Updated Health Risk Assessment for EAF Slag

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Outline of Presentation

I. Relative Bioavailability Study for Manganese (Mn) in EAF Slag

II. Update of the Health Risk Assessment for Residential Exposure for EAF slag

III. Responding to the Challenges Posed by EPA to the National Academies Committee

IV. Future Risk Assessment Work

Slag on road shoulder

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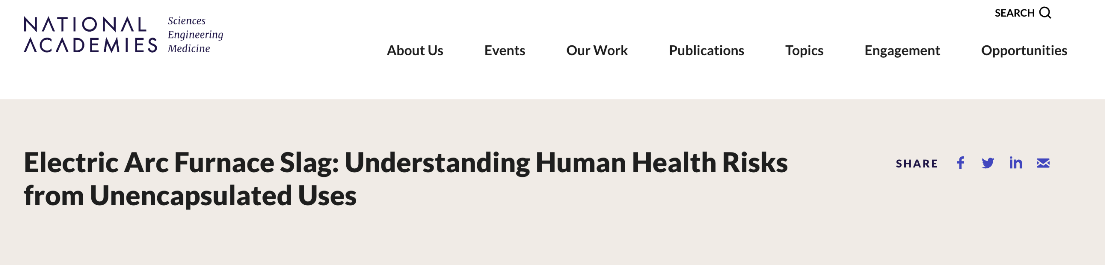
NASEM Charge Points Considered in Risk Assessment



1. Chemical and Physical Properties of Slag
2. Bioavailability
3. Magnitude of human exposure and comparison with epidemiology study data
4. Variability of metals by particle size
5. Cumulative impact from non-chemical stressors
6. Concise characterization of health risk

NASEM Panel Review was Sponsored by EPA with Region 8 as Lead

Relative Bioavailability (RBA) Study

OXFORD
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academic.oup.com/toxsci

Toxicological Sciences, 2023, 1–10
https://doi.org/10.1093/toxsci/kfad037
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Research article

Manganese relative oral bioavailability in electric arc furnace steel slag is influenced by high iron content and low bioaccessibility

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In vivo relative bioavailability study

- RBA studies evaluate the relative bioavailability (absorption into tissues) of a chemical (manganese) in an environmental matrix (slag) relative to the bioavailability of the chemical in the form administered in toxicity tests that are the basis of the RfD (diet).
- Published paper was submitted to the NASEM Committee

EAF Slag <150 μm

AIN-93G Cookie Dough Transgenic Rodent Diet

30:1 Dough to EAF Slag, ~1,000 mg/kg Mn

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RBA Study Design

Group	N	Treatment	Approximate Mn Dose mg/kg/day*	Mn Dose from Diet	Mn Dose from Slag	Notes
1	6	Untreated (Control)	0.6	0.6	0	Control AIN-93G diet with 10 mg/kg Mn
2	6	Mn-Enriched Diet—Low (250 ppm Mn in diet)	15.7	15.7	0	AIN-93G diet enriched to 250 mg/kg Mn formulated by Bio-Serv
3	6	Mn-Enriched Diet—High (500 ppm Mn in diet)	31.4	31.4	0	AIN-93G diet enriched to 500 mg/kg Mn formulated by Bio-Serv
4	8	EAF Slag—Low + Control Diet	19.4	0.4	19	Control diet + 3.5 g slag doughball with 1000 mg/kg Mn
5	8	EAF Slag—Medium + Control Diet	24.3	0.3	24	Control diet + 6 g slag doughball with 1000 mg/kg Mn
6	8	EAF Slag—High + Control Diet	36.2	0.2	36	Control diet + 8 g slag doughball with 1000 mg/kg Mn

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Bioaccessibility Test Results

	Mn		Fe		Cr	
Sample ID	Concentration (mg/kg)	BA (%)	Concentration (mg/kg)	BA (%)	Concentration (mg/kg)	BA (%)
S1	18,000	43	130,000	13	1,400	15
S2	30,000	21	140,000	11	2,700	4.8
S3	7,300	62	35,000	27	450	27
S4	39,000	15	180,000	8.4	2,300	5.7
S5	11,000	55	61,000	23	840	31
Mean	**21,060**	**39**	**109,200**	**16**	**1,120**	**11.1**

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Mean Doses by Dose Group

Dose Group (description)	Average Dose from Chow (mg/kg/day)	Average Dose from EAF Slag Doughball (mg/kg/day)	Total Mn Dose (mg/kg/day)
1 (10 ppm Chow)	0.24	0	0.24
2 (250 ppm Chow)	9.8	0	9.8
3 (10 ppm Chow)	20.3	0	20.3
4 (3.5 g Doughball)	0.24	18	18
5 (6 g Doughball)	0.22	28	28
6 (8 g Doughball)	0.20	39	39

> 1000-times higher than EPA's Reference Dose

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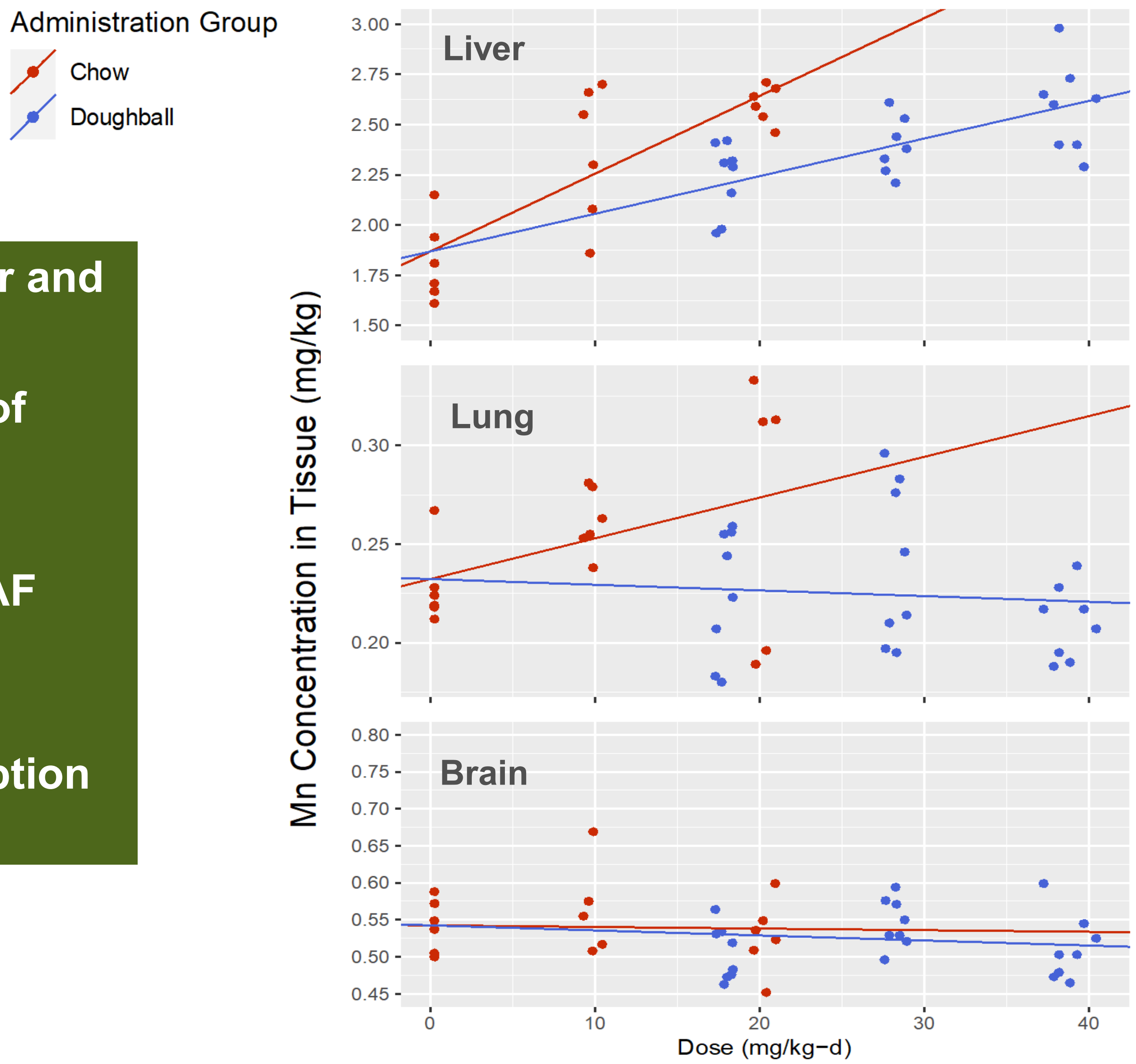
Results

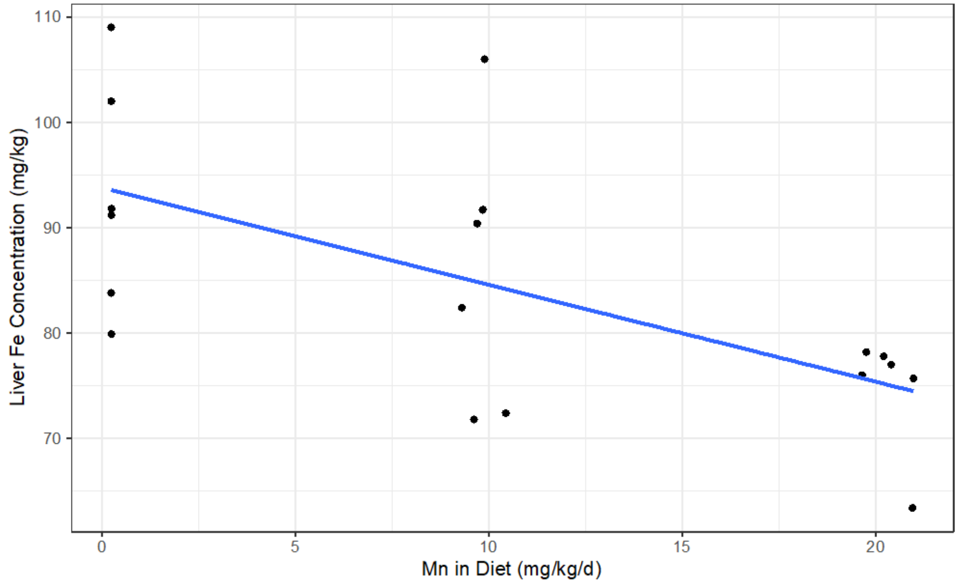
- **RBA Values of 48% in the liver and 14% in the lung**
- **Lung is more representative of systemic dose for use in risk assessment**
    - **Absorption of Mn from EAF slag was decreased with increasing dose in lung**
    - **No evidence of Mn absorption in brain tissue**



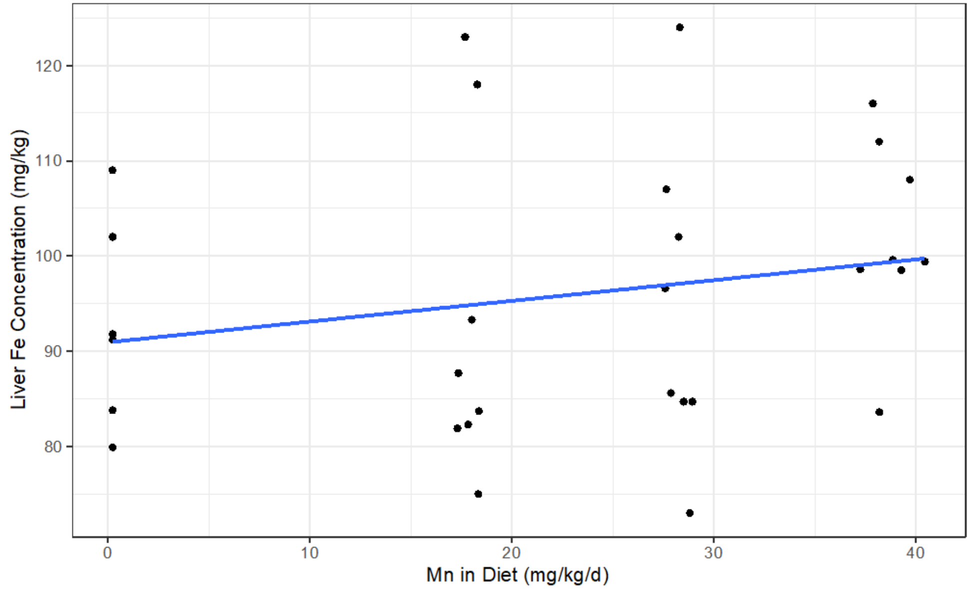
Protective Role of Iron in Slag

- Iron and Mn compete for the same absorption transporters
- Although Mn typically out competes iron for binding, the 6-fold higher levels of iron compared to Mn in EAF slag result in increased iron absorption and decreased Mn absorption
- Essentially, high iron content of EAF slag reduces Mn absorption and provides protective effect

Chow Dose Group



EAF Slag Dose Group



2023 Update of the Health Risk Assessment

Submitted for Publication in *Risk Analysis Journal*

Update of the EAF Slag Risk Assessment

- Probabilistic Risk Assessment (PRA) to calculate excess risk and hazard quotients for all Constituents of Interest (COIs)
  - Evaluated two residential exposure scenarios—the landscape/driveway scenario and the resident near an EAF slag covered rural road
- Used New Model of Mn Relative Bioavailability
- Used New PBPK model for Mn to evaluate potential accumulation of Mn in the brain
- Prepared manuscript for peer-review and publication in the scientific literature.
- Submitted manuscript to NASEM for review

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Results

2023 update of the HRA

Metals Concentrations in EAF Slag Current Study

Metal	Detection Frequency	KM Mean (mg/kg)	95 UCL (mg/kg)	Maximum (mg/kg)	EPA RSL (mg/kg)
Aluminum	100%	25,400	28,104	63,000	77,000
Antimony	**67%**	**14.9**	**19.02**	**79**	**31**
Arsenic	**36%**	**2.24**	**2.806**	**7.3**	**0.68**
Barium	100%	600	661.2	1,200	15,000
Beryllium	97%	2.54	2.776	4.6	160
Cadmium	69%	0.812	0.96	2.2	7.1
Calcium	100%	193,000	204,631	320,000	NA
Chromium	100%	3,320	3,733	7,700	120,000
CrVI	**90%**	**9.30**	**24.68**	**104**	**0.30**
Cobalt	62%	4.33	5.206	15	23
Copper	100%	166	191.8	415	3,100
Iron	**100%**	**182,000**	**196,904**	**315,000**	**55,000**
Lead	82%	14.6	17.61	160	400
Magnesium	100%	54,600	57,335	80,000	NA
Manganese	**100%**	**32,900**	**34,952**	**49,000**	**1,800**
Nickel	92%	55.9	89.28	515	1,500
Potassium	10%	73.4	85.84	160	NA
Selenium	82%	11.9	13.14	24	390
Silver	72%	5.21	5.863	11	390
Sodium	64%	227	261.5	690	NA
Thallium	0%	<1.1	--	0.51	0.78
Vanadium	**100%**	**626**	**678.8**	**1,200**	**390**
Zinc	100%	257	398.5	2,100	23,000
Mercury	41%	0.00714	0.00845	0.031	11

Calculations from EPA ProUCL

- Constituents of Interest measured above residential RSLs are bolded
- Cr(VI) analyzed by 3060A/7199
- Results for As and T analyzed by EPA method 6020, all others by method 6010

Presence of and levels of CrVI in EAF slag are being investigated

- Higher detection frequency and concentrations measured in 2019 than in previous assessments
- Crushing samples prior to analysis may have resulted in oxidation of CrIII to CrVI in digestion
- CrVI results as reported are used in the HRA but may be revised after analytical QC is complete

2021 Bioaccessibility Data

- Bioaccessibility (BA) testing using EPA Method 1340 conducted on 5 representative EAF slag samples
- Samples were crushed in the lab to prepare samples of <150 μm for analysis—expected to increase solubility of metals due to effect on particle surface chemistry
- CrVI was not tested because previous studies have shown that all results will be non-detect due to reduction to trivalent chromium in the acidic extraction fluid.
- Conservatively assumed that oral bioaccessibility and bioavailability is 100% for CrVI for risk and hazard results presented herein
- For arsenic, EPA equation used to calculate RBA from IVBA
- IVBA = 65%, Calculated RBA = 45% for arsenic in EAF Slag

Toxicity Criteria

Metal	Comment
Antimony	Noncarcinogen—RfC and RfD based on current USEPA IRIS values
Arsenic	Carcinogenic and Noncarcinogenic criteria based on current USEPA IRIS values
Hexavalent Chromium	Carcinogenic and Noncarcinogenic—EPA RfD and inhalation cancer slope factor from 2022 EPA Draft IRIS file were used. Assumes mutagenic mode of action and used Age-dependent Adjustment Factors.
Iron	Only toxicity criteria is oral PPRTV RfD
Manganese	Noncarcinogenic—EPA RfD is 0.14 mg/kg-day based on upper-bound of dietary intake, EPA recommends accounting for normal dietary intake, resulting in an RfD of 0.071 mg/kg-day. EPA also recommends a 3-fold modifying factor for non-dietary exposures relating to neonatal and drinking water exposure of 0.024 mg/kg-day. The RfD of 0.071 mg/kg-day is preferred for EAF slag HRA Used ATSDR chronic inhalation MRL (3E-4 mg/m^3)
Vanadium	Noncarcinogen—RfC and RfD based on current USEPA IRIS values Assumed that Vanadium in EAF slag is unlikely to be in pentoxide form

Results □ Residential Roadside Scenario – Arid Conditions (Fresno met data)—Inhalation only

	Cancer Risk Target ≤ 1E-06		Hazard Index – Child Target ≤ 1		Hazard Index – Adult Target ≤ 1	
Constituent of Interest	50th Percentile	90th Percentile	50th Percentile	90th Percentile	50th Percentile	90th Percentile
Antimony	--	--	2E-05	2E-04	8E-06	7E-05
Arsenic	6E-10	4E-09	1E-04	6E-04	4E-05	2E-04
Hexavalent Chromium	3E-09	5E-08	2E-04	3E-03	6E-05	1E-03
Manganese	--	--	1E-01	4E-01	3E-02	1E-01
Vanadium	--	--	5E-03	2E-02	2E-03	8E-03

Results Residential Driveway Scenario

	Cancer Risk Target ≤ 1E-06		Hazard Index – Child Target ≤ 1		Hazard Index – Adult Target ≤ 1	
Constituent of Interest	50th Percentile	90th Percentile	50th Percentile	90th Percentile	50th Percentile	90th Percentile
Antimony	--	--	3E-02	2E-01	1E-03	1E-02
Arsenic	2E-07	7E-07	5E-03	2E-02	3E-04	2E-03
Hexavalent Chromium	1E-07	2E-06	4E-03	5E-02	2E-04	4E-03
Iron	--	--	7E-02	2E-01	4E-03	2E-02
Manganese[1] (RfD = 0.024 mg/kg-day)	--	--	3E-01	*1E+00*	2E-02	1E-01
Manganese2 (RfD = 0.071 mg/kg-day)	--	--	1E-01	*5E-01*	7E-03	4E-02
Vanadium	--	--	1E-01	5E-01	8E-03	4E-02

Manganese RfD 1 is corrected for background diet and includes 3-fold modifying factor
Manganese RfD 2 is corrected for background diet

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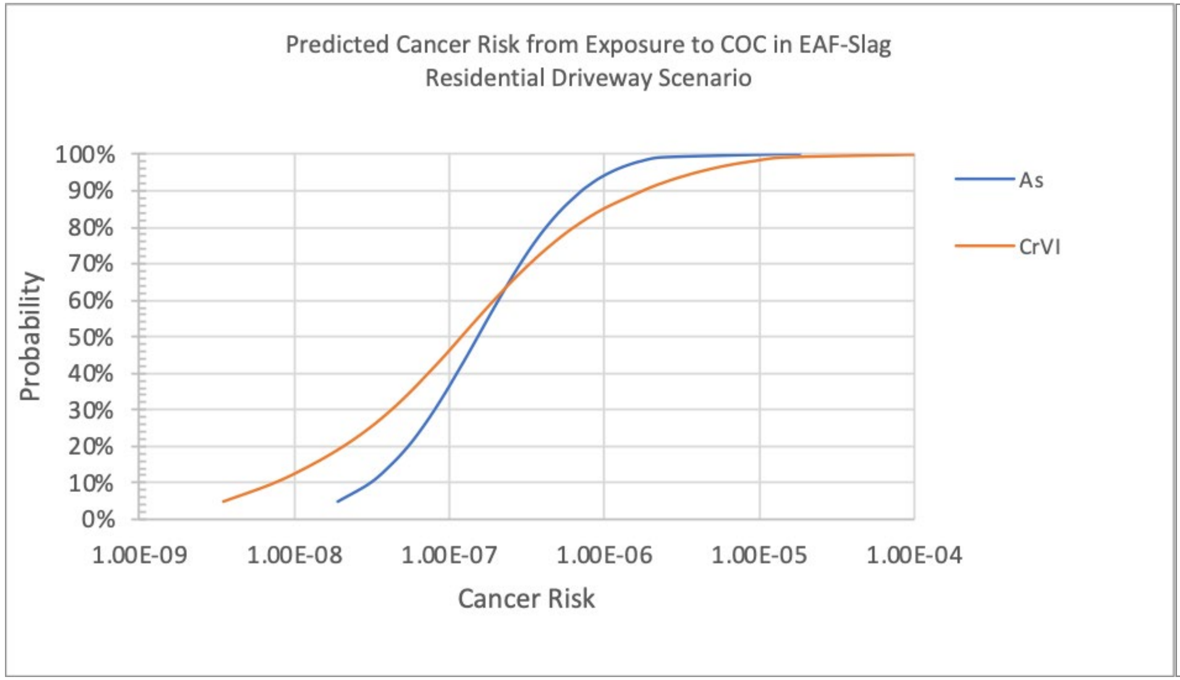
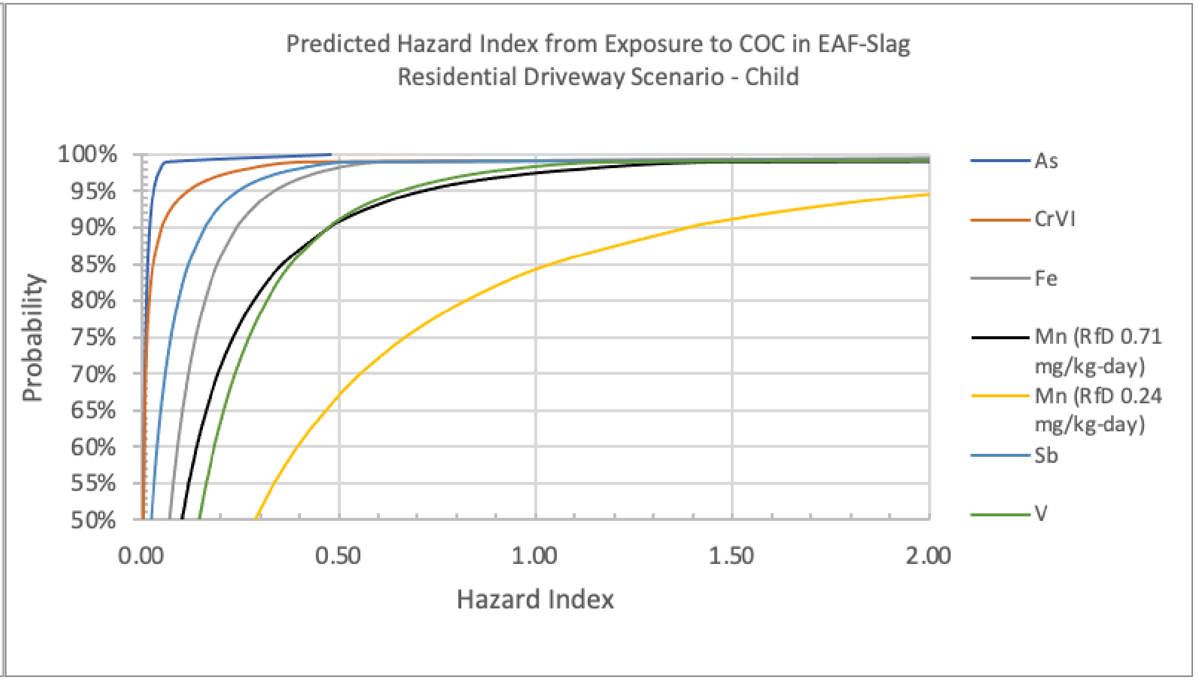
Probability Distributions for Cancer Risk and Hazard Index





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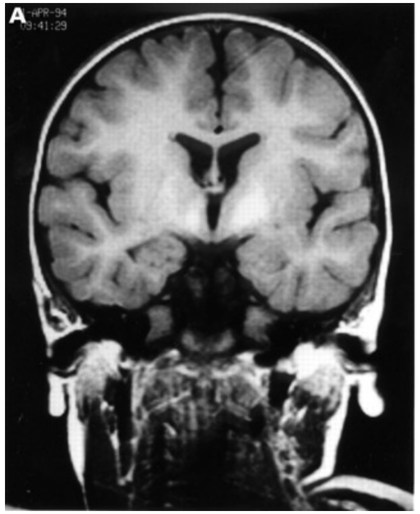
PBPK Modeling of Mn
Residential Exposure Scenarios



Mn is paramagnetic and can be seen in an MRI

New Published Model Campbell et al. 2022

- Models exposure from ages 3-60 years
- Sexes combined
- Brain (Globus Pallidus) is target tissue
- New model includes transporter mediated rapid uptake and elimination

PBPK Modeling Results for Residential Exposure Scenarios

Receptor and Exposure Percentile	Manganese Concentration (μg/g)					
	Brain		Whole Blood		Liver	
Driveway Exposure Scenario (Oral + Inhalation)						
	Background	Exposure	Background	Exposure	Background	Exposure
50th Percentile	0.575	0.579	0.00932	0.00940	2.66	2.68
90th Percentile		0.601		0.00983		2.76
Roadside Exposure Scenario (Inhalation Only)						
50th Percentile	0.575	0.575	0.00932	0.00932	2.66	2.66
90th Percentile		0.576		0.00935		2.66

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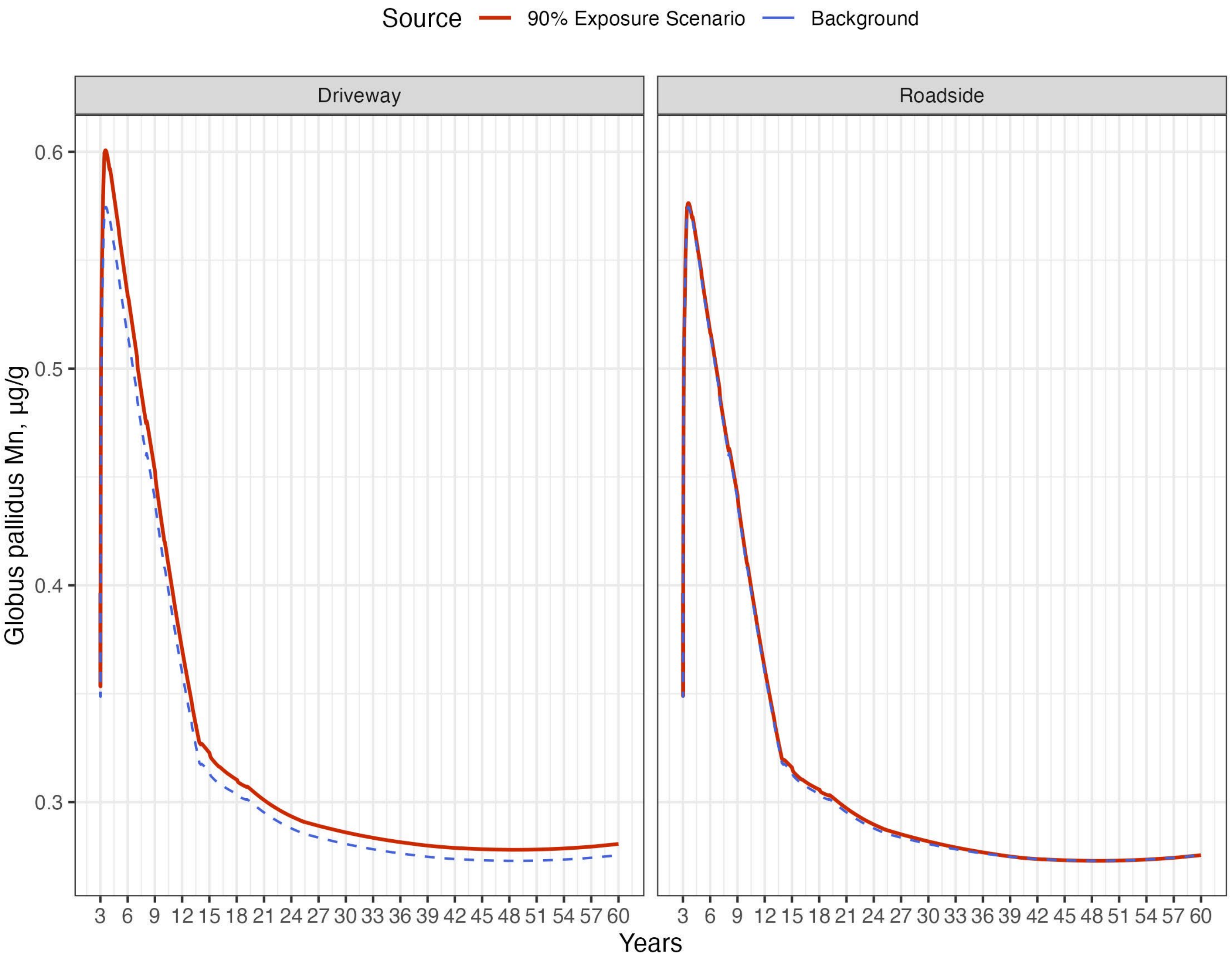
PBPK Model Predictions for Globus Pallidus for both scenarios at 90th percentile of exposure



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Comparison of PBPK results with NOAELs

The PBPK model predictions for peak Mn in the globus pallidus were slightly increased (as high as 0.6 µg/g) for residential exposures compared to diet alone (0.58 µg/g) at age 3 years

Predicted Mn concentrations were lower than NOAELs (0.7-0.9 µg/g) reported in the literature from human and primate studies (Schroeter et al. 2012; Gentry et al. 2017).

- Incidental slag ingestion exposure was the primary exposure pathway, and inhalation contributed negligibly
- PBPK modeling results support lack of neurological hazard associated with residential exposures to EAF slag

Findings of HRA

Using conservative toxicity criteria, PRA methodology and Mn RBA, measures of *in vitro* BA as relative bioavailability for other metals (except for CrVI), the calculated cancer risks and hazard indices are low

- Assuming CrVI is an oral carcinogen at low exposures, and 100% bioavailability by ingestion, results in a cancer risk of 2E-6 at 90th percentile
- Using EPA's most conservative oral RfD for manganese results in a Hazard Index of 1 at 90th percentile and 0.5 at 50th percentile.
- Inhalation exposure for both driveway/landscape and roadway scenarios is not significant even when using Fresno met data

Current Conclusions

- Current RBA study results support that accumulation of Mn in the brain or other tissues from EAF slag ingestion will not occur even at very high Mn doses. Homeostasis is not overwhelmed and iron in slag has a protective effect.
- Current PRA risk assessment findings do not support an increased hazard posed by EAF slag for residential exposure scenarios as Hazard Indices do not exceed one using more conservative EPA RfD
- The PBPK model provides additional support for findings because Mn levels in the globus pallidus do not exceed NOAELs for neurological effects published by others

NASEM Charge Addressed in Risk Assessment

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Electric Arc Furnace Slag: Understanding Human Health Risks from Unencapsulated Uses

SHARE

1. Chemical and Physical Properties of Slag ☑
   - *All EAF slag chemical characterization, particle size and SPLP data included in risk assessment*
2. Bioavailability ☑
   - *Mn RBA study results and Bioaccessibility using EPA Method 1340 provided*
3. Magnitude of Human Exposure and Comparison with Epidemiology Study Data ☑
   - *Quantified dose for two scenario, can be compared with occupational epidemiology data*
4. Variability of metals by particle size ☑
   - *Provided metal concentrations by particle size from 2011 HRA in supplemental material*
5. Cumulative impact from non-chemical stressors ☑
   - *Currently no Risk Assessment Guidelines for Cumulative Impact or Risk Assessment exists*
   - *Might have been argued that Mn absorption is increased among people who are deficient in iron (anemic or poor diet); however RBA study shows that intrinsic iron content of EAF slag is protective of increased Mn absorption*
6. Concise characterization of health risk ☑

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Future Risk Assessment Work

1. Respond to journal peer-reviewer comments and publish risk assessment paper
2. Respond the NASEM report and recommendations for additional research needs
3. Conduct risk assessment for other forms of slag (BF, EAF, Ladle, etc)
4. Prepare white sheets to readily communicate risk assessment findings to non-technical stake holders

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Questions?

Thank You!