Summary of Technical Information and Scientific Conclusions for Designating Spray Polyurethane Foam Systems with Unreacted Methylene Diphenyl Diisocyanates as a Priority Product

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Contents

I. Executive Summary

The purpose of this document is to present the scientific information the Department of Toxic Substances Control (DTSC) relied on to identify and prioritize spray polyurethane foam (SPF) systems containing unreacted methylene diphenyl diisocyanates (MDI)[1] for listing as a Priority Product. DTSC conducted an extensive literature review on the associated hazard traits and exposure potential of MDI and the potential for these chemicals in SPF products to contribute to or cause significant or widespread adverse impacts. This report summarizes the technical information evaluated and presents the conclusions of this evaluation.

Isocyanates are low molecular weight chemicals that act as haptens (Bernstein 1982). *In vivo*, haptens bind with larger proteins such as albumin or glutathione and may elicit an immune response known as respiratory sensitization (Janeway et al. 2001). Respiratory sensitization can lead to an elicitation of asthma in subsequent exposures to isocyanates, even when exposures are very low (< 1ppb) (OEHHA 2016). Therefore, it is generally accepted that isocyanates, including MDI, are asthmagens (AOEC 2014) and are associated with work-related asthma (CDPH 2013).

Work-related asthma is defined by the California Department of Public Health (CDPH) as asthma that is caused or aggravated by conditions or substances in the workplace. In order to qualify as work-related asthma, the asthma must be diagnosed by a physician and shown to have started after the possible workplace exposure began. The California Work-Related Asthma Prevention Program surveillance data (1993-2008) recorded 47 cases of work-related asthma associated with isocyanate exposure, with eight cases specifically attributed to MDI exposure (Lefkowitz et al. 2015).

Inhalation of airborne MDI is a common route of exposure to MDI during and soon after application of SPF products (ACC 2014d) and is of particular concern to DTSC. In addition to respiratory sensitization, scientific evidence has demonstrated that exposure to MDI in the workplace can cause immuno-, respiratory, and dermato-toxicities, which are summarized in more detail under “Section IV” of this document. MDI-induced fatalities have been documented for workers using spray polyurethane paints (NIOSH 1996a; NIOSH 2006) and resins containing MDI (Carino et al. 1997).

[1] The purpose of using this term “unreacted MDI” is to differentiate airborne MDI at the time of spraying from polymerized MDI. Polymerized MDI in finished SPF is beyond the scope of this report. The general term “MDI” is used throughout this document to refer to all unreacted MDI monomers and oligomers that are typically present in technical-grade MDI mixtures used in SPF systems. Section II discusses the use of the term, MDI, and the specific chemicals in more detail.

In addition to inhalation, applicators may also be exposed to MDI through dermal contact during handling activities (ACC 2014d; Bello et al. 2007; HSDB 2011; Liljelind et al. 2010; Lockey et al. 2015).

Human exposure to isocyanates may occur with use of either high- or low-pressure SPF systems, including home use kits. High-pressure SPF systems are distributed in unpressurized drums and totes, which are preheated and pressurized to between 1,000 and 1,600 pounds per square inch (psi) during mixing and spraying (ACC 2015). Low-pressure fillable systems and one-time use kits are sold pressurized at about 250 psi and passively mixed through the spray gun (ACC 2015). During spraying, inhalable materials containing MDI, including vapors, aerosols, dusts (U.S. EPA 2013c), and other respirable particles, become airborne.

Studies, including some from the SPF industry, found that workers may be exposed to MDI during spraying of SPF products, especially when they do not use any protective measures.[2] In some studies, airborne MDI levels exceeded 51 µg/m^3, which is both the Threshold Limit Values (8-hour Time Weighted Average) set by the American Conference of Governmental Industrial Hygienists (ACGIH 2015) and the Permissible Exposure Limits (PEL) of the California Division of Occupational Safety and Health (Cal/OSHA) (Cal/OSHA 2015).[3] In other studies, MDI exceeded 200 µg/m^3, which is the Occupational Safety and Health Administration (OSHA) PEL (15-minute ceiling) (NIOSH 2010). It is important to note that PELs do not protect all workers (Marlow et al. 2014); some sensitive workers may develop adverse health effects when they are exposed to MDI concentrations below PELs (Bello et al. 2007). Studies also suggested that exposure to very low concentrations of MDI can trigger adverse reactions in previously sensitized individuals ((Bello et al. 2007; Lemiere et al. 2002). According to recently established reference exposure levels (RELs) by OEHHA, individuals may develop adverse health effects if they are occasionally exposed to MDI levels above 12 µg/m^3 for an hour (Acute REL) or 0.16 µg/m^3 for 8 hours each day, 5 days a week (8-hour REL) (OEHHA 2016).

Occupational exposures to harmful substances, such as MDI in SPF systems, should be addressed via a well-documented hazard control methodology widely accepted by

[2] DTSC is primarily concerned about potential human exposure to unreacted MDI during the process of spraying. DTSC is aware of ongoing studies and reports on exposure scenarios where individuals entering or residing at locations after SPF application could be exposed to chemical hazards; however, these exposure scenarios are not the focus of this document.

[3] The PEL is the maximum concentration of a chemical that workers may be exposed to for a certain period, from 15 minutes to a typically 8-hour work shift. Workers may be exposed to concentrations that exceed the PEL provided they do not exceed the time-weighted average specific to that PEL or any applicable excursion limits.

the industrial hygiene profession and safety organizations, such as OSHA. Following the OSHA approach, hazards are controlled via a “hierarchy” of potential solutions (CDC 2015). This hierarchy, in order of preference, is: 1) elimination of the hazard; 2) substitution with a different chemical; 3) engineering controls, including processes and systems such as exhaust ventilation, which are designed to remove the hazard at the source, before it comes in contact with the worker; 4) administrative controls, including the implementation of policies, procedures, and employee training; and 5) the use of personal protective equipment (PPE) (CDC 2015).

Eliminating the chemical hazard entirely, or substituting a less hazardous chemical, is the most effective means of minimizing potential occupational exposures to workers. Engineering controls can be effective, especially when their use is combined with the use of administrative controls and PPE. However, compared with hazard elimination, administrative controls and PPE, which are the recommended controls by the industry, are considered to be the least desirable approaches to control potential occupational exposure (CDC 2015). This is largely because the original hazard is still present in the workplace. The level of workers’ training, experience, and supervision, as well as a range of physical and environmental variables, may reduce the effectiveness of administrative controls and PPE (Parr 2015). Worker exposure that can lead to injuries or illness is often a consequence of failing to use PPE, using it improperly or failing to follow administrative controls. Workers may not use PPE because it is uncomfortable, particularly under hot conditions, often fits poorly, and is bulky. Additionally, employers may not supply workers with adequate PPE nor enforce its use (Arcury et al. 2014; Farooqui et al. 2009; Lombardi et al. 2009; Salazar et al. 1999). OSHA estimates that only about 64% of construction workers wear proper PPE on a regular basis (Farooqui et al. 2009). Even when worn properly, PPE may place workers at risk due to reduced dexterity, visual acuity, and mobility; it may also increase the likelihood of trip, slip and fall accidents as well as developing heat-related illness (Lombardi et al. 2009; Salazar et al. 1999)

Of the two categories of SPF systems, workers who operate high-pressure systems are more likely to complete industry-recommended training and certification programs, follow safety procedures, and to be provided with PPE. However, as stated above, engineering and administrative controls and the use of PPE are at the bottom of the hierarchy of control methods, and therefore are the least effective in protecting workers from exposures to occupational hazards. DTSC has determined that industry recommended engineering and administrative controls and use of PPE reduces the likelihood of exposure, but cannot eliminate worker exposure to MDI during spraying of high-pressure systems.

Depending on the size of the project, workers may apply SPF continuously for shifts that typically range from four and six hours. High-pressure SPF systems are heated and pressurized and, as a result, atomization of these materials occur during spraying (ACC 2015). Regardless of the curing time and level of ventilation, SPF aerosols and particles containing MDI will be present in the workers' breathing zone during the entire work shift. In addition to handling-related exposures, workers may also be exposed to MDI through accidental spills or leaks, cleaning and maintenance of the equipment (Lockey et al. 2015; Marlow et al. 2014). Failure to use (Kavanaugh 2016) , improper use of, imperfect fit or malfunction of PPE.

Compared with high-pressure SPF systems, low-pressure SPF systems, including re-fillable systems and single-use kits, are packaged under lower pressures and not heated at the time of mixing and spraying (ACC 2015). Low pressure systems are used by insulation contracting businesses, including those with employees (ACC 2015) and sole proprietors, and by individual consumers engaged in "do-it-yourself" projects. Sole proprietors and individual consumers are exempt from federal OSHA and Cal/OSHA requirements (Environment Canada 2014a; Levinson et al. 2014; Lockey et al. 2015; U.S. EPA 2011a). Any consumer can purchase low-pressure single-use kits from the internet and home improvement centers (Levinson et al. 2014; U.S. EPA 2013c). Limited data from the industry suggested that spraying of low-pressure systems generates less airborne MDI than spraying of high-pressure systems, but in several studies, measurable MDI was detected around applicators' breathing zones during application (ACC 2015; Bloom 2012; Levinson et al. 2014; Wood 2013). Applicators increase their risk of exposure to MDI when they assume low-pressure systems are safer than high-pressure systems, and fail to use engineering controls such as local exhaust ventilation and PPE that are otherwise available to them. The SPF industry has occasionally identified and sanctioned contractors who failed to use PPE while publicly demonstrating the use of SPF (Kavanaugh 2016).

DTSC is particularly concerned about exposures to MDI by sole proprietors and individual consumers who apply SPF through low-pressure systems because they are unlikely to use engineering controls and PPE or industry recommended administrative controls (Environment Canada 2014a; Lockey et al. 2015; U.S. EPA 2011a). Some consumers may not be aware of the hazardous nature of these products (U.S. EPA 2013c). Monitoring studies suggest that any SPF applicators should wear PPE (i.e. full-face respirator, coveralls, head and foot covers, and gloves) at all times while in the work area and individuals without the proper PPE should remain outside of the work area (Marlow et al. 2014).

Based on the information presented above, DTSC determined that applying SPF through high- and low-pressure systems, including home use SPF kits, has the potential to cause significant or widespread adverse impacts to human health. The proposed Priority Product has the potential to harm not only workers of highly specialized commercial operations; it also can harm any applicator who is either improperly protected or unprotected against MDI exposures such as sole proprietors and individual consumers in California.

II. Identification of the Priority Product and Chemicals of Concern

DTSC has identified SPF systems containing MDI as a Priority Product. An SPF system is composed of two liquid chemical mixtures that are sold or distributed together and are referred to as “sides.” “Side A” of the system consists of MDI, and “Side B” consists of a mixture of polyols and other ingredients, which may include catalysts, blowing agents, flame retardants, and surfactants. The chemical mixtures in the sides react when mixed together to form polyurethane foam that is used for insulation, roofing, or sealing and filling voids and gaps (U.S. EPA 2013a).

The proposed Priority Product excludes: (a) one-component spray polyurethane foam sold in cans; (b) pre-fabricated flexible or rigid polyurethane foam; (c) assembled products containing polyurethane foam, or (d) polyurethane products that are applied by methods other than spraying (e.g. rolling, pouring, or brushing).

SPF systems may be packaged under either high- or low-pressure (Table 1). High-pressure SPF systems require considerable investment in equipment and are typically marketed for use by highly specialized commercial applicators (ACC 2014d). Low-pressure SPF systems require less investment in the use of specialized equipment and may be purchased by both commercial applicators and non-commercial users such as individual consumers for indoor or outdoor applications (Table 1).

Table 1. Overview of SPF systems (U.S. EPA 2013c) †

SPF Systems Overview		
	High-Pressure	Low-Pressure
SPF Types	• Open-Cell (low density, half lb.) • Closed-Cell (medium density,2lb.) • Closed-Cell (high density, 3 lb.)	Not applicable
Uses	• Larger insulation applications • Air sealant in hybrid insulation • Installation with fiberglass or other insulation materials • Roofing applications (Closed-Cell, high density, 3 lb.)	• Air sealant adhesive • Smaller insulation applications • Weatherization activities
Applicator	• Professional installer	• Professional installer • Weatherization worker • Do-it-yourselfers
Container size	• 55 gallon drum containers	• Typically three to five gallons per container from the system house, but can be purchased in larger containers over the internet or in some retail markets.
Application Process	Sides A and B are pumped through heated hoses from supply tanks into a nozzle where the two components react and are spray applied at elevated temperatures (>150°F) and pressure (1200 psi).	Sides A and B combined at application site and sprayed on as a stream or bead. After the foam is applied, has expanded, and has cured, it may then be trimmed or cut, if needed.
Chemical Exposure Potential	***Chemical exposures may occur***: • During application • After application • During heat-generating processes such as drilling, welding, or sanding • During fires ***Through***: • Aerosols • Vapors • Dust that may contain unreacted chemicals	
Hazards	• Sensitization • Asthma • Lung damage • Other respiratory and breathing problems • Skin and eye irritation	
Re-Entry	Some manufacturers recommend 24 hours after application for worker re-entry without the use of PPE and for re-occupancy by residents and other building occupants, but the recommended time may vary.	

† Adopted with format and language modifications.

The Chemicals of Concern are members of a highly reactive group of compounds called isocyanates. An isocyanate is any chemical that contains in its structure at least one isocyanate group (i.e., –N=C=O). A chemical containing two such isocyanate groups is referred to as a diisocyanate (3M Australia 2008). The term 'isocyanates' is more general and will be used in this document for simplicity.

The names and Chemical Abstract Service Registry Numbers (CAS #) of the Chemicals of Concern include:

- 4,4′-Methylene diphenyl diisocyanate (4,4′-MDI), CAS #: 101-68-8
- Generic methylene diphenyl diisocyanate (generic MDI), mixed isomers, CAS #: 26447-40-5

For the purpose of this document, the Chemicals of Concern are collectively referred to as MDI, which includes isocyanates that are referred to as 4,4′-MDI or pure MDI (ACC 2001), generic MDI, and technical grade MDI, all of which contain 4,4′-MDI (CAS # 101-68-8).[4] This approach is based on the rationale described below:

- MDI can be produced in a relatively pure form [4,4′-MDI isomer (CAS #: 101-68-8)], and they may be referred to as "pure MDI" (ACC 2001). The term "MDI" is often used for pure MDI (ACC 2014d).

- MDI generally can exist in more than one isomeric form, and can be produced as a mixture of isomers. This mixture contains 4,4′-MDI (CAS # 101-68-8) and may be referred to as "generic MDI" (ACC 2001). According to one authoritative body, the CAS #: 26447-40-5 for "generic MDI" includes the isomeric mixtures as well as all other specific isomers, including those with unique CAS numbers (U.S. NLM 2015).

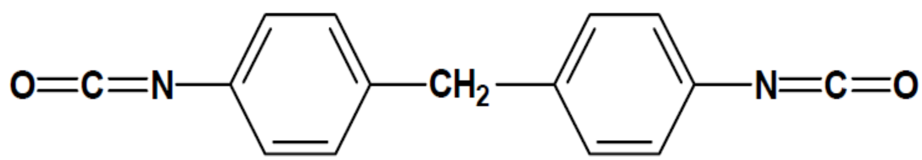
- Technical grade MDI contains 30 to 80% w/w 4,4′-MDI with the remainder consisting of other isomers, oligomers, and homologues (Wiley-VCH 2012).

[4] Technical grade and generic MDI are sometimes referred to as "polymeric MDI" (ACC 2014d; IARC 1987, Wiley-VCH 2012) by the SPF industry and in the scientific literature. However, they are not polymers, but liquid mixtures of MDI and higher molecular weight oligomers of MDI. It is important to distinguish the use of the term "polymeric MDI" (or PMDI) in this document from the use of the same term the report titled "Methylene Diphenyl Diisocyanate Reference Exposure Levels (Monomeric and Polymeric Forms) – Technical Support Document for the Derivation of Noncancer Reference Exposure Levels – Appendix D1 (OEHHA, 2016). The PMDI discussed in the OEHHA report is a polymer with a different CAS# (9016-87-9). To avoid confusion, the authors of this document only use the term "polymeric MDI," or PMDI, when it was used by authors of the literature cited in this report.

Additional information on the Chemicals of Concern:

- Molecular formula for both 4,4′-MDI (IARC 1987) and generic MDI (U.S. NLM 2015):
  - $C_{15}H_{10}N_2O_2$
- Chemical Abstract Names (ACC 2001; IARC 1987):
  - CAS # 101-68-8: benzene, 1,1'-methylenebis(4-isocyanato)
    - Short Name: 4,4′-MDI
  - CAS # 26447-40-5: benzene, 1,1′-methylenebis(4-isocyanato)
    - Short Name: generic MDI
- IUPAC Systematic Names:
  - CAS # 101-68-8: 1-isocyanato-4-(4-isocyanatobenzyl)benzene (ACC 2001), Isocyanic acid, methylenedi-paraphenylene ester (IARC 1987)
  - CAS # 26447-40-5: No IUPAC name for mixtures (ACC 2001)

- Chemical structures (HSDB 2011; IARC 1987):



MDI, CAS # 101-68-8

- 4,4'-MDI Common synonyms or trade names (ACC 2001)

  MDI
  Pure MDI
  Monomeric MDI
  Bis-(p-isocyanatophenyl)methane
  Bis-(4-isocyanatophenyl)methane
  Di-(4-isocyanatophenyl)methane
  Diphenylmethane-4,4′-diisocyanate
  Isocyanic acid, methylenedi-p-phenylene ester
  Methylenebis(p-phenyl isocyanate)
  Methylenebis(p-phenylene isocyanate)
  Methylenebis(4-phenyl isocyanate)
  Methylenebis(4-phenylene isocyanate)
  4,4′-Diisocyanatodiphenylmethane
  4,4′-Diphenylmethane diisocyanate

4,4′-Methylenebis(phenyl isocyanate)
4,4′-Methylenediphenyl diisocyanate
4,4′-Methylenediphenylene isocyanate

- Generic MDI common synonyms or trade names (ACC 2001)

  Methylene diphenyl diisocyanate
  Diisocyanatodiphenylmethane
  Methylenediphenylene diisocyanate
  Diphenylmethane diisocyanate
  Diphenyl methane diisocyanate
  Di-(isocyanato phenyl)methane
  Methylenebis(phenylisocyanate)
  Diphenylmethyl diisocyanate

MDI meets the conditions specified in California Code of Regulations, title 22, section 69503.6(a) in that it appears on one or more of the authoritative lists in California Code of Regulations, title 22, section 69502.2(a)(1) and is a chemical listed in California Code of Regulations, title 22, section 69502.2(a)(2):

- MDI is listed on the Air Toxics Hot Spots list of chemicals whose emissions must be quantified and the Office of Environmental Health Hazard Assessment (OEHHA) has inhalation Reference Exposure Levels for respiratory toxicity.
- MDI is classified by the European Commission as a respiratory sensitizer.
- MDI is identified by the California Air Resources Board as a Toxic Air Contaminant.

III. Physicochemical Properties of MDI

For MDI with CAS # 101-68-8:

- Color: White to light yellow (NIOSH 2010)
- Molecular weight: 250.25 g/mol (Haynes 2010)
- Density: 1.197 g/mL at 70 °C (Haynes 2010)
- Specific gravity: 1.23 (solid at 25 ^{o}C); 1.19 (Liquid at 50 ^{o}C)(NIOSH 1997)
- Melting point: 37 °C (Haynes 2010)
- Boiling point: 314 °C (OEHHA 2016)
- Log K_{ow}: 5.22 (est.) (U.S. EPA 2011b)
- Water solubility: 1.51 mg/L at 25°C, estimated (U.S. EPA 2011b)
- Vapor pressure: 5.0 x 10^{-6} mmHg at 25 °C (NIOSH 1997)

IV. Hazard Traits of MDI

MDI is a respiratory sensitizer and generally considered as an asthmagen (AOEC 2014) associated with work-related asthma (CDPH 2013). Once sensitized, re-exposure to even low concentrations of MDI (<1 ppb) may trigger severe asthma attacks in some people (OEHHA 2016). In addition to respiratory sensitization, exposure to MDI in the workplace can cause other adverse respiratory effects including inflammation and irritation, as well as dermatotoxic effects such as allergic contact dermatitis.

1. Allergic Sensitization[5]

A number of studies in animals have demonstrated that isocyanates, including MDI, are respiratory sensitizers. Several animal models of asthma have been developed for both respiratory and dermal sensitization to MDI or PMDI (Pauluhn and Poole 2011; Pauluhn et al. 2000; Rattray et al. 1994; Wisnewski et al. 2011). In mice and guinea pigs with previous MDI skin exposure (≥1% MDI in solution) significant airway inflammatory responses to respiratory MDI challenge have been demonstrated (Rattray et al. 1994; Wisnewski et al. 2011). Both high acute exposures and lower level exposures may induce sensitization (OEHHA 2016). Dermal sensitization to MDI can also result in allergic contact dermatitis.

- Short duration, high concentration (1,000 mg PMDI/m^3 for 10 minutes) repeated inhalation exposure in rats followed by PMDI inhalation challenge (40 mg/m^3) resulted in increased neutrophils in bronchoalveolar lavage fluid (BALF) and delayed-onset respiratory changes (Pauluhn and Poole 2011).
- Topical application of polymeric MDI to rats followed by inhalation of MDI resulted in increased neutrophils in BALF and a delayed respiratory response (as determined by breathing patterns; enhanced pause [Penh]). During the dermal sensitization phase, rats were dosed contralaterally two times, seven days apart. Two weeks after the second dermal dose, rats underwent four inhalation challenges, in two week intervals. The first three inhalation challenges were ~38 mg MDI/m^3 and the fourth challenge was either 8, 18, or 39 mg/m^3. Rats were lavaged and sacrificed one day after the fourth inhalation challenge. The degree of respiratory response was

[5] For the purposes of this document, the term "Allergic Sensitization" covers the toxicological hazard traits "Immunotoxicity" and "Dermatotoxicity". These toxicological hazard traits are specified in Title 22, California Code of Regulations Chapter 54 and are cited in the proposed regulation to list SPF systems with unreacted MDI as a Priority Product. DTSC elected to use this term in response to comments from the external scientific peer reviewers.

more dependent on the inhaled dose during elicitation, than the dose applied topically during induction/sensitization (Pauluhn 2008).

- Topical application of MDI on mice resulted in systemic sensitization, with increased total antibody production of IgE and MDI-specific antibodies (IgE, IgG1, and IgG2a). Dermally -exposed mice (>1% MDI weight/volume administered on days 0 and 7) and challenged seven days later via intranasal droplet (days 14, 15, 18, and 19) with MDI-albumin adducts had significant increases of inflammatory cells (eosinophils and lymphocytes) in the BALF. These observations suggest that dermal sensitization may result in respiratory inflammation (Wisnewski et al. 2011).
- Fifty-four patients suspected of having occupational skin disease, underwent patch testing for dermal sensitization to MDI, TDI, HDI, isophorone diisocyanate, and methylenedianiline (MDA), the metabolite/reaction product of MDI (U.S. EPA 1998). Twelve patients reacted to MDI and forty-four patients reacted to MDA. MDA is an important marker of MDI hypersensitivity (Aalto-Korte et al. 2012).
- Seventeen workers exposed to MDI-based polyurethane semi-rigid foam in a vehicle equipment factory had work related skin symptoms, which appeared from three days to six months after their first occupational exposure. Symptoms included itchy, stinging and/or burning skin lesions, localized on the exposed, bare skin areas. Diagnosis of allergic contact dermatitis for seven subjects was based on dermal sensitization patch test results where responses to MDA, but not MDI, were positive (Kieć-Świerczyńska et al. 2014).

2. Respiratory Toxicity

Many studies in both animals and humans demonstrate respiratory toxicity of MDI. The toxicological endpoints include the following:

a. Respiratory irritation

- Inhalation of aerosolized MDI (7-59 mg/m^3) for four hours by mice resulted in decreased respiratory rate (as determined by plethysmography) and increased lung weight. In contrast to toluene diisocyanate (TDI) and hexamethylene diisocyanate (HDI), MDI acted primarily as a pulmonary irritant rather than a sensory irritant. Decreased respiratory rate was also observed in mice exposed to MDI aerosol via tracheal cannulation, which bypasses the trigeminal nerve and therefore sensory irritation. This study demonstrates the stimulation of lower respiratory tract receptors rather than the trigeminal nerve (Weyel and Schaffer 1985).

b. Pulmonary Inflammation
    - An acute six hour inhalation exposure to PMDI (10, 30, or 100 mg/m^3) by rats resulted in concentration-related increases of inflammatory cells (neutrophils and alveolar macrophages), total protein, and enzyme activities (lactate dehydrogenase, alkaline phosphatase, and N-Acetyl glucosaminidase) in BALF at post-exposure days 1 and 3. Complete recovery was observed by post-exposure day 30 (Kilgour et al. 2002).

c. Pathology and Fibrosis
    - Chronic inhalation exposure to MDI in rats induced a dose dependent interstitial and peribronchiolar fibrosis (i.e., narrowing and fibrotic wall thickening of small airways) that was significantly increased in all treatment groups in comparison to controls (Ernst et al. 1998; Hoymann et al. 1998).
    - Chronic inhalation exposure to high concentrations of polymeric MDI in rats resulted in focal fibrosis around accumulations of alveolar macrophages after one year. After two years, high concentrations resulted in collagen synthesis and basement membrane thickening (Reuzel et al. 1994).
    - Chronic inhalation exposure to high concentrations of polymeric MDI in rats resulted in increased basal cell hyperplasia of nasal olfactory epithelium (Reuzel et al. 1994).

d. Airways hypersensitivity and Asthma
    - A prospective study of the respiratory effects of MDI exposure evaluated the lung health of workers in a new wood products manufacturing plant in which MDI resin was used as a binder. Fifteen of 56 workers with high exposure had new onset of asthma after 2 years vs. 0 of 43 workers with low exposure.(Petsonk et al. 2000)
    - Eleven foundry workers exposed to MDI and formaldehyde had bronchial hyperreactivity and respiratory symptoms compatible with asthma. MDI-induced asthma was confirmed in six workers after specific inhalation challenge (SIC) to MDI (12 ppb over 60 minutes) resulted in ≥20% decrease in forced expiratory volume in one second (FEV_1). These six workers did not react after SIC to formaldehyde (2.5 ppm for 30 minutes. One patient reacted to both MDI and formaldehyde, but the bronchoconstriction was attributed as an irritant response rather than sensitization (Zammit-Tabona et al. 1983).
    - A foundry worker, frequently exposed to MDI with no previously reported respiratory symptoms, was diagnosed with reactive airways dysfunction syndrome (RADS) after an acute high-level inhalation exposure to MDI produced by an accidental spill in his work area. Symptoms included

headache, sore throat, cough, and chest tightness. After the incident, chest symptoms worsened at work with increased wheeze and chest tightness. A spirometric test revealed moderate airflow obstruction with FEV_1 of 2.5 L (83% predicted) and forced vital capacity (FVC) of 4.5 L (121% predicted). Occupational asthma was confirmed after a inhalation challenge with MDI (15 ppb for 60 minutes) resulted in a 22% fall in FEV_1 seven hours post exposure (Leroyer et al. 1998).

e. Hypersensitivity pneumonitis
   - In a review of company physician's case histories of 1,780 isocyanate workers, fourteen patients were suspected of having isocyanate-induced hypersensitivity pneumonitis following isocyanate exposure with work-related symptoms of dyspnea, fever, and malaise. Nine of these patients were exposed to MDI only (the other patients were exposed to TDI, HDI, or a combination with MDI). Diagnosis was based on chest x-ray films, levels of IgE and IgG antibodies to isocyanate-human serum albumin, lung function tests, and analysis of lymphocytes in BALF. Hypersensitivity pneumonitis symptoms were also confirmed in five subjects who underwent inhalation challenge with MDI, symptoms occurred after a latency period of two to eight hours (Baur 1995).
   - Eight subjects who worked in a woodchip board manufacturing plant that used PMDI resin as a binding agent developed hypersensitivity pneumonitis with symptoms of chest tightness, cough, and shortness of breath associated with myalgia, chills, headaches, and nausea. Three to seven hours following inhalation challenge with MDI vapor, subjects experienced systemic symptoms and significant falls in both FEV_1 and FVC, hypoxia, increased blood neutrophils, increased neutrophils and lymphocytes in BALF, and significant levels of IgG and IgE antibodies to MDI-human serum albumin (Vandenplas et al. 1993).

V. Environmental Fate of MDI

MDI may be released to the environment via either accidental discharge or normal use of the Priority Product, which may contribute to airborne MDI, deposition to soil and/or surface waters in the vicinity where releases occur.

1. Air

MDI can exist in both vapor and particulate phases in the atmosphere as indicated by a vapor pressure of 5.0×10^{-6} mmHg at 25 ^oC. Airborne MDI does not readily react with water vapors in the atmosphere (Tury et al. 2003). Atmospheric MDI tends to form aerosols by condensing onto airborne particulates and water (Environment

Canada 2014b). MDI has been detected in air with concentrations ranging from 0.1 to 1,320 µg/m^3 (Environment Canada 2014b). Vapor-phase MDI is degraded in the atmosphere via reaction with photochemically-produced hydroxyl radicals with a reaction half-life estimated to be between 11 (HSDB 2011) and less than 24 hours (Tury et al. 2003).

Particulate-phase MDI will be removed from the atmosphere by wet or dry deposition (HSDB 2011) onto soil and water particles, structures, and equipment (Environment Canada 2014b).

MDI is not expected to be susceptible to direct photolysis by sunlight (European Chemicals Bureau 2005; HSDB 2011).

Once SPF is installed and cured, airborne concentrations of MDI are expected to be negligible. Most isocyanates will remain bound in the matrix as part of a rigid material under normal ambient conditions. However, it can undergo thermal degradation and release toxic chemicals (ACC 2014c; U.S. EPA 2013b). Thermal degradation may be caused by fires and other heat-generating processes such as welding, soldering, grinding, sawing on or near SPF insulation, which may generate a range of airborne degradation chemicals including isocyanates, hydrogen cyanide, and others (ACC 2014c; Blomqvist 2005; Blomqvist et al. 2003; U.S. EPA 2013b).

2. Water

Although MDI is hydrophobic (Environment Canada 2014b), it reacts with water to form predominantly insoluble polyureas and carbon dioxide. Studies suggest that the heterogeneous hydrolysis reaction occurs slowly at the MDI-water interface and can last for a considerable amount of time (Yakabe et al. 1999). This is due to the fact that the major product of such a reaction is polyurea, which tends to form quickly, starting on the outside and forming a crust that may restrict ingress of water and egress of amines such as methylene dianiline (MDA) and urea (Heimbach et al. 1996; Yakabe et al. 1999). The amines (e.g., MDA) are expected to bond with soil and sediments and biodegrade (Cowen et al. 1998). Hydrolysis reaction rates of MDI and reaction byproducts are dependent on many factors such as the starting concentration of MDI and aquatic temperatures (Environment Canada 2014b). Although there is little data describing degradation of MDI in various aquatic environments, it is generally presumed that MDI will not accumulate in aquatic systems or the food chain (Environment Canada 2014b; HSDB 2011).

3. Soil

Depending on soil temperature, particle size, and density, MDI released to or deposited onto the soil may be transported from the soil to adjacent waters, air, or freeze before reacting with moisture and slowly forming polyureas and small amounts of amines (e.g., MDA) (Environment Canada 2014b; Sendijarevic et al. 2004). Although degradation data in various soil media are not available, MDI is presumed not to leach or adsorb to solids, volatilize, or bioconcentrate due to hydrolysis of MDI in the soil in the presence of water (HSDB 2011).

VI. Exposure Potential of Humans to MDI in SPF Systems

1. Market Presence

a. The global market for building insulation (fiberglass, SPF, and others) is projected to grow from $18.5 billion in 2011 to $24 billion by 2016 (Markets and Markets 2014a). The global market for insulation foams will have a compound annual growth rate (CAGR) of 5.8% from 2011 to 2016, and is projected to reach $10 billion by 2016 (Markets and Markets 2014a).
b. Within the global polyurethane industry, the SPF sector is currently estimated to be worth $800 million, and is projected to grow to $1.1 billion by 2015. Global demand for SPF is projected to grow 13% per year from 2013 to 2015 (Business Wire 2013).
c. In 2015, the SPF industry reported between 460 and 490 million pounds of SPF were used for roofing and insulation in the U.S. and Canada, and reached the milestone of $1 billion market (Kavanaugh 2016).
d. In North America, demand for SPF for residential construction and updating grew about 15% per year from 2013 to 2015 (Kavanaugh 2016).
e. In California, approximately 83 polyurethane-related facilities, including those producing polyurethane foam, reported a total of $616.6 million in sales in 2011 (C. Barnes & Co. 2010).
f. The Spray Polyurethane Foam Alliance (SPFA) currently lists 38 California SPF contractors among its members (SPFA 2015).
g. The Center for the Polyurethane Industry (CPI) estimated that two-component SPF market in California to be $55-60 million (ACC 2016a)
h. In California, the use of SPF materials is rapidly expanding due to its effectiveness as insulation and from financial incentives for energy conservation upgrades offered by both government agencies and non-government organizations. These incentives are generally offered as tax credits or subsidies through contractors and utilities to increase energy efficiency in residential and commercial establishments (Energy Upgrade California 2016). The number of businesses and individual consumers that

are trying to conserve energy through upgrades is also growing due to awareness of government incentives and educational outreach by governments, non-profit organizations, and advocacy groups. In Northern California, for example, newly constructed homes are being insulated entirely with SPF in Placer County (Bozorgchami 2013).

2. Worker Exposure Routes

a. Exposure to isocyanates via inhalation or dermal contact can occur in the following ways (Marlow et al. 2014; NIOSH 2006; Petsonk et al. 2000; Rundman 2013; U.S. EPA 2013b; U.S. EPA 2013c; U.S. EPA 2014):
   - Via inhalation of vapors, aerosols, and particles generated when a product is sprayed. Inhalation exposures during some SPF applications exceeded OSHA PELs (ACC 2012; Lesage et al. 2007; U.S. EPA 2013c). Even when MDI concentrations were maintained below PELs, studies suggested that applicators should still use PPE to protect themselves from potentially harmful exposures (Marlow et al. 2014).
   - Via inhalation and dermal contact with degradation products, including isocyanates, from heat-generating processes such as drilling, welding, soldering, grinding, sawing, or sanding on or near foam insulation (U.S. EPA 2013c).
   - Via inhalation and dermal contact with isocyanates and other toxic chemicals released during fires (ACC 2014c; Blomqvist 2005; Blomqvist et al. 2003).

b. When neither engineering controls nor PPE are mandated, sole proprietors in the construction and weatherizing industries, and individual consumers using low-pressure SPF systems for do-it-yourself projects are at risk for exposure to MDI.

c. Many factors, including worker's physical characteristics, training, experience, and supervision as well as physical and environmental variables, can reduce the effectiveness of PPE (Parr 2015). These factors are included in the inspection procedures of the OSHA NEP as potential causes of occupational exposures to isocyanates (Rundman 2013).

d. The SPF industry has occasionally identified and sanctioned commercial contractors who were supposed to use PPE but failed to use protection during spraying of SPF products (Kavanaugh 2016).

e. Leaks and spills can also occur, which can expose workers via inhalation and dermal and mucous membrane contacts. During a 2012 NIOSH site survey, a leak developed in the line that feeds Side A (MDI component) to the spray gun, which took some time to repair (Marlow et al. 2014).

3. Monitoring Studies

There have not been many monitoring studies conducted to measure airborne concentrations of MDI during SPF applications. Data from available studies vary widely due to differences in (1) sampling and MDI recovery techniques, (2) analytical methods, (3) types of SPF systems, (4) operating parameters including heat and pressure, and (5) other factors such as distances from the application, air movement/ventilation, and other environmental conditions.

a. Limited monitoring data, including some from the SPF industry, suggest that workers may be exposed to MDI during spraying, especially when they do not use any protective measures. A 2014 NIOSH report reviewed the results from three MDI monitoring studies and found that applicators' exposure to MDI ranged from 7.0 to 205 µg/m^3 (Marlow et al. 2014). During 13 separate indoor applications, MDI has been detected in the applicators' breathing zones at concentrations that ranged from 12 to 570 µg/m^3 (Crespo and Galan 1999). A NIOSH monitoring study detected MDI concentrations that ranged from 4.85 to 18.7 µg/m^3 for the applicator and from 0.18 to 7.89 µg/m^3 for the helper. This study was conducted over three work shifts with samples taken up to 50 feet from the application equipment and in adjacent rooms, (Marlow et al. 2014). Other studies also detected measurable levels of airborne MDI up to 20 feet from the applicators' breathing zones for a considerable amount of time after spraying (ACC 2015; ACC 2012; Lesage et al. 2007; Roberge et al. 2009; Wood 2013). A recent Canadian review found that airborne MDI concentrations ranged from 0.1 to 1,320 µg/m^3 in European and US monitoring studies (Environment Canada 2014b).

b. In some monitoring studies, airborne MDI levels exceeded 51 µg/m^3, which is both the Threshold Limit Values (8-hour Time Weighted Average) set by the American Conference of Governmental Industrial Hygienists (ACGIH 2015) and the Permissible Exposure Limits (PEL) of the California Division of Occupational Safety and Health (Cal/OSHA) (Cal/OSHA 2015). In some studies, MDI exposures exceeded 200 µg/m^3, which is the Occupational Safety and Health Administration (OSHA) PEL (15-minute ceiling) (NIOSH 2010).

c. Despite the adoption of PELs, not all workers will be protected from adverse health effects even though their exposures are maintained below these levels (Marlow et al. 2014). People who are already sensitized can have adverse reactions to concentrations of MDI below the PEL (Bello et al. 2007; Lemiere et al. 2002). In addition, exposures below the PEL may induce sensitization, with dermal contact as a contributory factor (Reilly et al. 2001). Recently, the

California Office of Environmental Health Hazard Assessment has established MDI RELs in air (OEHHA 2016). These RELs were established to protect susceptible individuals of the general population. According to OEHHA, individuals could develop adverse health effects, particularly respiratory problems, if they are occasionally exposed to MDI at concentrations above 12 $\mu g/m^3$ for an hour (Acute REL) or 0.16 $\mu g/m^3$ for 8 hours each day, 5 days a week (8-hour REL) (OEHHA 2016).

4. MDI-induced Worker Fatalities

a. A maintenance worker developed isocyanate-induced hypersensitivity pneumonitis and died after repairing an MDI foaming system at a facility that made artificial plants with polyurethane foam bases (NIOSH 1994a).
b. A 45-year old worker died due to an acute asthma attack after 12 months on the job spraying MDI-based bed liners onto the floor and sides of cargo vans (NIOSH 2006).
c. A 39-year-old worker in a mold and core processing plant where resins containing MDI were used died from asthma. The worker was previously diagnosed with MDI-induced asthma at age 34. Several of his colleagues also developed asthma despite wearing personal respiratory devices. Although this fatality is not due to exposure to MDI in SPF products, it demonstrates that individuals sensitized to asthmagens, such as MDI, are at risk not only for active asthma but also for asthma death (Carino et al. 1997).

5. MDI-induced Occupational Asthma

Exposures to isocyanates have been identified as an attributable cause of work-related asthma for some exposed workers (Creely et al. 2006; Mapp et al. 1988; OEHHA 2016; U.S. EPA 1998; U.S. EPA 2011a). NIOSH has issued multiple hazard summaries and alerts warning of asthma and deaths resulting from occupational exposure to isocyanates (NIOSH 1996a; NIOSH 2004; NIOSH 2006). Harmful or fatal incidents involved workers spray-painting cars, applying spray-on polyurethane foam truck bed liners, installing foam in buildings, or exposed to MDI-based adhesives used in coal mining.

a. Ten workers with no preexisting asthma developed MDI-induced asthma after 1-8 months on the job at an engineered wood products plant. All 10 workers reported respiratory symptoms when they were in areas where MDI was used (NIOSH 1996b).
b. Nine spray-paint workers in a large airplane assembly plant developed asthma (Seguin et al. 1987). MDI in aerosols was one of the attributable isocyanates identified in this study.

c. A 29-year-old male working for a company that installed spray-on truck bed liners developed isocyanate-induced asthma (Bonauto and Lofgren 2004).
d. Isocyanate-induced asthma was reported in a 30-year old man who worked for a truck bed lining company (Bonauto and Lofgren 2004; NIOSH 2006).
e. A 22-year-old worker developed isocyanate-induced asthma after working in the truck bed lining industry for 18 months (Bonauto and Lofgren 2004; NIOSH 2006).
f. Coal miners complained of respiratory difficulties, asthma, and shortness of breath, dizziness, headache, sore throat, fatigue, and contact dermatitis after exposure to MDI-based polyurethane rock glues. Company medical records showed nine reports of health problems attributed to rock glue exposure (NIOSH 1994b).
g. In 2010, 119 isocyanate-induced occupational diseases were claimed in Germany with 30 attributable to MDI (25%) (Baur and Bakehe 2014)

6. Non-Occupational Exposure Potential

There are over 50 SPF products containing MDI readily available to consumers (Household Products Database 2015). Although consumer use appears to be rising, it is difficult to attribute specific cases of non-occupational illness, such as asthma or allergic sensitization, to the use of SPF products that contain MDI. Despite the paucity of data, DTSC remains concerned that consumers who use low-pressure SPF systems have an elevated risk of exposure because they are least likely to understand or take steps to mitigate the hazards posed by MDI.

According to latest national and state statistics on the incidence of asthma among children and adults in the U.S., 7.7% of the total U.S. population, or over 24 million people, currently have asthma (CDC 2014a). Approximately 11% of those with asthma live in California, constituting 8.7% of all Californians (CDC 2014b).

Incidence of asthma from chemical exposures, such as MDI, in the non-occupational setting is difficult to determine. Neither national nor state data for asthma triggered by isocyanates and application of SPF by non-occupational applicators are presently available. This is attributable to a general lack of epidemiological studies; confounding among different causative agents, such as sensitization by a chemical in one product and later triggered by the chemical in a different product; presumed under-reporting of illnesses; and lack of follow-up studies.

It is well known that many biological and chemical triggers causes asthma, which include triggers from indoor, outdoor, and in the workplace (CDC 2010), but the total number of such triggers remains unknown. Statistical data for each specific major causative agents are not available. A comprehensive review of more than 3,000 papers on occupational asthma identified 372 causative agents of allergic and 184 different causes of irritant occupational asthma (Baur 2013; Baur and Bakehe 2014). Some of these causative agents such as isocyanates are likely to cause non-occupational asthma. Due to the many triggers and numerous exposure routes, it is inherently difficult to attribute asthma from non-occupational settings to a specific causative agent such as isocyanates.

It is also difficult to attribute cases of MDI sensitization to specific SPF products, particularly in non-occupational settings. Unprotected consumers could unknowingly become sensitized to isocyanates following exposure to MDI in low-pressure SPF systems. Additional exposure to isocyanates in a variety of products, including SPF systems, could trigger serious asthma attacks. Given uncertainty in the specific causes for these types of asthma attacks, they are hard to trace and may be underreported. The reason for underreporting is likely similar to the underreporting in isocyanates-induced occupational asthma: primary care physicians may be unaware of the causative agents and fail to thoroughly investigate the patient's history using valid questionnaires and a comprehensive diagnostic setup (Baur and Bakehe 2014). The lack of non-occupational data does not dismiss the fact that isocyanates are sensitizers and potent asthmagens, which the SPF industry recognizes fully in its product and educational literature (ACC 2014b; ACC 2016b). For example, the industry published guides for occupational uses and stated that "exposure to high airborne concentrations of MDI can lead to respiratory sensitization, which may result in occupational asthma. Exposure of a sensitized individual to MDI can result in skin and/or respiratory reactions. Respiratory effects (asthma attacks) can be severe (or fatal) even at very low levels of exposure in sensitized individuals (ACC 2016b). There is no evidence that exposure to MDI at non-occupational settings are safe and do not cause asthma. These literature and guidance may be helpful to some commercial workers, sole proprietor and individual consumer will not benefit from them as they will neither use ventilation nor PPE specified in the guidance document.

VII. Sensitive Subpopulations with Potential for Adverse Impacts from MDI

DTSC is concerned about the potential for adverse human health impacts for people who may inhale, contact, or be in close proximity to MDI from the use of SPF systems. The population subgroups of greatest concern to DTSC are commercial operators using high- and/or low-pressure SPF systems employing only lower tiers of protection, unprotected workers in any commercial businesses, sole proprietors, and individual consumers who purchase SPF system for various do-it-yourself projects. The latter two groups generally use little or no protective measures against hazards associated with SPF systems.

a. Workers who work with or around isocyanates may be susceptible to both acute and chronic exposure to MDI via the inhalation and dermal routes. Inhalation exposures to isocyanates including MDI in excess of the OSHA PEL have been documented among workers during spray-on applications of foam roofs and insulation foam (ACC 2012; Crespo and Galan 1999; Hosein and Farkas 1981; Lesage et al. 2007; NIOSH 2005; NIOSH 2006; U.S. EPA 2011a). During spray foam applications, approximately 20% of the spray foam aerosol was found to be in the respirable size range (Lesage et al. 2007). Inhalation exposures have been documented after thermal degradation (welding or grinding) of isocyanate-containing products (OEHHA 2016; U.S. EPA 2011a). Both inhalation and dermal exposures to isocyanates are thought to contribute to the development of isocyanate-induced asthma (Bello et al. 2007; Liljelind et al. 2010).
b. Exposure to isocyanates is recognized as a cause of occupational asthma (Bakerly et al. 2008; Bello et al. 2004; U.S. EPA 1998; Vandenplas 2011). Asthmatic symptoms may occur immediately upon exposure, be delayed for several hours after exposure, or consist of both an immediate and delayed reaction.
c. The polyurethane industry, through the SPFA and American Chemistry Council, has developed industry training and certification programs for SPF workers and contractors. These stewardship programs address medical monitoring, recommendations, best practices, training materials, and health and safety guidance for workers (ACC 2014a; ACC 2014b; CPI 2014) to mitigate hazards associated with SPF products containing unreacted MDI. Large commercial operations may be willing and able to invest in training, and purchasing of equipment for engineering controls and personal protection for their workers.
d. There is little evidence that applicators who are exempt from state and federal worker protection standards, such as sole proprietors and individual consumers, receive industry recommended training or certification, invest in engineering controls, or hire industrial hygienists. As a result, sole proprietors and individual consumers may not understand the hazards associated with exposure to MDI or how to protect themselves before they apply SPF for commercial or do-it-yourself projects (U.S. EPA 2013c). Because SPF professional certification programs are offered through private industry associations, it is difficult to estimate worker participation rates in these programs in California. Among the numerous sole proprietors and individual consumers, a certain percentage is presumed to be susceptible to sensitization following exposure to MDI from SPF applications.

This percentage is expected to be similar to the percentages of commercial workers.

e. Despite industry's certification program for some applicators of SPF systems (SPFA 2013), accidental spills, leaks, cleaning and maintenance of equipment create situations where exposure to isocyanates can occur (Lockey et al. 2015).
f. The SPF industry sanctioned at least one contractor who was found on a Youtube video voluntarily spraying SPF products without protection (Kavanaugh 2016).
g. Despite industry guidelines and access to personal protective equipment and engineering controls, safety violations (Rundman 2013) and spills (Marlow et al. 2014) may occur.
h. Individual consumers can purchase low-pressure kits either online or from suppliers of SPF systems (Levinson et al. 2014; U.S. EPA 2013c). These consumers are of particular concern (Environment Canada 2014a; Lockey et al. 2015; U.S. EPA 2011a; U.S. EPA 2014) because these kits are typically sold without a Safety Data Sheet or the necessary PPE (ACC 2015). Most consumers may not fully understand the potential hazards associated with SPF products (U.S. EPA 2013c), and do not utilize engineering controls or PPE (U.S. EPA 2011a).
i. OSHA recognized the potential harm associated with isocyanates, and developed a national emphasis program specifically designed for protecting workers from exposure to isocyanates in June 2013. However, the OSHA Isocyanates National Emphasis Program (NEP) was a limited, temporary enforcement action, which expired in May 2016. Each OSHA Area Office was required to make only three (3) inspections per year (Rundman 2013). Despite multiple attempts, DTSC could not find any further information on program implementation and the number of inspections in the State of California. These inspections are specific only to the use of isocyanates, not SPF. Thus, OSHA inspections specific to SPF may or may not be conducted. The NEP did not cover sole proprietors, or individual consumers.

Some professional applicators have the benefit of workplace medical monitoring programs: employers remove workers who develop symptoms of sensitization from duties where exposure to MDI is likely. Although removal can prevent further MDI exposures, it does not reverse or cure the allergic sensitization that has already occurred. These workers can suffer future adverse impacts, including severe asthma attacks, if they are exposed to MDI or other isocyanates in either the workplace or elsewhere.

While not all applicators exposed to MDI in SPF products develop allergic sensitization, it is critical to note that this condition is not reversible. The number of people who are sensitized to MDI, and who are a risk of life-threatening asthma attacks from subsequent exposures is unknown, but may grow as the popularity of SPF insulation grows.

VIII. Conclusions

DTSC identified high-pressure and low-pressure SPF systems containing MDI as a proposed Priority Product. Following a review of available scientific data, including peer-reviewed journal articles, government reports, and information from the SPF industry, DTSC concluded that applicators, including workers, sole proprietors, and consumers, may be exposed to unreacted MDI through the use of both high- and low-pressure systems in either commercial or do-it-yourself project sites. Exposures to MDI in SPF systems may result in respiratory and dermal sensitization, chronic asthma, hypersensitivity pneumonitis, respiratory irritation, pulmonary inflammation, and contact dermatitis.

The scientific and public health communities generally consider isocyanates such as MDI asthmagens. Isocyanates are the cause of some documented cases of work-related asthma. Isocyanates bind with proteins, such as albumin or glutathione, and may cause respiratory sensitization that can lead to an elicitation of asthma in subsequent exposures to isocyanates, including MDI. People who have become sensitized to isocyanates could experience life-threatening asthma attacks when subsequently exposed to extremely low levels of isocyanates from any MDI-containing consumer products.

Measurable concentrations of MDI have been detected in applicators' breathing zones to as far as 50 feet from the applicator during work shifts. In some cases, particularly with high-pressure SPF systems, work-shift airborne concentrations exceeded the OSHA PEL of 200 $\mu g/m^3$ (15-minute ceiling), a national regulatory standard. Although airborne concentrations of MDI are generally greater during the use of high-pressure systems, respirable materials containing elevated MDI are also present in the applicators' breathing zones during the use of low-pressure SPF systems.

Businesses that own and operate high-pressure systems generally follow State and federal worker safety standards to train, supervise, and provide employees who apply SPF products with appropriate PPE and engineering controls, such as ventilation. Many workers who apply high-pressure SPF systems also participate in industry-sponsored certification programs and are aware of industry safety recommendations. By contrast, low-pressure systems are readily available to and widely used by a large number of sole proprietors and individual consumers. Sole proprietors and individual consumers are not required to comply with State or federal worker safety standards. They are also unlikely to be aware of industry-sponsored training programs or the need to protect themselves by following product SDS or using appropriate PPE and engineering controls.

PPE and engineering controls are considered the lowest tiers in the hierarchy of controls against occupational exposure to hazards because any user-error or malfunction can result in exposure to the hazard. Applicators who have not been trained how to wear PPE properly or who have been provided with ill fitting, poorly maintained, or improper PPE are at the greatest risk of exposure to MDI. Those who understand the hazards associated with applying SPF and protect themselves through the proper use of PPE and engineering controls still risk exposure to airborne MDI if these controls malfunction or fail. Because SPF applications produce measurable concentrations of airborne MDI in the breathing zone, any person involved in, or near, the application risks exposure to MDI even when protective measures are used. Any applicator who does not use PPE or engineering controls, through choice or negligence, may be exposed to potentially elevated concentrations of respirable MDI.

Therefore, DTSC concluded that workers, consumers, and bystanders could be exposed to MDI during the use of either high-pressure or low-pressure SPF systems that contain MDI. These exposures have the potential to contribute to or cause significant or widespread adverse impacts on the health of a considerable number of people in the State of California.

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APPENDIX A. Glossary and Abbreviated Terms

ACC: American Chemistry Council
ACGIH: American Conference of Governmental Industrial Hygienists
BALF: Bronchoalveolar lavage fluid
CARB: California Air Resources Board
Cal/OSHA: Division of Occupational Safety and Health, California Department of Industry Relations
CAS #: Chemical Abstract Service Registry Numbers
Cal/OSHA: California Division of Occupational Safety and Health (DOSH, commonly referred to as Cal/OSHA)
CDPH: California Department of Public Health
Diisocyanates: Isocyanates (see definition below) that have two isocyanate (–N=C=O) groups
DTSC: Department of Toxic Substances Control, State of California
FEV_1: Forced expiratory volume in one second
FVC: Forced vital capacity
HDI: Hexamethylene diisocyanate
HSDB: Hazardous Substances Data Bank maintained by the U.S. National Library of Medicine of the National Institutes of Health and Prevention, U.S. Department of Health & Human Services
IARC: International Agency for Research on Cancer
Isocyanates: Organic compounds that contains an isocyanate group (–N=C=O) with the general formula R–N=C=O.
MDA: Methylenedianiline
MDI: Methylene diphenyl diisocyanate
NIOSH: National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention, U.S. Department of Health & Human Services
OEHHA: Office of Environmental Health Hazard Assessment, State of California
OSHA: Occupational Safety and Health Administration
PEL: Permissible Exposure Limits
PMDI: Polymeric MDI . In this document, PMDI is only used when cited in the literature where it typically refers to technical grade MDI.
Polyurethane: A polymer composed of a chain of organic units joined by carbamate (urethane) links. Polyurethane polymers are formed by reacting an isocyanate with a polyol. Both the isocyanates and polyols used to make polyurethanes contain on average two or more functional groups per molecule
PPE: Personal protective equipment
PSI: Pounds per square inch
RADS: Reactive airways dysfunction syndrome
RELs: Reference Exposure Levels
SIC: Specific inhalation challenge
SPF: Spray polyurethane foam
SPFA: Spray Polyurethane Foam Alliance
U.S. EPA: United States Environmental Protection Agency

APPENDIX B. Summary of Revisions

The Department of Toxic Substance Control (DTSC) revised this document following external scientific peer review in September 2016, to correct minor errors, include additional references, and improve the focus and clarity of the report. The following table summarizes revisions made in response to the reviewers' recommendations.

Section	**Summary of Revisions**
Entire document	For readability, DTSC eliminated "unreacted" from the term "unreacted MDI." A footnote was added on page 3 to explain that the term "MDI" refers to all unreacted MDI monomers and oligomers that are typically present in technical grade MDI mixtures used in SPF systems.
Section I. Executive Summary	• Moved monitoring data to Section VI. Under Subheading 3. • Updated California Work-Related Asthma Prevention Program surveillance data. • Updated information regarding high-pressure systems to include a range of operating pressures used in the field. • Expanded the discussion about PELs and added information about OEHHA RELs for MDI. • Added information from a monitoring study indicating the need for applicators to wear PPE even when concentrations of MDI are below PELs.
Section II. Identification of the Priority Product	• Revised the product-chemical description and exclusions to match the proposed regulation language. • Updated Table 1 to reflect EPA revisions concerning re-entry time
Section IV. Hazard Traits of MDI	• Adopted the term "Allergic Sensitization" to cover the hazard traits 'immunotoxicity' and 'dermatotoxicity.' • Moved the bullets under former sections "Dermatotoxicity" and "Allergic Contact Dermatitis" to the "Allergic Sensitization" section. • Moved Summary statement "Dermal sensitization to MDI exposed skin can result in allergic contact dermatitis" to the end of the Allergic Sensitization summary paragraph. • Clarified that patients involved in a dermal sensitization study were "suspected of having occupational skin disease" prior to undergoing patch testing. • Clarified that workers diagnosed with allergic contact dermatitis had been exposed to "semi-rigid" foam in the workplace. • Added concentration ranges used for the respiratory irritation study.
Section IV. Hazard Traits of MDI *Subsection 1. Market Presence*	Deleted bullet (e): "In North America, the polyurethane foam market revenue was $203 million in 2009, and is projected to reach $273 million by 2016, with a CAGR of 4.2% (Markets and Markets 2014b)." The information was an underestimate and contradicted more recent information elsewhere in this section.
Section IV. Hazard Traits of MDI *Subsection 2. Worker Exposure Routes*	• Added a discussion of the continued need for PPE even when MDI concentrations were maintained below the PEL. • Deleted some information in bullet (c) regarding the OSHA Isocyanates National Emphasis Program because it was redundant; the same information is presented on page 25. • Added a discussion of MDI exposure related to leaks and spills.

Section	Summary of Revisions
Section IV. Hazard Traits of MDI *Subsection 3. Monitoring Studies*	• Added an introductory paragraph discussing the lack of MDI monitoring studies and the variability within data that exists. • Added monitoring information from two NIOSH studies to subsection (a). • Revised and expanded the discussion of PELs and RELs in subsection (c).
Section IV. Hazard Traits of MDI *Subsection 4. MDI-Induced Worker Fatalities*	• Added information about a worker who had been previously diagnosed with MDI-induced asthma died after being exposed to MDI-containing resins.
Section IV. Hazard Traits of MDI *Subsection 5. MDI-Induced Occupational Asthma*	• Added information about isocyanate-induced occupational diseases reported in Germany.
Section IV. Hazard Traits of MDI *Subsection 6. Non-Occupational Exposure Potential*	• Revised this section to acknowledge the lack of non-occupational exposure data, a brief analysis of why these data are lacking, and how the available data show that there is "potential" for both exposure and harm.
Section VII. Sensitive Subpopulations with Potential for Adverse Impacts from MDI	• Expanded discussions of MDI sensitization and industry practices in subsections (c), (d), and (f).
Section VIII. Conclusions	• Minor edits to reflect changes in the body of the report. • Deleted the following statement: "Studies and documented consumer complaints also suggest that bystanders and building occupants have the potential to be exposed to MDI if they re-enter treated areas without adequate protection." The focus of this document and DTSC's proposed regulation is primarily on the potential for SPF applicators to be harmed following exposure to MDI.
Section. IX. References	The following references were added to this document: • ACC 2016b. Potential Health Hazards of SPF Chemicals. https://spraypolyurethane.org/HealthHazards, accessed October 14, 2016. • Arcury T, A., Summers P, Carrillo L, Grzywacz JG, Quandt SA, Mills III TH (2014) Occupational safety beliefs among Latino residential roofing workers. American Journal of Industrial Medicine 57:718–725. • Baur X (2013) A compendium of causative agents of occupational asthma. J Occup Med Toxicol 8, 1-8. • Baur X, Bakehe P (2014) Allergens causing occupational asthma: an evidence-based evaluation of the literature. Int Arch Occup Eviron Health 87, 339-363. • CDC. 2010. Common Asthma Triggers. https://www.cdc.gov/asthma/triggers.html. Accessed October 14, 2016. • CDC 2014a. Most Recent Asthma Data. http://www.cdc.gov/asthma/most_recent_data.htm. Accessed October 13, 2016. • CDC 2014b. Most Recent Asthma State Data. http://www.cdc.gov/asthma/most_recent_data_states.htm. Accessed October 13, 2016. • Farooqui RU, Panthi K, Azhar S (2009) Addressing the Issue of Compliance with Personal Protective Equipment on Construction Worksites: A Workers' Perspective. The International Proceedings of the

Section	Summary of Revisions
	45th Annual Conference, the Associated Schools of Construction (ASC), at the University of Florida Gainesville, Florida, April 1 - 4, 2009. Edited and Published by Tulio Sulbaran, Ph.D. (Editor), University of Southern Mississippi & Carlos Sterling (Assistant Editor), University of Southern Mississippi. Available online at http://ascpro0.ascweb.org/archives/cd/2009/TOC.htm or http://ascpro0.ascweb.org/archives/cd/2009/paper/CPRT176002009.pdf. Accessed February 17, 2017. • Lefkowitz D, Pechter E, Fitzsimmons K, et al. (2015) Isocyanates and work-related asthma: Findings from California, Massachusetts, Michigan, and New Jersey, 1993-2008. Am J Ind Med 58(11):1138-49 doi:10.1002/ajim.22527 • Lemiere C, Romeo P, Chaboillez S, Tremblay C, Malo J-L. 2002. Airway inflammation and functional changes after exposure to different concentrations of isocyanates. J Allergy Clin Immunol 110:641–646. • Lombardi DA, Verma SK, Brennan MJ, Perry MJ (2009) Factors influencing worker use of personal protective eyewear. Accident Analysis and Prevention 41:755-762. • Marlow D, DeCapite J, Garcia A (2014) Spray Polyurethane Foam Chemical Exposures during Spray Application. Engineering and Physical Hazards Branch (EPHB) Report No. 005-163. National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention. December 2014. • Reilly MJ, Rosenman KD, Peck JH. 2001. Work-related asthma from exposure to isocyanate levels below the Michigan OSHA permissible exposure limit. Isoycnates: Sampling, analysis and health effects, ASTM STP 1408. In: Lesage J, editor. American society for testing and materials. West Conshohocken: PA. • Salazar MK, Takaro TK, Connon C, Ertell K, Pappas G, Barnhart S (1999) A Description of Factors Affecting Hazardous Waste Workers' Use of Respiratory Protective Equipment. Applied Occupational and Environmental Hygiene 14(7): 471-479.