Bull. Environ. Contam. Toxicol. (2005) 74:4–7

DOI: 10.1007/s00128-004-0572-0

Bulletin of Environmental Contamination and Toxicology

Authors' Response

Mr. Cleet raises questions about the methods used in our analysis of residual isocyanates in flexible polyurethane (PU) foams. One concern was modification to the standard protocol for the "SWYPE" test that uses mineral oil to sample for workplace isocyanate contamination. Mineral oil is employed because of its low toxicity and volatility, and high co-solubility for isocyanates. In addition, the reagents which react colorimetrically to detect isocyanates and are impregnated on the SWYPE pad, have poor solubility in mineral oil. It is preferable when testing work surfaces that the reagents are retained in the SWYPE pad to minimize work surface discoloration. In a PU foam matrix, detection of bound isocyanate is accomplished by substitution of acetone for the mineral oil. The reagents in the SWYPE pad are soluble in polar solvents such as acetone. Wetting the SWYPE pad with acetone allows the reagents to diffuse into the polymer matrix and react with the bound isocyanate functional groups. The use of mineral oil would fail to detect this bound isocyanate. Based on our review of the literature and our SWYPE analyses, we agree that the vast majority of isocyanate residue is bound in the foam polymer matrix.

Our HPLC method for extractable isocyanate used tagging of isocyanate groups with a chemical label (MAMA) and screening for its presence using multiple detection modalities. This general approach has become the standard for determination of free isocyanate in air samples (e.g., MDHS 25, NIOSH 5522, NIOSH 5525, ISO 16702). Furthermore, Damant et al. (1995) also used the same MAMA reagent with a solvent extraction in a study of residual isocyanate in PU food packaging plastics. Analysis of 19 commercial PU packages demonstrated that the method was not prone to interference and residual isocyanate monomer concentration ranged from 0.1 to 1 μg/g.

The criteria we used to identify MAMA-labeled TDI and TRIG in our foam samples employed response factors for fluorescence and UV absorbance at two wavelengths along with retention time (for the TDI monomers). Three reagent/system blanks were prepared and analyzed along with the PU samples. Neither TDI nor TRIG were detected in any of the blanks. It is highly unlikely that other possible compounds present in the PU foam would satisfy all these criteria and result in a false positive. Thus, the HPLC results taken together with the positive SWYPE tests, representing two completely independent analytical techniques, provide compelling evidence, in our view, that free isocyanate was present in these PU foam samples.

Mr. Cleet's letter states that "several studies, described below, indicate that free TDI is not present in foams"; the first three studies appear to be unpublished "industry evaluation or studies". There is insufficient detail to properly evaluate or interpret the methods used or the results of these studies. For example, if glacial acetic acid were used as the extraction medium, it is not surprising that the corresponding amines were not detected because isocyanate reacts with carboxylic acids to form substituted amides and ureas. In order to hydrolyze

isocyanates to corresponding amines, the presence of mineral acid and water in addition to the carboxylic acid would be needed.

We are aware of industry reports of residual TDI in various flexible foam formulations. In 1990, the Society of the Plastics Industry, Inc. published data regarding PU foams and compliance with the State of California's Proposition 65 that requires warnings for products containing potential carcinogens (such as TDI). The average level of residual TDI in eight consumer product foam formulas ranged from 0.07 ppm to 1.1 ppm, although some levels as high as 2.1 ppm were reported. Our analyses found up to 20 ppm in a PU foam.

Hugo et al. (2000) did not detect airborne TDI release from a PU foam and when "TDI-laden air was passed through the foam, the TDI was not released into the air; that is, free TDI actually was captured into the foam". Our concern, stated in our paper and still remaining, is for the fate of the TDI "captured on the foam". Hugo et al. did not attempt to extract, analyze, or account for the TDI loaded onto the foam. The possibility remains that trapped TDI could be available for absorption by dermal contact with foam products. The Society of the Plastics Industry (1990) document on PU foams states, in a section on likely routes of exposure, "For consumer products, dermal exposure and inhalation exposure would be the primary routes of exposure to TDI ."

Mr. Cleet states that "respiratory sensitization requires exposures to high concentrations" and cites a 28-year old reference (Weill et al 1975). We believe the statement is overly broad and highly interpretive of the results from the cited reference. Furthermore, the cited paper was a preliminary report of a 5-year study of workers in a new TDI plant. At the end of the 5-year study, 12 workers had become clinically sensitive to TDI, 8 of whom had less than four months of exposure prior to sensitization. Of the 12 sensitized workers, in only 6 was there a history of high level exposure during TDI spills (Weill et al. 1980). Several decades later, the consensus in the field is that the threshold-sensitizing dose in adults is still unknown although there appears to be an increase in risk with increasing exposure (e.g., Tarlo et al. 1997). No information on the sensitizing dose in children is available.

Early animal research on relationships between dermal contact and respiratory sensitization used relatively large dermal doses of undiluted (100%) isocyanate to elicit response (Karol et al., 1981). Among more recent studies is the development of a mouse model for isocyanate-induced asthma (Herrick et al 2002). This model used the dermal route for initial sensitization to diisocyanate (two applications, one week apart). Subsequent inhalation challenge produced lung inflammation identical to human isocyanate asthma. Moreover, it was shown that the lower dermal sensitization doses (0.1% versus 1% solutions) were much more potent in producing dermal contact hypersensitivity, as well as, the inflammatory lung infiltrates and mucous secretion after challenge. Thus, a small number of low-dose dermal exposures could sensitize and predispose to respiratory disease.

Many foam products are covered with a layer of cloth, however, others are not. The mattress pads we analyzed consisted of bare foam. Many modern wound dressings are made of polyurethanes. Direct skin contact durations of hours or even days occur with the use of these medical products. We suspect there may be many other uses of polyurethane that can contribute to a cumulative, unintentional isocyanate exposure.

We did not suggest foam bedding was the causal exposure leading to the development of childhood asthma. We summarized reports by others of an association between foam bedding and respiratory symptom elicitation. Two other large epidemiological studies have also linked synthetic bedding or foam mattresses with respiratory disease. An increase in childhood wheeze over the 13 year period from 1978 to 1991 was largely attributed to increasing use of synthetic pillows (Butland et al., 1997). A study conducted in urban and rural Ethiopia also linked foam mattresses and pillows to increased allergic symptoms and sensitivity; the risk of wheeze was positively associated with foam bedding (Yemaneberhan et al., 1997).

It seems clear that free isocyanates are present in some consumer PU foams and that direct dermal contact with foam does occur. There are too many unanswered questions regarding the exposure routes and doses, as well as, individual susceptibility factors (e.g., age, genetics, etc.) to preclude links between isocyanates in PU foams and respiratory disease. Thus, we continue to urge additional observational and experimental investigations.

Cheryl A. Krone, Applied Research Institute, P.O. Box 1969, Palmerston North, New Zealand
Tom D. Klingner, Colormetric Laboratories, 1261A Rand Road, Des Plaines, IL 60016
Roy J. Rando, Department of Environmental Health Sciences, Tulane University School of Public Health & Tropical Medicine, 1430 Tulane Ave. SL15, New Orleans, LA 70112
John T.A. Ely, Radiation Studies, Box 351310, University of Washington, Seattle, WA 98195

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