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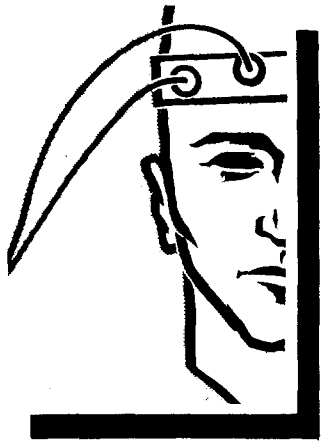
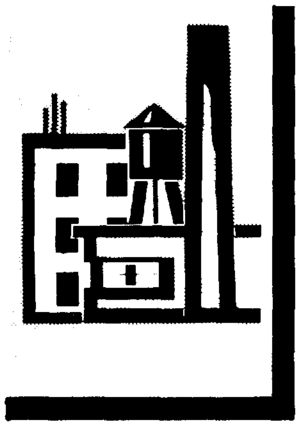
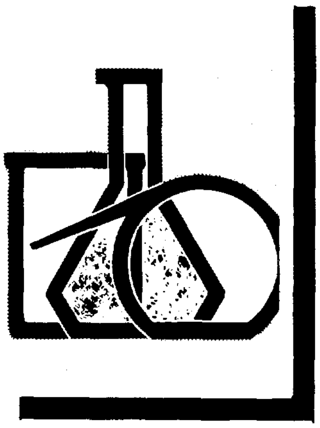
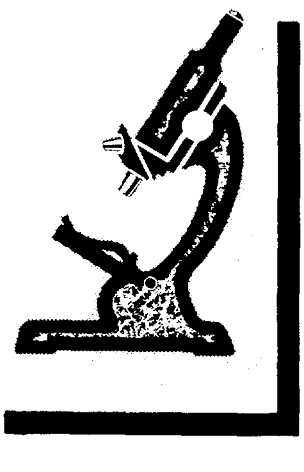


SPECIAL OCCUPATIONAL HAZARD REVIEW with CONTROL RECOMMENDATIONS





for ETHYLENE THIOUREA



U. S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
Public Health Service
Center for Disease Control
National Institute for Occupational Safety and Health

SPECIAL HAZARD REVIEW

WITH

CONTROL RECOMMENDATIONS

FOR

ETHYLENE THIOUREA

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U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
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National Institute for Occupational Safety and Health

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DISCLAIMER

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PREFACE

The Occupational Safety and Health Act of 1970 emphasizes the need for standards to protect the health and safety of workers exposed to an ever increasing number of potential hazards in their workplace. Consequently, the National Institute for Occupational Safety and Health (NIOSH) has implemented a program to evaluate the adverse effects of widely used chemical and physical agents. This program includes the development of Special Hazard Reviews which serve to support and complement the other major criteria documentation activities of the Institute.

The purpose of the Special Hazard Review is to assist employers in protecting the health and well-being of their employees.

The design of a Special Hazard Review is to analyze and document, from a health standpoint, the problems associated with a given industrial chemical, process, or physical agent, and to recommend the implementation of engineering controls and work practices to correct these problems.

Special Hazard Reviews are intermediate in scope to the more comprehensive NIOSH Criteria Documents and the briefer NIOSH Current Intelligence Bulletins. Generally, Special Hazard Reviews will concern those hazards associated with cancer or reproductive effects.

Dissemination of Special Hazard Reviews may be accomplished through appropriate trade associations, unions, industries, and members of the scientific community.

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The DCDSD review staff for this document consisted of Vernon E. Rose, Dr. P.H., Irwin P. Baumel, Ph.D., and Frank L. Mitchell, D.O. (Chairman).

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SPECIAL HAZARD REVIEW
ETHYLENE THIOUREA
(ETU)

CONTENTS

I. INTRODUCTION

On April 11, 1978, NIOSH issued a Current Intelligence Bulletin (CIB) which called attention to the carcinogenic and teratogenic potential of ethylene thiourea (ETU) in the workplace (Ethylene Thiourea, Current Intelligence Bulletin #22). While this bulletin alerted industry to known ETU hazards, the following Special Hazard Review presents a further report of the current occupational exposure to ethylene thiourea, and a more detailed and extensive appraisal of its mutagenic, teratogenic, and carcinogenic potential hazard in the workplace. This review was compiled so that a reliable source of information can be readily available to management and labor to assess the preventive measures available, and form a basis for the development of those better work practices needed to adequately protect the worker from exposure to ETU.

ETU is an organic compound chemically known as 2-imidazolidinethione. Its primary use is as an accelerator for vulcanization of elastomers (The Condensed Chemical Dictionary, 1977; Merck Index, 1977; Hill, 1977). It has also been used for a variety of other applications including: a clearing agent in metallic electroplating baths, and an intermediate in dyes, synthetic resins, antioxidants, and pharmaceuticals (Merck Index, 1977).

The effects of prolonged exposure to ETU in experimental animals are: hypothyroidism and neoplastic transformation of body tissues (Graham et al, 1973; Gak et al, 1977).

ETU is also an in-vitro and in-vivo breakdown product of the ethylenebisdithiocarbamate type of fungicides (Bontoyan, 1973, 1975; Newsome et al, 1975). Mainly on the basis of the potential pollution of the environment by ETU from these fungicides, EPA has issued a Rebuttable Presumption Against Registration (RPAR) for ethylene bisdithiocarbamates (Federal Register, #154, 1977).

In the Russian publication "Harmful Substances in Industry," reference is made to ETU as the toxic breakdown product from the ethylenebisdithiocarbamate fungicides as the basis of hazard therefrom (Lazarew, 1978).

The Food and Drug Administration has revoked use of neoprene and rubber products which contain ETU that may come in contact with drugs, cosmetics or medical devices (Federal Register, 1973, 1974).

The World Health Organization (WHO) has not established a permanent Allowable Daily Intake (ADI) for ETU, but has set guidelines for residues (on crops) which vary from 0.01 to 0.1 ppm (WHO, Personal Communications, March, 1978; Ethylene Thiourea, IUPAC, 1977).

ETU was evaluated by the International Agency for Research on Cancer (Ethylene Thiourea, IARC Monograph, Volume 7, 1974), and on the evidence presented, ETU was designated "carcinogenic."

No Federal regulations limiting industrial exposure of workers to ETU have been established in the United States, nor by any foreign government reporting their regulations to the World Health Organization (Permissible Levels of Toxic Substances, 1977).

ETU is listed under the heading of "Carcinogenic Substances and Agents Whose Use Presents Significant Potential Hazard," by the

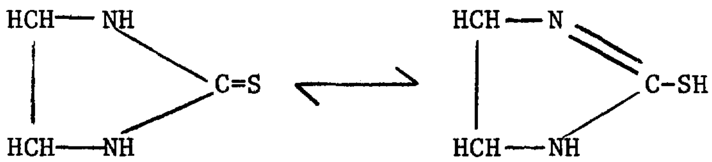
International Labour Office of the World Health Organization (Occupational Cancer--Prevention and Control, 1977).

II. CHEMICAL AND PHYSICAL PROPERTIES

At room temperature pure ETU is a colorless, odorless crystalline solid with a bitter taste (Kare and Muller, 1965). Some of the properties of ETU are listed in Table I.

Table I

Properties of Ethylene Thiourea

MW	102.17
Composition	C 3 N 2 S H 6
Structural formula	
Physical state	colorless short needle crystals or prisms
Melting point	203C
Vapor pressure	unknown
Flash point	252C
Water solubility	2% at 30C, 9% at 60C 44% at 90C

(Weast, 1977; The Condensed Chemical Dictionary, 1977; Hill, 1975)

ETU is stable in air or in solution over a wide range of temperatures and pH levels (Cruickshank and Jarrow, 1973). Ultraviolet radiation breaks down ETU to ethylene urea if a sensitizer, such as acetone or riboflavin, is added.

III. CHARACTERISTICS OF EXPOSURE

A. Manufacture

Hofman first synthesized ETU from ethylene diamine and carbon disulfide while attempting to prepare a mustard oil (Hofman, 1872). Most of the methods now used for the synthesis of ETU are variations of this, but Matolcsy (1968) demonstrated that it could also be synthesized from KCN and CS2.

In industry, ethylene thiourea is synthesized from ethylene diamine and carbon disulfide (Merck Index, 1976). Most of the production results in colorless to light green to yellow crystals with a light amine odor. This crystalline form melts at approximately 197C (The Condensed Chemical Dictionary, 1977). These crystals are crushed into a very fine powder in order to promote good dispersion into the elastomer. This flour-like dust tends to stick to the hands or on agitation becomes dispersed into the air (E.I. du Pont, 1972; Health Hazard Evaluation, 1977).

At least three major companies produce a safer type of formulation of ETU for use in the neoprene fabricating industry. The manufacturers intercalate finely divided ETU powder inside a matrix of an elastomer or a wax which is compatible with the final product. This "encapsulated" form of ETU is then used as the accelerator additive for vulcanization. In this form, ETU is least likely to become dispersed into the air that is respired by employees in facilities fabricating chloroprene products.

B. Production Volume

Production estimates of ETU are not available, the information being considered proprietary in nature by all companies (Synthetic Organic Chemicals, 1976). ETU production is closely tied to chloroprene (2-chlorobutadiene) polymer production and vulcanization. An estimate of the total production of ETU can thus be made from the production of chloroprene. A NIOSH criteria document has been prepared on occupational exposure to chloroprene (Criteria Document, 1977). Chloroprene is the monomer used to produce both chloroprene polymer latexes which are soft, as well as "dry" rubbers which are more resilient. Chloroprene polymer production is estimated at 440 million pounds per year (Chemical Profile, 1976). Inasmuch as ETU is reported to be added to chloroprene polymer at a rate of approximately one percent (1%) (E.I. du Pont, 1972), the best estimate of the production of ETU on this basis is 4.4 million pounds per year. Such an estimate does not include use in the acrylate base elastomers or in other uses, such as in electroplating, intermediates in the manufacture of other compounds, or as a contaminant found in fungicides (IARC, 1974; Bontoyan et al, 1975; Merck Index, 1977; The Condensed Chemical Dictionary, 1977).

Chloroprene polymer use has increased 5-6% per year from 1950-1974 (Criteria Document, 1977). The future growth has been estimated at 2.4% per year (Chemical Profile, 1976). The production of chloroprene polymers has been diminished by the use of plastics, especially in the wire and cable end-use area. Chloroprene polymer demand is dependent largely on the auto and construction industries, and, therefore, chloroprene polymer production is correlated with the general economy (Chemical Profile, 1976). The U.S. International Trade Commission lists two major producers of ETU (Synthetic Organic Chemicals, 1976): E.I. du Pont de Nemours and Co., Inc., and Fike Chemicals, Inc. Current information indicates ETU is distributed and available from most major chemical companies in small as well as bulk quantities (personal communications, 15 chemical companies, 1977).

C. Uses

Ethylene thiourea is used extensively as an accelerator in the vulcanization of various elastomers, including polychloroprene. Neoprene is E.I. du Pont's trade name for chloroprene polymer (polychloroprene). Chloroprene polymer, unlike natural rubber or most synthetic rubbers, is capable of being vulcanized or "cured" without the addition of any curing agents or accelerators, but the state of cure is usually unacceptable for most applications, and the rate of cure is too slow to be economically feasible (Neal, 1950). Because of this weakness in ability to vulcanize readily without additives, metal oxides, usually zinc oxide and manganese oxide, are employed as curing agents, and for most applications additional accelerators are desirable (Neal, 1950). The metal oxides furnish the free radicals for inducing the cross-linking of the monomer molecules. ETU initiates the free radical production at a more rapid rate. Neal (1950) discovered that in addition to producing a more rapid vulcanization, ETU was effective in producing "good age resistance, high elastic efficiency, and remarkable resistance to permanent deformation under conditions of compression." To date, no well accepted substitute for ETU has been found (personal communications, du Pont, Wyrough and Loser, St. Clair Rubber Co., 1977, 1978).

ETU can be used in nearly every type of polychloroprene formulation compound when a rapid rate of cure is desired. It can be used alone or in combination with other accelerators and curing agents. Variation in rate of addition can produce the most desired balance of properties in the vulcanizate. In general, modulus, resilience, and compression-set resistance all increase in proportion to the amount of ETU added up to "several" parts per hundred parts of elastomer. At the same time, processing safety, as indicated by the Mooney scorch test, (E.I. du Pont, 1972) decreases as ETU concentration increases. The various types of chloroprene polymer are somewhat different in their ETU requirements. In certain types, it is especially important to include a modifying secondary accelerator, such as thiuram, to produce the desired properties (E.I. du Pont, 1972; Bikales, 1965)

In thiacril rubbers, ETU meets the criteria of good curing performance and good storage characteristics, as well as adding the advantages of being non-adhesive to the mold and non-corrosive (E.I. du Pont, 1972).

Most uses other than as an accelerator in vulcanization are regarded by industry as proprietary information, but Merck Index (1977) lists its use in the electroplating of metals, and as an intermediate in the manufacture of dyes, synthetic resins, antioxidants, and pharmaceuticals.

D. Extent of Occupational Exposure

Based on a national survey conducted from 1972 to 1974, NIOSH estimated that approximately 17,000 employees in 24 different occupations are potentially exposed to ETU in the working environment (see Appendix C). The preliminary report of a Health Hazard Evaluation of ETU in a chloroprene fabrication plant estimates the major exposure routes to be inhalation and skin contact (Salisbury, 1978). This preliminary report also establishes that occupational exposure is less likely to occur when an "encapsulated" formulation of ETU is utilized rather than ETU powder.