Canadian Environmental Protection Act

Priority Substances List Assessment Report

3,5'-Dimethylaniline

Government of Canada | Gouvernement du Canada
Environment Canada | Environnement Canada
Health and Welfare Canada | Santé et Bien-être social Canada

Canada

CANADA'S GREEN PLAN

Canadian Environmental Protection Act

PRIORITY SUBSTANCES LIST ASSESSMENT REPORT

3,5-DIMETHYANILINE

Government of Canada
Health and Welfare Canada
Environment Canada

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Synopsis

The substance 3,5-dimethylaniline, which is reported to be mainly used as an intermediate in the manufacture of azo dyes, is not produced or imported into Canada. It is anticipated that 3,5-dimethylaniline will not persist in the environment since, by analogy to aniline, it should readily undergo biological degradation in water and soil, and photolysis in water, air and on soil. No information was found in the literature on the concentrations of 3,5-dimethylaniline in air, surface waters, ground water, biota, soil or sediment in Canada or elsewhere.

Available data on the toxic effects of 3,5-dimethylaniline on aquatic organisms indicate that concentrations in the low mg/L range would be required before adverse effects could be predicted; however, such levels are unlikely given the lack of use of this substance in Canada. No data on its toxicity to wild mammals, birds, sediment or soil biota were identified.

3,5-Dimethylaniline is expected to be of low to moderately volatility, and to readily photolyze in air. Consequently, it is unlikely that this substance would contribute to ozone depletion, global warming or the formation of ground-level ozone.

The available information was considered inadequate to quantitatively estimate the exposure to 3,5-dimethylaniline by the general population in Canada, or the associated potential health risk.

Based on these considerations, the Minister of the Environment and the Minister of National Health and Welfare have concluded that 3,5-dimethylaniline is not entering the environment in a quantity or concentration or under conditions that constitute a danger to the environment or to the environment upon which human life depends. The Ministers have concluded that there are insufficient data to determine whether 3,5-dimethylaniline constitutes a danger in Canada to human life or health.

1.0 Introduction

The Canadian Environmental Protection Act (CEPA) requires the Ministers of the Environment and of National Health and Welfare to prepare and publish a Priority Substances List that identifies substances, including chemicals, groups of chemicals, effluents and wastes, that may be harmful to the environment or constitute a danger to human health. The Act also requires both Ministers to assess these substances and determine whether they are "toxic" as interpreted in Section 11 of the Act, which states:

> "…a substance is toxic if it is entering or may enter the environment in a quantity or concentration or under conditions
>
> (*a*) having or that may have an immediate or long-term harmful effect on the environment;
>
> (*b*) constituting or that may constitute a danger to the environment on which human life depends; or
>
> (*c*) constituting or that may constitute a danger in Canada to human life or health."

Substances assessed as "toxic" according to Section 11 may be placed on the List of Toxic Substances (Schedule I of the Act). Consideration can then be given to developing guidelines, codes of practice or regulations to control any aspect of their life cycle, from the research and development stage through manufacture, use, storage, transport and ultimate disposal.

The assessment of whether 3,5-dimethylaniline is "toxic", as interpreted under CEPA, was based on the determination of whether it enters or is likely to enter the Canadian environment in a concentration or quantities or under conditions that could lead to exposure of humans or other biota to levels that could cause harmful effects.

Data relevant to the assessment of whether 3,5-dimethylaniline is "toxic" under CEPA were identified through the evaluation of published reference texts and literature identified through on-line searches of various databases (HSDB, RTECS, IRIS, CCRIS, TOXLINE, TOXLIT, ENVIROLINE, CHEMICAL ABSTRACTS, BIOLOGICAL ABSTRACTS, ELIAS, AQUAREF, MICROLOG, CODOC). Information was also obtained from the CEPA Domestic Substances List and from Statistics Canada. An unpublished review of the environmental behaviour and health effects of 3,5-dimethylaniline prepared under contract by Cambridge Environmental Inc. (Croy and DeVoto, 1990) was consulted where appropriate. In addition, a number of provincial authorities were requested to provide any available information on the levels of 3,5-dimethylaniline in the drinking water in their provinces. Data relevant to the assessment of the effects of 3,5-dimethylaniline on the environment and human health obtained after April, 1992 and October, 1992, respectively, were not considered for inclusion.

All studies that form the basis for determining whether 3,5-dimethylaniline is "toxic" under CEPA have been critically evaluated by the following staff of Health and Welfare

Canada (human exposure and effects on human health) and Environment Canada (entry and environmental exposure and effects):

R.G. Liteplo (Health and Welfare Canada)
R.J. Maguire (Environment Canada)
M.E. Meek (Health and Welfare Canada)

A summary of technical information critical to the assessment, and which is presented in greater detail in an unpublished Supporting Document, is presented in Section 2. The assessment of whether 3,5-dimethylaniline is "toxic" is presented in Section 3.

The environmental sections of this report were reviewed by Drs. C.M. Auer and W.H. Farland of the U.S. Environmental Protection Agency. Sections related to the effects on human health were approved by the Standards and Guidelines Rulings Committee of the Bureau of Chemical Hazards of Health and Welfare Canada. The Assessment Report was reviewed and approved by the Environment Canada/Health and Welfare Canada CEPA Management Committee.

Copies of this Assessment Report and the Supporting Document are available upon request from:

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2.0 Summary of Information Critical to Assessment of "Toxic"

2.1 Identity, Properties, Production and Uses

3,5-Dimethylaniline (Chemical Abstracts Service Registry Number 108-69-0) is one of six isomeric dimethylanilines, or xylidines, with a molecular formula of $C_8H_{11}N$. It is a pale to yellow oily liquid at room temperature (Weast *et al*., 1984). Synonyms for 3,5-dimethylaniline include 3,5-xylidine, 3,5-dimethylphenylamine, 3,5-dimethylbenzamine and 1-amino-3,5-dimethylbenzene. There are no experimentally determined values for its vapour pressure or solubility in water; estimated values are a vapour pressure of 7.4 Pa at 25°C (Grain, 1982) and a water solubility of 248.5 mg/L at 25°C (Kenaga and Goring, 1980). Reported values for the log n-octanol/water partition coefficient are 2.21 (calculated) (Newsome *et al*., 1987) and 3.04 (measured) (Tonogai *et al*., 1982).

3,5-Dimethylaniline can be produced by the reduction of 3,5-dimethylnitrobenzene with iron in strong acid (Sandridge and Staley, 1978). 3,5-Dimethylaniline and other xylidine isomers are reported to be mainly used as intermediates in the manufacture of azo dyes (Northcott, 1978; Budavari, 1989). It is also reportedly used in the manufacture of pharmaceuticals, curing agents, antioxidants and antiozonants, gasoline additives and detergents, wood preservatives, wetting agents for textiles, frothing agents for ore dressing, special lacquers and metal complexers.

3,5-Dimethylaniline is not produced or imported into Canada Environment Canada, 1990; 1991a; 1991b). There is no information on its incorporation in products imported into Canada. Production in the United States in 1986 was reported to total 19.2 tonnes; none was produced in 1990 (U.S. EPA, 1992).

2.2 Entry into the Environment

Based on the lack of domestic production and use, there do not appear to be any commercial sources or releases of 3,5-dimethylaniline into the Canadian environment. No information was identified in the literature on the presence of 3,5-dimethylaniline in effluents or emissions in Canada or other countries. 3,5-Dimethylaniline can be produced in various coal conversion processes (Schultz *et al*., 1978), and also by the reduction in aquatic environments of 3,5-dimethylnitrobenzene. However, there is no information which indicates that either process is relevant in Canada. The substance does not occur naturally, and there is no indication that it is involved in transboundary atmospheric transport.

2.3 Exposure-related Information

2.3.1 *Fate*

There is insufficient information (measured physical and chemical data and degradation rate constants) to permit an estimation of the relative importance of various pathways of distribution and transformation of 3,5-dimethylaniline in the environment. Based on the estimated vapour pressure and aqueous solubility, the half-life for volatilization of 3,5-dimethylaniline from surface waters (1 m deep, flowing at 1 m/s, with wind velocity of 3 m/s) to the atmos-

phere at 20°C was estimated to be 29.5 h (according to a method described by Thomas (1982)). This indicates that 3,5-dimethylaniline has low-to-medium volatility.

By analogy with aniline, it is anticipated that 3,5-dimethylaniline will be relatively non-persistent in the environment and that biological degradation will be a major process determining its persistence in the aquatic and soil environments. The photolysis of 3,5-dimethylaniline by sunlight may also play an important role in the degradation of this substance in water, on soil and in air. Based on a comparison of its pK_a (4.89) (Perrin, 1965) with that of aniline (pK_a = 4.63), it is anticipated that 3,5-dimethylaniline may bind more strongly to clays than to organic matter in soils. Data on the persistence of 3,5-dimethylaniline in the environment are limited to a report by Baird *et al*. (1977), in which the half-life for the degradation of 3,5-dimethylaniline by activated sludge was similar to that for aniline (i.e., less than 1 week).

3,5-Dimethylaniline is not expected to accumulate to any significant extent in either terrestrial or aquatic organisms.

2.3.2 *Concentrations*

No quantitative data on the levels of 3,5-dimethylaniline in drinking water, surface water, ground water, soil or sediment, biota or foodstuffs within Canada (or elsewhere) were identified. No information on the level (if any) of 3,5-dimethylaniline that may be present in consumer products containing dyes derived from this substance was identified.

2.4 Effects-related Information

2.4.1 *Experimental Animals and* In Vitro

Available (quantitative) data on the toxicity of 3,5-dimethylaniline in experimental animals are limited to values of the LD_{50} for the oral administration of this compound to rats and mice (Vernot *et al*., 1977) and the formation of methaemoglobin in cats injected (intravenously) with 3,5-dimethylaniline (McLean *et al*., 1969). Information on the toxicological effects produced by either the short-term, subchronic or chronic exposure of experimental animals to 3,5-dimethylaniline, or data on the reproductive, developmental, neurological and/or immunological effects of this compound in experimental animals have not been identified. Quantitative information on the metabolism of 3,5-dimethylaniline in experimental animals was also not identified.

Information on the mutagenicity/genotoxicity of 3,5-dimethylaniline is limited. Although Zimmer *et al*. (1980) and Nohmi *et al*. (1984) reported that 3,5-dimethylaniline was not mutagenic in various strains (TA98, TA100, TA1537) of *Salmonella typhimurium* (either with or without metabolic activation), Zeiger *et al*. (1988) reported "weak" mutagenic activity of 3,5-dimethylaniline (94% purity) in *Salmonella typhimurium* in the presence of metabolic activation. The (intraperitoneal) administration of 3,5-dimethylaniline (100 mg/kg b.w.) to male mice had no effect upon the synthesis of DNA in the testis (Seiler, 1979).

2.4.2 *Humans*

No quantitative information on the toxicological effects produced in humans following chronic exposure to 3,5-dimethylaniline was identified.

2.4.3 *Ecotoxicology*

Baird *et al*. (1977) reported that 3,5-dimethylaniline (20 mg/L) had some (unquantified) inhibitory effect on the respiration of organisms in activated sludge while this substance was being degraded, suggesting that a metabolite or metabolites may be responsible for the observed toxicity. Kaiser and Palabrica (1991) reported EC_{50}s of 14 to 19 mg/L 3,5-dimethylaniline for light output (photoluminescence) in a bacterium, *Photobacterium phosphoreum*. Schultz *et al*. (1978) reported a 48-h LC_{100} of 273 mg/L for a ciliate, *T. pyriformis*. Tonogai *et al*. (1982) reported 24- and 48-h LC_{50}s of 35 and 17 mg/L, respectively, for medaka fish (*Oryzias latipes*). Kaiser (1992) estimated a 96-h LC_{50}s of 22 mg/L for fathead minnow (*Pimephales promelas*), 11 mg/L for rainbow trout (*Oncorhynchus mykiss*) and 14mg/L for golden orfe (*Leuciscus idus melanotus*), based on structure-activity relationships.

No data on the toxicological effects of 3,5-dimethylaniline in wild mammals, birds, sediment or soil biota were identified.

3.0 Assessment of "Toxic" under CEPA

3.1 CEPA 11(*a*): Environment

3,5-Dimethylaniline is not produced or imported into Canada, indicating that there are no commercial sources or releases of this compound in this country. It is not expected to persist in the environment since, by analogy to aniline, it should readily undergo biological degradation in water and soil, and photolysis in water, air, and on soil. No reports were identified concerning its presence in biota or environmental media in Canada or elsewhere. Limited data were found that provided insight into the toxicity of 3,5-dimethylaniline to environmental biota. Levels in the low mg/L range in water would have to be reached before adverse effects would be predicted; however, these are unlikely, even if 3,5-dimethylaniline were to enter the Canadian environment.

Therefore, on the basis of available data, 3,5-dimethylaniline is not considered to be "toxic" as defined under paragraph 11(*a*) of CEPA.

3.2 CEPA 11(*b*): Environment on Which Human Life Depends

There are no data suggesting that 3,5-dimethylaniline is entering or may enter the Canadian environment. Furthermore, due to its estimated low-to-medium volatility and its tendency to photolyze readily in air, it is not expected to contribute to ozone depletion, global warming or the formation of ground-level ozone.

Therefore, on the basis of available data, 3,5-dimethylaniline is not considered to be "toxic" as defined under paragraph 11(*b*) of CEPA.

3.3 CEPA 11(*c*): Human Life or Health

Data on concentrations of 3,5-dimethylaniline in air, water and food within Canada (or elsewhere) have not been identified. Consequently, the available information is considered inadequate to (quantitatively) estimate the exposure of the general population in Canada to 3,5-dimethylaniline.

Available (quantitative) data on the toxicity of 3,5-dimethylaniline in experimental animals (or humans) are limited to values of the LD_{50} for the oral administration of this compound to rats and mice and the formation of methaemoglobin in cats following the intravenous injection of this compound. Additional identified information on the toxicity of 3,5-dimethylaniline is restricted to limited data on the mutagenicity/genotoxicity of the substance.

Thus, the information on human exposure and available toxicological data are considered inadequate (EHD, 1992) to serve as a basis for the determination of whether or not 3,5-dimethylaniline is "toxic" as defined under paragraph 11(*c*) of CEPA.

Therefore, there are insufficient data to assess whether 3,5-dimethylaniline is "toxic" as defined under paragraph 11(*c*) of CEPA.

3.4 Conclusion

On the basis of available data, 3,5-dimethylaniline is not considered to be "toxic" as defined under paragraphs 11(*a*) and 11(*b*) of CEPA. It has been concluded that available data are insufficient to assess whether 3,5-dimethylaniline is "toxic" as defined under paragraph 11(*c*) of CEPA.

4.0 Recommendations for Research

To permit a more comprehensive assessment of the effects of 3,5-dimethylaniline on human health and the environment, additional data are required on the levels of this substance in the environment and its fate in various environmental media, on its toxicological effects on aquatic and terrestrial organisms, and from well-designed sub-chronic, chronic (carcinogenicity), reproductive and developmental toxicity studies in mammalian species. Since negligible amounts (if any) of 3,5-dimethylaniline may be entering the country, the priority for research is considered to be low.

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