ABSTRACT

In 2016, the American Conference of Governmental Industrial Hygienists (ACGIH) lowered the 8-hour Threshold Limit Value (TLV) for toluene diisocyanate (TDI) from 5 ppb to 1 ppb, and the 15-minute short term exposure limit (STEL) from 20 ppb to 5 ppb, to protect against respiratory effects. However, the human evidence indicates that maintenance of 8-hour TWA concentrations less than or equal to 5 ppb and peaks less than 20 ppb is unlikely to prevent all cases of occupational asthma (OA) in most workers, and is also protective of lung function decrements and other respiratory effects. Several of the available studies that suggest cases of OA are associated with airborne concentrations less than 5 ppb likely affected by very high airborne exposures, well above 20 ppb. Advances in industrial hygiene measures have reduced peak exposures and the incidence of up to 40% of cases of OA are still observed in industries with moderate levels of exposure. The animal literature supports the human evidence and indicates that TDI-induced asthma is a threshold phenomenon. The evidence does not indicate that the lower TDI TLVs will result in a lower incidence of respiratory effects, including OA.

BACKGROUND

• TDI is an organic compound used to synthesize polyurethane foams. Two isomers are used commercially: 2,4-TDI (CAS # 107-10-1) and 2,6-TDI (CAS # 108-20-9).
• TDI is an occupational allergen that can cause high airborne concentrations.
• ACGIH published its first TDI TLV in 1959 and has made several revisions to the TLVs since that time (Figure 1).
• In 2016, ACGIH lowered the 8-hour TWA-TLV for TDI from 5 ppb to 1 ppb, and lowered the 15-minute TLV-STEL from 20 ppb to 5 ppb.
• The revised TLVs appear to be driven by the goal of further reducing the incidence of OA and respiratory symptoms in workers exposed to TDI.

RESULTS

Occupational Asthma

• Studies of occupational TDI exposure indicate that new cases of OA are not likely to occur if facilities are in compliance with TDI TWAs of 5 ppb and maximum peak concentrations of 20 ppb (Table 2).

• Animal studies, including Paulson et al. (2001) and Selgray et al. (2006), support a threshold for TDI-induced respiratory sensitization and suggest that dermal TDI exposure, in the absence of inhalation exposure, is insufficient to induce OA.

• Several studies have observed airway neutrophilia after inhalation of TDI in mice that are dermally sensitized to TDI, but only with a sufficient exposure duration (e.g., 60 minutes, relative to 10 minutes).

• In all dermally sensitized animals, multiple induction “boosts” (inhalation exposures at high concentrations) were needed to induce a response after respiratory challenge.

Methods

• Critically reviewed the human and animal evidence on which the TDI TLVs were based.
• Focused on key evidence relied upon by ACGIH to set the TDI TLVs.
• Evaluated the likelihood of a TDI exposure threshold for respiratory effects and the influence of peak exposures on the risk of these outcomes.

Lung Function

• A series of studies conducted in the early 1980s reported yearly declines in lung function in workers exposed to TDI TWAs of up to 40 ppb that were larger than expected; however, these studies’ measurements were not properly adjusted for factors affecting individual lung function, such as smoking status and age (Table 2).

• No significant decrements in lung function (adjusted values) were reported in other studies of workers with average exposures <5 ppb TDI (Table 2).

Table 2  Selected Studies of Lung Function in TDI-exposed Workers

<table>
<thead>
<tr>
<th>Study</th>
<th>Location</th>
<th>Year</th>
<th>TDI TWAs (ppb)</th>
<th>FEV1</th>
<th>FVC</th>
<th>FEV1/FVC ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Olsen et al. (1982)</td>
<td>Sweden</td>
<td>1978-1980</td>
<td>0.3-2.7</td>
<td>2.7</td>
<td>1.6</td>
<td>0.8</td>
</tr>
<tr>
<td>Griese et al. (1983)</td>
<td>Germany</td>
<td>1960-1969</td>
<td>0.01-1.4 (2,4-TDI); 0.05-2.7 (2,6-TDI)</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Caimi et al. (2004)</td>
<td>Italy</td>
<td>1967-1992</td>
<td>0.03-0.1</td>
<td>1.8</td>
<td>1.2</td>
<td>0.8</td>
</tr>
</tbody>
</table>

Notes: FEV1 = Forced Expiratory Volume in 1 Second; FVC = Forced Vital Capacity.

Évaluation des seuils pour les effets respiratoires du diisocyanate de toluène

MÉTHODES

• Critiquement révisé les preuves humaines et animales sur lesquelles les TLV-TDI étaient basées.
• Focussé sur les preuves clés sur lesquelles ACGIH s’appuie pour fixer les TLV-TDI.
• Évalué la probabilité d’un seuil d’exposition TDI pour les effets respiratoires et l’influence des expositions à pic sur le risque de ces outcomes.

CONCLUSIONS

• La documentation ACGIH pour les TLV-TDI ne révèle pas intégralement les résultats des preuves humaines et animales d’exposition TDI.

• Un examen critique de l’évidence humaine indique que les précédents 8-heures TLV-TWA et 15-minute STEL (5 ppb et pic max jusqu’à 20 ppb) sont protecteurs contre l’OA dans la majorité des travailleurs et sont aussi protecteurs contre les effets fonctionnels respiratoires et d’autres effets respiratoires.

• L’animalité soutient l’évidence humaine et indique que l’asthme induit par TDI est un phénomène de seuil.

REMERK

This work was funded by the American Chemistry Council (ACC) Diisocyanates Panel. The authors have sole responsibility for the writing and contents presented, which represent the professional opinions of the authors and not necessarily those of ACC.

ACKNOWLEDGMENTS

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