



8EHQ-0402-15122

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Office of Toxic Substances  
U.S. Environmental Protection Agency  
Ariel Rios Building  
1200 Pennsylvania Avenue N.W.  
Washington, D.C. 20460  
Attn: 8(e) Coordinator

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2002 MAY -3 AM 7:39

Re: Benzene, 1,3-diisocyanatomethyl-  
CASRN 26471-62-5

Dear Sir/Madam:

The following information is being submitted by The Dow Chemical Company (Dow) pursuant to current guidance issued by EPA indicating EPA's interpretation of Section 8(e) of the Toxic Substances Control Act. Dow has made no determination as to whether a significant risk of injury to health or the environment is actually presented by the findings.

The attached abstract is from a study (which includes NIOSH investigators) for presentation at Federation of American Societies for Experimental Biology (FASEB) meeting beginning April 20, 2002.

Sincerely,

Linda C. Burgert  
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jt

Attachment



8EHQ-02-15122



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Mechanisms of Toluene Diisocyanate (TDI) Asthma in a Subchronic Mouse Model  
Joanna M Matheson <sup>1</sup>, Ranulfo Lemus <sup>2</sup>, Meryl Karol <sup>2</sup>, Michael I Luster <sup>1, 1</sup>, TMBB,  
DHHS/CDC/NIOSH, 1095 Willowdale Road, Morgantown, WV 26505, <sup>2</sup> Center for Env.  
& Occupational Health & Toxicology, University of Pittsburgh, Pittsburgh, PA

Nearly 9 million workers are exposed to chemical agents associated with occupational asthma with isocyanates representing the chemical class most responsible. Isocyanate-induced asthma has been difficult to diagnose and control, in part because the biological mechanisms responsible for the disease and the determinants of exposure have not been well defined. To address these issues a mouse model was established to better reflect the exposures that were likely occurring in the workplace. It was hypothesized that isocyanate-induced asthma is characterized by cellular and humoral immune responses. To explore this hypothesis, C57BL mice were sensitized by inhalation (20 ppb, 4 hours/day, 5 days/week) for 6 weeks, and challenged 14 days later by inhalation (20ppb; 1 hour) with TDI. Airway inflammation, goblet cell metaplasia, epithelial cell damage and non-specific airway reactivity to methacholine challenge, measured 24 hrs following the last challenge, were significantly increased in the challenged mice. Adoptive transfer experiments demonstrated that T lymphocytes were primarily responsible for the airway hyperreactivity elicited by TDI challenge. In addition, significant but low levels of specific IgG antibodies were detected and their reactivity demonstrated by serum passive transfer. These results suggest that T cells play an important role in TDI sensitization in a non-irritating low dose exposure subchronic model (the current permissible workplace exposure level).