March 9, 2018

Dr. Meredith Williams
Deputy Director
Department of Toxic Substances Control
1001 I Street
P.O. Box 806
Sacramento, California 95812-0806

RE: Safer Consumer Products Draft Three Year Priority Product Work Plan 2018 – 2020 (February 8, 2018)

Dear Dr. Williams:

The American Chemistry Council Diisocyanates Panel, Aliphatic Diisocyanates Panel and the Center for the Polyurethanes Industry (collectively hereinafter referred to as "ACC") [1] appreciate the opportunity to provide the following comments on the Department of Toxic Substances Control ("DTSC or Department") Safer Consumer Products Draft Three Year Priority Product Work Plan 2018-2020 ("Work Plan") issued on February 8, 2018.

I. Broad Scope of the Building Products Category Does Not Provide Sufficient Level of Predictability to Stakeholders

Isocyanates and diisocyanates, as a class of chemicals, are identified as potential candidate chemicals in the now broadened "Building Products and Materials Used in Construction and Renovation" product category ("Building Products category"). The Building Products category in the 2015-2017 Work Plan was narrower in scope, and focused on painting products, adhesives, sealants and flooring. The new Work Plan expands this product category to include "products or materials used to construct, renovate, or repair any building designed or intended as a commercial, office, industrial, or child-occupied space where people work or learn, or that is designed for human habitation, or that contains a habitable space." While DTSC states that the Work Plan is "intended to provide a higher level of predictability regarding

[1] The Diisocyanates Panel includes the U.S. manufacturers and importers of toluene diisocyanate (TDI) and methylene diphenyl diisocyanate (MDI). The Aliphatic Diisocyanates Panel includes the U.S. manufacturers and importers 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. CPI is also providing separate comments specific to its polyurethane-related interests.

potential regulatory actions DTSC will take in the future," it actually creates more uncertainty and confusion. The present examples provided for the Building Products category encompass a wide range of products, making it difficult for manufacturers to engage in an informed manner in the early stages of priority product selection. For example, it is unclear whether DTSC is targeting the manufacture of building products or their subsequent use in constructing a building. ACC urges the Department to focus its resources toward the most compelling chemical and product risks affecting California's citizens and the environment, with consideration of both hazard and exposure. Furthermore, contrary to the methods used to identify the initial draft Priority Products in March 2014, decision-making must meet benchmarks of objectivity, transparency, and scientific accuracy in order for the public and other stakeholders to have sufficient confidence in the Department and the process.

II. Once a Product is Cured, the Diisocyanate is No Longer Present in its Original Form Because it is Reacted into the Finished Polyurethane Product

Curing refers to the reaction that occurs between the two primary chemicals used to form a polyurethane product. In some products these primary chemicals are commonly referred to as the "A-side" (diisocyanate) and "B-side" (polyol or other co-reactant). The A-side material is highly reactive and curing begins immediately upon mixing with the B-side material. The majority of polyurethane products are cured completely before they are sold and therefore considered "inert". As EPA notes in the toluene diisocyanate (TDI) and methylene diphenyl diisocyanate (MDI) Chemical Action Plans, "[c]ompletely cured products are fully reacted and therefore are considered to be inert and non-toxic."[2] This means that the original reactive ingredients - the diisocyanate and polyol or co-reactant - are no longer present in their original form in the cured polyurethane product. They were transformed during the chemical reaction into the finished polyurethane product. ACC has developed a whiteboard video available on our website that further explains the reactivity of isocyanates chemistry: https://www.americanchemistry.com/DII-Chemical-Building-Block-Video.html.

III. Finished Consumer Products Made with Diisocyanates Do Not Expose the Consumer to Uncured Diisocyanates

For building products, the Work Plan provides a number of examples of building materials, but offers no details as to which of these materials may include certain diisocyanates or how they could result in consumer exposure to diisocyanates. As such, ACC wants to ensure the Department is aware that fully cured products do not contain unreacted diisocyanates. Therefore, diisocyanates cannot be transferred to a consumer via the air or by direct contact with the product. As stated previously, EPA specifies in the TDI and MDI Action Plans that "[c]ompletely cured products are fully reacted and therefore are considered to be inert and non-toxic." ACC urges the Department to very carefully articulate the chemical of concern in each product category to ensure valuable Department and industry resources are not expended addressing misguided initiatives on products that no longer contain the chemicals of concern to DTSC. We also urge DTSC to not foster unnecessary public fear or concern that the product as installed (e.g. insulation) may be of a health/environmental concern.

[2] Environmental Protection Agency. Toluene Diisocyanate (TDI) and Related Compounds Action Plan [RIN 2070-ZA14]. April 2011. Available at: https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/toluene-diisocyanates-tdi-action-plan

IV. Consumer and Community Exposures to Uncured Diisocyanates are Expected to be of Very Low Magnitude and Frequency

There are a very limited number of consumer products containing uncured diisocyanates. The vast majority of diisocyanates are manufactured for industrial use. Consumer products containing uncured diisocyanates generally are accompanied by product safety information like warning labels, which can include the characteristics of the chemicals, their approximate cure time, and how to properly protect oneself while handling the product. To protect consumers, these products have precautionary labeling subject to Federal Trade Commission (FTC)/Consumer Product Safety Commission (CPSC) and the Federal Hazardous Substances Act (FHSA) requirements.

Further, a significant potential for community exposure to diisocyanates used in the industrial setting has not been demonstrated. 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. 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."[3] 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. The diisocyanates monitored included MDI, TDI and HDI. The EPA analysis concluded that diisocyanates were non-detectable, therefore well below levels of concern. More information can be found on the EPA website: http://www.epa.gov/schoolair/schools.html.

V. Isocyanates Should Not be Considered Human Carcinogens

The Department unjustifiably lists carcinogenicity as a hazard trait associated with the isocyanates class of chemicals in the Building Products category. This listing is flawed for several reasons. Isocyanates are a broad category of chemicals with different physical/chemical properties. The scientific evidence shows that none of the isocyanates including toluene diisocyanate (TDI), methylene diphenyl diisocyanate (MDI) hexamethylene diisocyanate (HDI), isophorone diisocyanate (IPDI) and methylene dicyclohexyl diisocyanate (H_{12}MDI), would be carcinogenic under the relevant and primary routes of human exposure (i.e. inhalation and dermal contact).

The carcinogenicity listing for isocyanates in the Work Plan is likely based solely on one conceptually and technically flawed bioassay with the TDI mixture performed over 30 years ago by the National Toxicology Program (NTP, 1986). Due to its high reactivity, NTP could not administer TDI via the diet. Thus, NTP chose to administer TDI, stored in corn oil for up to one week, by oral gavage directly into the acidic environment of the rodent stomach. Not only did levels of TDI reaction products (e.g., TDA) begin to appear at progressively higher levels during this one week of storage (Appendix I of 1986 NTP study; Seel et al., 1999), but the low pH of the stomach, found nowhere else in the body, favors the transformation of TDI to TDA (see discussion by Prueitt et al., 2013). While the NTP investigators

[3] North Carolina Department of Health and Human Services (NCDHHS) & the Agency for Toxic Substances and Disease Registry (ATSDR) (2010). North Carolina TDI Community Health Report. Available at: http://epi.publichealth.nc.gov/oee/tdi/TDICommunityHealthReport.pdf

(Dieter et al., 1990) qualitatively recognized the similar tumor spectra produced by both the TDI mixture and 2,4-TDA in rodents, they dismissed these study flaws with their belief that transformations of TDI to 2,4-TDA would also occur in the more pH-neutral environments found elsewhere in the body. However, subsequent studies have shown this not to be the case as TDA has not been detected under normal physiological exposure conditions such as inhalation (Timchalk et al., 1994) and dermal contact (Rosenberg and Savolainen, 1985).

The misclassification of TDI as a human carcinogen is further supported by several observations. First, in rodents, the inhalation of TDI mixture (CAS 26471-62-5), the primary exposure route in humans, at a maximum tolerated concentration, has not been found to cause tumor formation in rodent tissue (Loeser, 1983). Second, a robust statistical analysis of the tumor spectra seen across rodent species, sexes, and organ systems with 2,4-TDI / 2,6-TDI and 2,4-TDA (Sielken et al., 2012) noted that the carcinogenic response seen by NTP with TDI was consistent with 5% of the TDI being transformed to TDA either before and/or after gavage administration. Third, a weight-of-the-evidence evaluation of *in vitro* and *in vivo* studies concluded that TDI was not a human carcinogen (Prueitt et al., 2013). Although TDI can produce tumors if administered as a bolus dose directly into the stomach via gavage[4], this is an unrealistic exposure route in humans. TDI has not been shown to transform to TDA when TDI is inhaled, the primary route of exposure in humans, or in contact with the skin.

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, Kennedy and Brown). 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 a large amount 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 reflected in 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 (a) the absence of epidemiological evidence of carcinogenicity in TDI exposed workers (Prueitt et al., 2013), (b) the observation that 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 for a lifetime at a maximum tolerated concentration of 150 ppb (150-fold higher than the ACGIH TLV), (d) the inability to detect free TDA in rats following a 6-hour inhalation exposure to TDI vapor at 2 ppm (Timchalk et al., 1994), a concentration 2000-fold higher than the TDI TLV, and (e) three epidemiological studies with updates, representing the combined long-term mortality experience of more than 17,000 PU foam production workers, failed to find an association between occupational exposure to

[4] TDI entering the mouth would not be carcinogenic as it would react with macromolecules present in the buccal cavity just as it does when depositing in the lungs. The subsequent passage of TDI-macromolecular conjugates through the gastrointestinal system does not result in the release of TDA (Timchalk et al., 1994).

diisocyanates and an increased risk of cancer (Hagmar et al., 1993a, b, updated by Mikoczy et al., 2004; Schnorr et al., 1996; Sorahan and Pope, 1993, updated by Sorahan and Nichols, 2002).

A tacit acknowledgment of the flaws with the NTP study of TDI is the recent decision by the Michigan Department of Environmental Quality (MDEQ) to eliminate its cancer-based ambient air concentrations for TDI. The Department recognized that the disposition of inhaled TDI is quite different from that of orally administered TDI and this difference does not support using the NTP gavage data to assess the cancer risk posed by inhaled TDI. The Department specifically concluded that the "oral carcinogenicity data for TDI is not appropriate to use to derive an inhalation unit risk for a cancer risk assessment because the pharmacokinetics (absorption, metabolism, distribution and elimination) are so different between the two routes (emphasis added)." [5]

In conclusion, the carcinogenicity of TDI has only been demonstrated when TDI is placed in a non-aqueous medium and subsequently given under aphysiological exposure conditions that facilitate its transformation to TDA, a chemical that is not detected in biological fluids under relevant exposure conditions. The evidence shows relevant modes of physiological exposures to TDI do not result in carcinogenicity. Further, none of the other isocyanates are considered carcinogenic by IARC. Therefore, the Department should remove carcinogenicity as a hazard trait associated with the isocyanates class of chemicals.

VI. Biomonitoring Data Alone Does Not Signify Adverse Health Risk

In the building products category in which isocyanates are listed, the Department states that "Biomonitoring studies show that people are exposed to some of the Candidate Chemicals in these products and that human exposure is widespread." It is inappropriate to make such broad claims without specific substantiation or additional information to clarify to which chemicals the statements apply. Furthermore, it is important to recognize that biomonitoring data is limited in the information that it provides. When considering results from any biomonitoring analysis, it is important to recognize that the detection of a substance in the body indicates only that an exposure has taken place; it does not indicate an adverse health effect. Biomonitoring data do not provide information about (1) the source(s) of an exposure, (2) how long a substance has been in the body, or (3) what effect, if any, a substance may have on human health. Biomonitoring data alone is not indicative of adverse health effects. Biomonitoring data alone does not constitute a complete exposure assessment. Studies of absorption, distribution, metabolism and excretion are needed to convert biomonitoring data into more useful information that in turn must be evaluated with toxicological data before they can be used to predict potential health risks. As the CDC states, "Just because people have an environmental chemical in their blood or urine does not mean that the chemical causes disease." [6]

[5] Email correspondence between Mike Depa, MDEQ Toxicologist, and Sahar Osman-Sypher, Director, Diisocyanates Panel, Nov 2017.
[6] Centers for Disease Control and Prevention. Second National Report on Human Exposure to Environmental Chemicals. CDC; 2003. p.2.

VII. Industry Consultation is a Critical Part of the Process

The regulations require DTSC to "consider the extent and quality of information available"[7] as a factor to identify and prioritize product-chemical combinations. In selecting the proposed initial priority products, the Department failed to adequately consult with industry, did not complete an appropriate survey of available resources of information, and was therefore unaware of the full suite of existing science available. This resulted in inaccurate Product Profiles that impacted California businesses and expended unnecessary use of government and stakeholder resources. While the inaccuracies in the Product Profiles were subsequently corrected, this issue could have been avoided.

The process outlined in the Work Plan to select future priority products demonstrates an improvement. A commitment to conversations with and the collection of data and information from the stakeholders who design, manufacture and use these products is a step in the right direction. Consumer product value chains are complex, however, and rarely reflect a direct line from the manufacturer to the point of sale. Therefore, to ensure that DTSC has a comprehensive understanding of the value chain, industry consultation should occur prior to publication of the product profile and should include dialogue about: responsible parties; chemistries; uses and potential exposures; product stewardship activities; toxicological data; voluntary programs; and, market impacts. Thorough research and the early consultation with manufacturers will greatly benefit the prioritization process and result in activities that not only avoid regrettable substitutions, but are more reliable, beneficial, and consistent with applicable requirements.

Thank you for the opportunity to provide comments on the Work Plan. We look forward to continued and productive collaboration and dialogue with the Department as it identifies the next set of Priority Products. 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,

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Sincerely,

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[7] Safer Consumer Product Regulations §69502.2.

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