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# Risk assessment for consumer exposure to toluene diisocyanate (TDI) derived from polyurethane flexible foam

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ABSTRACT

Polyurethanes (PU) are polymers made from diisocyanates and polyols for a variety of consumer products. It has been suggested that PU foam may contain trace amounts of residual toluene diisocyanate (TDI) monomers and present a health risk. To address this concern, the exposure scenario and health risks posed by sleeping on a PU foam mattress were evaluated. Toxicity benchmarks for key non-cancer endpoints (i.e., irritation, sensitization, respiratory tract effects) were determined by dividing points of departure by uncertainty factors. The cancer benchmark was derived using the USEPA Benchmark Dose Software. Results of previous migration and emission data of TDI from PU foam were combined with conservative exposure factors to calculate upper-bound dermal and inhalation exposures to TDI as well as a lifetime average daily dose to TDI from dermal exposure. For each non-cancer endpoint, the toxicity benchmark was divided by the calculated exposure to determine the margin of safety (MOS), which ranged from 200 (respiratory tract) to $3 \times 10^6$ (irritation). Although available data indicate TDI is not carcinogenic, a theoretical excess cancer risk ($1 \times 10^{-7}$) was calculated. We conclude from this assessment that sleeping on a PU foam mattress does not pose TDI-related health risks to consumers.



## 1. Introduction

Polyurethanes (PU) are polymers made by reacting diisocyanates (monomers with two isocyanate (NCO) groups) with polyols or chemically related compounds (Fig. 1). These polymers are manufactured in industrial settings for subsequent use in consumer products such as furniture, automotive interiors, bedding, carpet underlay, insulation and coatings. It is thought that any NCO groups present in the PU foam following curing are attached to large molecular weight heterogenous polymers that prevents their release by either evaporation or diffusion (Vangronsveld et al., 2012). The levels of attached NCO groups decline rapidly, probably by reacting with ambient atmospheric moisture (Cole et al., 1987). Fully cured PU products are considered toxicologically inert (USEPA, 2011a) since they contain neither unreacted TDI nor biologically available NCO groups (Dieterich et al., 1993).

Despite these generally held beliefs, there are reports that unreacted TDI is present in cured PU foam. Gagné et al. (2003) and

*Abbreviations:* BHR, bronchial hyperreactivity; BMDS, USEPA benchmark dose software; CSF, cancer slope factor; FEV, forced expiratory volume; FEV1, forced expiratory volume in one second; FVC, forced vital capacity; GPMT, guinea pig maximization test; LADD, lifetime average daily dose; LMS, linearized multistage; LLNA, local lymph node assay; LOAEL, lowest observable adverse effect level; MOS, margin of safety; MDL, method detection limit; NTP, national toxicology program; NESIL, no expected sensitization induction level; NOAEL, no observed adverse effect level; NOEL, no observed effect level; OEL, occupational exposure limit; POD, point of departure; PU, polyurethanes; RfC, reference concentration; TDI–GSA, TDI–guinea pig serum albumin conjugates; TWA, time-weighted-average; TDA, toluene diamine; TDI, toluene diisocyanate.

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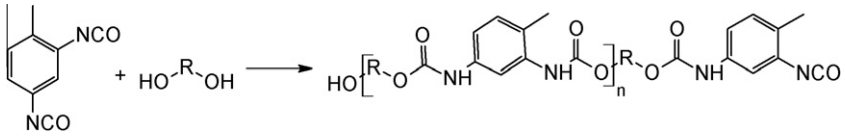


**Fig. 1.** Generic reaction of TDI with a polyol to form a polyurethane.

Krone et al. (2003) reported the presence of low concentrations of "free TDI" (i.e., residual unreacted TDI monomer) in PU products, even after prolonged aging. However, the presence of free TDI is unlikely. The absence of TDI emissions [limit of detection (LOD) of 0.2–0.5 ng/g] from PU foam spiked with TDI (Hugo et al., 2000) suggests that results reported by Gagné et al. (2003) are likely due to either degradation of the foam by the extraction procedure and/or reaction of the derivatization agent with other extractable, low-molecular weight components (e.g., oligourea) in the foam. In addition, the reliability of the Krone et al. (2003) results have been questioned based on the absence of both control samples and the positive identification of isocyanates, use of dimethyl sulfoxide as solvent, and the unusual ratios of putative TDI isomers in different samples (Cleet, 2005). The TDI commonly used in foam manufacture is an isomer mixture of 2,4- and 2,6-TDI (80:20). Toxicity tests have predominantly been performed on this isomer mixture, and in this manuscript TDI is used to refer generically to the isomer mixture or single isomers.

While few concerns are expressed about the safety of PU foams, this assessment quantitatively addresses the concern that unreacted TDI monomer may escape from the polymer matrix and pose a health risk. Sleeping on a PU foam mattress was the exposure scenario selected for this assessment since it represents a situation that would accentuate the potential for consumer exposure.

## 2. Methodology

It is generally accepted that risk assessment can be performed in the following four steps (National Research Council, 1983):

- Hazard assessment
- Dose–response assessment
- Exposure assessment
- Risk assessment

Risk is a function of both toxicity (hazard and dose–response) and exposure. The sections below detail the risk assessment process for TDI. By combining appropriate analytical data and exposure modelling with the toxicity benchmarks provided herein, similar risk characterizations can be made for other TDI-based PU products.

### 2.1. Toxicity assessment

Toxicity refers to the inherent property of every chemical to cause adverse health effects at some level of exposure. It can be determined by evaluating responses in experimental animals exposed to chemicals under defined laboratory conditions (most commonly) or in humans exposed to chemicals in their environment. Traditionally, toxic effects have been broadly divided into non-cancer and cancer endpoints. In this document, only toxicity endpoints relevant to TDI (i.e., skin irritation; skin sensitization; respiratory sensitization; lung irritation and decrement not related to asthma; and carcinogenicity) are considered. Dose–response data on the potential adverse health effects from TDI in PU products are likely the same as that for the monomer itself. Comprehensive information about the toxicity of TDI monomer is available in various reviews or agency documents (Bolognesi et al., 2001; Canadian Government, 2008; Collins, 2002; ECHA, 2011; European Commission Joint Research Centre, 2000; IARC, 1999; National Research Council, 2004; Ott, 2002; USEPA, 1995).

For non-cancer endpoints, toxicity benchmarks were identified by dividing each point of departure (POD) by a combined uncertainty factor. PODs (e.g., No Observed Adverse Effect Level, NOAEL) were selected following a review of relevant dose–response data for each endpoint. Combined uncertainty factors were calculated as the product of two or more factors that compensate for uncertainties associated with the POD (e.g., inter- and intra-species variability, extrapolation from less than lifetime-to-lifetime exposures and weakness of the toxicological database). Uncertainty factors were derived from regulatory and other expert guidance and refinements to these factors based on the toxicological database for TDI. For cancer, the cancer slope factor (CSF) was derived using the USEPA Benchmark Dose Software (BMDS) (http://www.epa.gov/ncea/bmds/dwnldu.html) version 2.2 and the USEPA preferred linearized multistage (LMS) cancer model to describe the relationship between risk and dose below the experimentally observed range. The CSF is defined as the upper 95% confidence limit on the slope of the risk–dose relationship with units of risk per mg/kg bw/day.

### 2.2. Exposure assessment

Exposure is a function of the mass of material in contact with the body as well as the exposure conditions under which contact occurs. In the case of dermal irritation and sensitization where contact alone is a key parameter, the appropriate dose-metric is mass per unit area (European Commission, 2010; Kimber et al., 2008; Loveless et al., 2010). Otherwise, exposures are commonly expressed in units of mg/kg bw/day, the amount of material contacted (mg) per mean body weight (kg) of the subject per unit of time (day). Exposures can be measured empirically or modelled based on the physical–chemical properties of the chemical, physiological characteristics of the receptor population (e.g., absorption rate, inhalation rate, body weight), and contact conditions (i.e., frequency, duration, and route) for the exposure scenario under study. Selected exposure variables typically represent a combination of average and upper-bound values designed to estimate the exposure experienced by individuals at the upper end (e.g., 90th percentile) of the exposure distribution. A common exposure metric for cancer endpoints is the Lifetime Average Daily Dose (LADD).

If there were to be human exposure to TDI monomer from PU products, in principle it would be most likely to occur via inhalation (release of TDI to air) and dermal contact (transfer of TDI to the skin). One scenario which would provide maximal opportunity for such exposure via these routes would be sleeping on a flexible PU foam mattress. A high index (119) PU foam was selected for this assessment. The index refers to the stoichiometric ratio of TDI to polyol used to manufacture the foam, with a value of 100 indicating equal amounts of TDI and polyol. The index of commercial PU foam bedding typically ranges between 105 and 115. The high index PU foam used for this assessment was conservatively selected to represent PU foam most likely to contain residual unreacted TDI. The magnitude of other potential TDI exposures (e.g., ingestion of