Current Intelligence Bulletin 11

July 7, 1976

DIMETHYLCARBAMOYL CHLORIDE (DMCC) REVISED

July 7, 1976 (Revised)

Dear Colleague:

On February 11, 1976, Dr. Norton Nelson, Professor and Chairman of the Institute of Environmental Medicine at New York University Medical Center, informed the National Institute for Occupational Safety and Health (NIOSH) of the carcinogenic potential of dimethylcarbamoyl chloride (DMCC) by inhalation in laboratory rats.

Presently, the only known uses of dimethylcarbamoyl chloride in the United States are in the synthesis by Hoffmann-LaRoche, Inc. (Nutley, NJ) of pharmaceuticals used in the treatment of myasthenia gravis (neostigmine bromide, neostigmine methylsulfate, and pyridostigmine bromide) and as a reagent for the synthesis of carbamates in chemical research laboratories.

Dimethylcarbamoyl chloride may be employed in the synthesis of carbamates (which are used as drugs and pesticides), in the synthesis of dyes, and in the synthesis of unsymmetrical dimethylhydrazine (a rocket fuel). It should also be noted that DMCC may be formed in side reactions during the manufacture of other products. For example, by letter of June 23, 1976, E.I. du Pont de Nemours & Company advised NIOSH that they have taken measures to protect their employees and customers due to the formation of up to 6 ppm (w/w) DMCC during Du Pont's production of phthaloyl chlorides.

Dimethylcarbamoyl chloride is prepared by the reaction of phosgene with trimethylamine. Domestic producers of DMCC have included Ashland Chemical Company (Great Meadows, NJ), Chemetron Corporation (La Porte, TX), Fabtex Corporation (Englewood Cliffs, NJ) and the Ott Division of Story Chemical Corporation (Muskegon, MI). The last known domestic commercial production of DMCC, approximately 3000 lbs., was manufactured about a year ago for use in pharmaceuticals. DMCC is manufactured in Germany by BASF, Aktiengesellschaft. DMCC is available from many suppliers of laboratory chemicals.

The very limited production and commercial use of DMCC in the United States suggests that only a small number of workers are exposed to this substance. It is estimated that fewer than 200 persons are at risk of occupational exposure to DMCC. Most of these would be intermittent exposures occurring in chemical laboratories; not included here are potential exposures to DMCC formed in side reactions during the synthesis of other products.

The acute toxic effects of DMCC that have been observed in laboratory animals include irritation to eye membranes, respiratory organs, and, after repeated contact, inflammation of the skin. The carcinogenic potential of DMCC was first reported by Van Duuren (Institute of Environmental Medicine, NYU Medical Center) in a 1972 preliminary report (J Nat Cancer Inst 48:1539-1541, 1972) and in 1974 (J Nat Cancer Inst 53:695-700, 1974). In this study, Van Duuren observed a high incidence of skin tumors and subcutaneous sarcomas, along with some papillary tumors of the lung in ICR/Ha Swiss mice following applications of DMCC to skin by both subcutaneous injection and intraperitoneal injection.

In the current study by Drs. Sidney Laskin and Marvin Kuschner (Institute of Environmental Medicine, New York University), reported to NIOSH by Dr. Nelson, rats exposed by inhalation to 1 ppm DMCC developed squamous cell carcinomas of the nose within 200 days. These tumors were seen in 89 of the 93 rats exposed. This very high incidence of nasal cancer and the short latency period in rats suggests a potentially serious hazard for workers exposed to DMCC. Therefore, NIOSH is distributing this Current Intelligence Bulletin to inform the occupational health community of these findings.

Sincerely yours,

John F. Finklea M.D.

John F. Finklea, M.D.
Director

NIOSH

Current Intelligence Bulletin

Reprints-Bulletins 1thru18 (1975-1977)

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