

201-14715A

**HIGH PRODUCTION VOLUME (HPV)  
CHEMICAL CHALLENGE PROGRAM**

**TEST PLAN**

**For**

**N, N, N', N'- tetramethyl-1,2-ethanediamine,  
CAS No. 110-18-9**

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**Submitted to the US EPA  
By  
Crompton Corporation.**

## Table of Contents

### Test Plan for N, N, N', N'-tetramethyl-1,2-ethanediamine

1.	General Information	3
1.1	CAS No.	3
1.2	Molecular weight	3
1.3	Structure and formula	3
1.4	Introduction	3
2.	Review of Existing Data and Development of Test Plan	3
A.	Evaluation of Existing Physicochemical Data and Proposed Testing	4
B.	Evaluation of Existing Environmental Fate Data and Proposed Testing	4
C.	Evaluation of Existing Ecotoxicity Data and Proposed Testing	5
D.	Evaluation of Existing Human Health Effects Data and Proposed Testing	5
3.	Evaluation of Data for Quality and Acceptability	6
4.	References	7

## 1. General Information

1.1 CAS Number: 110-18-9

1.2 Molecular Weight: 116.21

1.3 Structure and formula: C<sub>6</sub>H<sub>16</sub>N



### 1.4 Introduction

N, N, N', N'-tetramethyl-1,2-ethanediamine (TMEDA) may be used in the preparation of epoxy curing agents; polyurethane formation; corrosion inhibition; as a textile finishing agent; as an intermediate for quaternary ammonium compounds; acrylamide polymerisation catalysis and as a reagent in organolithium compound formation.

## 2. Review of Existing Data and Development of Test Plan

Crompton Corporation has undertaken a comprehensive evaluation of all relevant data on the SIDS endpoints of concern for TMEDA. The availability of the data on the specific SIDS endpoints is summarized in Table 1. Table 1 also shows data gaps that will be filled by additional testing.

Table 1: Available adequate data and proposed testing for TMEDA

CAS No. 110-18-9	Information Available?	GLP	OECD Study?	Other Study?	Estimation Method?	Acceptable?	SIDS Testing required?
	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N
<b>Physicochemical</b>							
Melting Point	Y	N			N	Y	N
Boiling Point	Y	N			N	Y	N
Vapour Pressure	Y	N			Y	Y	N
Water Solubility	Y	N			Y	Y	N
Partition Coefficient (Kow)	Y	N			N	Y	N
<b>Environmental Fate</b>							
Biodegradation	Y				Y	Y	N
Hydrolysis	N						N
Photodegradation	Y				Y	Y	N
Transport and Distribution between Environmental Compartments	Y				Y	Y	N
<b>Ecotoxicology</b>							
Acute Fish	Y				Y	Y	N
Acute Daphnia	Y				Y	Y	N
Acute Algae	Y				Y	Y	N
<b>Toxicology</b>							
Acute Oral	Y	Y		Y		Y	N
Repeat Dose toxicity	Y	Y		Y		N	Y
Genetic toxicity – Gene mutation	Y	Y	Y			Y	N

Genetic toxicity – Chromosome aberration	N						Y
Reproductive toxicity	N						Y
Developmental toxicity/teratogenicity	N						Y

#### **A. Evaluation of Existing Physicochemical Data and Proposed Testing**

##### 1. Melting Point

The melting point of TMEDA is reported as -55°C in a peer-reviewed publication.

##### 2. Boiling Point

The boiling point of TMEDA is reported as 121°C in a peer-reviewed publication.

##### 3. Vapour Pressure

The vapour pressure of TMEDA was calculated to be 20 hPa at 25°C using MPBPWIN v1.40.

##### 4. Water Solubility

The water solubility of TMEDA was calculated to be 877,700 mg/L at 25°C using WSKOW v1.40.

##### 5. Partition Coefficient

The log Pow of TMEDA is reported as 0.3 in a peer reviewed publication. The value estimated using KOWWIN v1.66 is log Pow = -0.26.

**Summary of Physicochemical Properties Testing: Existing data for melting point, boiling point, vapour pressure, water solubility and partition coefficient are considered to fill these endpoints adequately and, therefore, no further testing is planned.**

#### **B. Evaluation of Existing Environmental Fate Data and Proposed Testing**

##### 1. Biodegradation

The biodegradation of TMEDA has been estimated using Biowin v4.00 and the results indicate TMEDA not to be readily biodegradable.

##### 2. Hydrolysis

There are no hydrolysable groups in the chemical structure, and the substance is therefore predicted to be hydrolytically stable.

##### 3. Photodegradation

The potential for photodegradation of TMEDA has been estimated using the AOP Program v1.90, and indicated atmospheric oxidation via OH radicals reaction with a half-life of 0.8 hours.

##### 4. Transport and Distribution between Environmental Compartments

An Epiwin Level III Fugacity Model calculation has been conducted for TMEDA and indicates even distribution between soil and water for emissions of 1000 kg/hr simultaneously to air water and soil compartments.

**Summary of Environmental Fate Testing:** Existing data for photodegradation and transport and distribution between environmental compartments are considered to fill these endpoints adequately. TMEDA contains no hydrolysable or biodegradable groups, therefore no hydrolysis or biodegradation testing is proposed.

### **C. Evaluation of Existing Ecotoxicity Data and Proposed Testing**

1. Acute Toxicity to Fish

Estimation using ECOSAR v0.99g gives an LC<sub>50</sub> (96 h) of 392 mg/L.

2. Acute Toxicity to Algae

Estimation using ECOSAR v0.99g gives an LC<sub>50</sub> (96 h) of 24 mg/L.

3. Acute Toxicity to Daphnia

Estimation using ECOSAR v0.99g gives an LC<sub>50</sub> (48 h) of 23 mg/L.

**Summary of Ecotoxicity Testing:** TMEDA belongs to the Ecosar class of aliphatic amines. The predicted values for acute toxicity to fish, daphnia and algae are regarded as being valid for this material and no testing is proposed.

### **D. Evaluation of Existing Human Health Effects Data and Proposed Testing**

1. Acute Oral Toxicity

The acute oral toxicity has been determined in a number of studies, two of which are considered reliable. The first study (EPA OTS 798.1175, rat, GLP) reported an LD<sub>50</sub> value of 891 mg/kg b.w. (males) and 406 mg/kg b.w. (females). A second study (similar to guideline method, rat, GLP) reported an LD<sub>50</sub> value of 268 mg/kg b.w. (females) and >250 mg/kg b.w. (males).

2. Acute Inhalation Toxicity

This non-SIDS endpoint has been determined in a number of studies. In the most reliable of these (EPA OTS 798.1150, rat, GLP) the reported LC<sub>50</sub> (4 h) was >1180 ppm.

3. Acute Dermal Toxicity

This non-SIDS endpoint was determined in a valid study (EPA OTS 798.1100, rabbit, GLP) and the LD<sub>50</sub> was reported to be 1230 mg/kg b.w.

4. Skin Irritation

This non-SIDS endpoint has been evaluated for TMEDA in a number of studies. In the most reliable study (EPA OTS 798.4470, rabbit, GLP) the substance was found to be severely irritating via the dermal route of exposure.

5. Eye Irritation

This non-SIDS endpoint has been evaluated for TMEDA. In the most reliable study (EPA OTS 798.4500, rabbit, GLP) the substance produced severe, persistent irritation.

6. Repeat Dose Toxicity

The repeat dose toxicity of TMEDA has been determined in a 9-d (similar to guideline method, rat, GLP) via the inhalation route. The NOAEL was reported to be <50 ppm. As the repeat dose toxicity has not been evaluated over a minimum of 28 d, this endpoint will be determined using OECD Method 422.

7. Genotoxicity

TMEDA was determined to be non-mutagenic in two reliable Ames reverse mutation assays (similar to OECD 471, *S. typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538, GLP) and (similar to OECD 471, *S. typhimurium* TA98, TA100, TA1535 and TA1537).

The *in vitro* cytogenicity of TMEDA will be determined using OECD Method 473.

8. Reproductive and Developmental Toxicity

The developmental and reproductive toxicity of TMEDA in rat will be determined using OECD Method 422.

**Summary of Human Health Effects Testing: The endpoints for repeat dose toxicity, developmental toxicity and reproductive toxicity (OECD 422) and genotoxicity (OECD 473), will be determined. The other human health endpoints have been filled adequately.**

3. Evaluation of Data for Quality and Acceptability

The collected data were reviewed for quality and acceptability following the general US EPA guidance [2] and the systematic approach described by Klimisch et al [3]. These methods include consideration of the reliability, relevance and adequacy of the data in evaluating their usefulness for hazard assessment purposes. This scoring system was only applied to ecotoxicology and human health endpoint studies per EPA recommendation [4]. The codification described by Klimisch specifies four categories of reliability for describing data adequacy. These are:

- (1) **Reliable without restriction:** Includes studies or data complying with Good Laboratory Practice (GLP) procedures, or with valid and/or internationally accepted testing guidelines, or in which the test parameters are documented and comparable to these guidelines.
- (2) **Reliable with Restrictions:** Includes studies or data in which test parameters are documented but vary slightly from testing guidelines.
- (3) **Not Reliable:** Includes studies or data in which there are interferences, or that use non-relevant organisms or exposure routes, or which were carried out using unacceptable methods, or where documentation is insufficient.
- (4) **Not Assignable:** Includes studies or data in which insufficient detail is reported to assign a rating, e.g. listed in abstracts or secondary literature.

#### 4. References

- [1] US EPA, EPI Suite Software, 2000
- [2] USEPA (1998). Guidance for Meeting the SIDS Requirements (The SIDS Guide). Guidance for the HPV Challenge Program. Dated 11/2/98.
- [3] Klimisch, H.-J., et al (1997). A Systematic Approach for Evaluating the Quality of Experimental Toxicological and Ecotoxicological Data. Regul. Toxicol. Pharmacol. 25:1-5
- [4] USEPA (1999). Determining the Adequacy of Existing Data. Guidance for the HPV Challenge Program. Draft dated 2/10/99.