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MS1-04 HOW CAN INFORMATION ON ORAL BIOAVAILABILITY IMPROVE HUMAN HEALTH RISK ASSESSMENT FOR LEAD-CONTAMINATED SOILS?

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In the Netherlands, in present human health risk assessment of contaminated soils a relative bioavailability factor of "1" is used. This means that it is assumed that there is no difference in the bioavailability of a contaminant from soil compared to the bioavailability from the matrix used in the studies underlying the Intervention Value for remediation, which is typically a food or water matrix. However, there is ample evidence demonstrating that the bioavailability of a contaminant from a soil matrix can be considerably lower than from food or water. This presentation addresses how the assessment of human health risks due to exposure to lead through soil ingestion can be improved by using specific information on oral bioavailability of lead in the human body. The research focused on the contaminant lead, since lead is frequently encountered in soil at high concentrations. Furthermore, soil ingestion is an important pathway of exposure for lead, especially for children, leading to potential adverse effects. Therefore, the need for a realistic but still protective risk assessment for human health is high.
RIVM has developed a simple experimental tool, an *in vitro* digestion model, to supply information on the bioavailability of a contaminant in the human body after ingestion of contaminated soil. In this presentation, a concrete proposal is given for using information on oral bioavailability obtained with the *in vitro* digestion model into procedures to assess the soil quality according to the Dutch Soil Protection Act. To this purpose, a tiered approach is used.
In addition to the approach to implement specific information on oral bioavailability into risk assessment, also the scientific basis of the RIVM *in vitro* digestion model is addressed. The relationship between the results of the digestion model and the relative bioavailability factor will be described. Furthermore, the results of the *in vitro* digestion model are compared to bioavailability data obtained in *in vivo* studies with juvenile swine (soils and bioavailability data kindly provided by Dr. Casteel (University of Missouri, USA)). Together this provides a state-of-the-art overview of the proposal for application of information on oral bioavailability of soil contaminants into risk assessment in the Netherlands.

MS1-05 FACTORS AFFECTING THE BIOACCESSIBILITY AND BIOAVAILABILITY OF HEXAVALENT CHROMIUM AND DIOXIN CONTAMINANTS IN SOIL, AND THEIR RELEVANCE TO RISK ASSESSMENT

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When assessing the risks to chidren and adults due to contaminated soil and/or housedust, it has become clear over the past 25 years that ingestion does not equal the absorbed dose. That is, not all of the chemical in these media will be absorbed due to a myriad of chemical interactions with the different types of soil and dust present in the environment. To characterize the likely absorbed dose, many factors need to be considered. Theoretically, physiochemical characteristics should govern interactions between the contaminant and soil matrix and may affect solublization, gastrointestinal absorption, and subsequently absolute oral bioavailability. Once solubilized and bioaccessible, a chemical must undergo absorption from the gut into systemic circulation. Absorption is most affected by chemical ionization, lipophilicity and solubility. However, nearly 3 decades of research have not given sufficient insight to develop a universal model for predicting bioaccessibility. In this paper, we examine two markedly different chemicals and the factors that influence the bioavailability: dioxin (TCDD) and hexavalent chromium (Cr(VI)), which will be discussed, based on previous work from our group. Scenarios involving childhood and adult exposures will be addressed.
TCDD is uncharged and highly lipophilic, chemical properties expected to give high oral bioavailability, yet only 25-50% oral bioavailability has generally been reported for TCDD present in contaminated soil in animal studies. Strength of TCDD binding to soils may increase over time, termed "aging", which reduces bioavailability of environmental TCDD and possibly risk estimates. Oral bioavailability of TCDD was determined by measuring the amount deposited in the liver of rats, following ingestion of contaminated soil and reported to be approximately 43%. It is unclear if rodent studies properly predict the human GI tract.
Conversely, hexavalent chromium [Cr(VI)] represents a charged, water-soluble metal known to be absorbed by anion transport. Following acute ingestion by human volunteers, Cr(VI) was 6.9% bioavailable, while Cr(III) was less than 1% bioavailable regardless of pH. Cr(VI) is rapidly reduced in the liver and serum to Cr(III), which is incapable of cellular transport, absorption and toxicity. Environmental and physiological reduction of Cr(VI) represent primary protective aspects of chromium toxicity, reducing the potential risk from oral exposure. Cr(VI) sequestering capacity of erythrocytes and reducing capacity of whole blood may limit systemic toxicity. Due to its low oral toxicity, a number of human studies have been conducted. Overall, no significant increases in urinary Cr excretion were found above background in treatment groups that have been exposed to reasonable doses, suggesting that Cr is not sufficiently bioavailable for biomonitoring using urine at doses of 200 micrograms/day in soil.

MS1-06 HEALTH CANADA APPROACHES AND ACTIVITIES WITH RESPECT TO BIOAVAILABILITY OF CONTAMINANTS IN SOIL

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Under the Canadian Federal Contaminated Sites Action Plan (FCSAP), Health Canada is responsible for the provision of guidance, training and advice on human health risk assessment (and related topics) to federal departments with custodial responsibilities for contaminated sites. This presentation will provide an overview of Health Canada funded research into the relevance and applicability of in vitro simulated lung fluid solubility assays, in vitro dermal penetration of various soil-borne contaminants using viable human skin, and factors affecting oral bioavailability. One way to improve human health exposure estimates is to apply an increasingly realistic understanding of the fate of particulates and the substances they carry. A review of *in vitro* studies for the pulmonary tract indicated that given the complexity of particulate distribution, clearance, dissolution, and interaction with macrophages in the pulmonary tract, there is insufficient experimental evidence for other types of solubility assessments to allow for the confident use of *in vitro* assays as estimates of *in vivo* contaminant bioavailability. Based on the currently available studies, any arguments for decreased bioavailability of substances derived from inhaled particulates are necessarily accompanied by a very low level of confidence. Ongoing *in vitro* studies are being conducted at Health Canada to examine bioavailability through viable excised skin. It is anticipated that this will provide more relevant data for human exposures than studies with cadavar skin or animal studies. Contaminated soils are applied to the tissue for various durations as well as soils spiked with chemicals. A database of these results will be compiled for a variety of chemicals that are commonly found at contaminated sites. With regard to oral bioavailability, Health Canada has funded numerous studies to evaluate oral bioavailability of soil-borne contaminants. Health Canada is working toward having a standardized *in vitro* test that can be used to evaluate site-specific bioaccessibility of metals in soils as the soil characteristics and chemical speciation can have a significant impact on the bioavailability. Each of these pathways can have significant influence in the estimates of exposures in human health risk assessment, including childhood exposures to metals in soils and housedust in residential environments. This presentation will provide information on the above studies and recommendations toward regulatory approaches with respect to bioavailability of contaminants in soils and housedust.