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An approach for assessing human exposures to chemical mixtures in the environment

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ABSTRACT

Humans are exposed daily to multiple chemicals, including incidental exposures to complex chemical mixtures released into the environment and to combinations of chemicals that already co-exist in the environment because of previous releases from various sources. Exposures to chemical mixtures can occur through multiple pathways and across multiple routes. In this paper, we propose an iterative approach for assessing exposures to environmental chemical mixtures; it is similar to single-chemical approaches. Our approach encompasses two elements of the Risk Assessment Paradigm: Problem Formulation and Exposure Assessment. Multiple phases of the assessment occur in each element of the paradigm. During Problem Formulation, analysts identify and characterize the source(s) of the chemical mixture, ensure that dose–response and exposure assessment measures are concordant, and develop a preliminary evaluation of the mixture's fate. During Exposure Assessment, analysts evaluate the fate of the chemicals comprising the mixture using appropriate models and measurement data, characterize the exposure scenario, and estimate human exposure to the mixture. We also describe the utility of grouping the chemicals to be analyzed based on both physical–chemical properties and an understanding of environmental fate. In the article, we also highlight the need for understanding of changes in the mixture composition in the environment due to differential transport, differential degradation, and differential partitioning to other media. The Results section describes the application of the method to various chemical mixtures, highlighting issues associated with assessing exposures to chemical mixtures in the environment.

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Introduction

Humans continually encounter chemical mixtures in their environment. These environmental chemical mixtures typically arise from three broad circumstances: incidental release from a source (e.g., chemical disinfection of drinking water), intentional use (e.g., herbicide application), and coincidental occurrence (e.g., occurrence of volatile organic compounds [VOCs] in urban air due to releases from multiple sources) (ATSDR, 2004a). Human encounters with environmental chemical mixtures can lead to exposures. Exposures typically are described as contact between the chemical mixture and the body's exchange boundaries (skin, lung, and gastrointestinal tract) across which the chemicals can be absorbed (U.S. EPA, 1992).

Human health concerns from exposures to chemical mixtures in the environment have resulted in specific United States federal legislation. The 1980 Comprehensive Environmental Response, Compensation, and Liability Act, as amended in 1983 and 1986, and the 1996 Food Quality Protection Act require the U.S. Environmental Protection Agency (U.S. EPA) and other federal agencies to evaluate human health risks associated with exposures to multiple chemicals. While risk analysts have developed a number of methods to address the use of dose–response and toxicity information for estimating chemical mixture-related human health risks (e.g., U.S. EPA, 1986, 2000a; ATSDR, 2004a), there has not been a similar level of effort expended in developing and describing general approaches to estimate human exposures to environmental chemical mixtures.

Exposure assessment includes the quantitative evaluation of the intensity, frequency, and duration of chemical contact, the route of exposure (e.g., dermal, oral, or respiratory), the rates (intake or uptake), the resulting amount of chemical that actually crosses the exchange boundary, and the amount of chemical absorbed (internal dose) (U.S. EPA, 1992; Paustenbach, 2000). Exposure assessment also can include the identification and quantification of the exposure pathways that characterize the movement of a chemical mixture from its source(s) to an exposed individual. Several analysts have evaluated exposures to specific environmental chemical mixtures, including the

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dioxin-like compounds (DLCs) (Lorber et al., 1994; Lorber and Phillips, 2002; U.S. EPA, 2003b), polychlorinated biphenyls (PCBs) (Tsongas et al., 2000), polybrominated diphenyl ethers (PBDEs) (Lorber, 2007), drinking water disinfection by-products (DBPs) (Teuschler et al., 2004), organophosphorous pesticides (OPs) (U.S. EPA, 2001a), and gasoline (Foster et al., 2005).

Fig. 1 presents a conceptual model depicting the fate of multiple chemicals released into the environment from multiple sources and subsequent human exposures. Sources release chemicals into receiving media, and these media can then transport the mixture through the environment. Due to physical, biological, and chemical processes, the composition of a mixture in the environment can change substantially over time. Humans can encounter environmental chemical mixtures through their activity patterns (e.g., daily activities such as, work, and recreation). By considering these patterns and identifying the types and locations of affected media, analysts can characterize demographically the types of people who might be exposed to chemical mixtures of interest. Analysts can quantify the uptake of an environmental chemical mixture by combining appropriate exposure factors with measured or modeled concentrations of the chemicals in the affected media.

In this manuscript, we propose an iterative approach (see Fig. 2) for assessing exposures to environmental mixtures that focuses on the synthesis of information typically collected during the Problem Formulation and Exposure Assessment elements of the Risk Assessment Paradigm (NRC, 1983, 1994; U.S. EPA, 1998a, 1999b, 2003a). Other elements of this paradigm include Hazard Identification, Dose–Response Assessment, and Risk Characterization. Recognizing the problem of considerable data gaps for environmental mixtures combined with resource constraints for assessments, our practical approach takes advantage of existing information and is consistent with previous single-chemical exposure assessment approaches (U.S. EPA, 1989, 1992, 1998b, 2005a; Paustenbach, 2000). Problem Formulation is an iterative element of the Risk Assessment Paradigm that includes the development of an initial understanding of key relationships between the environmental mixture and human health endpoint(s) of concern. Exposure Assessment also is an iterative paradigm element where analysts identify and quantify the information needed to characterize human contact and uptake, and develop human estimates of chemical exposures. We illustrate our approach in the Results section through examples from several different mixtures that highlight issues not routinely encountered in single-chemical assessments. The overall objective of this effort is to strengthen the characterization of human exposures to chemical mixtures in the environment.

Method

Our proposed approach for assessing human exposures to environmental mixtures occurs during the Problem Formulation and Exposure Assessment elements of the Risk Assessment Paradigm. Reflecting this, we divide the description of our approach into two parts highlighting issues unique to assessing exposures to environmental chemical mixtures.

Phases considering chemical mixtures exposures during Problem Formulation

While Problem Formulation involves a number of interrelated phases, the emphasis of this article is on exposure analysis. Therefore, the following discussion focuses on the phases of Problem Formulation relevant to exposure analysis including the chemical mixture source(s), environmental fate, and existing dose–response metrics for chemical mixtures. Together these inputs will subsequently frame the detailed exposure assessment in our approach.

Chemical mixture sources. From the exposure analysis perspective, Problem Formulation commonly begins with the identification and characterization of the source(s) of the chemicals. During source identification, analysts must determine whether the candidate sources are anthropogenic or natural, whether they represent point or non-point sources, and where they are located.

Source characterization describes the nature of the release (continuous or episodic), the frequency of release, and the environmental medium (or media) into which the chemicals are released. During source characterization, analysts also quantify the composition of the chemical mixture as it is released into the receiving medium if such data are available. The quantities of chemical mixture components released either can be measured or simulated using process models. Because sampling and analysis can be

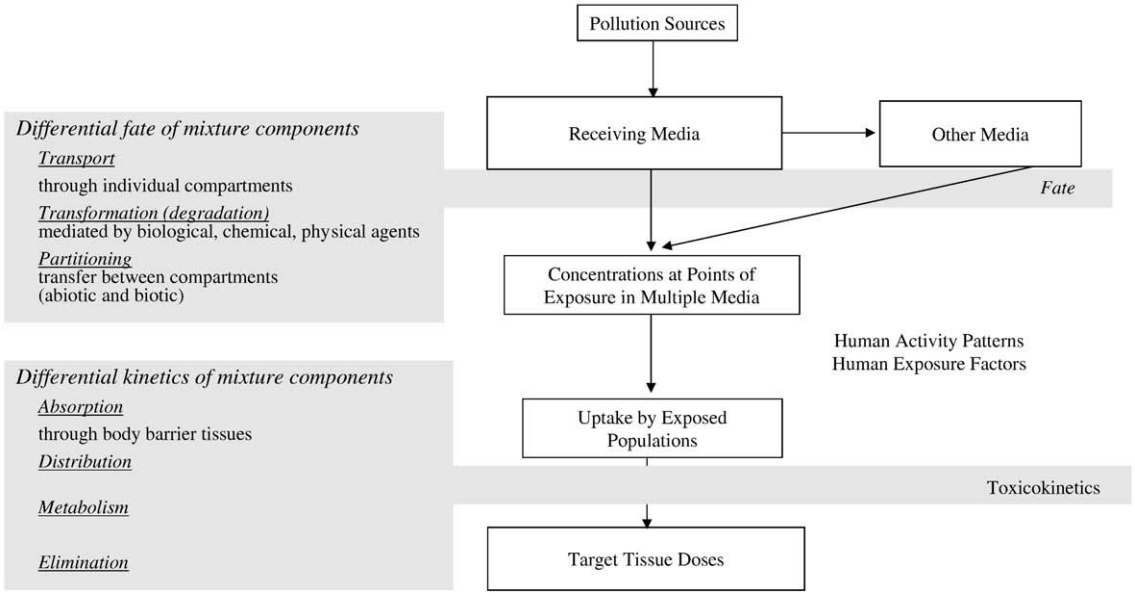

Fig. 1. A conceptual model of the environmental fate and human exposures to a chemical mixture. This figure depicts a conceptual model of the fate of multiple chemicals released to the environment from multiple sources, and the subsequent human exposures. These sources release the chemicals into the receiving medium (e.g., the local atmosphere into which emissions are released from a waste combustor). The *concentrations* of the components of the mixture will change in the receiving medium. The chemical *composition* of a mixture can change substantially in the receiving medium over time due to differences in the fates of its components, notably differential transport within the receiving medium, differential transformation of some components into other compounds, and differential partitioning of some components to other environmental media. Humans can encounter these mixtures in the environment through their activity patterns. By identifying the types and locations of affected media, analysts can demographically characterize people who might be exposed to the chemical mixture of interest. Analysts can estimate human uptake quantitatively by combining appropriate exposure factors with measured or estimated concentrations of the mixture in the affected media. In some cases, human exposures also may be assessed using biomarker information, such as for levels of lead and methyl mercury in blood and kinetic information that relates these concentrations to chemical intake rates. Estimating mixture component levels in specific human tissues requires an understanding of the possible differential absorption, distribution, metabolism, and elimination by the body. Chemical-to-chemical interactions can affect the transport and kinetic processes depicted.