

## HEALTH RISK ANALYSES FOR DIOXIN: LITERATURE SEARCH STRATEGY AND STATUS

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### INTRODUCTION

Dioxin is a general term that describes a family of hundreds of chemicals that have a similar chemical structure and induce harm through a similar mechanism. Dioxins have been characterized by the U.S. Environmental Protection Agency (EPA) as likely human carcinogens, and there is also concern that they might cause a number of noncancer health effects. Fortunately, levels of dioxin and dioxin-like compounds (DLCs) in the environment have been declining since the early 1970s as a result of federal regulations to reduce emissions. However, current exposure levels remain a concern to communities and environmental organizations because of their potential toxicity combined with relatively long half-lives in the environment and in human tissues.

The EPA undertook an extensive assessment more than twenty years ago (1980s) to address extant environmental health concerns. In response to evolving information, the Agency initiated a comprehensive update in the early 1990s. That draft reassessment was provided for initial review to the EPA Science Advisory Board (SAB) in 1995, then revised to address SAB comments, distributed for interagency review, and resubmitted for SAB review in 2000. Following subsequent revision and interagency review, the dioxin reassessment (1) was provided to the National Academy of Sciences (NAS) for review in November 2004. In July 2006, the NAS panel released its review report identifying several key technical issues and areas for improvement (2).

The goal of the EVS dioxin project is to help EPA complete the dioxin assessment, by strengthening the understanding of potential health risks from dioxin through a systematic evaluation of toxicity information and assessment methodologies. The near-term scope involves: (1) assessing key technical issues from the NAS review, (2) identifying and evaluating current scientific information to address those issues (note that thousands of dioxin articles have been published since the draft 2003 reassessment document), (3) involving experts and soliciting public input on key studies and technical issues, and (4) summarizing these inputs to guide the technical work plan for completing the dioxin assessment.

### METHODS

The initial stages of this project focused on developing a systematic strategy for searching the extensive dioxin literature, to identify candidate toxicity and health effect data for detailed analysis. Comprehensiveness at this stage is crucial, especially considering the issues raised by NAS regarding selection of data sets for the modeling efforts (limiting criteria excluded potentially useful data) and the need to integrate data across many health endpoints (e.g., cancer, reproductive, developmental, and immunological effects) and other technical topics (e.g., toxicokinetic modeling and uncertainty analysis). Thus, it is vital to maintain a clear, transparent, and practical process for identifying and selecting priority studies for further evaluation.

The strategy for identifying, retrieving, and assessing data to guide

completion of the dioxin assessment consists of three stages. The first is preliminary framing, which involves scoping activities such as identifying search terms and information sources (including the annual dioxin conference, and peer-reviewed publications identified via PubMed, a National Library of Medicine database), reviewing short papers from the conference proceedings as well as abstracts identified from the peer-reviewed literature to assess relevance, and coding them for priority retrieval. The second stage involves determining which studies contain quantitative data that could be useful for addressing NAS comments (including to better explain and justify the dose-response models and uncertainty characterization). The third involves extracting specific data and synthesizing information across health endpoints, to frame upcoming inputs from national and international experts.

### RESULTS

Under the first step of the literature search strategy, approximately 6,000 references have been identified and their abstracts have been reviewed and coded for priority retrieval. This involved assessing roughly 500 search terms covering more than 15 technical areas. Upon completion of this step, it is anticipated that upwards of 10,000 to 20,000 publications will have been identified for initial relevance review.

The full paper retrieval, review, and data compilation phases are just getting underway, and evaluation criteria are being developed to guide the selection of studies for detailed review. These activities are expected to be relatively straightforward, although they will take considerable time. A Web-based database of candidate references will be developed over the next several months to support public access to the extensive literature, and an open workshop is planned for early 2009 at which key studies, technical issues, and candidate approaches for quantitative dose-response modeling will be discussed. The overall aim is to improve our understanding of health effects from dioxin to guide appropriate risk management measures.

### REFERENCES

1. U.S. Environmental Protection Agency (EPA), *Exposure and Human Health Reassessment of 2,3,7,8-Tetrachlorodibenzo-p-Dioxin (TCDD) and Related Compounds*, NAS review draft, Volumes 1-3 Washington, DC (December 2003).
2. National Academy of Sciences (NAS), *Health Risks from Dioxin and Related Compounds: Evaluation of the EPA Reassessment*, National Academies Press, Washington, DC (July 2006).

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