A Dimethyl Mercury Inhalation Risk Screening Concentration for Public Health Protection

WP-31

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Abstract

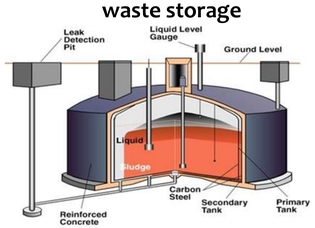
Dimethyl mercury (DMM), CASRN 593-74-8, is a small component of headspace gas in some waste storage tanks near the Hanford nuclear waste treatment plant. DMM vapor is also emitted by municipal landfills; is a trace gas in the global mercury cycle; and is sometimes detected in fish tissue along with monomethyl mercury (CH_3Hg^+). Acute DMM exposures of as little as 5 mg/Kg body weight have caused delayed brain damage and death in humans. Fetal neurological development is likely the most sensitive effect at very low maternal exposures.

Occupational exposure limits for alkyl mercury compounds have been published; however, no reference inhalation limits such as an MRL or RfC for public exposure to any alkyl mercury compounds are available. This presentation shows how I derived a risk screening concentration for DMM of 0.14 µg/m³ (daily time-weighted average) using published data and some assumptions about its absorption, distribution, metabolism, and elimination kinetics. The available literature suggest DMM is biologically inactive until it undergoes demethylation. Public exposure outside the Hanford area boundary from inhalation and ingestion of DMM emissions from the waste tank transfer ventilation systems is 6.9E-07 µg/kg body weight per day or less. These emissions appear to pose no appreciable off-site health risks.

$H_3C—Hg—CH_3$

Mass	230.659
Log Kow	2.59
Melting Point	- 43 C
Boiling Point	92 - 94 C
Vapor pressure	58.8 @ 23.78 C
Atmospheric T1/2	7.865 h

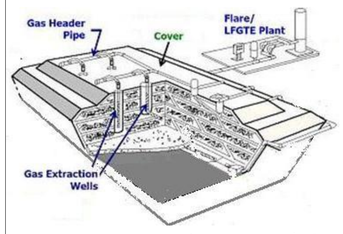
Fuel rod plutonium extraction waste storage



Headspace gas in some tanks
Max. 251 ng/m³

Most exposed public access
Max. 24-h avg. 7.7e-05 ng/m³

Municipal solid waste landfills

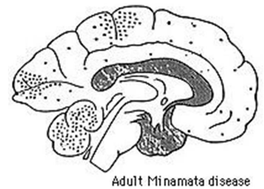


Washington landfills	Min.	7.1 ng/m³
	Max.	46.1 ng/m³
Florida landfills	Mean	30 ng/m³

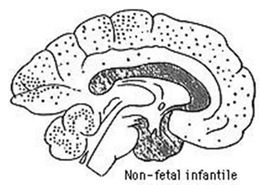
Background DMM		ng/m³
Antarctica	Mean	0.04 ± 0.01
	Max.	0.63
	Min.	0.00
Seattle	Mean, s.d.	0.003 ± 0.004
	Max.	0.007
	Min.	0 .000
Mid-Atlantic Ocean air		<0.1

Potential for Neurodevelopmental Effects

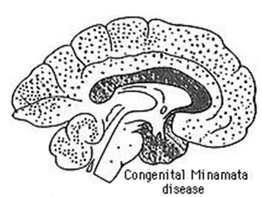
- Subtle neurodevelopmental effects of DMM are unknown but likely
- Acute DMM symptoms resemble those observed in acute Minamata disease
- Fetal neurological development is likely the most sensitive effect
- in the Minamata outbreak, severe neurodevelopmental effects occurred *from in utero* exposure, even among asymptomatic mothers



Adult Minamata disease



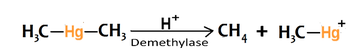
Non-fetal infantile Minamata disease

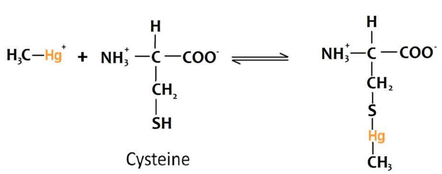


Congenital Minamata disease

(Chang, LW. 1984)

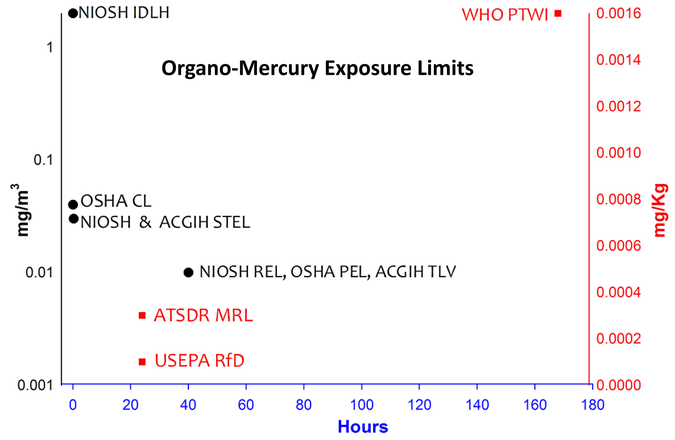
Metabolism





Cysteine

- LAT1 and 2 transport cysteine-Hg into CNS where some dissociates to $HgCH_3^+$ then demethylates to Hg^{++}, which reacts with endogenous Se, SH and NH_3 groups
- DMM can diffuse through the blood-brain barrier at unknown rates



Differences between organo-mercury compounds

- Primary route of exposure
- CNS uptake and elimination rates
- Non-monotonic dose to time-to-onset relationships
- Metabolic de-alkylation of alkyl mercury compounds is faster for ones with longer chain alkyl groups

DMM neurological effects bioassay

5 Groups of male SD rats, gavaged at age 60-days then observed for 8 weeks *(Cabela et al 1974)*

		mg Hg/Kg b.w.
Equilibration test of motor coordination	ED50	65.9 ± 1.7
"	NOEC	30
"	LOEC	39
Maze learning performance	LOEC	30

Allometric scaling: $Dose_{human} = Dose_{rat} (Bw_{human} / BW_{rat})^{0.67 \text{ or } 0.75}$

$Dose_{human}$ ranges from 5.0 - 17.6 mg Hg/Kg bw
> proposed human lethal dose 5 mg Hg/Kg bw

$HgCH_3^+$

- No RfC
- RfD 0.1 µg/Kg-day, U.F. 10, based on BMD of neurodevelopmental data in the Faroe Islands longitudinal prospective study of mother-infant pairs, and other studies.
- Mol. wt. 215.6239

With continuous DMM exposure to steady concentration

- Hg would accumulate in proportion to exposure and elimination of the $HgCH_3^+$ metabolite (constant: 0.014/day)
- Second elimination phase rates of injected $HgCH_3^+$ and DMM are near equal in mice.
- In humans, how much DMM metabolized to $HgCH_3^+$ is unknown.
- If all is metabolized to $HgCH_3^+$, the RfD for DMM would be the same as molecular wt. adjusted tolerable internal dose (TID) of $HgCH_3^+$

Tolerable Internal Dose of $HgCH_3^+$

GI tract primary exposure route by consumption of contaminated fish. In adult humans, >94% $HgCH_3^+$ in food is absorbed from the GI.

0.95 x 0.1 µg/Kg-d (RfD) = 0.095 µg/Kg-d $HgCH_3^+$

Equivalent DMM TID based on $HgCH_3^+$

$$0.095\ \mu g/Kg \cdot d \times \left(\frac{230.6589}{215.6239}\ mol.wt.ratio\right) = 0.102\ \mu g/Kg \cdot d$$

For someone weighing 67 Kg

0.102 µg/Kg-d x 67 Kg = 6.8086 µg DMM/d

Dose by Inhalation

- During pregnancy, women have higher daily ventilation volumes than prior to pregnancy (~55% increase)
- Overweight and obese women use higher volumes than normal and underweight ones do.

Overweight and obese daily ventilation volumes during pregnancy

Percentile	m³/d
50	23 – 25
95	32 – 35
99	41– 47

- To absorb this by breathing 47 m³/d, air would have to contain

$$\frac{6.8086\ \mu g\ DMM/m^3}{47\ m^3/d} = 0.14\ \mu g/m^3$$

- Less extreme physical and exposure conditions result in tolerable concentrations up to 0.19 µg DMM/m³

Conclusions

- 0.14 µg DMM/m³ daily TWA should be sufficient to screen ambient air concentrations for *in utero* exposure neurodevelopmental hazards, even with steady exposure throughout a pregnancy in which maternal daily ventilation volume is in the 99th percentile, and there is complete absorption of DMM.
- Inhalation and ingestion exposures to DMM from waste tank transfer ventilation systems outside the Hanford area boundary has been estimated to be <6.9E-07 µg/Kg day (Rumburg 2011). These emissions appear to pose no appreciable off-site risks
- Municipal landfill emissions also appear to pose no appreciable risk

The opinions expressed in this presentation are those of the author. They do not necessarily reflect the views of the Washington Department of Ecology, and no official endorsement should be inferred.

Poster presentation – International Society of Exposure Science Conference, October 28 - November 1, 2012, Seattle, WA