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ROBUST SUMMARY FOR HEXAMETHYLENEIMINE

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Summary

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 and water solubility at 25°C of 8.09 mm Hg and 3.19×10^4 mg/L, respectively, and an estimated log Kow of 1.7. Hexamethyleneimine has a flash point of 37.2°C and flammability limits in air of 1.6-2.3%.

Hexamethyleneimine's production and use as an intermediate in the synthesis of a pesticide product may result in its release to the environment through various waste streams. 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 adsorb to suspended solids and sediment in water based upon the estimated Koc of 170. Volatilization of the free amine from water surfaces is expected to be an important fate process based upon this compound's Henry's Law constant. However, 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. 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.

ECOSAR (Meylan and Howard, 1999) was used to estimate the missing aquatic toxicity data for hexamethyleneimine to fish, *Daphnia* (planktonic freshwater crustaceans), and algae. Predicted $\log_{10}$ Kow values were used as input for the ECOSAR model. Based on the ECOSAR predictions, hexamethyleneimine would be moderately toxic to aquatic organisms, with a 96-hour LC_{50} in fish of 36.5 mg/L, a 48-hour EC_{50} in Daphnia of 2.6 mg/L, and a 96-hour EC_{50} in green algae of 4.4 mg/L. ECOSAR predictions are generally substantiated by comparing the values obtained in the model to those obtained from actual testing of an analogous compound. Since no measured test data for an analogous chemical were available, fish, *Daphnia*, and algae studies (generally following OECD Guidelines 203, 202, and 201, respectively) are recommended to determine the actual aquatic toxicity potential of this test substance.

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 1000 mg/kg (slightly toxic). Hexamethyleneimine was moderately toxic via inhalation with an ALC in rats of 2.45 mg/L. 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 of 1260-2000 mg/kg when tested in rabbits, is 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. Although repeated dose data are available, and there are some evaluations of the gonads and gonadal products, they are not sufficient to adequately describe the potential toxicity from repeated exposure to the test substance or data to evaluate the potential reproductive or developmental effects. Hence, a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD Guideline 422) is recommended.

Hexamethyleneimine was negative in *Salmonella typhimurium* and *Escherichia coli* when tested in the *in vitro* bacterial reverse mutation assay. Since no additional information regarding genetic toxicity was available, an *in vitro* chromosome aberration study in human blood (generally following OECD Guideline 473) is recommended to fulfill the required HPV endpoint for potential chromosomal aberrations.

Exposure Assessment for HMI

HMI (Hexamethyleneimine) is manufactured at four DuPont facilities (Victoria, Sabine River Works, Maitland, and Wilton). HMI is a raw material used in the production of a new chemical contained in a FIFRA registered herbicide. 73% of the HMI is sold into this application and the remaining 27% is burned for fuel value.

The potential for exposure is the greatest during the loading and unloading of HMI, since closed processes are used at the sites. The sites can have from 430 to 2000 personnel working (construction, contractor, and plant employees). The areas where the substance is manufactured will have from 2 to 5 operators during normal operations and 30 to 60 people during a shutdown or major construction activity. HMI is manufactured at all four sites, but three sites ship their material to Victoria or a toller where the HMI is refined. All sites that produce HMI have effective safety, health and environmental practices and procedures in addition to engineering controls, environmental controls, and personal protective equipment to control exposure. Adequate safety equipment, such as safety showers, eyewash fountains, and washing facilities, are available in the event of an occupational exposure. Individuals handling HMI should avoid contact with eyes, skin, or clothing, should not breathe vapor or mist, and should wash thoroughly after handling.

DuPont practices Responsible Care and assesses the ability of a potential toll manufacturer or any customer to safely handle HMI, prior to commencing a commercial relationship. This assessment includes reviews and audits of PPE (personal protective equipment), safety equipment and procedures, structural integrity, and safety practices. The Toller has procedures, practices, and controls in place to manage the risk of exposure. DuPont also assess the capability of a customer using the Product Stewardship System prior to selling a product. The Product Stewardship System works with customers to understand their applications and any issues associated with PPE, safety equipment (safety showers, eyewash stations, ventilation needs,

etc.), storage concerns, disposal requirements, and MSDS questions. No DuPont sites, tollers, or customers reported any SHE incidents from the handling of HMI.

Air monitoring has been conducted on HMI and results 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 validation 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 μg/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. LOGAN (lognormal analysis) is a computerized statistical method for characterizing occupational exposures to chemicals, noise, and other environmental hazards. LOGAN uses sequential collection of data and makes decisions on the minimum amount of data. It helps make cost-effective, accurate decisions that ensure a healthy workplace. LOGAN uses inferential statistics to estimate the true workplace conditions, in the same way that public polling estimates opinions by sampling a representative percentage of the public. LOGAN is designed to limit the risk of employee occupational overexposure to less than 5%.

The DuPont Acceptable Exposure Limit (AEL) for HMI is 0.5 ppm as an 8-hour TWA (time-weighted average). No other limits have been established. None of the samples taken suggest the probability of exposure in excess of the current recommended AEL of 0.5 ppm 8-hour TWA.

EXPOSURE DATA

People	No. of Results	Avg. of TWA (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

References for the Summary:

Meylan, W. M. and P. H. Howard (1999). User's Guide for the ECOSAR Class Program, Version 0.993 (Mar 99), prepared for J. Vincent Nabholz and Gordon Cas, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics, Washington, DC, prepared by Syracuse Research Corp., Environmental Science Center, Syracuse, NY 13210 (submitted for publication).

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

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TEST PLAN FOR HEXAMETHYLENEIMINE

Hexamethyleneimine CAS No. 111-49-9	**Data Available**	**Data Acceptable**	**Testing Required**
Study	**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	N	Y
Acute Toxicity to Invertebrates	Y	N	Y
Acute Toxicity to Aquatic Plants	Y	N	Y
MAMMALIAN TOXICITY			
Acute Toxicity	Y	N	N
Repeated Dose Toxicity	Y	N	Y
Developmental Toxicity	N	N	Y
Reproductive Toxicity	Y	N	Y
Genetic Toxicity Gene Mutations	Y	Y	N
Genetic Toxicity Chromosomal Aberrations	N	N	Y