

CURRENT INTELLIGENCE BULLETIN 22

ETHYLENE THIOUREA (ETU)

April 11, 1978

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IDENTIFIERS AND SYNONYMS FOR ETHYLENE THIOUREA

Chemical Abstracts Service

Number 96-45-7

NIOSH RTECS Number NI96250

Chemical Formula $C_3H_6N_2S$

4,5-Dihydroimidazole-2(3H)-thione

4,5-Dihydro-2-mercaptoimidazole

N,N'-(1,2-Ethanediy)thiourea

Ethylene thiourea

Ethylenethiourea

1,3-Ethylene-2-thiourea

1,3-Ethylenethiourea

N,N'-Ethylenethiourea

ETU

Imidazolidinethione

Imidazoline-2-thiol

2-Imidazolidinethione

2-Imidazoline-2-thiol

Imidazoline-2(3H)-thione

Mercaptoimidazoline

2-Mercaptoimidazoline

2-Mercapto-2-imidazoline

NA 22

NA-22-D

Pennac CRA

Rhodanin S 62

Sodium-22 Neoprene accelerator

Tetrahydro-2H-imidazole-2-thione

2-Thiol-dihydroglyoxaline

Warecure C

ETHYLENE THIOUREA (ETU)

April 11, 1978

The National Institute for Occupational Safety and Health (NIOSH) recommends that ethylene thiourea be handled in the workplace as if it were a human carcinogen and teratogen. During development of a NIOSH Special Occupational Hazard Review on ethylene thiourea (scheduled for issuance later in 1978) it became apparent that exposure to ethylene thiourea poses a risk of teratogenesis, particularly to the central nervous system, which is greater than has been generally recognized. The NIOSH literature review clearly shows ethylene thiourea to be a teratogen and a carcinogen in laboratory rats with supportive studies in other species. Pending completion of a NIOSH Special Occupational Hazard Review, this Current Intelligence Bulletin has been prepared to provide early dissemination of the information since NIOSH believes it would be prudent to minimize occupational exposure to ethylene thiourea. There is no current Occupational Safety and Health Administration (OSHA) exposure standard for ethylene thiourea.

Background

Ethylene thiourea is a white crystalline solid which is used extensively as an accelerator in the curing of polychloroprene (Neoprene) and other elastomers. NIOSH estimates that approximately 3,500 workers in the rubber industry have potential occupational exposure to ethylene thiourea. This estimate is based on the NIOSH National Occupational Hazard Survey which was conducted between 1972 and 1974, and included over 500,000 employees at 4,775 facilities. In addition, exposure to ethylene thiourea also results from the very widely used ethylene bisdithiocarbamate fungicides. Ethylene thiourea may be present as a contaminant in the ethylene bisdithiocarbamate fungicides and can also be formed when food containing the fungicides is cooked.

Commercial ethylene thiourea is available as a solid powder, as a dispersion in oil (which retards the formation of fine dust dispersions in workplace air), and "encapsulated" in a matrix of compatible elastomers. In this latter form, ethylene thiourea may be least likely to escape into the workplace air.

Laboratory Animal Studies

Ethylene thiourea has been shown to be carcinogenic and teratogenic (causing malformations in offspring) in laboratory animals. In addition, ethylene thiourea can cause myxedema (the drying and thickening of skin, together with a slowing down of physical and mental activity), goiter, and other effects related to decreased output of thyroid hormone.

In a recent publication from E. I. du Pont de Nemours and Company's Haskell Laboratory, for example, Stula and Krauss report "marked teratogenic effects were demonstrated" when ethylene thiourea was applied to the skin of laboratory rats.¹ In this study, 50 milligrams ethylene thiourea per kilogram body weight was applied as a 20% solution in dimethylsulfoxide (DMSO) to the skin of pregnant, female Sprague-Dawley rats on the twelfth and also on the thirteenth day of gestation. Malformations were observed in all of seventy-three fetuses upon sacrifice of the pregnant females on the twentieth day of gestation. Appropriate control animals showed no fetal abnormality. A number of other reports in the literature further document the teratogenic potential of ethylene thiourea (e.g., ² and references cited therein).

The Stula and Krauss study¹ further demonstrates that dose as well as day of gestation on which exposures occur are critical factors. When 50 mg/kg ethylene thiourea applications were made as above, but on the tenth and eleventh day of gestation, only five of eighty-three fetuses exhibited abnormalities; DMSO controls in this case exhibited one abnormality in forty fetuses. However, no fetal abnormalities were found among pregnant rats similarly exposed to 25 mg/kg ethylene thiourea on the tenth and also on the eleventh day of gestation.

Ethylene thiourea has been shown to cause cancer in laboratory animals. In one study, for example, Charles River CD rats were fed ethylene thiourea at 175 or 350 ppm in their diets for eighteen months and then observed while on a control diet for an additional six months.³ Thyroid carcinomas were observed in seventeen of twenty-six males² with pulmonary metastases) and eight of twenty-six females at the high dose level, as well as three of twenty-six males and three of twenty-six females at the low dose level. In addition, solid-cell adenomas of the thyroid were observed in one female at the high dose level as well as two females at the low dose level. No thyroid carcinoma was found among the thirty-two male or thirty-two female controls. The International Agency for Research in Cancer (IARC) has concurred that oral administration of ethylene thiourea produces thyroid carcinoma in rats.⁴ authors^{5,6} also reported carcinogenic effects of ethylene thiourea in laboratory animals.

A more complete review of animal experiments on ethylene thiourea will be presented in the forthcoming NIOSH Special Occupational Hazard Review.

NIOSH Recommendation

Pending completion of the NIOSH Special Occupational Hazard Review and the development of specific recommended control measures for ethylene thiourea, the National Institute for Occupational Safety and Health recommends, as an interim and prudent measure) that occupational exposure to ethylene thiourea be minimized exposure should be limited to as few employees as possible, while minimizing workplace exposure levels with engineering and work practice controls. Although substitution is a possible control measure, alternatives to ethylene thiourea or ethylene bisdithiocarbamate fungicides should be fully evaluated with regard to possible human health effects.

[signature]

J. Donald Millar, M.D.

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Acting Director

SUGGESTED GUIDELINES FOR MINIMIZING EMPLOYEE EXPOSURE TO ETHYLENE THIOUREA (ETU)

NIOSH recommends that it would be prudent to handle ethylene thiourea in the workplace as if it were a human carcinogen and teratogen. Exposure to ethylene thiourea should be limited to as few employees as possible) while minimizing workplace exposure levels. The area in which it is used should be restricted to only those employees essential to the process or operation.

Exposure Monitoring

Initial and routine employee exposure surveys should be made by competent industrial hygiene and engineering personnel. These surveys are necessary to determine the extent of employee exposure and to ensure that controls are effective.

The *NIOSH Occupational Exposure Sampling Strategy Manual*, NIOSH Publication #77-173, may be helpful in developing efficient programs to monitor employee exposures to ethylene thiourea. The manual discusses determination of the need for exposure measurements, selection of appropriate employees for exposure evaluation, and selection of sampling times.

Employee exposure measurements should consist of 8-hour TWA (time-weighted average) exposure estimates calculated from personal or breathing zone samples (air that would most nearly represent that inhaled by the employees). Area and source measurements may be useful to determine problem areas, processes, and operations.

Minimizing Employee Exposure

There are four basic methods of limiting employee exposure to ethylene thiourea. None of these is a simple industrial hygiene or management decision and careful planning and thought should be used prior to implementation of any of these.

- **Product Substitution**

The substitution of an alternative material with a lower potential health and safety risk is one method. However, extreme care must be used when selecting possible substitutes. Alternatives to ethylene thiourea should be fully evaluated with regard to possible human effects. Unless the toxic effects of the alternative have been thoroughly evaluated, a seemingly safe replacement, possibly only after years of use, may be found to induce serious health effects.

- **Contaminant Controls**

The most effective control of ethylene thiourea where feasible, is at the source of contamination by enclosure of the operation and/or local exhaust ventilation.

If feasible, the process or operation should be enclosed with a slight vacuum so that any leakage will result in the flow of air into the enclosure.

The next most effective means of control would be a well designed local exhaust ventilation system that physically encloses the process as much as possible, with sufficient capture velocity to keep the contaminant from entering the work atmosphere.

To ensure that ventilation equipment is working properly, effectiveness (e.g., air velocity static pressure, or air volume) should be checked at least every three months. System effectiveness should be checked soon after any change in production process, or control which might result in significant increases in airborne exposures to ethylene thiourea.

- **Employee Isolation**

A third alternative is the isolation of employees. It frequently involves the use of automated equipment operated by personnel observing from a closed control booth or room. The control room is maintained at a greater air pressure than that surrounding the process equipment so that air flow is out of, rather than into, the room. This type of control will not protect those employees that must do process checks, adjustments, maintenance, and related operations.

- **Personal Protective Equipment**

The least preferred method is the use of personal protective equipment. This equipment which may include respirators, goggles, gloves, and related items, should not be used as the only means to prevent or minimize exposure during routine operations.

Exposure to ethylene thiourea should not be controlled with the use of respirators except:

- During the time necessary to install or implement engineering or work practice controls; or
- In work situations in which engineering and work practice controls are technically not feasible; or
- For maintenance; or
- For operations which require entry into tanks or closed vessels; or
- In emergencies.

Only respirators approved by the National Institute for Occupational Safety and Health (NIOSH) should be used. Refer to *NIOSH Certified Equipment, December 15, 1975*, NIOSH publication #76-145 and *Cumulative Supplement June 1977, NIOSH Certified Equipment*, NIOSH publication #77-195. The use of faceseal coverlets or socks with any respirator voids NIOSH approvals.

Quantitative faceseal fit test equipment (such as sodium chloride, dioctyl phthalate, or equivalent) should be used. Refer to *A guide to Industrial Respiratory Protection*, NIOSH publication #76-189 for guidelines on appropriate respiratory protection programs.

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