April 29, 2014

Dr. Meredith Williams
Deputy Director
California Department of Toxic Substances Control
1001 I Street
Sacramento, CA 95814

Re: Comments on the DTSC Priority Product Profile for "Spray Polyurethane Foam Systems Containing Unreacted Diisocyanates," March 2014

Dear Dr. Williams,

The American Chemistry Council Diisocyanates Panel, Aliphatic Diisocyanates Panel and the Center for the Polyurethanes Industry Spray Foam Coalition ("ACC") [1] are pleased to have the opportunity to submit comments to the California Environmental Protection Agency‟s Department of Toxic Substances Control ("Department" or "DTSC") regarding the recent "Spray Polyurethane Foam ("SPF") Systems Containing Unreacted Diisocyanates" Priority Product Profile issued in March 2014. The following bullets summarize ACC‟s general comments, while the attachment includes a more in-depth response and provides additional details regarding our concerns.

- The scope of the Priority Product Profile document is overly broad and the Department needs to clearly articulate the specific consumer product(s) it may intend to evaluate. All references to other polyurethane applications that are not SPF systems and therefore outside the scope of the Profile, such as truck bed liners, coatings, and adhesives, should be removed. As written, the Priority Product Profile document does not provide an adequate basis for evaluating the product or the Department‟s subsequent regulation.

- MDI and its oligomers are the only diisocyanates used in SPF systems. TDI and HDI are not used in SPF systems; therefore all references to the chemicals as components of SPF should be immediately removed from the Priority Product Profile to avoid confusion.

[1] The DII Panel includes U.S. manufacturers of TDI and/or MDI: BASF Corporation, Bayer Material Science, The Dow Chemical Company, and Huntsman Corporation. The ADI Panel is comprised of the U.S. manufacturers of hexamethylene diisocyanate (HDI), isophorone diisocyanate (IPDI) and methylene dicyclohexyl diisocyanate ($H_{12}MDI$). CPI membership includes raw material producers, systems suppliers, processing machinery and equipment manufacturers, as well as users of polyurethane materials that manufacture products made of or from polyurethanes.

Furthermore, the physiochemical properties of TDI and HDI are significantly different from MDI.

- If industry recommendations are followed, studies have shown that installation of SPF insulation in homes, schools and other public buildings is not a source of exposure to isocyanates. Studies on high pressure two-component systems have shown that airborne concentrations of MDI are non-detectable within 30 minutes to 2 hours after application.

- For one-component foam, airborne concentrations of MDI are non-detectable at the time of application. To protect customers, these products have precautionary labeling in accordance with Federal Trade Commission (FTC)/Consumer Product Safety Commission (CPSC) and the Federal Hazardous Substances Act (FHSA) requirements.

- SPF industry recommendations by manufacturers are intended to specifically limit or prevent potential MDI exposures to occupants and bystanders.

- There is currently no known substitute for isocyanates to produce rigid SPF insulation and roofing that provides the qualities required for these applications. The unique qualities of SPF insulation and roofing include:
    - higher energy efficiency through consistent thermal performance under a wide range of temperatures
    - low air permeability, qualifying SPF as an air barrier material
    - low moisture transmission, qualifying SPF as a vapor retarder material beneficial in colder climates
    - permanent adhesion to substrates and long-term durability - no settling or sagging
    - low water absorption* - FEMA-approved flood resistant insulation
    - high strength and stiffness* - providing structural enhancement for building assemblies

      **Closed-cell SPF only*

- Although diisocyanates have been mentioned as one of the leading attributable causes of asthma in the workplace, various national data collection programs on worker exposure and disease incidence present a consistent picture, showing a reduction of diisocyanates-related asthma cases over the last decade due to improved work practices and better medical surveillance programs.

- The Department‟s very narrow selection of peer-reviewed articles and information to support its position appears to demonstrate a bias.

- No demonstrated potential for community exposure to diisocyanates used in the industrial setting has been observed.

- Regardless of the route of induction of "sensitization," inhalation exposures are necessary to exhibit a respiratory response. Thus, the role that dermal contact with diisocyanates plays in the development of occupational asthma remains unresolved for humans.

- Exposure of adults and children to diisocyanates in everyday life from fully cured products, such as SPF, is not supported by the evidence. Diisocyanates are not released from SPF in normal and correct use. Thus, the emphasis on a unique health concern affecting children potentially exposed to diisocyanates is not supported by scientific evidence.

- The reported symptoms (dizziness, nausea, sore throat, and breathing difficulties) in the Jan et al. 2009 study are consistent with an exposure to xylene, a known central nervous system (CNS) depressant and upper respiratory tract irritant, that was used as a solvent for the applied MDI (0.1% MDI in xylene). It is inaccurate to attribute the symptoms to MDI. In addition, no hydrolyzed MDI was found in the urine of the school children indicating a lack of exposure. ACC recommends DTSC remove this reference.

- A review of the Verschoor and Verschoor 2014 paper reveals a number of inaccuracies and false assumptions. Thus use of this review article as a basis for determining health effects is flawed.

- TDI is not used in SPF systems. Furthermore, there is no evidence that TDI is carcinogenic in humans.

- TDI is not used in SPF systems. In addition, the current American Conference of Governmental Industrial Hygienists (ACGIH) limits are sufficiently protective of workers. ACC does not believe a reduction in the TDI TLV-TWA or TLV-STEL is supported by the data and research available to date, or that such reductions would reduce the incidence of occupational asthma.

- TDI is not used in SPF systems. Furthermore, the ACGIH rationale for the Biological Exposure Index for TDI is scientifically flawed and needs to address the importance of using a specific biomarker of TDI exposure.

ACC urges the Department to consider our comments and revise the Priority Product Profile accordingly. We look forward to continuing to work with the Department as it determines next steps with the state‟s Safer Consumer Products Regulations. If you have any questions or need additional information, please contact either Sahar Osman-Sypher at (202) 249-6721, Sahar_Osman-Sypher@americanchemistry.com, or Lee Salamone at (202) 249-6604, Lee_Salamone@americanchemistry.com.

Sincerely,

Sahar Osman-Sypher
Director, Diisocyanates/Aliphatic Diisocyanates Panels

Sincerely,

Lee Salamone
Senior Director, Center for the Polyurethanes Industry/Spray Foam Coalition

Attachment: ACC Critique of the California DTSC Priority Product Profile for Spray Polyurethane Foam Systems Containing Unreacted Diisocyanates

***Pg. 2 - Scientific studies have shown that diisocyanates are the leading attributable cause of asthma in the workplace, and asthma is common among workers in the polyurethane industry.***

**Comment: Although diisocyanates have been mentioned as one of the leading attributable causes of asthma in the workplace, various national data collection programs on worker exposure and disease incidence present a consistent picture, showing a reduction of diisocyanates-related asthma cases over the last decade due to improved work practices and better medical surveillance programs.**

Various national data collection programs on worker exposure and disease incidence present a consistent picture, showing a reduction of diisocyanates-related asthma cases over the last decade in Finland, Ontario, Germany, Belgium, and France, against a background of increasing production and use around the world. (Piipari and Keskinen, 2005; Buyantseva et al., 2011; DGUV, 2011; Vandenplas et al., 2011; Paris et al., 2012). To understand the prevalence of disease, a reasonable approach is to use the national statistics and estimates of workers in the industry. In the Canadian Province of Ontario, Buyantseva et al., reported a reduced annual rate of successful isocyanate-related claims of occupational asthma for the period 1998-2002 (7.4 claims/year) compared to 1980-1993 (30.5 claims/year). Using the CareEx data of 12,000 isocyanates workers in Ontario, one can derive a prevalence of 0.06 % (7.4/12000) (http://www.carexcanada.ca/en/toluene_diisocyanates/occupational_estimate/).

The underlying reason for the reduction in isocyanate-related asthma is multi-factorial, including better compliance with exposure standards, improved work practices, use of less volatile isocyanate forms (e.g., prepolymers) and better medical surveillance programs (*See* Appendix 1). As several organizations have recognized, some specific tasks, notably spray painting, are associated with higher asthma incidence (McDonald et al., 2000; Karjalainen et al., 2002; Naylor and Curran, 2004; Cowie et al., 2005; Pronk et al., 2007; Buyantseva et al., 2011). Improving work practices in these applications could offer the opportunity to reduce cases of asthma even further.

The reduction in asthma cases in the last decade may be attributed to heightened awareness from medical surveillance programs and improvements in occupational hygiene (Buyantseva et al., 2011). The German Committee on Hazardous Substances (AGS, 2006) concluded that if TDI exposure concentrations are kept below 10 to 20 ppb (0.07 - 0.14mg/m$^3$), few new cases of asthma are observed. Also, they found that healthy workers were unaffected by occasional TDI exposures at or near a ceiling of 20 ppb. It appears control of exposures and compliance with current occupational exposure limits have shown that isocyanate asthma can be minimized. This

is evidenced by the production site data where there is training, surveillance, and exposure controls. (*See* Appendix 1 for more information).

There have been no large epidemiology studies of incidence and prevalence for MDI asthma. Review of individual studies reveal that the higher prevalence of 7-27% in two earlier studies (Liss, 1988; Zammit-Tabona, 1983) was not evident in a third cross-sectional study in a urethane mold plant designed to minimize MDI exposure. In that plant, a low prevalence of occupational asthma of 1.2%. was found. The authors concluded that aggressive environmental control of diisocyanate exposure decreased the expected prevalence of occupational asthma in this setting. This was supported by a large retrospective study involving 6,308 workers from the Ontario Ministry of Labour computerized database that included diisocyanate air sampling determinations conducted by the Ministry (Tarlo et al., 1997) that estimated an incidence of 0.9% per 4 years.

According to the NIOSH work-related asthma statistics, isocyanates are number 8 in frequency of reported cases with total numbers 2 to 3.5 times lower than the top 3 categories, *available at* http://www2a.cdc.gov/drds/WorldReportData/FigureTableDetails.asp?FigureTableID=2607&GroupRefNumber=F09-01

***Pg. 2 - Exposure to unreacted diisocyanates and other chemical ingredients in SPF systems may harm both workers who are not using exposure controls or personal protective equipment, and consumers or bystanders at the time of application and after the materials have been installed.***

**Comment: Extensive product stewardship efforts are in place to address the safe handling and use of SPF applications. Installation of SPF insulation in homes, schools and other public buildings is not a potential source of exposure to isocyanates if industry recommendations are followed. Studies on two component systems have shown that airborne concentrations of MDI are non-detectable within thirty minutes - two hours after application. For one component foam in aerosol cans, industrial hygiene monitoring has shown airborne concentrations of MDI are non-detectable at the time of application.**

Data demonstrates that no MDI exposure exists within thirty minutes to two hours after application. Lesage (2007) found that airborne MDI could not be detected approximately 1 hour following application of SPF in residential structures. In a subsequent study by IRSST (2009) using analytical techniques with lower detection limits, airborne MDI could not be detected approximately 2 hours following SPF application. More recently, work conducted in three residential structures found that airborne MDI could not be detected approximately 1 hour following SPF application (Robert et al., 2013). In this work, active ventilation was used during and following SPF application. Recently, in a study conducted by the Center for the Polyurethanes Industry (Wood, 2013), airborne MDI could not be detected approximately 30 minutes following SPF application. Similar to the Robert et al. study, active ventilation was used during and following SPF application.

Current SPF industry recommendations by manufacturers are as follows and can prevent potential MDI exposures to occupants and bystanders:
1) The building should be vacated during SPF application;
2) Where the building cannot be vacated, the spray application area should be contained/isolated and ventilated;
3) The spray area should be ventilated for a period of time following SPF installation;
4) Building occupants should not return until after the manufacturer‟s recommended re-occupancy time (typically 24 hours) has elapsed. (For additional information, see: *Guidance on Best Practices for the Installation of Spray Polyurethane Foam* and *Ventilation Considerations for Spray Polyurethane Foam*.

SPF Suppliers and many SPF distributors offer a 2-3 day material and equipment training program for their customers. After the applicator is trained by the supplier or distributor, the Spray Polyurethane Foam Alliance (SPFA) offers a voluntary ISO-compliant Professional Certification Program for all SPF applicators. This four-level program helps to assure that SPF applicators have the knowledge, skills and ability to apply SPF insulation and roofing systems with attention to quality and safety. No other insulation technology offers an industry-level certification program for its installers. For additional information, visit http://www.sprayfoam.org/certification.

CPI developed and launched SPF training programs which are available free to weatherization professionals, SPF applicators and helpers who work with low pressure and/or high pressure SPF. There are two (2) online courses, one focused on high pressure SPF and the other on low pressure SPF. Both provide information about the use, handling and disposal of SPF, potential health hazards and control measures, including engineering controls and personal protective equipment (PPE). The online courses are available in English and Spanish and can be taught in an instructor led setting as well. Since its release in 2010 more than 11,000 people have participated in the high-pressure health and safety training either in English or Spanish. More than 1,500 people have accessed the low-pressure health and safety training since it launched in December 2012 in English and Spanish. The low pressure training was developed with support of a Susan Harwood Grant (OSHA). Completion of CPI‟s high pressure training is a prerequisite for anyone who takes the SPFA PCP certification exam. For additional information, visit http://www.spraypolyurethane.org.

In addition, we question the inclusion of "other chemical ingredients in SPF systems." Other ingredients are out of the scope of this document and should not be referenced.

***Pg. 3-4 - SPF systems typically contain MDI including MDI mixed isomers, polymeric MDI, and HDI. TDI may be found in SPF systems either as a minor component or as a residual constituent, particularly in systems containing polyurethane-based materials such as coatings, which may contain TDI.***

**Comment: HDI and TDI are not used in SPF systems. In order for the Priority Product Profile to be accurate, the Department should remove all references to HDI and TDI.**

MDI and its oligomers are the only diisocyanates used in SPF systems. TDI and/or HDI could be used in roof coating systems. However, neither TDI nor HDI is included in SPF roofing systems. The SPF roofing systems and roof coating systems are completely separate systems independent of one another. Typically, the SPF roofing system is applied and fully cured, and then a separate roof coating system containing TDI and/or HDI may be applied as a top coat to meet certain performance characteristics such as resistance to harsh weather conditions.

Since neither TDI nor HDI are used in SPF systems, we request all references to the chemicals as components of SPF be removed from the Priority Product Profile to avoid confusion. Furthermore, the physiochemical properties of TDI and HDI are significantly different from MDI.

***Pg. 4 - When the two sides are mixed in a spray applicator, a series of chemical reactions and physical processes occur, and a polyurethane foam is generated that will „cure" into a rigid foam. In the process, human exposure to diisocyanates is likely. Curing time may range from hours to weeks depending on the type and conditions of application (U.S. EPA, 2013c).***

**<u>Comment:</u> If industry recommendations are followed, studies have shown that installation of SPF insulation in homes, schools and other public buildings is not a source of potential exposure to isocyanates. Studies on two component systems have shown that airborne concentrations of MDI are non-detectable within thirty minutes - two hours after application. For one component foam in aerosol cans, industrial hygiene monitoring has shown airborne concentrations of MDI are non-detectable at the time of application.**

Curing refers to the reaction that occurs between the two primary chemicals used to form a polyurethane product. These primary chemicals are commonly referred to as a diisocyanate (A-side material) and a polyol (B-side material). The A-side material, or diisocyanate, is highly reactive and curing begins immediately upon mixing with the B-side material. The cure time varies depending on the type of polyurethane product being produced, the ingredient formulations and other factors in the manufacturing process.

Many polyurethane products are completely cured and therefore considered "inert" before they are sold, such as mattresses, pillows, furniture cushions, car seating, refrigerator insulation, footwear, ski bindings or inline skates. This means that the original reactive ingredients, the diisocyanates and polyols, are no longer present in their original form in the cured polyurethane product.

SPF insulation is unique because the reaction between the A-side material (MDI for rigid foam insulation) and the B-side material (polyol) occur at the customer site. The diisocyanate (MDI) reacts quickly with the polyol to begin forming the foam insulation. Research studies by Lesage et. al., 2007 report that by the time 60 minutes has passed (post application time), airborne concentrations of MDI are below the analytical detection limit. Lesage 2007 also monitored the foam surface with isocyanate-indicating colorimetric wipes at various times after application. Their results showed the presence of removable isocyanate on the foam immediately after spraying, but in all cases (20 samples) no removable isocyanate was detectable on the foam surface 15 minutes after application.

There are various ways to define when SPF insulation is fully cured. Some look at certain physical properties of the installed SPF and believe when these have been achieved the insulation is cured (the SPF is tack-free within several minutes of application, and may achieve its desired physical properties within 24 hours of application). Others may look at the amount of unreacted isocyanate (which appears to be below the limit of detection on the surface of the foam within 15 minutes and below the limit of detection in the air within 2 hours after application). Additional discussion may be needed in this area to agree on an accepted definition of cured SPF. However, each SPF manufacturer is knowledgeable about the curing characteristics of its particular SPF product(s). This information is used by the manufacturer in recommending re-occupancy times after SPF installation. Also, while curing time and re-occupancy time may be related, they are not necessarily one and the same.

In conclusion, there is a big difference between curing as it relates to completion of the physical characteristics of the product and emissions of airborne isocyanate (air emissions) from the product as it begins to cure immediately after application. It may take some polyurethane products up to 24 hours to completely mature or develop all of its physical characteristics. However, MDI is generally non-detectable within the air (two hours) and on the surface (15 minutes) of the polyurethane product after application without engineering controls (ventilation). Of course, with engineering controls, re-entry time can be significantly decreased.

***Pg. 5 - One-component SPF kits/cans: These SPF products are premixed as a one-component mixture under pressure. They are typically sealed in 16-ounce cans, and are widely available in home improvement centers, hardware stores, and other retail locations.***

**<u>Comment:</u> One-component SPF cans do not contain TDI nor HDI. Various studies completed by manufacturers show that during spraying of one-component foam, MDI levels are non-detectable to thousandths less than the OSHA PEL of 0.20 mg/m3. To protect consumers, these products have precautionary labeling in accordance with Federal Trade Commission (FTC)/Consumer Product Safety Commission (CPSC) and Federal Hazardous Substances Act (FHSA) requirements.**

One-component SPF cans do not contain TDI nor HDI. Once the cans are filled with the components at the manufacturing site, reactions occur in the can reducing the amount of unreacted isocyanates and leaving pre-polymers. These materials react as soon as they are expelled from the can and cure very quickly, thus post application chemical exposure potential is extremely low. This is seen in the tack free times reported. Due to the high reactivity of the isocyanates, the surface of any foam is considered entirely reacted, as is a thin film of material. As the surface of the foam or film reacts to form the polymer chains it is physically tacky. Once the surface is tack-free it is considered entirely reacted and of sufficient robust state to resist damage from touching; thus tack-free time is a diagnostic time that characterizes cure. Various studies completed by manufacturers show that during spraying of a one component foam, MDI levels are non-detectable to thousandths less than the OSHA PEL of 0.20 mg/m3 (Fishback, 2012). There is no data to suggest that dust from these applications contains unreacted chemicals when properly applied. To protect consumers, these products have precautionary labeling in accordance with FTC/CPSC and FHSA requirements.

***Pg. 10 - Diisocyanates are known to undergo thermal degradation and release toxic chemicals.***

**<u>Comment:</u> The Department has misquoted the source regarding thermal degradation. The source for this statement is referring to polyurethanes, not diisocyanates, undergoing thermal degradation.**

The source that the Department is citing for the statement above is the CPI guidance document, "Polyurethanes and Thermal Degradation" (ACC, 2014). This document highlights the toxic products that may be of concern when polyurethanes are thermally degraded, and some worker safety and health precautions to consider. The Department has misquoted the document and should instead state the following, "When polyurethanes undergo thermal degradation, some potentially hazardous chemicals may be emitted." The source is available at: http://polyurethane.americanchemistry.com/Resources-and-Document-Library/6936.pdf .

***Pg. 12 - Antibodies to TDI have been detected in some residents living near a facility that manufactured polyurethane foam, indicating that exposures may be occurring from environmental releases from the plant and sensitizing some individuals (Orloff et al., 1998; Darcey, 2002).***

**<u>Comment:</u>. The potential for community exposure to diisocyanates used in the industrial setting has been studied and no demonstrated potential for exposure has been observed. Furthermore, TDI is not used in SPF systems. Therefore, all references to the chemical as a component of SPF should be removed from the Priority Product Profile.**

In 2007, the North Carolina Department of Health and Human Services (NCDHHS) and the Agency for Toxic Substance and Disease Registry (ATSDR) conducted a joint study of environmental exposure to TDI and potential community health effects. Data were collected from ten NC communities in four counties. Half were communities near facilities with reported TDI emissions (target areas) and half were communities where no TDI emissions were reported (comparison areas). The study results were released in May 2010 and did not find any significant health-related concerns associated with communities near plants using TDI. State and federal researchers concluded, "[w]e did not find a scientific connection between respiratory problems and exposure to TDI…Overall, we did not find that people living near the plants that emit TDI have recent or current exposure to TDI at levels of health concern." The publication on this study by Wilder et al. (2011) concluded that "[o]verall, air sample and antibody test results are not consistent with recent or ongoing exposure to TDI." The DTSC Priority Product Profile should be updated to reflect the findings from this study. The full TDI Community Health Report can be found online at: http://www.epi.state.nc.us/epi/oee/tdi/TDICommunityHealthReport.pdf.

In March 2009, EPA initiated its School Air Monitoring Project that monitored the air in 22 states around 62 schools that were located near industrial facilities or in urban areas. Seven schools in six states were selected for diisocyanates air monitoring. EPA released analyses for 5 of the 7 schools, concluding that diisocyanates were non-detectable and well below levels of concern. Therefore, EPA is no longer monitoring at those schools. For 2 of the 7 schools, which are located a ½ mile apart in the same city, results are still pending. EPA has decided to continue

air monitoring at these schools once the nearby facility is operating at a level closer to normal capacity. More information can be found on EPA website: www.epa.gov/schoolair.

In conclusion, the potential for community exposure to diisocyanates used in the industrial setting has been studied and a demonstrated potential for exposure has not been observed.

***Pg. 12 - Carcinogenicity of TDI: Most authoritative bodies generally accept that TDI is a reasonably anticipated human carcinogen (WHO, 1987; IARC, 1999; NIOSH, 2006). Oral exposure to TDI results in TDI hydrolysis in the gut, thereby generating toluene-2,4-diamine (TDA), a carcinogen. These oral route studies found that TDI exposure caused tumors at several different tissue sites in rats and mice (Timchalk et al., 1994; OEHHA, 2009, 2010).***

**Comment: TDI is not used in SPF systems. Therefore, all references to the chemical as a component of SPF should be removed from the Priority Product Profile. Furthermore, there is no evidence that TDI is carcinogenic in humans. Three epidemiological studies representing the combined long-term mortality experience of more than 17,000 polyurethane foam production workers, did not find an association between occupational exposure to diisocyanates and an increased risk of cancer. Inhalation exposures of rodents to TDI, the most relevant route of exposure, are not carcinogenic. Lifetime inhalation exposures of rats and mice to TDI vapor (150 ppb) did not elicit a carcinogenic response. Rodents tumors were observed only when contaminated TDI was administered by an aphysiological route (gavage) that favored the formation of a known rodent carcinogen (TDA), a reaction not known to occur under normal exposure conditions.**

The claim that TDI is carcinogenic lacks foundation. In humans, three epidemiological studies with updates, representing the combined long-term mortality experience of more than 17,000 polyurethane foam production workers, failed to find an association between occupational exposure to diisocyanates and an increased risk of cancer (Hagmar et al., 1993a and 1993b, updated by Mikoczy et al., 2004; Schnorr et al., 1996; Sorahan and Pope, 1993, updated by Sorahan and Nichols, 2002).

In combined chronic inhalation toxicity and carcinogenicity studies, male and female rats, as well as male and female mice, were exposed for 6 hours/day, 5 days/week for approximately 2 years to TDI (80/20) vapor concentrations of 0, 5 or 150 ppb. Histopathology of the organs/tissues investigated showed that the type and incidence of tumors and the number of tumor-bearing rats were similar in both control and TDI treated groups. In summary, TDI was not carcinogenic in rats and mice after long-term inhalation to vapor concentrations of up to 150 ppb. Lifetime inhalation exposures of rats and mice to TDI vapor (150 ppb) did not elicit a carcinogenic response (Löser, 1983; Owen, 1984), despite the lesions noted in the upper and lower respiratory tract at this maximum tolerated concentration. The claim that TDI is carcinogenic is based on the increased tumor incidences observed by the NTP (1986) when TDI in corn oil was administered directly into the stomach of rodents by oral gavage. However, this study was flawed both technically (i.e., mishandling of the test material) and conceptually (i.e., gavage exposures) resulting in the formation of toluene diamine (TDA), a known animal carcinogen, both prior to and after TDI administration (NTP, 1986, Appendix I, Dieter et al.,

1990). Given the qualitative similarity between the carcinogenic responses seen in rodents exposed to TDI and TDA (NCI, 1979), the NTP (Dieter et al., 1990) concluded that the degradation of TDI to TDA could explain the carcinogenic effects noted with TDI. Quantitative support for this conclusion comes from two studies. In the first (Timchalk et al., 1994), rats were gavaged with either 60 mg/kg TDI in corn oil (same dose as used by NTP) or 3 mg/kg TDA. Urinary analyses indicated that both produced comparable metabolic profiles of free TDA, N-acetylated TDA, and TDI/TDA conjugates. This finding is consistent with about 5% of the TDI gavage dose (i.e., 3 mg/kg of the 60 mg/kg TDI dose) being converted to TDA. In the second (Sielken et al.,2012), a statistical comparison of the carcinogenic responses seen with TDI (NTP, 1986) and TDA (NCI, 1979) support the conclusion that the carcinogenic responses to TDI are consistent with 5% of the gavaged TDI being transformed to TDA either before and/or after exposure. The NTP (Dieter et al., 1990) dismissed concerns over its flawed study by stating that TDA would be similarly formed if exposures occurred via inhalation. This misconception persists in the scientific community despite data to the contrary.

The reactivity of TDI and its propensity to form TDA is different in pure aqueous versus complex biological systems. Whereas the formation of ureas and polyureas is the predominant reaction pathway in water at neutral pH, conjugation with biomolecules dominates in complex biological systems (Day et al., 1997; Mormann et al., 2006; Seel et al., 1999). The reactions of TDI in biological systems can be influenced by the pH of the *in vivo* environment. The pH neutral and macromolecule-rich environments associated with physiological exposures (i.e., inhalation, dermal, buccal) to TDI favor conjugation with macromolecules with no detectable free TDA (Mormann et al., 2006; Rosenberg and Savolainen, 1985; Timchalk et al., 1994). In contrast, the introduction of TDI directly into the acidic environment of the stomach (i.e., bolus dose by gavage) favors the formation of free TDA, which can be detected systemically (Jeffcoat, 1988; Kennedy and Brown, 1998; Timchalk et al., 1994). A testament to the influence of pH on the conversion of TDI to TDA is the laboratory practice of using acid hydrolyses to convert TDI/TDA conjugates in biological fluids to free TDA (Skarping et al., 1994). The *in vivo* conversion of TDI to TDA and the subsequent induction of a carcinogenic response only under aphysiological (i.e., gavage) exposure conditions is consistent with the observations that (a) the absence of epidemiological evidence of carcinogenicity in TDI exposed workers, (b) free TDA was not detected in the urine of TDI exposed workers before subjection to acid hydrolysis (Skarping et al., 1994), (c) the absence of carcinogenic effects in rodents exposed to TDI vapors at a maximum tolerated concentration of 150 ppb (30-fold higher than the ACGIH TLV), and (d) free TDA was not detected in rats following a 6-hour inhalation exposure to TDI vapor at 2 ppm (Timchalk et al., 1994), a concentration 400-fold higher than the TDI TLV.

In conclusion, there is no evidence that TDI is carcinogenic in humans or animals under physiological exposure conditions. Furthermore, since TDI is not used in SPF systems, we request all references to the chemical as a component of SPF be removed from the Priority Product Profile.

***Pg. 12 - The polyurethane industry fully recognizes the hazardous nature of the SPF systems (ACC, 2014b). Through the American Chemistry Council and industry alliances and trade***

***associations, the industry has developed training materials and health and safety guidance for workers (ACC, 2014c; CPI, 2014).***

**Comment:** The fundamental principle of toxicology is "the dose makes the poison," accepting that everything can be toxic at some dose. It is also well accepted that everything can be used in a safe manner. Health and safety are priorities for the polyurethanes industry, as evidenced by our commitment to product stewardship activities and our partnership with other user groups and associations and our ongoing efforts to provide information and conduct research regarding our products. Industry has been working with federal agencies for several years to improve the dissemination of product stewardship information on the safe use and handling of our products. The American Chemistry Council (ACC) Center for the Polyurethanes Industry (CPI) provides a number of guidance documents on safety considerations when using SPF as well as health and safety training programs.

In addition, the CPI Spray Foam Coalition, a group representing about 90% of the manufacturers of SPF systems in the U.S., has recently approved a Code of Conduct that further demonstrates the member companies‟ commitment to the safe use of SPF throughout the value chain and helps provide a framework to drive continuous improvement in chemical health and safety and product stewardship. This is the first commitment of its kind in the SPF industry. The Code of Conduct is available here: http://polyurethane.americanchemistry.com/Spray-Foam-Coalition/Spray-Foam-Coalition-Code-of-Conduct.pdf.

***Pg. 12 – Frequent violations have occurred and been documented for the Occupational Safety and Health Administration (OSHA) regulated workers (Rundman, 2013).***

**Comment: We believe this statement is misleading because isocyanate-related violations are not frequent.**

Under the NEP, we have only been aware of one violation for a facility being above the PEL. Other violations have been for programs like hazard communications, PPE, and respirator standard. These sorts of violations are common in many OSHA inspections.

***Pg. 13 - Inhalation exposures in excess of the OSHA permissible exposure limit have been documented among workers during spray-on applications of truck bed liners, foam roofs, and insulation foam (NIOSH, 1996a, 2005, 2006; U.S. EPA, 2011b; Karlovich, 2010; Hosein and Farkas, 1981; Crespo and Galan, 1999; Lesage et al., 2007).***

**Comment: The reference to the Karlovich paper to support the statement that "inhalation exposures in excess of the OSHA permissible exposure limit have been documented" is completely inaccurate.**

The reference to the Karlovich paper to support the statement that "inhalation exposures in excess of the OSHA permissible exposure limit have been documented" is completely inaccurate The paper did not in fact report any overexposure to an OSHA PEL. We ask that this reference be removed from the Product Profile Document as it does not support the statement. Furthermore, we urge the Department to remove any references to other polyurethane

applications such as truck bed liners (TBL) as that is outside the scope of the document. TBL is a completely different application than SPF and should not be used to characterize SPF.

***Pg. 13 - Dermal exposure has been associated with isocyanate sensitization and/or asthma, even when airborne isocyanate concentrations were below occupational exposure levels (U.S. EPA, 2011a, b).***

**<u>Comment:</u> Diisocyanates can cause allergic contact dermatitis (dermal sensitization) but it appears to be a rare occurrence. The role that dermal contact with diisocyanates plays in the development of occupational asthma remains unresolved for humans. Regardless of the route of induction of "sensitization," inhalation exposures are necessary to exhibit a respiratory response. MDI has low volatility and is not available as respirable particles unless heated or sprayed.**

Diisocyanates are considered as dermal sensitizers and can cause allergic contact dermatitis in some individuals. It appears to be a rare event, however, as there are minimal case reports of diisocyanate contact dermatitis. The ability of diisocyanates to induce respiratory sensitization in some individuals, and asthma in some cases, is also a known potential adverse health effect in humans after inhalation exposure to concentrations above workplace exposure limits. Although there is still no validated experimental animal model accepted by regulatory agencies that adequately reflects the respiratory sensitization process and constellation of symptomology associated with occupational diisocyanate asthma, several researchers have shown respiratory changes (e.g., alterations in respiratory rate, non-specific hyperreactivity, influx of inflammatory cells) and/or antibody production in animals after dermal induction exposure and subsequent inhalation challenge with MDI or TDI. (e.g., Pauluhn and Poole 2011; Rattray et al.; 1994**,** Pauluhn, 1994**;** Pauluhn and Mohr, 1994; Pauluhn, 1995; Blaikie et al 1995).

Of interest is a Brown Norway rat MDI respiratory sensitization study that demonstrated the existence of a threshold for the elicitation of respiratory hypersensitivity responses (Pauluhn and Poole, 2011). In addition, a high-dose MDI topical induction protocol using Brown Norway rats demonstrated a neutrophilic and eosinophilic inflammatory response in the lung following repeated inhalation challenge to MDI. These topically „sensitized" rats did not exhibit marked respiratory changes after repeated inhalation challenges unless irritating concentrations of MDI aerosol were used (Pauluhn et al., 2005). It was demonstrated that at least three to four adequately spaced challenge exposures using moderately irritant concentrations of MDI are required, after topical application(s), to elicit a typical asthma phenotype (Pauluhn, 2005).

Data on this issue, including evidence from the workplace, have been considered (Graham et al., 2002) and it was concluded that while animal and human data suggest the immune system can be activated by topical exposures to MDI and TDI, experimental animal studies suggest that dermally-mediated activation of the immune system without a subsequent exposure of the respiratory tract is not sufficient to initiate a respiratory hypersensitivity response.

In conclusion, regardless of the route of induction of "sensitization," inhalation exposures are necessary to exhibit a respiratory response. Thus, the role that dermal contact with diisocyanates plays in the development of occupational asthma remains unresolved for humans.

***Pg.14 - TDI may be found in SPF systems either as a minor component or as a residual constituent. For Example, TDI is declared in the MSDS of one manufacturer in California (UPI Inc., 2012)…Some SPF systems on the market today are SPF systems containing polyurethane based coatings, sealants, or adhesives which are likely to contain TDI. For this reason, TDI is included in this Priority Products listing***.

**<u>Comment:</u> The UPI MSDS cited in the Priority Products List is for a polyurethane construction coating, which is not an SPF application.**

The UPI MSDS cited in the Priority Products List is for a polyurethane construction coating, which is not an SPF application. The product is a single-component, liquid-applied polyurethane waterproofing coating used as a base coat in most of UPI's polyurethane deck and roof coating systems. TDI is not used in SPF systems and therefore all references to TDI should be removed from the Priority Product Profile.

***Pg. 14 Worker Exposures: Potential for exposure to isocyanates comes from inhalation of or dermal contact with the material in these ways (Petsonk et al., 2000; NIOSH 2006; U.S. EPA, 2013b, 2013c, and 2014; Rundman, 2013): Dust that may contain unreacted isocyanates, generated from cutting or trimming the foam as it hardens… Degradation products, including isocyanates, from heat-generating processes such as drilling, welding, soldering, grinding, sawing, or sanding on or near foam insulation… Isocyanates and other toxic chemicals release during fires (Blomqvist, 2005; Karlovich et ..al., 2011).***

**<u>Comment:</u> In a study conducted by the ACC Center for the Polyurethanes Industry, data on the potential for dust, MDI, and pMDI generation during the trimming of open-cell and closed-cell insulation foams was gathered. In all cases MDI and pMDI were not detected. In addition, the industry has published a guidance document and warning signs that describe fire protection measures to avoid heat-generating processes to prevent overheating and combustion of SPF. The Blomqvist 2005 reference simply mentions the possibility of isocyanate release during polyurethane combustion.**

A study was initiated to evaluate the potential exposure of workers to inhalable and respirable particulates, as well as MDI and pMDI, during the post-application trimming and cutting of open cell and closed cell SPF insulation in interior applications. This study employed a written protocol under controlled laboratory conditions designed to simulate an extreme case trimming situation.

SPF insulation was applied to sections of timber drywall assemblies to simulate actual interior wall application. Extra spray was applied so that the resulting foam extended well past the studs to provide adequate foam to lengthen times for trimming and cutting in this study. Once the wall sections had cured for 1-2 hours, short-term (11-17 min) task personal exposure sampling and source air sampling was conducted during trimming and cutting. Various trimming tools, categorized as "low" or "high" dust potential, were used for both types of foam. In all cases MDI and pMDI were not detected. (M. Spence, C. Graham; Evaluation of Particulates Generated During Trimming and Cutting of Spray Polyurethane Foam Insulation, CPI Conference Paper,

2010 *available at*: http://polyurethane.americanchemistry.com/Resources-and-Document-Library/Evaluation-of-Particulates-Generated-During-Trimming-and-Cutting-of-Spray-Polyurethane-Foam-Insulat.pdf).

CPI has published a guidance document on SPF fire safety titled "Fire Safety Guidance: Working with Polyurethane Foam Products During New Construction, Retrofit and Repair" to specifically address fire protection of foams during heat generating processes (*Available at*: http://polyurethane.americanchemistry.com/Resources-and-Document-Library/11365.pdf) (ACC, 2011). SPFA has also published ANSI/OSHA compliant warning signs to be posted at all jobsites to warn other workers about potential fire hazards of exposed foam. Drilling, grinding, sanding and sawing operations are highly unlikely to generate enough heat to initiate any substantial isocyanate emissions.

The Blomqvist 2005 thesis paper (cited in the DTSC Priority Product Profile) focuses on measurement of standard combustion by-products from organic materials, such as CO, HCl, HCN, $CO_2$ and $NO_x$. Diisocyanates were only mentioned in passing and the thesis does not provide any quantitative isocyanate release data, nor does it specify the source polyurethane materials of concern for isocyanate release. Further, a paper measuring the toxic combustion by-products and oxygen depletion released from a variety of polyurethane products including foams shows that the release profile (LC50) from these materials is not significantly different than that of burning wood (Landry et al., 2007).

Finally, the reference to the Karlovich et al 2011 paper to support the statements regarding dust generation and the formation of degradation products from heat-generating processes is inappropriate. There is no mention of these items in the referenced document. We ask that this reference be removed from the Product Profile Document as it does not support the statements.

***Pg. 15 - Long-time researchers of isocyanates and asthma have become concerned about the potential relationship between isocyanates in consumer products, including SPF, and the increasing prevalence of asthma in the general population, especially children, and point to the urgent need for further research (Krone and Klingner, 2005).***

**Comment: Exposure of adults and children to diisocyanates in everyday life from fully cured products, such as SPF, is not supported by the evidence. Diisocyanates are not released from SPF in normal and correct use. Thus, the emphasis on a unique health concern affecting children potentially exposed to diisocyanates is not supported by scientific evidence.**

The special needs and safety of children is an integral consideration in the establishment of community exposure limits. The case is often made that children are more susceptible to asthma, and the exacerbation of pre-existing asthma, than adults. On a generic level, the physiological differences between children and adults (*e.g.*, breathing rates, lung size) can result in the lungs of children receiving a higher dose of any asthmogen at any given air concentration (Schwartz, 2004). Thus, an increase in the incidence of asthma in children could be more reflective of higher asthmogenic doses rather than an inherently higher susceptibility to asthma in general. This does not mean that the underlying cellular and biochemical processes that mediate an asthmatic

response are more active or efficient in children. That is, a comparison of age-dependent toxicities based on lung surface area to body mass is an inappropriate metric for diisocyanate toxicity. The chemical reactivity of diisocyanates results principally in portal-of-entry toxicity with no reproducible evidence of systemic adverse health effects. Thus, it is dose per unit area of exposed skin or lung epithelial surface that determines toxicity. Age-related pharmacodynamics that relate to the etiology of allergic dermatitis or asthma are not well understood for diisocyanates.

Specifically with regard to diisocyanates, it is becoming increasingly clear that the macromolecular and cellular pathways that are associated with childhood asthma and predominate in early childhood (Th2) are different from those associated with the full manifestation of diisocyanate asthma in adults (Th1). This dichotomy in pathophysiology indicates that children are likely to be less susceptible to any given dose of diisocyanate-induced asthma than adults.

For example, while childhood asthma is characterized by the actions of Th2-type interleukins as well as the presence of IgE antibodies and eosinophilia (Levine and Wenzel, 2010; Liu and Wisnewski, 2003), IgE antibodies are found in only a small fraction (5-30%) of workers diagnosed with diisocyanate (TDI and MDI) asthma (Tee et al., 1998; Ott et al., 2007). Furthermore, Th1 pathway cytokines (e.g., interferon γ) participate in the full manifestation of the asthmatic response (e.g., bronchial hyperreactivity) of children to environmental allergens (Heaton et al., 2005) as well as the human (Liu and Wisnewski, 2003) and animal responses (Matheson et al., 2005) to TDI. Since the Th2 pathway generally predominates in early life while the Th1 pathway is less well developed, children can be less sensitive – not more sensitive – to the expression of atopy if exposed to diisocyanates because the Th1 pathway is required for full manifestation of an asthmatic response. Therefore, based on the above, ACC contends that the emphasis on a unique health concern of children potentially exposed to diisocyanates is not supported by scientific evidence.

In conclusion, exposure of people and children to diisocyanates in everyday life from fully cured products, such as SPF is not credible, as diisocyanates would not be released from SPF in normal and correct use. Thus, the emphasis on a unique health concern affecting children potentially exposed to diisocyanates is not supported by scientific evidence. Notably, children live safer, healthier lives thanks in part to the development of many products and technologies made with diisocyanates chemistry that improve public health and safety.

***Pg. 15 - Although there is much evidence relating adverse health effects on workers to diisocyanate exposures, the evidence of harm to the general public and consumers is more limited. However, extrapolation from what is known about occupational exposure risks to the less-protected settings in which wet SPF is used by independent contractors and DIYers indicates a high potential for adverse exposures to diisocyanates among the general population during the use of this product. A recent study found that rising use of isocyanate-based materials in consumer products is leading to an increased burden of disease, with an increase in nonoccupational exposure (Verschoor and Verschoor, 2014).***

**<u>Comment:</u> A review of the Verschoor and Verschoor paper reveals a number of inaccuracies and false assumptions. The use of this review article as a basis for determining health effects is flawed.**

The Department is using a secondary reference instead of reading and referencing the primary references which would not lead to the same conclusions. The Verschoor and Verschoor (2014) paper is a review and personal opinion paper on exposure. No new or convincing data is presented. Most references are misquoted, taken out of context, or completely inaccurate. A comprehensive and detailed "Letter to Editor" will be offered to the journal. At the time of submission, ACC will share the individual details. In the meantime, it is highly recommended that the Department obtain the primary references and review the information to correct the Product Profile.

***Pg. 16 - There are also anecdotal reports of strong odors and physiological reactions (headaches, dyspnea) following installation of insulation in various settings (Green Building Advisor, 2010).***

**<u>Comment:</u> This is an anecdotal report and not a peer-reviewed research paper, and provides no scientific evidence on isocyanate exposure to building occupants. Odors inside a building can come from many sources if minimum indoor ventilation rates are not achieved.**

MDI is an odorless chemical and it is therefore highly likely that the odors cited in this article were from other sources. The presence of odors inside a building is very subjective, and is strongly dependent on an individual‟s olfactory sensitivities. Humans can detect odors of many chemical compounds at levels far below safe exposure limits. In terms of SPF application in buildings, ventilation of the spray zone for a few hours after spraying can eliminate these odors in most cases. In addition, the air sealing feature of SPF will dramatically reduce air leakage in a building to levels below the natural ventilation minimum of 0.35 $ACH_n$ recommended by ASHRAE 62.1. Without minimum ventilation, emissions from many other sources can accumulate within the building. When SPF is installed, a common practice is to perform an air leakage test of the building after installation to determine if minimum ventilation rates are achieved or if additional mechanical ventilation is needed.

***Pg. 16 - Incidental exposure to MDI and xylene caused asthma-like symptoms in 203 students in Taiwan, where students from two adjacent schools were exposed to MDI and xylene (Jan et al., 2008).***

**<u>Comment:</u> The reported symptoms (dizziness, nausea, sore throat, and breathing difficulties) in the Jan et al. 2009 study are consistent with an exposure to xylene, a known CNS depressant and upper respiratory tract irritant, that was used as a solvent for the applied MDI (0.1% MDI in xylene). It is therefore inaccurate to attribute the symptoms to MDI. In addition, no hydrolyzed MDI was found in the urine of the school children indicating a lack of exposure. ACC recommends DTSC remove this reference.**

The Department assumes that purported asthma-like symptoms observed in school children were due to a MDI exposure (Jan et al., 2008). However, the reported symptoms (dizziness, nausea, sore throat, and breathing difficulties) are more likely attributable to xylene, a known CNS depressant and upper respiratory tract irritant that was used as a solvent for the applied MDI. This theory is based on the following: (a) air monitoring was not conducted for either volatile organic compounds or MDI, and (b) despite the claim by Jan and coworkers, an earlier work referenced by the authors did not detect MDI near polyurethane tracks up to a week after application. Examination of another reference (Chang et al., 1999) reveals no mention of MDI measurements. Further supporting an absence of an exposure to MDI is the determination that no MDA was detected in the hydrolyzed urine of school children purportedly exposed to MDI.

The sizeable difference in volatility between xylene and MDI, the high xylene content compared to MDI in the applied product (0.1% MDI in xylene), as well as the symptoms consistent with xylene or other solvent exposure, indicate that the symptoms observed were most likely due to the inhalation of xylene.

Therefore, ACC asks the Department to remove this reference because the Reactive Airways Dysfunction Syndrome (RADS)-like effects (*e.g.*, dyspnea, cough, headache) seen can be attributed to the irritating and highly volatile solvent, xylene. Significantly, a more detailed critique of the Jan et al. (2008) paper concludes that due to significant lapses of proper scientific consideration, this paper should be regarded as unreliable, and should not be used as evidence of health effects attributable to MDI exposure. This review is attached to these comments as Appendix 2.

In conclusion, the reported symptoms (dizziness, nausea, sore throat, and breathing difficulties) are consistent with an exposure to xylene, a known CNS depressant and upper respiratory tract irritant, that was used as a solvent for the applied MDI (0.1% MDI in xylene) and it is inaccurate to attribute the symptoms to MDI asthma. In addition, no hydrolyzed MDI was found in the urine of the school children indicating a lack of exposure. ACC recommends that DTSC remove this reference for these reasons.

***Pg. 19-20 - Recent research has focused on the development of non-isocyanate chemistries especially for polyurethane adhesives, sealant and coatings, such as soy-based polyurethane (Javni et al., 2008), and linear or network non-isocyanate-based polyurethane (NIPU) produced by reaction of cyclocarbonate resins and amines (Figovsky and Shapovalov, 2006)…There exist very few isocyanate-free alternatives in the rigid spray foam market. The only reported commercialized product is an isocyanate-free expanding foam product for insulation applications utilizing a hybrid silane terminated polymer technology (Soudal,* **2010).**

**<u>Comment:</u> There is currently no known substitute of the use of isocyanates to produce rigid SPF insulation and roofing that provides the qualities required for these applications.**

There is currently no known substitute that would function as an appropriate alternative to the use of isocyanates to produce rigid SPF insulation and roofing that provides the qualities required for these applications. The unique qualities of SPF insulation and roofing include

consistently higher energy efficiency through thermal performance under a wide range of temperatures and low air permeability (air barrier material), low moisture transmission (vapor retarder material), low water absorption* (FEMA flood resistant material), improved physical strength and stiffness* (structural enhancement), adhesion to substrates and long-term durability. **Closed-cell SPF only.*

The technology described by Figovsky may have some applicability in the coatings area as curing at elevated temperatures can be more easily achieved. Its use in the rigid foam area appears extremely limited due to the reported difficulties in obtaining a fast curing system. Additionally, the technology described by Soudal is intended for one-component foam and does not meet the requirements for SPF.

***Pg.18 - The ACGIH is proposing a TLV-TWA of 0.001ppm for TDI, and a 15-Minute STEL of 1.3 ppm, and lists the basis for the TLV as being "Asthma."***

**<u>Comment:</u> TDI is not used in SPF systems. Therefore, all references to the chemical as a component of SPF should be removed from the Priority Product Profile. Furthermore, based on the available information, the current ACGIH limits are sufficiently protective of workers. ACC does not believe that a reduction in the TLV-TWA or TLV-STEL is supported by the available science, or that such reductions will reduce the incidence of occupational asthma.**

ACC has submitted extensive scientific information to ACGIH explaining the Panel‟s position that the proposed TLV values are not justified by the evidence and that the existing values are sufficiently protective of workers. The Panel does not believe a reduction in the TLV-TWA or TLV-STEL is supported by the science, or that such reductions would reduce the incidence of occupational asthma. The Panel‟s previous comments have discussed the following:

1) <u>No New Scientific Information.</u> The ACGIH Notice of Intended Changes (NIC) levels are not based on any new information that ACGIH did not have when it evaluated TLV levels for TDI in 2004. The draft documentation does not present any new scientific data that demonstrate a need to lower the TLVs.

2) <u>Unsupported Rationale</u>. The rationale for lowering the TLV-TWA reflects a belief that lowering the TLV the last time resulted in reduced incidence of occupational asthma, and a supposition that lowering the TLV again should lead to further reductions in occupational asthma. No empirical support for that first proposition is presented in the draft documentation. Nor is any scientific evidence presented to support the supposition that a further reduction in the TLV would lead to a further reduction in occupational asthma.

3) <u>Technical Feasibility of Monitoring at Lower Levels Using Direct Reading Instruments</u>. Direct reading instruments (DRIs) are commonly used to assess airborne concentrations of TDI because of their ability to provide a quick evaluation of the potential inhalation hazard in the work environment. The proposed TLV values push the limits of technology for monitoring compliance when using DRIs. For example, it may be possible to measure compliance with the proposed TLV-TWA (8-hour value) using passive

samplers, but it would not be possible to measure to the proposed TLV-STEL based on the current detection range of these devices.

In conclusion, ACC believes that based on available information, the current ACGIH limits are sufficiently protective of workers. ACC does not believe a reduction in the TLV-TWA or TLV-STEL is supported by available science, or that such reductions will reduce the incidence of occupational asthma.

***Pg. 18 - In addition, ACGIH has published a "Biological Exposure Index" for TDI based upon toluene diamine in urine, collected at the end of the work shift.***

**<u>Comment:</u> TDI is not used in SPF systems. Therefore, all references to the chemical as a component of SPF should be removed from the Priority Product Profile. Furthermore, the ACGIH rationale for the Biological Exposure Index (BEI) for TDI is scientifically flawed and should instead address the importance of using a specific biomarker of TDI exposure.**

ACC has submitted extensive comments questioning the scientific validity of the development of a Biological Exposure Index for TDI based upon toluene diamine in urine. Previous comments have discussed the following:

1) <u>TDA is not an Expected Metabolite of TDI in Humans</u>
   Under normal physiologic exposure conditions, the formation of free TDA from TDI has not been demonstrated *in vivo*. The text in the draft documentation of the BEI for TDI that refers to the presence of free TDA in the metabolic scheme of TDI should be revised to accurately reflect the current understanding of TDI metabolic pathways.

2) <u>Non-Specificity of the Proposed Biomonitoring Method</u>
   The inability to specifically assess TDI exposure and to differentiate TDI from TDA exposures is considered a limitation of this method. This limitation downgrades the use of this biomonitoring method as a screening or surveillance tool and does not permit a more definitive and quantitative assessment of exposure to TDI.

3) <u>Specific Biomarkers of TDI Exposure are Available</u>
   A TDI-specific biomonitoring method such as that based on albumin conjugates are available and should be considered rather than the non-specific urine hydrolysis method.

4) <u>Description of the Recommended Analytical Method Should be Expanded</u>
   Additional details of the proposed analytical method should be provided along with validation of the procedure before it is adopted for use as a biomonitoring method to screen TDI workers for potential exposure.

5) <u>Non-Occupational Exposure to TDI is Very Limited</u>
   TDI-based products should not be listed as sources of non-occupational exposure. Further, the BEI Documentation inaccurately mentions several product types that may

represent sources of non-occupational exposure to TDI. These product types (e.g., SPF, one-component foams) contain MDI, not TDI, therefore do not present opportunities for non-occupational exposure to TDI.

6) References to Urinary TDA in the Documentation Require Qualification
To prevent a misinterpretation of the text in BEI documentation, we strongly recommend that each reference to "TDA in urine" or "plasma TDA" or "TDA elimination in urine" or similar statements be qualified to indicate that the urine was hydrolyzed prior to measurement of TDA levels. This is to preclude a reader from mistakenly assuming that such statements indicate the presence of free TDA in workers.

7) Basis of a Proposed BEI for TDI Should be the Current TLV
Any proposed BEI for TDI should be based on the current 8-hour TWA of 5 ppb and not in anticipation of a proposed change to the TLV to 1 ppb.

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# Appendix 1

## Are Diisocyanate Occupational Asthma Cases Declining?
## Poster Presented at the Isocyanates and Health Conference
## Potomac, Maryland, April 3-4, 2013

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# Are Diisocyanate Occupational Asthma Cases Declining?

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## Study Objective

To review recent publications and Surveillance databases in order to evaluate trends of diisocyanate-related occupational asthma (OA).

## BACKGROUND

Diisocyanates are often cited as a leading cause of occupational asthma. We reviewed trends of diisocyanate-related OA in order to evaluate the effect of compliance with current occupational exposure limits aimed at preventing new cases.

## METHODS

A literature search was done on recent publications. Information was gathered from national or state/province-based registries, surveillance schemes and compensation statistics of various metrics for rates of diisocyanate-related occupational asthma. European manufacturer data on occupational asthma incidence (unpublished data) was collected. Data was reviewed to assess possible trends.

## RESULTS

**USA, Center for Disease Control** (CDC) Work-Related Lung Disease Surveillance System (eWoRLD):

The categories for Diisocyanates n.o.s. (221.00), TDI (221.01), MDI, (221.02), and HDI (221.04) were included for the years 1993-1999, 1993-2002, and 1993-2006. Unfortunately these numbers include work-aggravated asthma cases, reactive airways dysfunction syndrome cases, and confirmed but unclassified cases which may not be diisocyanate asthma.

An average of 30.7 cases per year have been reported during 1993-1999, which dropped to 21.33 cases per year during 2000-2002, and to 20.75 cases per year during 2003-2006.

| Years | Number of cases | Number of new cases | New Cases per year |
|---|---|---|---|
| 1993-1999 | 215 | | 30.7 |
| 1993-2002 | 279 | 64 | 21.33 |
| 1993-2006 | 362 | 83 | 20.75 |

### Michigan, USA:

MICHIGAN'S PROJECT SENSOR publishes annual reports on work-related illness and specifically, work-related asthma (WRA) to isocyanates. Asthma rates of Diisocyanates have fallen from 22.9 cases per year in 1988-1997 to a recent 6.4 cases per year in 2005-2010.

(http://www.oem.msu.edu/AnnualReports.aspx)

| Years | Number of cases | % of cases | Number of new cases | New Cases per year |
|---|---|---|---|---|
| 1988 - 1997 | 229 | 19.4 | | 22.9 |
| 1988 - 2000 | 295 | 18 | 66 | 22.0 |
| 1988 - 2005 | 351 | 14.6 | 56 | 11.2 |
| 1988 - 2010 | 383 | 12.7 | 32 | 6.4 |

### Ontario, Canada:

Annual rates of successful isocyanate-related worker compensation claims for occupational asthma have been recorded in the Canadian Province of Ontario. A recent publication reports a reduced annual rate of successful isocyanate-related worker compensation claims comparing **30.5 occupational asthma claims/year** during 1980-1993 with **7.4 claims/year** during the period 1998-2002 (Buyantseva *et al*., 2011).

### EU production sites for TDI:

**No asthma cases** were reported and only one case of other respiratory disease occurred during 2000-2005 in all TDI production plants (III, Unpublished data).

### United Kingdom:

Data from the period 1989-1991 showed the proportion of occupational asthma ascribed to isocyanates as **22%** (McDonald *et al*, 2000), while during the period 1992 – 2001 the annual rate attributed to diisocyanates was consistent at about **14%** of all occupational asthma, or an annual average of **84 cases** (McDonald et al 2005). Data for 2008-2010 reports a decline to an average of **44 cases** per year (UK HSE 2011).

### Netherlands:

For the years 2009-2011 isocyanate-related cases were reported as **none to 4** (Nederlands Centrum voor Beroepsziekten, 2012).

### Switzerland:

Diagnosis of occupational respiratory disease due to diisocyanates has remained similar in the period 2005-2009, accounting for about **5%** of all respiratory cases (SUVA 2011).

### France:

Work related asthma assigned to isocyanates declined over the period 2001-2009 from **12.7%** to **6.2%** of all cases. During this time the decline in isocyanate-related cases was significant (P=0.007) even while the total numbers of cases due to all agents also declined (Paris et al., 2012).

| Years | avg #cases/year | % of all WRA |
|---|---|---|
| 2001-2003 | 49 | 12.1 |
| 2004-2006 | 38.6 | 12.3 |
| 2007-2009 | 12.3 | 4.8 |

### Germany:

Total Diisocyanate asthma cases recorded as 'new pension because of recognized occupational disease' show a decline over the last 16 years (DGUV).

| Years | Average/year |
|---|---|
| 1995 - 1999 | 47 |
| 2000 – 2004 | 26.6 |
| 2005 – 2010 | 17.3 |

## CONCLUSIONS

**Metrics on diisocyanate-related asthma rates indicate a significant reduction in reported cases. The data variability can be accounted for by the difference in source and method of diagnosis, which varies from patient's association of symptoms with work and a physician diagnosis of asthma (UK) to specific challenge testing (Canada and Germany). We emphasize the importance of exposure control and medical surveillance which various authors advocate as strong methods of prevention.**

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# Appendix 2

## III Scientific Office

## Critique of Jan et al. (2008)

# III Scientific Office
# Critique of Jan et al. (2008)

## Summary and Conclusion

A paper published by Jan et al. has been cited in several regulatory reviews as an example of public health effects from use of a reactive polyurethane product. The paper reports health effects experienced by school children in Taiwan following the application of an MDI-containing outdoor track surfacing product. Upon even casual reading of the paper, numerous problems with the paper are evident. For example, simple items such as spelling errors (e.g. the use of "tract" when "track" is intended) call into question the quality of both peer review and editing that was applied to the paper. On the more scientific level, there is a fundamental question about attribution of health effects to MDI without considering the possible or probable role of other chemicals known to be present. Also, there is an apparent misunderstanding of air concentration data and exposure guidelines, as well as frankly erroneous attribution of MDI exposure data to a reference which, upon inspection, contains no such data. Because of these significant lapses of proper scientific consideration, this paper should be regarded as unreliable, and should not be used as evidence of health effects attributable to MDI exposure.

## Critique Details

The details of the major criticisms of the paper outlined above are given below;

- **False statement** - One of the most egregious errors in this paper appears to be a false statement concerning earlier work done by one of the authors: in the last page of the paper, the authors say, "We previously showed that polyurethane athletic tracks continue to release certain isocyanates and volatile solvents during the paving process and beyond. Adjacent to such tracks, air levels of MDI were easily detectable even after the first week of tract (sic) installation [11]" There is no mention of isocyanates in the 1999 paper referenced [Chan et al, 1999]; which measures and discusses individual and total VOCs.

- **Attribution of noted effects (CNS) to MDI** - Jan et al reports on acute respiratory symptoms following exposure to MDI and xylene.

They distinguish between immunologic and irritant-induced asthma or reactive airway dysfunction syndrome (RADS) and provide two references of previously reported MDI – induced RADS. Only one of the two actually involved MDI (Leroyer et al 1998) and interestingly enough this case also involved MDI mixed with a solvent. The exposure in the Jan paper was described to the raw material and not to MDI. The acute symptoms consisted of dizziness, nausea, sore throat, and breathing irregularities, symptoms associated with solvent exposure and specifically xylene, which is well known to cause acute to chronic CNS encephalopathy. MDI on the other hand, has not been associated with CNS symptoms, except in the presence of other confounders such as when mixed with solvents and other chemicals (Herbert et al 1995, Longley 1964), litigation cases (Reidy 1994) and a detailed review found no evidence of CNS effects of MDI exposure (Carson et al 2011). In conclusion, we do not believe that the health effects reported by Jan et al, can be linked to MDI exposure. In addition, local newspaper reports of the incident attributed the children's symptoms to xylene (per communication of Alex Xu, BASF via William Robert, BASF)

- **Misstatements concerning MDI concentrations** – in the abstract, the authors state, "In a simulation, we found the raw material used for tract (sic) surfacing, primarily MDI dissolved in xylene, to be present at a concentration (870 ppm w/w) more than 8000-fold the level defined as safe for a working environment". In the results section, the authors explain, "The raw material used for track surfacing was found to be primarily MDI dissolved in xylene at a concentration of 870 ppm w/w, by use of the reference Occupational Safety and Health Administration analytical method 42 [6], more than 8000-fold the recommended safe minimum inhalation concentration for a working environment [7]". It appears that the authors have a poor understanding of the application of OSHA occupational exposure limits (OELs). The OEL referenced is the NIOSH REL – 0.005 ppm (8-h TWA), 0.02 ppm (Ceiling) in air on a molar volume (i.e., v/v) basis. From the authors statement, I can only conclude that they somehow applied the OSHA Method 42 (1,2-pyridyl piperazine derivatization air monitoring filter method) to assay the composition of the bulk liquid solution (as further indicated by the weight basis designation (i.e., w/w), as would be typical for reporting liquid solution compositions). They apparently then proceeded to compare the liquid concentration with the air concentration somehow, although it is unclear how they arrived at the factor of 8000: 870 ppm / 0.02 ppm = 4100; 820 ppm / 0.005 ppm = 164,000; 820 ppm / 8000 = 0.1025 ppm.

**Poor logic is statement of attribution of effects to MDI** – In the results section of the paper, the authors make the statement, "The direct cause-effect relationship for MDI exposure and health effects on the students was confirmed by an inverse linear relationship between the incidence of students in various classrooms and the distance from the site of MDI spillage (r = -0.48, p<0.05) [Fig. 2]" *(Note: the text reports a value of -0.48 for r yet the figure indicates 0.51)*. Figure 2 is included below for reference. The poor correlation indicated might demonstrate some association of effects in the children with the site of the spill, but says nothing about what aspect of the spill caused the effects – if xylene were the causative agent, the data would look the same.

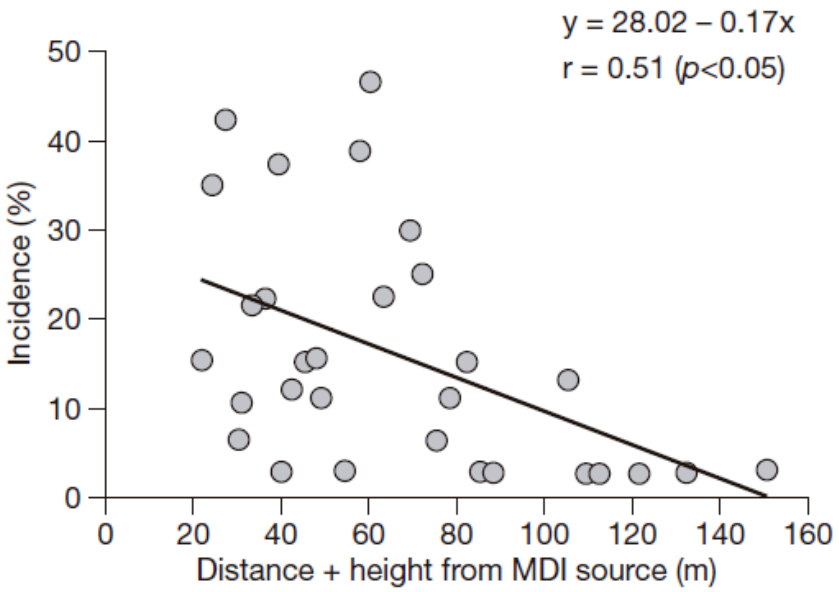


**Fig. 2.** Linear relationship between the incidence of affected students in various school classrooms and distance/height combinations from the suspected methylene diphenyl diisocyanate (MDI) emission source.

M Spence
M Collins
16 March 2012

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