

NORTH AMERICAN POLYELECTROLYTE PRODUCERS ASSOCIATION

1250 Connecticut Avenue, N.W. • Suite 700 • Washington, D.C. 20036
Phone: 202-419-1500 • Fax: 202-659-8037

April 11, 2008

Rob Dewoskin
Chemical Manager
National Center for Environmental Assessment
US Environmental Protection Agency
Research Triangle Park, NC 27711
Via e-mail: dewoskin.rob@epa.gov

Re: Comments on EPA's December 2007 External Review Draft Acrylamide IRIS Assessment; Docket No. EPA-HQ-ORD-2007-1141

Dear Dr. Dewoskin:

The North American Polyelectrolyte Producers Association (NAPPA) respectfully submits the attached comments on EPA's draft acrylamide IRIS assessment¹ (the "draft Assessment"). NAPPA represents the major North American manufacturers and users of acrylamide, which currently includes Ashland Inc., Ciba Corporation, Kemira Water Solutions, Inc., Nalco Company and SNF Holding Company.

NAPPA would like to thank the Agency for granting an extension of time to provide comments on the draft Assessment per its February 12, 2008 letter. As mentioned in our January 28, 2008 letter, review of the draft Assessment is not a trivial undertaking and has required significant time and effort given the complex nature of the 388-page draft report and the over 340 underlying references. As the Agency is well aware, considerable effort was expended over several years to prepare the draft Assessment and we maintain that stakeholders should have ample time to review.

NAPPA's efforts regarding the draft Assessment will not culminate with the submission of these comments. NAPPA anticipates providing the Agency supplemental information as additional issues and information are identified. Specifically, NAPPA is not addressing in these comments issues relating to the physiologically-based pharmacokinetic (PBPK) model since the model and technical documentation was just made available on April 4. We appreciate that EPA recognizes the importance of making this information available to stakeholders as noted in your remarks on this subject at the March 10-11 Science Advisory Board (SAB) Acrylamide Review panel meeting. We concur with your comments that before, or simultaneously with, the release of a model's results, the Agency should also make the underlying model available. As you are well aware, input from the SAB and the public requires access to all supporting materials in a timely manner.

¹ Toxicological Review of Acrylamide (CAS No. 79-06-1) – In Support of Summary Information on the Integrated Risk Information System (IRIS). December 2007. External Review Draft.

Given the complex nature of the draft Assessment, NAPPA has sought the technical input of several highly experienced experts (their comments are attached):

- Ernest Eugene “Gene” McConnell, DVM, DABT – Dr. McConnell (ToxPath, Inc.) is a board certified pathologist (ACVP) and toxicologist (ABT) with over 30 years experience in the design, conduct and interpretation of rodent bioassays. He was Chief of the Pathology Branch at the National Toxicology Program, and was responsible for assuring the diagnoses from the NTP bioassays were accurate. Dr. McConnell also served as Director of the Toxicology Research and Testing Program of the NTP where he directed all aspects of their studies. He has participated in more than 200 cancer bioassays, including the examination of the histopathological slides.
- Errol Zeiger, PhD, JD – Dr. Zeiger (Errol Zeiger Consulting) has more than 30 years experience with FDA and NIEHS. He was responsible for the development, design, and management of the National Toxicology Program Genetic Toxicity Testing Program. He has been involved with the design, management, and interpretation of *in vitro* and *in vivo* test validation studies. Among other responsibilities, Dr. Zeiger has been a member of EPA’s Interagency Testing Committee, ICCVAM Committee and the NTP Management Committee. He served as Editor-in-Chief of Environmental and Molecular Mutagenesis and has over 180 peer-reviewed publications and book chapters.
- Annette Shipp, PhD – Dr. Shipp (Environ International Corporation) has more than 17 years of experience in quantitative risk assessment, including evaluations of chemicals in environmental or occupational settings, as well as investigations of cancer risk assessment methodology. Dr. Shipp has a strong background in toxicology and the biological sciences and years of experience in the use of risk assessment in regulatory decision-making.

In revising its acrylamide IRIS assessment, NAPPA encourages EPA to consider not only the views of stakeholders and the input provided by the SAB, but also to incorporate into its Assessment the significant new information from the extensive research program underway by FDA’s National Cancer for Toxicological Research (NCTR). NCTR’s ongoing research is directly relevant to many of the critical issues regarding the carcinogenic and mutagenic potential of acrylamide. Some of the key projects include:

- **Carcinogenicity of Acrylamide and its Metabolite, Glycidamide, in Rodents: Neonatal Mouse Bioassay (E0718501).** Principal Investigator: Frederick A. Beland. Objective: To compare the carcinogenicity of acrylamide and its metabolite glycidamide in B6C3F1 mice treated neonatally.
- **Genotoxicity and Carcinogenicity of Acrylamide and its Metabolite, Glycidamide, in Rodents (E0215001).** Principal Investigator: Frederick A. Beland. Objective: To compare the carcinogenicity of acrylamide and its metabolite glycidamide in B6C3F1 mice and F344 rats treated chronically for two years.
- **Development of a PBPK/PD Model for Acrylamide (E0721201).** Principal Investigator: Daniel R. Doerge. Objectives: 1) To develop a physiologically based

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pharmacokinetic/pharmacodynamic (PBPK/PD) model for acrylamide and glycidamide; 2) To determine mutagenicity of acrylamide and its metabolite glycidamide in Big Blue® rats; and 3) To determine the DNA adduct levels and the extent of mutagenicity of furan and its metabolite cis-2-buten-4-dial in neonatal B6C3F1/Tk+/- mice.

- **Genotoxicity, Mutagenicity, and Exposure Biomarkers of Acrylamide and Its Metabolite, Glycidamide, in Rodents (E0214601).** Principal Investigator: Daniel R. Doerge. Objectives: 1) To synthesize chemically and characterize spectroscopically the major glycidamide-DNA adducts; 2) To develop and validate LCES/ MS/MS assays to quantify the major glycidamide-DNA adducts; 3) To determine glycidamide-DNA adduct levels in rodent tissues following short-term exposures of rodents to acrylamide and to glycidamide; 4) To determine toxicokinetics and compare bioavailability of acrylamide and glycidamide following exposure by intravenous, oral gavage, and dietary administration; 5) To correlate the levels and kinetics of glycidamide-DNA adducts in target tissues and circulating lymphocytes with acrylamide- and glycidamide-hemoglobin adducts in rodent exposure studies for future use in monitoring human exposure through occupation, smoking, and the diet; and 6) To determine *in vivo* mutagenesis of acrylamide and glycidamide using transgenic mice (Big Blue®).

These studies will provide significant new information directly relevant to EPA's IRIS assessment. Our understanding is that most of the information from this testing program will be available in time for EPA to consider in revising its Assessment. The additional information will greatly enhance the database for acrylamide and the quality and robustness of the final Assessment.

Lastly, NAPPA would like to meet with the Agency in the near future to discuss the overall draft Assessment and the research recommendations identified by the SAB, which could have significant influence on the industry's research agenda. Please contact me if you have any questions about these comments or the attached documents. I will be contacting you shortly to schedule a time to meet and discuss this information.

Sincerely,

Robert J. Fensterheim
Executive Director

cc: Suhair Shallal, shallal.suhair@epa.gov
Linda Tuxen, tuxen.linda@epa.gov
Office of Environmental Information Docket, ord.docket@epa.gov