INTERACTION PROFILE FOR A MIXTURE OF PCBS, TCE AND RADIONUCLIDES

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Introduction

The Agency for Toxic Substances and Disease Registry (ATSDR) is building upon its applied research program to address mixtures of potentially hazardous substances by developing interaction profiles. The primary purpose of interaction profiles is to evaluate mixtures that are of special importance to environmental public health, based on results reported in the scientific literature, on assessments based on the weight-of-evidence (WOE) methodology, and on other health assessment tools. The interaction profiles are peer and publically reviewed documents to ensure the accuracy of data presented and the validity of conclusions.

Review of ATSDR's documents with site-specific information showed that radionuclides coexist with other chemicals at hazardous waste sites. Specifically, a mixture of strontium, cesium, cobalt, trichloroethylene (TCE), and polychlorinated biphenyls (PCBs) was found at several sites. In the event of exposure, the primary route of exposure of nearby populations to these chemicals in soil is likely to be oral, resulting from contamination of soil and/or groundwater. Available reports of chemical use and prior chemical release concerning these sites indicate that strontium, cobalt, and cesium radionuclides, rather than the stable forms of these metals, are of greatest concern for possible adverse health effects. Although data on the effects of ingested strontium radionuclides are available, data on the toxic and/or carcinogenic effects of radiocobalt and radiocesium following oral exposure are lacking. However, as the most sensitive effects of the radionuclides are expected to come from emitted radiation, a reasonable estimate as to potentially sensitive targets for oral exposure to radiocobalt and radiocesium can be made from examining the toxicokinetics of the stable compounds, as well as the tissues that are sensitive to external exposure to cobalt or cesium radiation.

Methods

Interaction profiles provide environmental health scientists with ATSDR's evaluation concerning whether interactions occur among the chemical components in the mixture, the types of interactions that would be expected, and make recommendations regarding how to incorporate concerns regarding the expected interactions or additivity into the public health assessment of the contaminated site. Interaction profiles provide the results of experimental and theoretical studies available in current literature, an assessment of toxic interactions, recommendations for exposure-based assessments of the potential impact of joint toxic action of the mixture on public health, and generalizable rules that might be used inferentially for other related exposure scenarios.

The WOE method to evaluate joint toxic actions of binary submixtures consists of two biological categories: mechanistic understanding and toxicological significance. The scoring component for mechanistic data is divided into three classifications: direct (I), indirect (inferred from the structure-

Table 1. Matrix of BINWOE Determinations for Hematological, Immunological, Neurological, Developmental, Reproductive, Hepatic, and Carcinogenic Effects of Intermediate or Chronic Simultaneous Oral Exposure to Chemicals of Concern

		ON TOXICITY OF				
		Strontium	Cobalt	Cesium	Trichloro-ethylene	PCBs
EFFECT OF	Strontium		=IIC r =IIC i =IICd =IIC c	=IIC r =IIB i =IIC d =IIB c	?	?
	Cobalt	? h =IIC i =IIC c		=IIB r =IIB i =IIB d =IIB c	?	?
	Cesium	=IIB h =IIB i =IIB c	=IIB r =IIB i =IIB d =IIB c		?	?
	Trichloro-ethylene	?	?	?		?
	PCBs	?	?	?	>IIB p >IIB n	

h / hematological, i / immunological, n / neurological, d / developmental, r / reproductive, p / hepatic, c / cancer
Direction: = additive; > greater than additive: < less than additive; ? indeterminate
For mechanistic (I, II, III) and toxicological (A, B, C) scoring : see the Methods section above

activity relationships) (II), and inadequate or ambiguous (III). The scoring for toxicological significance has components for directly demonstrated (A) and unclear (C) toxicological interactions; the middle rating (B) is applied to either inferred toxicological significance or the demonstration of toxicologically significant interactions in related compounds. A detailed explanation of the WOE method and its use in calculating an adjusted hazard index can be found in the original paper (2).

Results and Discussion

No studies were located that examined health effects in humans or animals exposed to mixtures containing strontium, cobalt, cesium, TCE, and PCBs. No physiologically-based pharmacokinetic/ pharmacodynamic (PBPK/PD) models for this mixture have been developed. Because suitable exposure-response data, joint action models, and PBPK models are lacking for the complete mixture,

the recommended approach for the exposure-based assessment of joint toxic action of this mixture (for noncancer health hazards) is to use a hazard index approach with a target-organ toxicity dose (TTD) modification and a qualitative WOE assessment of joint toxic actions of binary mixtures of the components. Available information on toxic actions of the individual components indicates that joint additive actions of radiostrontium, radiocobalt, radiocesium, TCE, and PCBs on several toxicity targets are plausible, including hematological effects, immunological effects, reproductive effects, altered neurodevelopment, neurological alterations, hepatic injury, and cancer. The WOE analysis indicates that scientific evidence for greater-than-additive or less-than-additive interactions among these components is limited to a potentially greater-than-additive effect of PCBs on TCE-induced hepatic and neurological effects (see Table 1). Data are inadequate to characterize the possible modes of joint action on most of the pertinent toxicity targets, although there is mechanistic evidence to support the additive action of radiation from the radionuclides on cancer and immunological, neurodevelopmental, and reproductive effects. For assessment of cancer risks from joint toxic action of the mixture, a similar component-based approach is recommended that involves multiplication of intakes of the components by U.S. Environmental Protection Agency (EPA) cancer slope factors and summation of the resultant risk estimates. The recommended approaches, based on additivity, are public health protective measures to use in exposure-based assessments of health hazards from exposures to mixtures of these components. It is recommended that their use should include qualitative consideration of the potential for greater-than-additive action of PCBs on TCE-induced effects.

References

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