(11) BASF AG, Department of Ecology, unpublished study, 1090/88, 19.12.1990

(12) BASF AG, Department of Product Safety, unpublished calculation, 04.09.2003

(13) BASF AG, Analytisches Labor; unveroeffentlichte Untersuchung, 307371, 28.04.1988

(14) Smyth H.F., Jr., Seaton, J. and Fischer, L., J. Ind. Hyg. Toxicol. 25:259-268 (1941).

(15) Yamamoto, K., 1991. Endogenously synthesized N-nitrosobis(2-hydroxypropyl)amine and its carcinogenic potential in rats. J. Nara. Med. Ass. 42:134-152

(16) Smyth H.F. and Carpenter C.P., J. Ind. Hyg. Toxicol. 30, 63-68 (1948)

(17) Zeiger E. et al.: Environ. Mutagen. 9, Suppl.9, 1-18 (1987)

(18) BASF AG, dept. of toxicology, unpublished data (26M0013/9[C196), 02/23/1995

(19) Toropkov V.V.: Tr. Leningr. San.-gigien Med.In-ta 130, 29 (1980).
cited in: BIBRA Toxicity Profile "Triisopropanolamine" (1990)

(20) BASF AG, dept. of toxicology, unpublished data (30R0013/93029), 07/14/1995