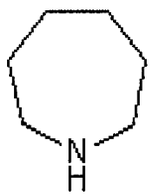
Summary and Test Plan for:

Hexamethyleneimine



CAS#: 111-49-9

U.S. EPA HPV Challenge Program Submission

Submitted by:

INVISTA S.à r.l.

SUMMARY

Under the U.S. Environmental Protection Agency (EPA) High Production Volume (HPV) Chemical Challenge Program, INVISTA S.à r.l ("INVISTA") is completing a commitment by DuPont to voluntarily compile a Screening Information Data Set (SIDS) that can be used for an initial hazard assessment of Hexamethyleneimine (HMI), CAS Registry No. 111-49-9. Robust summaries have been prepared for all key studies. The information described in this test plan is a summary of the data presented in the Robust Summaries and should only be used for the purposes of the HPV Program.

This assessment includes data for physicochemical, environmental fate, and mammalian and environmental effect endpoints included in the U.S. HPV Program in a manner consistent with the requirements of an OECD SIDS Level 1 data package. Data / information on use and exposure have also been supplied with this submission. Based on a literature search, combined with data from accepted models, adequate information is available for all endpoints.

The information that follows below has been taken from the Robust Summaries prepared for HMI, which include the original references for the data presented.

Hexamethyleneimine is a clear, colorless liquid with a fishy, ammonia-like odor. It has a melting/freezing point of - 37 °C, boiling point of 138 °C, and density of 0.8799 at 20/4 °C. Hexamethyleneimine has a vapor pressure of 8.09 mm Hg (Daubert and Danner, 1989). The Hazardous Substance Data Bank (HSDB) of the National Library of Medicine reports a water solubility of 3.19×10^4 mg/L at 25°C for hexamethyleneimine, which was taken from the Aquasol database of Aqueous Solubility. Additional support for the submitted water solubility value includes the EPIWIN v3.05 model value for hexamethyleneimine of 4.4×10^4 mg/L. This value corresponds closely to the above reported HSDB value. In addition, dipropylamine (CASRN: 142-84-7), an analog of hexamethyleneimine, has a measured solubility of 3.51×10^4 mg/L (HSDB) and a calculated (WSKOWIN v1.41) value of 4.4×10^4 mg/L. These values are consistent with the solubility values for hexamethyleneimine. No further testing is recommended.

Hexamethyleneimine has an estimated log K_{ow} of 1.7, which is a conservative estimate in terms of partitioning into living tissue (Meylan and Howard, 1995). Since hexamethyleneimine is an ionizable species in water, logK_{ow} may not be the most appropriate way to describe its lipophilicity. Instead, logD calculations using Advanced Chemistry Development (ACD) software, which takes into account both the ionization constants and logK_{ow} of various species formed in solution at different pH, is considered to be more appropriate. Calculated values for hexamethyleneimine at different pH values are shown below. At low concentrations in the environment, where pH is likely to be near neutral, the logD values are low (lower than the estimated logK_{ow}), predicting very little, if any, partitioning into living tissue. No further testing is recommended.

logD (LOGD)	-1.60	pH l	(1) ACD
logD (LOGD)	-1.60	pH 4	ACD[1]
logD (LOGD)	-1.57	pH 7	ACD[1]
logD (LOGD)	-1.37	pH 8	ACD[1]

logD (LOGD)	0.24	pH 10	ACD[1]

[1]Calculated using Advanced Chemistry Development (ACD) Software Solaris V4.67 ((C) 1994-2003 ACD)

Hexamethyleneimine's production and use may result in its release to the environment through various waste streams or directly to the air. If released to air, a vapor pressure of 8.09 mm Hg at 25°C indicates hexamethyleneimine will exist solely in the vapor phase in the ambient atmosphere. Vapor-phase hexamethyleneimine will be degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals; the half-life for this reaction in air is estimated to be 4.3 hours. If released into water, hexamethyleneimine is expected to have limited adsorption to suspended solids and sediment in water based upon the estimated K_{oc} of 20. A pKa of 11.07 indicates hexamethyleneimine will exist almost entirely in the protonated form in aqueous environments, and is not expected to volatilize from water surfaces. The maximum reported biodegradability for hexamethyleneimine was 1.19% over 28 days. In addition, hexamethyleneimine was toxic to the microbial inoculum at a test concentration of 2 mg active substance/L. An estimated BCF of 3.9 suggests the potential for bioconcentration in aquatic organisms is low (SRC, n.d.). Fugacity model prediction indicates that hexamethyleneimine will partition mainly to the soil and water, with virtually none going to the air or sediment.

Aquatic toxicity studies conducted with hexamethyleneimine on fish, invertebrates, and algae according to current OECD TG (203, 202, and 201, respectively) indicate low to moderate acute aquatic toxicity. LC_{50}/EC_{50} values were determined to be >100 mg/L for rainbow trout and *Daphnia* and 88 mg/L (growth index) for green algae and thus were of lower toxicity than predicted by the ECOSAR model (INVISTA S.á r.l. 2006, 456749) and (INVISTA S.á r.l. 2006, 456751).

Reported values for acute oral toxicity in rats with hexamethyleneimine ranged from highly toxic to slightly toxic. However, only 1 study specified the purity of the sample tested, which was 98.18%. In this study, the acute oral toxicity in rats was 1,000 mg/kg (slightly toxic). Hexamethyleneimine was moderately toxic via inhalation with an ALC in rats of 2.45 mg/L (DuPont Co. 1974). Organs showing possible test substance related effects included the lungs, trachea, and eyes; however, histopathologic effects were difficult to interpret in the absence of a concurrent control group. Hexamethyleneimine had a dermal MLD (Minimum Lethal Dose) of 1,260-2,000 mg/kg when tested in rabbits, was corrosive to the skin and eye, and produced sensitization reactions in 40% of mice tested using the mouse ear swelling test (MEST).

Hexamethyleneimine did not produce mortality, clinical signs of toxicity (other than some temporary discomfort at dosing), or evidence of treatment related pathological changes when administered orally to rats at a dose of 90 mg/kg, 5 times/week for 2 weeks. When administered as a single 10 mg/kg dose, hexamethyleneimine produced no effects upon plasma or interstitial fluid concentrations. At 10 mg/kg daily for 7 days, no morphological changes in testes, or abnormal changes in epididymal sperm morphology in male rats were observed.

Except for mucosal thickening of glandular/forestomach tissue observed at necropsy (without correlation to microscopic tissue damage), no other treatment related effects were observed up to the highest dosage tested (50 mg/kg/day hexamethyleneimine (by gavage) during a Combined Repeated Dose Toxicity and Reproductive/Developmental Toxicity Screen study (OECD 422). Additionally, no effects were observed on gonadal tissue or on reproductive parameters including mating, parturition or lactation in parental animals. No evidence of developmental or fetal effects were seen in offspring even at the highest dosage (50 mg/kg/day) tested (INVISTA S.á r.l. 2006, 456738).

Hexamethyleneimine was negative in *Salmonella typhimurium* and *Escherichia coli* when tested in the *in vitro* bacterial reverse mutation assay. No clastogenic effects were observed when hexamethyleneimine was tested in an *in vitro* chromosomal aberration study (OECD 473) in human lymphocytes, with and without incorporation of a mammalian metabolic activation system.

Exposure Assessment for HMI

At INVISTA locations, production and loading operations occur in a closed system. All sites that produce HMI have implemented safety, health and environmental practices and procedures in addition to engineering controls, environmental controls, and personal protective equipment to control exposure. Safety equipment, such as safety showers, eyewash fountains, and washing facilities, are available in the event of an occupational exposure.

Air monitoring has been conducted on HMI and the results that were previously reported by DuPont are shown in the table below. A sampling and analytical method validation study for HMI was conducted by Clayton Environmental Consultants in 1995 (Project No. 27051-00). Clayton's method of evaluation was based on a previous method for trans 1, 4-diaminocyclohexane, and included study of method performance, recovery efficiency, sample stability, and collection efficiency. Analysis was performed using gas chromatography/nitrogen phosphorus detection (GC/NPD). Samples were collected on 225 milligram (mg) silica gel sorbent tubes. Overall, the method has a wide linear range of 6.07 to 121.4 mg/sample and a recovery average of 92.2% for HMI. HMI is stable over 21 days and has an overall average collection efficiency of 97.7%. Prior to 1995 an in-house method was used.

An exposure limit of 0.5 ppm, as an 8-hour TWA (time-weighted average), had previously been recommended by DuPont. No other limits have been established. None of the samples taken suggest the probability of exposure in excess of 0.5 ppm.

EXPOSURE DATA

Exposure Group	No. of Results	Avg. of TWA[1] (ppm)	Min. of Results (ppm)	Max of Results (ppm)
HMD Operators (16)	104	0.056	<0.005	**0.31**

Power East Operators (20)	6	0.056	<0.049	0.06
HMD Maintenance (22)	25	0.053	<0.005	**0.10**

[1]Not specified if values are “arithmetic mean” or “geometric mean”.

References for the Summary:

Daubert, T. E. and R. P. Danner (1989). Physical and Thermodynamic Properties of Pure Chemicals Data Compilation, Taylor and Francis, Washington, DC.

DuPont Co. (1974). Unpublished Data, Haskell Laboratory Report No. 495-74 (also cited in TSCA fiche OTS0546547).

INVISTA S.á r.l. Internal Study (2006). NOTOX B.V. Project No. 456738.

INVISTA S.á r.l. l Internal Study (2006). NOTOX B.V. Study No.456749.

INVISTA S.á r.l. Internal Report (2006). NOTOX B.V. Study no. 456751.

Meylan, W. M. and P. H. Howard (1995). J. Pharm. Sci., 84:83-92 (HSDB/562).

SRC (Syracuse Research Corporation) (n.d.). (HSDB/562).

TEST PLAN FOR HEXAMETHYLENEIMINE

Hexamethyleneimine CAS No. 111-49-9	Data Available	Data Acceptable	Testing Required
	Y/N	Y/N	Y/N
PHYSICAL/CHEMICAL CHARACTERISTICS			
Melting Point	**Y**	**Y**	**N**
Boiling Point	**Y**	**Y**	**N**
Vapor Pressure	**Y**	**Y**	**N**
Partition Coefficient	**Y**	**Y**	**N**
Water Solubility	**Y**	**Y**	**N**
ENVIRONMENTAL FATE			
Photodegradation	**Y**	**Y**	**N**
Stability in Water	**Y**	**Y**	**N**
Transport (Fugacity)	**Y**	**Y**	**N**
Biodegradation	**Y**	**Y**	**N**
ECOTOXICITY			
Acute Toxicity to Fish	**Y**	**Y**	**N**
Acute Toxicity to	**Y**	**Y**	**N**
Acute Toxicity to Aquatic	**Y**	**Y**	**N**
MAMMALIAN TOXICITY			
Acute Toxicity	**Y**	**Y**	**N**
Repeated Dose Toxicity	**Y**	**Y**	**N**
Developmental Toxicity	**Y**	**Y**	**N**
Reproductive Toxicity	**Y**	**Y**	**N**
Genetic Toxicity Gene	**Y**	**Y**	**N**
Genetic Toxicity Chromosomal Aberrations	**Y**	**Y**	**N**