Printed from: Interstate Technology & Regulatory Council (ITRC). 2017. *Bioavailability of Contaminants in Soil: Considerations for Human Health Risk Assessment.* BCS-1. Washington, D.C.: Interstate Technology & Regulatory Council, Bioavailability in Contaminated Soil Team. http://bcs-1.itrcweb.org.

6.3 Methodology for Quantifying RBA of Lead in Soil

Several recent studies (some still in progress) correlate IVBA and in vivo bioavailability estimates (RBA) for lead. USEPA (2007b) and Drexler and Brattin (2007) presented RBA values for 19 different soils and soil-like materials. Other studies also have applied various in vivo methods and in vitro bioavailability estimation methods for lead (Ruby et al. 1999; Attanayake et al. 2014; Juhasz et al. 2009; Denys et al. 2012) and others. In vitro methods for estimating the RBA of lead from soil have been developed and have gained broad regulatory acceptance (USEPA 2007b; 2017c).

6.3.1 Default Assumptions

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The USEPA integrated exposure uptake biokinetic (IEUBK) model assumes that the absorption fraction depends on lead intake and age. At low soil lead intakes (<10 µg/day), the absorption fraction is approximately 30%, in the absence of any other sources of lead (for example, food and water). This value translates to an absolute bioavailability (ABA) of 30% (which is equivalent to a soil RBA of 60%) in the IEUBK model to predict blood lead levels in children. ABA, in this case, "is the amount of a substance entering the blood via a particular route of exposure (e.g., gastrointestinal) divided by the total amount administered (e.g., soil ingested)." USEPA derives the ABA of 30% based on the assumption that the bioavailability of lead in food and water is 50% and that from soil is 60%, hence 60% x 50% = 30% (USEPA 1999). The Parameter Dictionary (USEPA 2007a) cites a 1989 USEPA Office Air Quality Report (USEPA 1989a) as the source for the 30% ABA, which includes the following language (page A-18; item 17) :

> *Based on these data and the fact that ingestion of such materials occurs other than at mealtimes, allowing for potentially enhanced absorption, the CD [criteria document] estimates that 30% of the lead ingested in dust and soil is absorbed in a child (CD, p.10-10).*

More recently, USEPA (2007b) reported RBA values that were highly variable for 19 different soils and soil-like materials. The central RBA value from this exercise is 60%, suggesting that the default RBA value is appropriate on average. The wide variability in these RBA results, however, highlights the importance of characterizing site-specific RBA to improve risk assessments for lead exposure.

6.3.2 In Vivo Methods

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The methodology section discusses the basics of performing in vivo bioavailability studies. Although several in vivo models have been used to directly measure RBA of lead in soils (Ruby et al. 1999), the juvenile swine model of Casteel et al. 2006 has gained widespread acceptance internationally by regulatory agencies. USEPA (2007b) provides guidance applicable to the United States. The blood lead endpoint, quantified as the area under the curve (AUC) for the exposure duration, can be used to calculate the RBA, or the RBA can be based on an average of several endpoints (USEPA 2007b). Note that steady-state is a prerequisite assumption for the assessment of the RBA of lead (Casteel et al. 2006; Brattin and Casteel 2013).

6.3.3 In Vitro Methods

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Several published in vitro methods can be used to measure lead bioaccessibility, which then can be used to predict site-specific RBA values. IVBA methods may include simulated gastric extraction alone or sequential gastric to intestinal extraction with each phase considering several key GI tract physiological factors, including pH, chemical composition of gastrointestinal solutions, soil extraction time, and soil/gastrointestinal solution ratio (Basta and Juhasz 2014; Drexler and Brattin 2007; Scheckel et al. 2009; Zia et al. 2011). Most IVBA methods for predicting the RBA of lead from soils employ a gastric pH of 1.2–2.5. The chemical composition of IVBA solutions range from simple gastric phase systems that contain few constituents to highly complex solutions that contain several organic and inorganic components. Small variations in extraction times exist between different IVBA methods. Aside from the chemical composition of gastrointestinal solutions, IVBA methods are similar (see Table 6-3 for a list of published IVBA methods for lead).

Table 6-3. Published in vitro methods for lead that estimate site-specific RBA values.

Source: Adapted with permission from Henry, H., M.F. Naujokas, C. Attanayake, N.T. Basta, Z. Cheng, G. M. Hettiarachchi, M. Maddaloni, C. Schadt, and K.G. Scheckel, (2015). Bioavailability-based in situ remediation to meet future lead (Pb) standards in urban soils and gardens. Environmental Science & Technology, 49(15), pp.8948-8958. Copyright 2015 American Chemical Society.

Method	Key References	Notes
USEPA Method 1340 Also known as Relative Bioaccessibility Leaching Procedure (RBALP), Solubility/Bioavailability Research Consortium (SBRC)	Kelly et al. 2002	Method adopted by USEPA for United States. USEPA (2013d) provides official guidance. Limitations potentially include 1) the IVIVC reported in USEPA (2007b) only includes soils contaminated with mineral sources of Pb and 2) the overestimation of RBA values in P-treated soils.
	Drexler and Brattin 2007	
	Juhasz et al. 2009	
	USEPA 2007b	
	USEPA 2013d	
Unified BARGE Method (UBM)	Denys et al. 2012	BARGE 2016, ISO 17924 – widely used throughout Europe. Limitations include the omission of regression parameters in the published IVIVC study.
	Wragg et al. 2011	
Physiologically Based Extraction Test (PBET)	Ruby et al. 1996; Hettiarachchi et al. 2003	No regulatory guidance exists to support these methods.
	Attanayake et al. 2014	
	Defoe et al. 2014	
Urban Soil Bioaccessibility Leach Test (USBLT)	Chaney, Zia, and Codling 2011	No regulatory guidance exists to support this method.
In Vitro Gastrointestinal (IVG) Method	Schroder et al. 2004	No regulatory guidance exists to support this method.

6.3.4 In Vivo – In Vitro Correlation of Lead Relative Bioavailability and Lead Bioaccessibility

For in vivo – in vitro correlation (IVIVC) studies, direct measurements of lead RBA (%) from in vivo studies using multiple lead-contaminated soils of interest are expressed as a function of lead IVBA measurements, which is expressed as a percentage as follows:

IVBA Pb (%) = [bioaccessible Pb (mg/kg)] / [total soil Pb content (mg/kg)] * 100

Usually, a simple linear regression equation is developed that quantitatively equates in vivo RBA measurements (y-axis) to the IVBA measurements (x-axis) in units of percent. Regression parameters (slope and y-intercept) are necessary because published relationships deviate from unity, reflecting fundamental differences between bioaccessibility (IVBA) and bioavailability (RBA).

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Only a limited number of IVBA methods for lead have reported IVIVC as defined by USEPA (2007b). However, much variability exists among the r square values emphasizing the need for validation criteria. These values are summarized in Table 6-4.

IVBA Limitations

IVBA measurements are used to predict RBA values but are not direct surrogates. The most important consideration in selecting an IVBA method is the IVIVC. IVBA methods that have not been rigorously evaluated against in vivo bioavailability data (see Methodology) may not be reliable, and are not recommended for use in human health

risk assessments and the development of remedial action objectives.

Table 6-4. Published in vivo – in vitro correlation studies evaluating the ability of in vitro gastrointestinal methods to predict in vivo relative bioavailable lead

Reference	Method	Animal	Endpoint	Number of Soils	Source of Lead	Gastric IVIVC	r^2	Intestinal IVIVC	r^2
Ruby et al. 1996	PBET	Sprague-Dawley rat	Blood	7	Mining, smelting	Not reported	0.93	Not reported	0.76
Drexler and Brattin 2007	RBALP	Swine	Blood	19	Mining, smelting	RBA= 0.878*IVBA – 0.028	0.92	NA	
Denys et al. 2012	UBM	Swine	Bone	19	Mining, smelting	RBA =1.00*IVBA + 4.75	0.81	RBA =0.95*IVBA + 3.76	0.74
Schroder et al. 2004	OSU IVG	Swine	Blood	18	Residential, mining, smelting	RBA =1.22*IVBA + 12.4	0.79	RBA =1.22*IVBA + 40.6	0.14

USEPA (2007b) reports the results of an IVIVC and provides IVBA guidance consisting of the Drexler and Brattin (2007) method (see Table 6-4), which supersedes the RBALP method in the literature, and is now known as USEPA Method 1340. Although this is now the default IVBA method in the United States given federal guidance and a recent policy memo from USEPA's Office of Land and Emergency Management (USEPA 2016h), the in vitro gastric (IVG) method and the Unified Bioaccessibility Method (UBM) have also been validated with published IVIVC studies. The UBM IVBA method was developed by the Bioaccessibility Research Group of Europe (BARGE) and is validated both in terms of a statistically significant IVIVC (Denys et al. 2012) and inter- and intralaboratory reproducibility (Wragg et al. 2011). This method is used throughout the European Union. Similarly, the IVG method has been validated using a diverse suite of soils with contrasting physiochemical properties and lead sources, including relatively low diffuse concentrations (Schroder et al. 2004).

For USEPA Method 1340, nineteen soils and soil-like materials were evaluated exclusively from mining-impacted areas with mineral sources of lead (USEPA 2007b). Thus, mineral dissolution in the gut was the primary mechanism controlling bioavailability in the IVIVC study, rather than desorption from soil. While the lead sources consisted of a diverse suite of lead-bearing minerals, particle size distribution is the only physiochemical property reported. Other critical soil properties known to influence the bioaccessibility of lead at relatively lower concentrations are omitted, including pH, total organic carbon, and amorphous iron/manganese oxide content (Walraven et al. 2015). Therefore, applying USEPA Method 1340 and the corresponding predictive equation from the IVIVC (USEPA 2007b) to soils contaminated with lower concentrations of lead from other (nonmineral) sources may result in less accurate RBA estimates. In some situations, site- or region-specific IVIVC studies may be needed to validate USEPA 1340 and, if so, should reflect the pertinent range in physicochemical soil properties and lead sources.