N-oxydiethylenethiocarbamyl-N'-oxydiethylenesulfenamide Accelerator Revised Test Plan

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CAS Nos.: 13752-51-7

Rubber and Plastic Additives Panel
American Chemistry Council
December 2003

List of Member Companies in the Rubber and Plastic Additives Panel

The Rubber and Plastic Additives (RAPA) Panel of the American Chemistry Council (ACC) includes the following member companies: Alco Chemical Corporation; Bayer Polymers LLC; Ciba Specialty Chemicals Corporation; Crompton Corporation; Eliokem, Inc.; Flexsys America L.P.; The Goodyear Tire & Rubber Company; The Lubrizol Corporation; Noveon, Inc.; and R.T. Vanderbilt Company, Inc.

Executive Summary

The American Chemistry Council's RAPA Panel submits this Test Plan and accompanying Robust Summaries for N-oxydiethylenethiocarbamyl-N'-oxydiethylenesulfenamide (OTOS; CAS No. 13752-51-7). This submission constitutes part of a revision of documents previously submitted by the RAPA Panel. In the previous submission, dated December 3, 2001, OTOS was included in a category called "Sulfenamide Accelerators." After considering comments received, the Panel reconfigured the category and revised documentation for OTOS, which is now submitted as a single chemical rather than as part of a category. This current submission reflects consideration of comments received from EPA (dated August 14, 2002) and from Environmental Defense (dated May 7, 2002). While chemistry and hazard information for the chemicals in the former Sulfenamide Accelerators category overlap, the Panel is submitting revised documentation for the two sponsored category chemicals individually to more clearly explain and substantiate the data. Documentation for the remaining former category member [2-(morpholinothio)-Benzothiazole (MBS; CAS number 102-77-2)] was submitted separately on August 25, 2003.

In consideration of animal welfare concerns to minimize the use of animals in the testing of chemicals, the Panel has conducted an extensive literature search for all available data, published and unpublished. The Panel has also performed an analysis of the adequacy of the existing data.

As described in the report that follows, this sulfenamide accelerator, which has a structure consisting of two morpholine molecules (R_1/R_2) that are attached to a dithiocarboxy group [$R_1SC(S)R_2$], is used as a primary accelerator in natural and synthetic rubbers. Its use in rubber products requires negligible water solubility, high organic/oil solubility, relatively low melting point and low vapor pressure. Based on the current knowledge of the physical properties of this and other similar accelerators, OTOS is insoluble in water and is expected to be of low to moderate concern for aquatic toxicity, low concern for persistence/bioaccumulation and low concern with respect to acute mammalian toxicity. *In vitro* studies

have shown that it is mutagenic in a number of assays. It is also carcinogenic at high doses in rats. A number of studies including the absence of histopathological findings in reproductive tissues from a long-term feeding study in rats indicate that it is not a reproductive toxin.

After further review, the Panel concurs that some additional testing is appropriate for purposes of the HPV Program.

OTOS Accelerator Structure

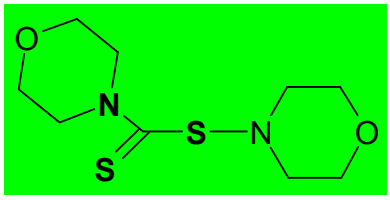

Figure 1. Chemical structure N-oxydiethylenethiocarbamyl-N'-oxydiethylenesulfenamide (OTOS) CAS No. 13752-51-7

Precursors

OTOS is produced by reacting two moles of morpholine with one mole of carbon disulfide.

Common Breakdown Products

OTOS is readily hydrolyzed to give the starting amine. It undergoes accelerated degradation when exposed to heat, humidity and/or acidic conditions.

Physicochemical Properties

The physicochemical properties of OTOS were reviewed and are described in Table 1. OTOS is a solid at room-temperature with a relatively low melting point, low vapor pressure, negligible water solubility, and high flash points.

A review of the physicochemical data indicates that some data are adequate while other end points need confirmation. Melting point data are adequate. The EPIWIN value of 124° C is close to the measured melting point range of 133.0° C to 140.0° C. Boiling point is not applicable; OTOS begins to decompose at the melting point range. Therefore, a boiling point test will not be conducted. Water solubility and partition coefficient studies will be conducted.

Fate and Transport Characteristic

The environmental fate and transport characteristics of OTOS have been reviewed. OTOS is expected to rapidly hydrolyze to its starting materials, especially under acidic conditions. The presence or absence of light does not significantly alter the degradation rate, so additional photodegradation data collection efforts are not necessary. Fugacity Level III calculations have also been provided. In practice, this material is not expected to partition to water or air if released into the environment due to its low water solubility and low vapor pressure. Calculated Bioconcentration Factors and Log P values indicate that this material is not Persistent Organic Pollutant (POP). Hydrolysis and biodegradation (OECD 301B) studies will be conducted. Level III fugacity modeling also will be recalculated using experimentally derived data.

Aquatic Toxicology

No adequate ecotoxicity data was located on OTOS. Fish (OECD 203), Daphnia (OECD 202), and algal (OECD 201) acute aquatic toxicity tests are proposed.

Mammalian Toxicology – Acute

Data on acute mammalian toxicity of OTOS were reviewed. The data were determined to be adequate for purposes of the HPV program. The findings indicate a low concern for acute toxicity.

Mammalian Toxicology – Repeated Dose Toxicity

Data from repeated-dose toxicity studies were reviewed. The data were determined to be adequate for purposes of the HPV program. The two-year feeding study established a NOAEL of 200 ppm for chronic effects of OTOS in rats. An increased incidence of urothelial tumors was observed in rats at the high dose (600 ppm).

Mammalian Toxicology - Mutagenicity

Data from bacterial reverse mutation assays, *in vitro* and *in vivo* chromosome aberration studies, as well as additional supporting *in vitro* and *in vivo* genetic toxicity studies were reviewed. The data were determined to be adequate for purposes of the HPV program. These studies show that OTOS is positive in a number of *in vitro* assays that have been used as screens for carcinogenic potential. These data are consistent with the increased incidence of tumors in the two-year feeding study.

Mammalian Toxicology - Reproductive and Developmental Toxicity

Data from the male fertility, dominant lethal, and two year feeding studies in rats with OTOS were reviewed. The data were determined to be adequate for purposes of the HPV program. Based on the absence of reproductive effects in the male fertility and dominant lethal studies and the absence of any histopathological changes in reproductive organs in the two-year feeding study, OTOS was determined to be a low concern for Reproductive Toxicity.

No adequate developmental studies have been located on OTOS. An OECD 421 developmental toxicity study is proposed.

Conclusion

Based upon EPA's comments and a further review of the data, additional testing will be conducted on OTOS.

Test Plan

The test plan for OTOS is summarized in Table 1.

Background Information: Manufacturing and Commercial Applications

Manufacturing

OTOS has been manufactured in the USA for approximately 25 years. It is manufactured by reacting morpholine, carbon disulfide, and bleach in an aqueous medium.

Commercial Applications

The sole known commercial use of OTOS is as a general purpose vulcanization accelerator for natural and styrene-butadiene rubbers. It is primarily used in the manufacture of tires. Typical usage for OTOS accelerators is from 0.5 to 2 parts accelerator per every 100 parts of rubber (phr).

Worker/Consumer Exposure

OTOS is sold to industrial users as ingredients for their rubber compounding processes. There are no known direct sales to the general public. Exposure of workers handling OTOS is likely to be the highest in the area of material packaging rather than from chemical manufacturing. Dustless forms that reduce the potential for inhalation exposure, coupled with the mechanized materials handling systems of the large industrial users, combine to help keep exposures to minimum levels.

The potential for consumer exposure is limited. OTOS is primarily used in rubber for retread tires and industrial applications. Only very small amounts are used in rubber processing. Furthermore, it becomes bound in the rubber matrix during the vulcanization process. Because consumers are expected to only have incidental and infrequent contact with the rubber, the potential for skin irritation, or possibly an allergic skin reaction in sensitive individuals from prolonged and repeated exposure is minimal to nil.

Table 1. Test Plan for OTOS Accelerator

End Point	Available Data	Assessment
Molecular Weight	248.36	A
Melting Point	130.0° C to 140.0° C; 124.3˚ C (EPI)[1]	A
Boiling Point	353˚ C (EPI)[1]	A
Relative Density	0.6 g/cm3	A
Vapor Pressure	1.53x10(-5)hPa	A
Partition Coef. (logPow)	-0.84 (EPI)[1]	T
Water Solubility	NV[1]	T
Photodegradation	$T_{1/2}$ = 0.6 hr (AOP)[2]	A
Hydrolysis	ND	T
Biodegradability	ND	T
Fugacity Level III	Air = <0.01%; Water = 50.2%; Soil = 49.7%; Sediment = 0.0927%	C
Acute Fish Toxicity	ND	T
Acute Invertebrate Toxicity	ND	T
Algal Toxicity	ND	T
Acute Toxicity	Oral LD50 = 5,200 mg/kg bw (rat)	A
Repeated Dose	NOAEL = 200 ppm (2 year feeding study, rats)	A
Mutagenicity:– gene mutation	Ames = negative; *E. coli* = negative; Mouse Lymphoma Assay = positive	A
Mutagenicity – chromosome	CHO chromosomal aberration assay = positive (-act); *E. coli* DNA Damage & Repair = positive; *In vivo* Dominant Lethal Assay = negative	A
Reproductive Toxicity	No reproductive effects in Male Fertility or DL Assays; No pathology changes in reproductive organs at doses up to 600 ppm in 2 yr rat feeding	A
Developmental Toxicity	ND	T

Legend for Table 1:
A = Adequate data available
C = Endpoint requirement fulfilled based on calculated data
T = Testing to be done
ND = Not Done
NV = Not Valid
(-act) = Without metabolic activation
CHO = Chinese hamster ovary cells

References

1. EPIWIN modeling Program. Meylan, W. and Howard, P. (1999), Syracuse Research Corporation. Environmental Science Center, 6225 Running Ridge Road, North Syracuse, NY 13212-2510.

2. AOP Program, version 1.89. EPIWIN modeling Program. Meylan, W. and Howard, P. (1999) Syracuse Research Corporation. Environmental Science Center, 6225 Running Ridge Road, North Syracuse, NY 13212-2510.