Health Information in Material Safety Data Sheets for a Chemical that Causes Asthma

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OBJECTIVE: To assess the quality of health information on material safety data sheets (MSDS) for a workplace chemical that is well known to cause or exacerbate asthma (toluene diisocyanate, TDI).

DESIGN: We reviewed a random sample of 61 MSDSs for TDI products produced by 30 manufacturers.

MEASUREMENTS AND MAIN RESULTS: Two physicians independently abstracted data from each MSDS onto a standardized audit form. One manufacturer provided no language about any respiratory effects of TDI exposure. Asthma was listed as a potential health effect by only 15 of the 30 manufacturers (50%). Listing asthma in the MSDS was associated with higher toluene diisocyanate concentrations in the product ($P < .042$). Allergic or sensitizing respiratory reactions were listed by 21 manufacturers (70%).

CONCLUSIONS: Many MSDSs for toluene diisocyanate do not communicate clearly that exposure can cause or exacerbate asthma. This suggests that physicians should not rely on the MSDS for information about health effects of this chemical.

KEY WORDS: asthmas; MSDSs; chemical exposure.
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The incidence of asthma has increased by more than 50% in the last two decades. The reasons for this increase are not entirely clear, but workplace exposures may cause asthma in some patients.¹⁻⁴ Occupations with excess risk for asthma include plastics manufacturing, spray painting, welding, baking, agriculture, and many others.⁵⁻⁸ Occupational asthma occurs when there is workplace exposure to an asthmagen and the worker develops recurrent wheezing, breathlessness, chest tightness, or coughing, plus variable airflow limitation.^{7,9} Chemicals that may cause occupational asthma include respiratory irritants or sensitizers. Many sensitizing agents induce specific IgE antibodies.^{7,10} Overall, more than 250 chemicals have been associated with occupational asthma.^{6-8,11}

Population-based surveys have reported that 5% to 21% of asthma cases are caused or exacerbated by occupational exposure.¹²⁻¹⁴ Extrapolating to the estimated 12 million adults in the United States who have asthma^{1,2} suggests between 500,000 and 2.5 million Americans have occupational asthma.

A complete evaluation of the adult patient with asthma should include an occupational history.^{15,16} For this task, consulting the material safety data sheet (MSDS) for products used in the workplace is recommended to evaluate chemical exposures.^{11,16} Material safety data sheets are regulated by the Occupational Safety and Health Administration (OSHA) through the Hazard Communication Standard.¹⁷ The OSHA standard stipulates that the MSDS must report the physical and chemical characteristics of the product, precautions for safe product handling, and health hazards from exposure to the product. The OSHA standard does not state how often an MSDS should be reviewed or updated.

There has been little research on MSDSs. One study found that 60% to 65% of MSDSs for chemicals that are reproductive hazards made no mention of reproductive effects.¹⁸ In a second study,¹⁹ a random sample of 150 MSDSs was assessed. For 28 products that contained a carcinogen, only 16 MSDSs (57%) stated that the substance contained carcinogenic material. Overall, the health effects information was judged to be accurate for 37% of the MSDS, partially accurate for 16% of the MSDSs, and inaccurate for 47% of the MSDS.

We assessed the MSDS for a chemical that is one of the most well-established occupational causes of asthma, toluene 2,4-diisocyanate (TDI).⁶⁻¹¹ Toluene 2,4-diisocyanate is used to manufacture plastics, polyurethane paints and coatings, and polyurethane foams used in furniture, insulation and packaging.^{7,8,10} The National Occupational Exposure Survey estimated that at least 19,921 workers are exposed annually to TDI (NIOSH, personal communication, 1999).²⁰ Although studies of asthma incidence among TDI-exposed workers are limited by cross-sectional design and other problems, existing evidence suggests that approximately 5% to 10% of isocyanate workers develop occupational asthma.¹⁰

Exposure to TDI usually occurs for a period of time before sensitization develops and symptoms begin (latent period). The worker may cough, experience shortness of breath, or wheeze while at work, or these symptoms may not appear until the evening. Symptoms may improve during vacations and weekends. The level of exposure to TDI required to develop asthma is not precisely known. If the patient reports that a large quantity of TDI is used without respiratory protection and that there are frequent spills, exposure levels may be high, increasing the likelihood of developing asthma.^{10,21} In addition to respiratory exposure, studies in rodents suggest that skin exposure to isocyanates may increase the likelihood that respiratory sensitization will occur.²²⁻²⁶ Once a worker becomes sensitized to TDI, relatively small exposures

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(below occupational exposure limits required by OSHA) can cause asthma symptoms.¹¹

About 50% of workers with TDI-induced asthma continue to have asthma after removal from TDI exposure.^{27–29} While the patient's asthma symptoms may have initially been associated only with TDI exposure, sensitized individuals may develop generalized airway reactivity on exposure to irritants, nonallergenic dusts, and sometimes perfumes and other chemicals.⁷

Because TDI can cause permanent asthma, MSDS for TDI-containing products should adequately explain its respiratory effects. Our primary goal in this study was to assess whether MSDSs for products containing TDI report that asthma is a potential health effect of exposure.

METHODS

Obtaining Material Safety Data Sheets

There is no national library for MSDSs. Massachusetts created a repository of MSDS for products containing certain types of chemicals, but funding was stopped after a few years.¹⁸ Therefore, we reviewed the major MSDS Internet sites in the United States. The Cornell MSDS Web site³⁰ had the most TDI MSDSs of any site located, with 309 MSDSs containing TDI. It is not known to what extent these MSDSs represent the universe of MSDSs for TDI.

We chose a random sample of 120 of these MSDSs for review (the study sample). We contacted the manufacturers to request the most current MSDS (1 phone call and 2 mailings). The sample size of 120 MSDSs was chosen to provide an estimate of the prevalence of asthma language in the MSDS with 10% precision,³¹ assuming that 96 independent MSDSs would be obtained (96/120, 80% response rate from manufacturers).

Auditing Material Safety Data Sheets

We developed an instrument to audit the MSDS and used the MSDS not chosen for the random sample to pilot test and revise the instrument (the test sample). The final instrument contained 6 items to assess language about respiratory effects, 4 items to assess language about preventing exposure and 2 items about managing sensitized workers or workers with respiratory problems.

Two pairs of physicians independently audited each MSDS and then met to resolve disagreements. To assess initial agreement between pairs of physician auditors, we calculated the overall percentage agreement as well as the κ statistic.^{32,33} The κ statistic is not a robust measure of agreement when the prevalence of the condition is very low or very high.³⁴ We report κ statistics only for language with a prevalence of 20% to 80% among the MSDSs.

Statistical Analysis

The manufacturer was the unit of analysis. This is because MSDSs for TDI issued by a single manufacturer

are likely to have similar language. Therefore, each MSDS is not statistically independent, invalidating commonly used tests for statistical significance³⁵ and altering prevalence estimates. We used the most conservative way to address nonindependence of multiple MSDSs produced by a single manufacturer by selecting 1 MSDS randomly per manufacturer.

Random numbers were generated using Epi-Info software (CDC, Atlanta, Ga). Descriptive statistics and univariate statistical tests were performed using the Statistical Package for the Social Sciences, version 7.5 (SPSS Inc., Chicago, Ill). Proportions were compared using Chi-square tests. If any cell of a 2-by-2 table contained an expected value of less than 5, a Fisher's exact test was computed. All tests were 2-tailed and used an α of 0.05.

RESULTS

Study Sample

The Cornell MSDS Web site revealed 309 MSDSs containing TDI, and a random sample of 120 of these MSDSs was chosen for study. Among the 120 MSDSs identified, 9 were found to be duplicates, leaving 111 MSDSs to obtain for analysis. There were 17 MSDSs with incorrect or missing contact information that could not be resolved. Manufacturers who were contacted reported that the product was obsolete for 12 MSDSs, that the product no longer contained TDI for 11 MSDSs. The product could not be identified from the information in the Cornell MSDS for 1 MSDS. Seventy MSDSs were eligible for study. Of these, 61 MSDSs were obtained from the manufacturer (87.1% response rate).

There were 30 manufacturers represented among the 61 MSDSs; 12 manufacturers had more than 1 MSDS in the test sample (range, 2 to 9 MSDSs for these manufacturers). Different TDI products from the same manufacturer had different concentrations of TDI or differences in other chemical constituents. One MSDS was randomly chosen to represent each manufacturer, yielding a final study set of 30 MSDSs. Characteristics of the TDI products and their MSDS are listed in Table 1.

Agreement Between Auditors

The overall percentage agreement between pairs of physician auditors ranged from 89% for presence of nonspecific respiratory symptoms to 98% for presence of a recommendation to use the product with adequate ventilation. The range for κ was .69 for respiratory irritation to .93 for asthma.

Language About Respiratory Effects

Language found in the MSDS about the potential respiratory effects of uncontrolled exposure is shown in Table 2. One MSDS contained no language about respiratory effects of exposure. The most common respiratory

Table 1. Characteristics of Toluene Diisocyanate (TDI) Products

Characteristic	All MSDS, <i>n</i> = 61	One MSDS per Manufacturer, <i>n</i> = 30
TDI formulation, <i>n</i> (%)		
Toluene-2,4-diisocyanate alone	42 (68.9)	22 (73.3)
Toluene-2,4-diisocyanate mixed with toluene-2,6-diisocyanate	19 (31.1)	8 (26.7)
Number of hazardous chemicals other than TDI, mean (median), range	2.5 (2.0) 0–9	3.2 (3.0) 0–9
TDI concentration as weight, %, mean (median), range	21.0 (1.0) 0.10–98	12.2 (1.0) 0.10–92
Year MSDS was last reviewed,* mean (median), range	1996 (1997) 1990–1998	1996 (1997) 1990–1998

* We obtained the Material Safety Data Sheet (MSDS) in late 1998.

effect listed was respiratory irritation. Only half of the MSDSs reported asthma as a potential health effect. A quarter of MSDSs (26.7%) contained neither the word “asthma” nor language about allergic or sensitizing respiratory reactions.

Listing asthma in the MSDS was associated with concentration of TDI in the product of greater than or equal to 25 weight percent ($P < .042$). A similar relationship was found between TDI concentration and stating that preexisting respiratory diseases could be aggravated by exposure ($P = .03$). There was also a nonstatistically significant tendency for MSDSs with high TDI concentrations to recommend excluding workers with preexisting respiratory problems from handling this product ($P = .052$)

Table 2. Language About Respiratory Effects and Exposure Prevention (*n* = 30)*

Language	Frequency (%) of MSDSs
Respiratory effects	
Respiratory irritation	23 (76.7)
Allergic or sensitizing respiratory reaction	21 (70.0)
Nonspecific respiratory symptoms (bronchitis, difficulty breathing, shortness of breath, chest tightness, or cough)	16 (53.3)
Asthma	15 (50.0)
Preexisting respiratory disorders may be aggravated	14 (46.7)
Respiratory symptoms may be delayed	9 (30.0)
Exposure prevention	
Ventilation	30 (100)
Respirator in selected circumstances	30 (100)
Gloves	30 (100)
Protective clothing	20 (66.7)
Managing workers with a respiratory problem	
Exclude from working with product if respiratory problem	8 (26.7)
Controls may not be adequate to protect sensitized workers	1 (3.3)

* MSDS indicates material safety data sheet.

and to state that exposure-related respiratory symptoms may be delayed until after the work shift ($P = .076$).

Language About Exposure Prevention

All MSDSs recommended using the product with adequate ventilation or respiratory protection. All MSDSs also recommended using chemical-resistant gloves. Only two thirds of MSDSs advised workers to use protective clothing. A few more of the MSDSs from products with TDI concentrations of at least 25% recommended using protective clothing when handling the product (4 of 20 vs 0 of 9), but this difference was not statistically significant ($P = .28$).

There was no relationship between language about health effects or exposure prevention and date on which the information in the MSDS had last been reviewed or updated by the manufacturer. It was not clear whether the date of last review listed on the MSDS always referred to performance of a literature review to assess whether the MSDS reflected current scientific knowledge, because the date of last review was listed as the date we requested the MSDSs for 9 of 30 MSDS (30%). Other MSDSs had not been reviewed for at least 4 years: 6 of 30 MSDSs (20%) listed the date of last review as 1990–1994. The date of last review was missing from 3 of 30 MSDSs (10%).

DISCUSSION

We found that information on the MSDS about the respiratory effects of TDI was limited. Although all but one MSDS listed some respiratory effect, the effects described were often nonspecific, such as “shortness of breath.” “Allergic respiratory sensitization” was listed by 70% of the manufacturers as an adverse effect, a phrase that may not communicate clearly that asthma is a risk. If the physician has received training in occupational medicine, he or she knows that TDI is an established cause of asthma and will not depend on the MSDS for a description of the product’s health effects. Unfortunately, because medical schools and residency programs provide little training in occupational

medicine,³⁶ the knowledge levels of physicians may be suboptimal.

We found a possible relationship between TDI concentration in the product and presence of the more specific respiratory terms such as "asthma" in the MSDS. This suggests that some MSDS writers may believe that asthma is only a significant risk when handling products with high TDI concentrations. Toxicologic data do not support this assumption. Skin exposure to small concentrations of isocyanates lowers the threshold for asthmalike reactions in laboratory animals.²²⁻²⁶ In a mouse model, TDI at a concentration of only 1% caused tracheal hyperreactivity when applied to the skin twice daily for only 2 days.²² The dermal dose of TDI required to sensitize 50% of a test group of mice is only 30.4 $\mu\text{mol/kg}$.²⁶ In a 70-kg human, the skin exposure equivalent would only be about 2.1 μmol . In addition, exposure to relatively low air levels over several years has been shown in humans to decrease pulmonary function.²¹ These data suggest that repeated exposure to TDI products at relatively low concentrations could be harmful. A history of dermal exposure may also be important in the asthma patient who works with TDI.

Many MSDSs (6 of 30) had not been updated since 1990-1994. These MSDS were written before the research on dermal exposure to TDI in rodents^{22,24-26} and the U.S. surveillance statistics on isocyanate-induced asthma^{9,13} were published.

Many MSDSs were hard to read. Although our investigators were looking for respiratory language, they did not always find terms relating to asthma or other pulmonary effects. Detection rates among physicians who quickly scan MSDSs in a clinic setting or among workers might be even worse than those found by our auditors.

This study is limited by small sample size. Although the Internet site appeared to provide a large number of products containing TDI, many of the products were obsolete or the contact information for the manufacturer was invalid. The sample size in a survey affects the precision of estimates of prevalence.²⁹ In this study, the final sample size allows the precision to be estimated for the prevalence of 50% of manufacturers that used the word "asthma" on the MSDS. This precision is reported as the "margin of error" in surveys or polls. Using an α of 0.05, our population of 30 TDI manufacturers yields a precision of plus or minus 18%. This means that if all TDI manufacturers were assessed, the prevalence of using the word "asthma" on the MSDS would probably be between 32% and 68%. Even if 68% of all TDI manufacturers used the word "asthma" in the MSDS, approximately one third of TDI manufacturers would still provide MSDSs that are unhelpful or even misleading for health education.

In conclusion, this study found worrisome omissions in health information on MSDSs for a well-recognized asthmagen. The consequences of underrecognition of the asthmagenic properties of TDI are clinically important for the asthma patient, because sequelae of continued exposure may be severe and permanent.^{27,29} If the worker

can not tell from the MSDS that TDI may cause a serious health problem such as asthma, he or she may be less likely to use optimal safety procedures to prevent exposure. Similarly, the employer has to be informed that the product could harm workers before he or she will endorse safety procedures and authorize expenditures for exposure control.

Because MSDSs are required by law, federal agencies responsible for in occupational safety and health should ensure that the information on MSDSs is accurate. This study, taken together with two previous studies, suggests that an investigation of the accuracy of health information on MSDSs for other hazardous chemicals would be worthwhile. Periodic review of MSDSs should be required, for instance, every 2 years. The main data used to determine health effects could be cited in a bibliography either at the end of the MSDS or in another, accessible publication. Experts from the medical, occupational safety, and consumer communities should assist in developing effective descriptions of serious health effects. Standardized language templates should be required on MSDSs for respiratory sensitizers to ensure that product users are told that exposure can cause permanent asthma. Until the accuracy of health information on MSDSs is assured, physicians need to rely on textbooks and literature searches to supplement the health information on the MSDS.

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