



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

DEC 21 2004

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

Courtney M. Price
Vice-President, CHEMSTAR
American Chemistry Council
1300 Wilson Boulevard
Arlington, VA 22209

Re: Request for Correction of the Isocyanates Profile pursuant to EPA's Information Quality Guidelines (IQG #04025)

Dear Ms. Price:

This is in response to your letter of September 8, 2004, requesting corrections to statements in the Toxicology section of the *Isocyanates Profile: Auto Refinishing Industry*, which is posted on EPA's Design for the Environment (DfE) Auto Refinishing Project Website at <http://www.epa.gov/dfe/projects/auto>.

Background - *Isocyanates Profile: Auto Refinishing Industry*

The *Isocyanates Profile: Auto Refinishing Industry* (Profile) dated May 1, 1997, was prepared by the Science Applications International Corporation under EPA Contract No. 68-D4-0098, as part of the New Chemicals Environmental Technology Initiative (ETI). The Profile and related reports on automotive spray coatings and control technologies were developed as an information base for the ETI project to promote dialog between EPA and industry on the use of diisocyanates (also known as isocyanates) during spray application of automotive coatings in collision repair shops. At that time, many manufacturers and users of automotive paints expressed an interest in working with the Agency to reduce exposures to diisocyanates (a leading cause of occupational asthma) and to develop alternative risk management approaches. EPA's Office of Pollution Prevention and Toxics (OPPT) held a public meeting on August 28, 1996, to discuss the findings in these draft reports and request comment from the automotive refinishing industry. Representatives from Air Products & Chemicals, BASF, Bayer, Cytec, DuPont, Olin, PPG, Sherwin Williams and the National Paint and Coatings Association attended the meeting and/or submitted comments. The OPPT compiled a Response to Comments document, dated April 1997, and revised the draft reports where appropriate.

The Toxicology section of the Profile summarizes the results of the available studies on diisocyanates as of 1996. The summary was developed to support the need for exposure reductions during spray applications of automotive coatings that generate mists containing diisocyanates. A list of more recent reviews of diisocyanates toxicology studies is enclosed with this letter.

Background - Design for the Environment (DfE) Auto Refinishing Project

The DfE program works in partnership with many industry sectors to identify cost-effective solutions to environmental issues that affect businesses and communities. In addition to its work with the automotive refinishing industry, DfE partners with chemical product formulators, chemical manufacturers, printers, furniture manufacturers, industrial designers, electronics manufacturers, environmental organizations and others. Since 1997, DfE has worked with collision repair shops to identify ways to reduce health risks to workers and other persons in the shop and surrounding community. In addition to sponsoring best practices site visits for collision repair shops and vocational technical schools, DfE conducts train-the-trainer workshops for technical assistance providers, collision repair instructors, paint suppliers, and the insurance industry. DfE demonstrated that shops adopting best practices can reduce toxic paint emissions in a cost-effective manner. Best practices benefit the worker, the industry and society as a whole, reducing not only exposures to toxic substances that cause asthma and other adverse health conditions, but also costly medical expenses to treat chronic illnesses.

Responses to specific correction requests

1. Request: Diisocyanates Health Endpoints. You indicate that you agree with the statement that the primary target of diisocyanates toxicity is the upper and lower respiratory tract, but would like EPA to delete the phrase "Although they may affect many organ systems" from the first paragraph of the Toxicology section.

Reply: EPA will change the word "many" to "other." Industry's product literature provides the following statement: "Overexposure to isocyanate products can cause skin, eye, nose, throat and lung irritation. It also can lead to skin or lung sensitization. A third effect for which there is some evidence is a chronic (long-term) loss of lung function."¹ It also is important to note that contact with skin may lead to respiratory sensitization or cause other allergic reactions.²

¹"Isocyanates Questions and Answers About Use and Handling", Product Safety Department, Bayer Corporation, Revised 1995, January 1999

²TSCA New Chemicals Program Chemical Categories, Diisocyanates, 1990, revised 1990, 1995, 1997 <<http://www.epa.gov/oppt/newchems/cat02.pdf> >

2. Request: Distinction between Aromatic and Aliphatic Diisocyanates. You request that the Profile be corrected to acknowledge the possible difference in carcinogenic potential between the aliphatic and aromatic diisocyanates. You thought the first sentence of the Conclusions section was contradicted by other information in the Toxicology section and by a later statement in the same paragraph.

Reply: Your quotation of the first sentence of the Conclusions section omitted an important qualifier. The complete sentence reads, "*In general*, there appears [sic] to be little or no difference between aromatic and aliphatic diisocyanates for the above-listed endpoints." The rest of the paragraph provides a more detailed comparison, including an indication that most members of the diisocyanates category have not been tested for carcinogenic potential. The paragraph further indicates that though the aromatic diisocyanates [methylene bis(4-phenylisocyanate) (MDI), toluene diisocyanate (TDI) and dianisidine diisocyanate (DADI)] tested positive and one aliphatic diisocyanate [hexamethylene diisocyanate (HDI)] tested negative in one species, it is premature to generalize about the carcinogenic potential of aromatic versus aliphatic diisocyanates.³ Accordingly, the paragraph as a whole does accurately summarize the available information on the listed endpoints, including carcinogenic potential.

3. Request: Distinction among Monomer, Prepolymer and Polymer.

A) Nomenclature. You provide distinctions in the terminology of "polymers" and "prepolymers."

Reply: EPA agrees that your clarifications would provide some additional useful information. As stated in Appendix A of the Profile, structures with an isocyanate equivalent weight of $\geq 5,000$ are presumed not to pose a hazard under any conditions. Typically, concerns are confined to those species with molecular weights $<1,000$.⁴

EPA will add your clarification as an editor's note in the Toxicology section of the Profile. EPA will also reference the definitions of monomers, prepolymers, and polyisocyanates as reported in the recent summary of diisocyanates health hazard evaluations published by the National Institute for Occupational Safety and Health (NIOSH)⁵ and the definition of "polymer" in the TSCA polymer exemption rule, 40 CFR 723.250(b).

³*Isocyanates Profile: Auto Refinishing Industry*, May 1, 1997
<http://www.epa.gov/dfe/pubs/auto/profile/index.htm>

⁴TSCA New Chemicals Program Categories, Diisocyanates, revised 2002.

⁵A Summary of Health Hazard Evaluations: Issues Related to Occupational Exposure to Isocyanates, 1989 to 2002, Department of Health and Human Services, January 2004, NIOSH Publication No. 2004-116 <<http://www.cdc.gov/niosh/docs2004-116>> or 1-800-356-4674.

B) Monomer Content in Prepolymers and Polymers. You indicate that residual monomer in an HDI prepolymer is less than 2% and that a fully cured polymer (polyurethane or polyisocyanurate) contains no residual monomer. You request that the Profile be corrected to reflect this.

Reply: EPA agrees that the discussion you provided contains additional useful background information. EPA will add your clarification as an editor's note in the Toxicology section of the Profile.

C) Differences in Toxicity of the Monomer and Prepolymer. You request that the Profile be corrected to show that the evidence indicates prepolymers are significantly less toxic than the associated monomers.

Reply: EPA does not agree with this request. The Profile was developed to support the need for exposure reductions during spray applications of automotive coatings that generate mists containing HDI polyisocyanates (prepolymers) and small amounts of HDI monomers. Health and safety information in industry's product literature report similar toxicities for the HDI monomer and HDI polyisocyanate prepolymer in acute inhalation studies, as follows: "Acute inhalation studies, in which rats have been exposed to aerosols (spray mist) of several polyisocyanates containing HDI, resulted in 4-hour LC₅₀ (concentration which resulted in death of 50% of the exposed animals) values of 137-1150 mg/m³, placing this material in the highly toxic by inhalation range. In addition, lung irritation and edema were observed during gross pathology. Rats exposed to HDI monomer aerosols (spray mist) have shown irritation to the respiratory tract and have shown a 4 hour LC₅₀ of 310-350 mg/m³."⁶

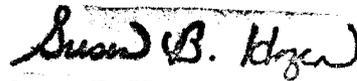
D) Differences in Toxicity of the Monomer and Polymer. You request deletion of the following sentence: "In addition, also based upon a very limited data set, it appears that diisocyanates polymers induce the same effects in repeated dose studies as the monomer, at similar doses." You express the opinion that this statement was based on studies of MDI and "so-called polymeric MDI (PMDI)," which you characterize as a monomer, since PMDI is not a polymer but a prepolymer. You also reference a 1982 study on finished polyurethane products as showing they are physiologically and chemically inert and a separate report of effects from polyurethane foam dust, which effects you indicate have not been validated by subsequent studies.

Reply: The Profile summarizes the data relevant to potential exposures of diisocyanates and polyisocyanates (prepolymers) during spray painting, but does not address studies on partially or fully cured polyurethane polymers. Since the sentence in question does not appear to be relevant to polyisocyanate prepolymers, EPA will delete this sentence from the Toxicology section.

⁶Health and Safety Information: Desmodur® N - Hexamethylene Diisocyanate Based Polyisocyanates, Bayer Corporation, 1991, p.5.

EPA has revised the Profile as indicated above and plans to revise the Webpage by January 30, 2005. EPA will add a Webpage note to reflect these revisions and notify you if unable to meet the intended date. If you are dissatisfied with EPA's response to your request, you may submit a Request for Reconsideration (RFR). EPA normally recommends that this request be submitted within 90 days of the date on this letter; however, should you decide to submit an RFR, we request that you submit it within 90 days of update of the Webpage. You may submit an RFR to the Agency's Information Quality Guidelines Processing Staff via email at quality@epa.gov, by mail at USEPA, 1200 Pennsylvania Avenue, NW, Mail Code 2811R, Washington, DC 20460. The RFR should reference the request number assigned to the original request for correction (RFC #04025). Additional information that must be included in the request is listed on the IQG Website at <http://www.epa.gov/quality/informationguidelines>.

Sincerely yours,



Susan B. Hazen
Acting Assistant Administrator

Enclosure

Enclosure for letter to American Chemical Council RFC#04025

List of recent reviews of diisocyanates toxicology studies

<http://www.cdc.gov/niosh/docs/2004-116/>

A Summary of Health Hazard Evaluations: Issues Related to Occupational Exposure to Isocyanates, 1989 to 2002, contains background information, health effects, exposure criteria, analytical methods and issues, recommendations, summaries of 14 years of NIOSH health hazard evaluations, and a list of 44 references.

<http://www.cdc.gov/niosh/topics/isocyanates/>

NIOSH-2 Search Isocyanates is a searchable bibliographic database of occupational safety and health publications, documents, grant reports, and journal articles supported in whole or in part by NIOSH.

<http://www.atsdr.cdc.gov/toxprofiles/tp120.html>

Toxicological Profile for Hexamethylene Diisocyanate, U.S. Health and Human Services, Agency for Toxic Substances and Disease Registry, August 1998. Comprehensive peer-reviewed profile of health and toxicologic information, potential for human exposure, regulations and advisories, references, and minimal risk level (MRL) worksheets.

<http://www.chem.unep.ch/irptc/sids/oecdsids/822060.pdf>

SIDS Initial Assessment Report for 12th SIAM (Paris, France, June 2001) on Hexamethylene diisocyanate, UNEP Publications.

<http://www.cdc.gov/niosh/asthma.html>

NIOSH ALERT, Request for Assistance in Preventing Asthma and Death from Diisocyanate Exposure, U.S. Department of Health and Human Services/NIOSH Publication No. 96-111, March 1996, 1-800-35-NIOSH

<http://www.osha-slc.gov/SLTC/isocyanates/index.html>

Isocyanates - Health and Safety Topics, U.S. Occupational Safety and Health Administration.

Isocyanate Exposures in Autobody Shop Work: The SPRAY Study, Judy Sparer et al, Yale School of Medicine, *Journal of Occupational and Environmental Hygiene* 1:570-581, September 2004. Part of an epidemiologic study of workers exposed to aliphatic polyisocyanates by inhalation and dermal contact.

Overview of diisocyanate occupational asthma, Jonathan A. Bernstein, University of Cincinnati Medical Center, Department of Medicine, Division of Immunology, *Toxicology* 111:181-189, 1996.