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Bioavailability of Organic Solvents in Soils: Input into Biologically Based Dose-Response Models for Human Risk Assessments

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Research Objective

The purpose of this study is to determine the bioavailability of organic solvents following dermal exposures to contaminated soil and water. Breath analysis is being used to obtain real-time measurements of volatile organics in expired air following exposure in rats and humans. Rhesus monkeys will be used as surrogates for humans in benzene exposures. The exhaled breath data is being analyzed using physiologically based pharmacokinetic (PBPK) models to determine the dermal bioavailability of organic solvents under realistic exposure conditions.

The end product of this research will be a tested framework for the rapid screening of real and potential exposures while simultaneously developing physiologically based pharmacokinetic (PBPK) models to comprehensively evaluate and compare exposures to organics from either contaminated soil or water.

Research Progress and Implications

This report summarizes work 7 months into a 3-year project. Method development has produced systems for solvent exposure from soil and water which mimic actual exposure, and for which animals and human volunteers can be safely tested. Soil exposure is generally open to the air (working the soil) while water exposure is generally immersion. For 6-8 hour test exposure, a patch has been developed where soil is contained against the skin by a non-occlusive membrane, while simultaneously allowing volatilization of test solvent to the environment (activated charcoal). The water counterpart is an occlusive glass culture dish, sealed to skin with silicone adhesive. Shorter term exposure is done by one hand immersion in a bucket containing circulating water or soil, the volunteer instructed to move fingers through the water or soil. Human volunteers and animals breathe fresh air via a new breath-inlet system that allows for continuous real-time analysis of undiluted exhaled air. The air supply system is self-contained and separated from the exposure solvent-laden environment. The system uses a Teledyne 3DQ Discovery ion trap mass spectrometer (MS/MS) equipped with an atmospheric sampling glow discharge ionization source (ASGDI). The MS/MS system provides an appraisal of individual chemical components in the breath stream in the single-digit parts-per-billion (ppb) detectable range for each of the compounds proposed for study, while maintaining linearity of response over a wide dynamic range.

1,1,1-Trichlorethane (methyl chloroform, MC) is rapidly absorbed through rat skin following exposure in soil. In humans, the length of time between exposure and appearance of MC in exhaled breath varies between subject and exposure scenario, but there appears to be a 30-60 minute post application delay. Exposure to solvent in the "hand in bucket" system is proving successful for short-term determinations; the patches are proving successful on both animals and human volunteers for longer exposure. [Figures](#) show examples of results.

Planned Activities

Following collection and analysis of all the MC exposure data for rats and humans, studies will be implemented to describe the dosimetry for perchlorethylene, trichlorethylene, benzene following dermal exposures. A working PBPK model for MC will be used as the basis for PBPK models that

describe the next three chemicals. Breath exhalation profiles will be determined for these volatile chemicals in rats and humans, except for benzene where Rhesus monkeys will be used to replace humans as study subjects.

Figure 1

Figure 2