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IMPLEMENTING A CANCER RISK ASSESSMENT FOR DIOXIN USING A MARGIN OF EXPOSURE APPROACH AND AN INTERNAL MEASURE OF DOSE

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Introduction

We recently proposed a safe exposure limit for the carcinogenic effects of tetrachlorodibenzo-*p*-dioxin (TCDD) that is based on epidemiology data, internal dose measures, and a threshold for cancer response.[1] The analysis included three internal dose metrics: peak, lifetime average, and integrated lifetime, or area-under-the-curve (AUC) TCDD serum level. From this analysis, we calculated safe (threshold) lifetime serum levels of TCDD (mean and lower fifth percentiles) that can be used in a margin-of-exposure analysis for calculating risks associated with exposures at a contaminated site (see table below). While we believe the concept of an internal-dose-based threshold value could become a critical element of human health risk assessments, we also acknowledge that non-traditional factors must be considered in order to properly apply the results of our analysis in a site-specific risk assessment. Specifically, as is required for assessing risks from lead exposures, a simple pharmacokinetic model is used in conjunction with site-specific scenarios to yield estimates of lifetime serum [TCDD] levels. The lifetime serum TCDD curves are then used to develop appropriate internal dose measures that can be compared with the thresholds in a margin-of-exposure analysis.

Comparison of Distribution for Background TCDD Blood Levels with Distributions for Cancer Threshold

	Total Cancer			
	Background		Threshold	
	Mean	95th %-ile	5th %-ile	Mean
AUC	158	316	617	1047
Avg	2	4	19	32
Peak	2	4	50	102

The units are serum lipid adjusted 2,3,7,8-TCDD (ppt)

This paper describes the manner in which a cancer risk assessment can be conducted using a margin-of-exposure analysis and internal dose measures. As a preliminary case study, we examine the margins of safety associated with current background TCDD exposures in the U.S.