Annex 2: Absolute in vivo bioavailability of metal compounds

In the Alloy LLC review, the soil studies have compared the gastric in vitro bioaccessibility (IVBA) of metals to their in vivo relative bioavailability (RBA). In some instances, the gastric IVBA values underpredict the RBA values. This could be misinterpreted as the IVBA not being conservative enough. However, the RBA values are calculated bioavailability values relative to that of a reference compound (usually a water soluble compound). The table below demonstrates that the absolute bioavailabilities (ABA) of the most water soluble metal compounds (corresponding to the metals considered in the Alloy LLC review) are always lower than 100%. This confirms that even if an IVBA is lower than an RBA, the IVBA will never be lower than the ABA and it will not underpredict metal bioavailability.

Metal compound	Water Solubility	Oral bioavailability	Oral absorption	Reference
Nickel sulfate hexahydrate	65 g/100 mL (20 °C)		11% rats	Ishimatsu S, Kawamoto T, Matsuno K, Kodama Y. 1995. Distribution of various nickel compounds in rat organs after oral administration. Biol. Trace Elements Res. 49(1):43-52
Cobalt chloride	52.9 g/100 mL (20 °C)	6.2% rats		Attachment 1 to Alloy LLC report
Mercuric chloride	6.9 g/L (20 °C)		7%-20% mice	https://cfpub.epa.gov/ncea/iris/iris_documents/documents/subst/0692_summary.pdf https://www.epa.gov/sites/production/files/2015-09/documents/volume5.pdf; Nielsen JB. Toxicokinetics of mercuric chloride and methylmercuric chloride in mice. J Toxicol Environ Health. 1992 Sep;37(1):85-122.
Sodium arsenate heptahydrate	listed as very soluble in water	40-70% monkeys		http://hawaiidoh.org/references/Roberts%20et%20al.%20%202006.pdf Roberts SM, Munson JW, Lowney YW, Ruby MV. 2007. Relative oral bioavailability of arsenic from contaminated soils measured in the cynomolgus monkey. Toxicol Sci. Jan;95(1):281-8. Roberts SM, Weimar WR, Vinson JR, Munson JW, Bergeron RJ. Measurement of arsenic bioavailability in soil using a primate model. Toxicol Sci. 2002 Jun;67(2):303-10.

Metal compound	Water Solubility	Oral bioavailability	Oral absorption	Reference
				USEPA. Bioavailability of Arsenic and Lead in Environmental Substrates. 1. Results of an Oral Dosing Study of Immature Swine. Superfund/Office of Environmental Assessment, Region 10, EPA 910/R-96-002, 1996.
Sodium selenite	85 g/100 ml (20 °C)	53% rats		Loeschner K, Hadrup N, Hansen M, Pereira SA, Gammelgaard B, Møller LH, Mortensen A, Lam HR, Larsen EH. Absorption, distribution, metabolism and excretion of selenium following oral administration of elemental selenium nanoparticles or selenite in rats. Metallomics. 2014 Feb;6(2):330-7.
Lead acetate Lead nitrate	44.31 g/100 mL (20 °C) anhydrous	60% swine		USEPA 2007 https://semspub.epa.gov/work/11/175416.pdf
Antimony trichloride	985.1 g/100 mL (25 °C)		2-7% mice-hamsters	ATSDR 2017 https://www.atsdr.cdc.gov/toxprofiles/tp23.pdf Gerber GB, Maes J, Eykens B Transfer of antimony and arsenic to the developing organism. Arch Toxicol. 1982 Jan;49(2):159-68. Felicetti SW, Thomas RG, McClellan RO. 1974. Metabolism of two valence states of inhaled antimony in hamsters. Am Ind Hyg Assoc J 355:292-300.
Beryllium sulfate	40.0 g/100 mL (20 °C)		<1% rats	ATSDR 2002 https://www.atsdr.cdc.gov/toxprofiles/tp4.pdf
Cadmium chloride	119.6 g/100 mL (25 °C) monohydrate		1.5-10.0% humans	TERA (Ruoff et al 1994) http://www.tera.org/Publications/Ruoff1994.pdf