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May 17, 2018

Via Electronic Mail & Federal Express
Jennifer Orme-Zavaleta, Ph.D.
Principal Deputy Assistant Administrator for Science
United States Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, D.C. 20460

Re: Chloroprene Request for Correction #17002
Status Report on PBPK Model Development for Chloroprene
Our File: 165671-00

Dear Dr. Orme-Zavaleta:

On April 6, 2018, on behalf of Denka Performance Elastomer LLC (DPE), we sent you a letter expressing DPE's intention to provide EPA with a Physiologically-Based Pharmacokinetic (PBPK) model that meets EPA's validation concerns and other requirements. As you know, the 2010 Toxicological Review of Chloroprene developed an inhalation unit risk (IUR) for chloroprene based on the most sensitive species (the female mouse) in laboratory exposure studies. As described in the EPA Cancer Guidelines (2005), the preferred approach for developing an IUR relevant to humans based on laboratory results from other animal species is through the use of PBPK models when these are available. Our letter of April 6, 2018, included a copy of our proposed "Workplan to Provide a Physiologically-Based Pharmacokinetic (PBPK) Model to Support the Inhalation Unit Risk (IUR) for Chloroprene," dated March 23, 2018, prepared by experts at Ramboll. The Ramboll team includes Dr. Harvey Clewell as a lead scientist, who was instrumental in work related to the development of PBPK models for chloroprene.

In the time since sending the April 6, 2018, letter, we have worked with Dr. Clewell and the Ramboll team to develop and document a PBPK model that addresses the technical questions and comments from EPA on prior chloroprene PBPK models. Dr. Clewell reports that his work updating and validating the chloroprene PBPK model is now close to complete. Dr. Clewell believes that the updated model resolves EPA's concerns. Ramboll is now in a position to provide EPA the computer code so that EPA can undertake its own validation of the model.

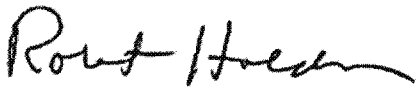
Although the updated PBPK modeling work is close to complete, DPE values EPA's review and comment on this model and would like to understand what the next steps are for providing this model to EPA. We specifically request:

- The opportunity to provide the PBPK model computer code and documentation to EPA for review;
- Guidance from EPA on best practices for obtaining peer review of the PBPK model and underlying data; and
- Guidance from EPA concerning next steps for correcting the IUR based on the EPA vetted and peer reviewed PBPK model.

The application of a PBPK model is an important step towards the application of the best available science in a chloroprene risk assessment. Without the application of a PBPK model, the IUR overestimates the human risk of chloroprene exposure. Correcting the erroneous IUR is an urgent matter for DPE, as the current IUR is creating immense burdens on DPE's Neoprene manufacturing facility in LaPlace, Louisiana, and threatens the long-term viability of the facility.

We are looking forward to working closely with you on this collaborative effort. We would like to schedule a meeting or a telephone conference with you to discuss the EPA review of the updated chloroprene PBPK model and a path forward. We will be in touch with your office to follow up on this request.

Yours very truly,



Robert E. Holden
Attorney for Denka Performance Elastomer LLC

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cc: *(Via Electronic Mail):*
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Stephen Fine, Ph.D. Acting Chief Information Officer
David Gray, EPA Region 6 Director of External Affairs
Vincia Holloman, Director of Enterprise Quality Management Division
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Kistina Thayer, ORD/NCEA IRIS Division Director
Richard Yamada, Ph.D. Deputy Assistant Administrator, Office of Research & Development
Samantha Dravis, Associate Administrator for Policy, Office of Policy, EPA

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