



# Addressing children's environmental health in the U.S. EPA's risk assessments and regulations

for APHA 2012

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*The views expressed in this presentation are those of the authors, and do not necessarily represent the views of the U.S. EPA*



## Presenter Disclosures

Matthew H. Davis

**(1) The following personal financial relationships with commercial interests relevant to this presentation existed during the past 12 months:**

**“No relationships to disclose”**

# Framework for analyzing actions: Science, Statutes, Policies, Impact



A sampling of recent EPA actions particularly relevant to children's environmental health (CEH):

- Regulatory Determination for Perchlorate in Drinking Water 2011

- Mercury and Air Toxics Rule 2011



- Integrated Risk Information System (IRIS) Toxicological Reviews of:

- Trichloroethylene (TCE) 2011

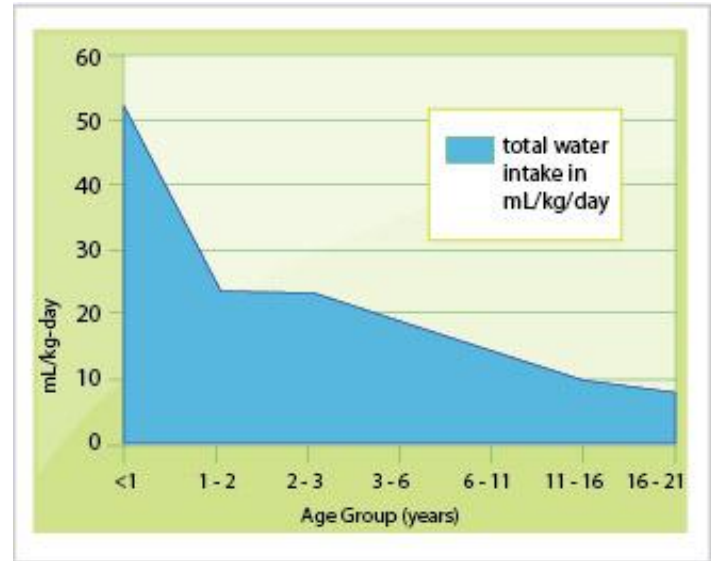
- Formaldehyde Inhalation Toxicity draft 2010

The screenshot displays the EPA IRIS website for Trichloroethylene (TCE). The page includes a navigation menu on the left, a main content area with a table of IRIS actions, and a detailed section for the 'Current Health Hazard Assessment for Trichloroethylene (TCE)'. The table lists actions such as 'IRIS Update', 'IRIS Review', and 'IRIS Review' with columns for 'Category (Action)', 'Status', and 'Last Revised'. The 'Current Health Hazard Assessment' section provides a summary of the assessment, including the 'Point of Departure' and 'Risk' for various exposure scenarios.

Category (Action)	Status	Last Revised
IRIS Update	In Review	9/10/2010
IRIS Review	In Review	9/10/2010
IRIS Review	In Review	9/10/2010



# Why are children more at risk?



Data from Exposure Factors Handbook (EPA 2011)

## Children's Behavior and Physiology at Different Lifestages



- Different Behaviors
- Different Physiology
  - Demands
  - Pathways
- Developing bodily systems across early lifestages





## Context, overarching policies:

- EPA Policy on Evaluating Health Risks to Children (1995):  
*“...consider the risks to infants and children consistently and explicitly as a part of risk assessments generated during its decision making process, including the setting of standards to protect public health and the environment.”*
- Executive Order 13045: Protection of Children from Environmental Health Risks and Safety Risks (1997):  
*“...each Federal agency: shall ensure that its policies, programs, activities, and standards address disproportionate risks to children that result from environmental health risks or safety risks.”*
- Guide to Considering Children's Health When Developing EPA Actions: Implementing Executive Order 13045 and EPA's Policy on Evaluating Health Risks to Children (2006)
- EPA Peer Review Handbook (2006)





# Regulatory Determination for Perchlorate in Drinking Water 2011

- Science: Perchlorate impedes iodide uptake in pregnant mother and infant, affecting neural development:

*“Poor iodide uptake and subsequent impairment of the thyroid function in pregnant and lactating women have been linked to delayed development and decreased learning capability in their infants and children.”*

-FR 76(29) February 11, 2011

- Statute: Safe Drinking Water Act (SDWA) requires the EPA Administrator to:

*“...take into consideration, among other factors of public health concern, the effect of such contaminants upon subgroups that comprise a meaningful portion of the general population (such as infants, children, pregnant women, the elderly, individuals with a history of serious illness, or other subpopulations) that are identifiable as being at greater risk of adverse health effects due to exposure to contaminants.”*

-42 U.S.C. § 300g-1(b)(1)(C)



# Regulatory Determination for Perchlorate in Drinking Water 2011



- Policies referred to when calculating the alternative Health Reference Level for perchlorate:
  - Guidance on Selecting Age Groups for Monitoring and Assessing Childhood Exposures to Environmental Contaminants (2005)
  - Child-Specific Exposure Factors Handbook (2008)

Life Stage	RfD (µg/Kg-day)	RSC <sup>a</sup>	Mean Ingestion Rate <sup>d</sup> (mL/Kg-day) <sup>b</sup>	Alt HRL (µg/L)	90 <sup>th</sup> Percentile Ingestion Rate <sup>d</sup> (mL/Kg-day) <sup>b</sup>	Alt HRL (µg/L)	95 <sup>th</sup> Percentile Ingestion Rate <sup>d</sup> (mL/Kg-day) <sup>b</sup>	Alt HRL (µg/L)
Birth to < 1 month	0.7	59%	137	3	235 <sup>c</sup>	2	238 <sup>c</sup>	2
1 to < 3 months	0.7	59%	119	3	228 <sup>c</sup>	2	285 <sup>c</sup>	1
3 to < 6 months	0.7	59%	80	5	148	3	173 <sup>c</sup>	2
Birth to < 6 months	0.7	59%	95	4	184	2	221	2
6 to < 12 months	0.7	59%	53	8	112	4	129	3
1 to < 2 years	0.7	44%	27	11	56	6	75	4
2 to < 3 years	0.7	44%	26	12	52	6	62	5
3 to < 6 years	0.7	60%	24	18	49	9	65	6
6 to < 11 years	0.7	71%	17	29	35	14	45	11
11 to < 16 years	0.7	84%	13	45	26	23	34	17
16 to < 18 years	0.7	80%	12	47	24	23	32 <sup>c</sup>	18
18 to < 21 years	0.7	80%	13	43	29	19	35 <sup>c</sup>	16
Pregnant Women <sup>e</sup>	0.7	62% <sup>c</sup>	14 <sup>c</sup>	31	33 <sup>c</sup>	13	43 <sup>c</sup>	10
Women Ages 15-44	0.7	80%	15	37	32	18	39	14

alternative HRL for 0-6 months (2 µg/L), vs. adult value (14 µg/L)

<sup>a</sup> RSC calculated for nearest age range based on the mean dietary intake from TDS (see Table 5 at 73 FR 60275, October 10, 2008), RSC for pregnant women and women ages 15-44 based on the 90<sup>th</sup> percentile dietary intake from NHANES-UCMR analysis (see Table 6 at 73 FR 60276, October 10, 2008).

<sup>b</sup> Drinking Water Ingestion Rates for consumers only in Community Water Systems taken from EPA's "Child-Specific Exposure Factors Handbook" (USEPA, 2008e). Except for values for infants from birth to 6 months, which are taken from Tables 5.2.A2 of EPA's "Estimated Per Capita Water Ingestion and Body Weight in the United States - An Update" (USEPA, 2004), and for Pregnant Women and Women Ages 15-44 which are taken from Table 6.2.A2 of EPA's "Estimated Per Capita Water Ingestion and Body Weight in the United States - An Update" (USEPA, 2004).

<sup>c</sup> The sample sizes for the estimates of ingestion rates for these life stages do not meet the minimum data requirements as described in the "Third Report on Nutrition Monitoring in the United States" (LSRO, 1995).

<sup>d</sup> Ingestion rate is adjusted for the self reported body weights from the CFSII.

<sup>e</sup> The most sensitive population identified by the NRC are the fetuses of pregnant women who might have hypothyroidism or iodide deficiency.





- Impact: The final decision was a positive determination to regulate levels of perchlorate in drinking water.
- EPA's determination was informed by:
  - the potential adverse neurological development effects of perchlorate,
  - children's drinking water rates, and the occurrence and levels of perchlorate in public drinking water systems, and
  - a meaningful opportunity for health risk reduction





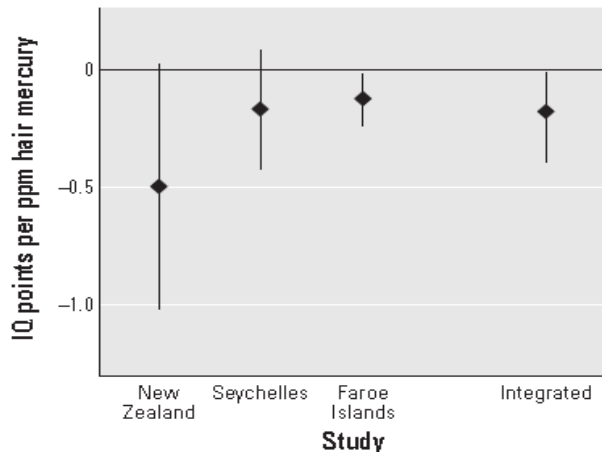


# Mercury and Air Toxics Standards 2011

- Science: children are more vulnerable to Hg, other HAPs than adults:

*“Because the primary measurable health effect of concern—developmental neurological abnormalities in children—occurs as a result of in-utero exposures to Hg, the specific population of interest in this case is prenatally exposed children.”*

- FR 77(32) February 16, 2012



**Figure 2.** Coefficients and 95% confidence intervals for the dose–response relationship between IQ and maternal hair mercury from the three epidemiologic studies and for the results of the integrated analysis.

*“Children are more vulnerable than adults to many HAPs emitted by EGUs due to differential behavior patterns and physiology.”*

- Regulatory Impact Analysis for the Final Mercury and Air Toxics Rule (EPA, 2011)





- Statute: Clean Air Act (CAA) requires EPA Administrator to:

*“...promulgate standards ... if promulgation of such standards is required in order to provide an ample margin of safety to protect public health...”*

- CAA 112 (f)(2)(A)

- CAA mentions mercury and sensitive populations in reference to a study:

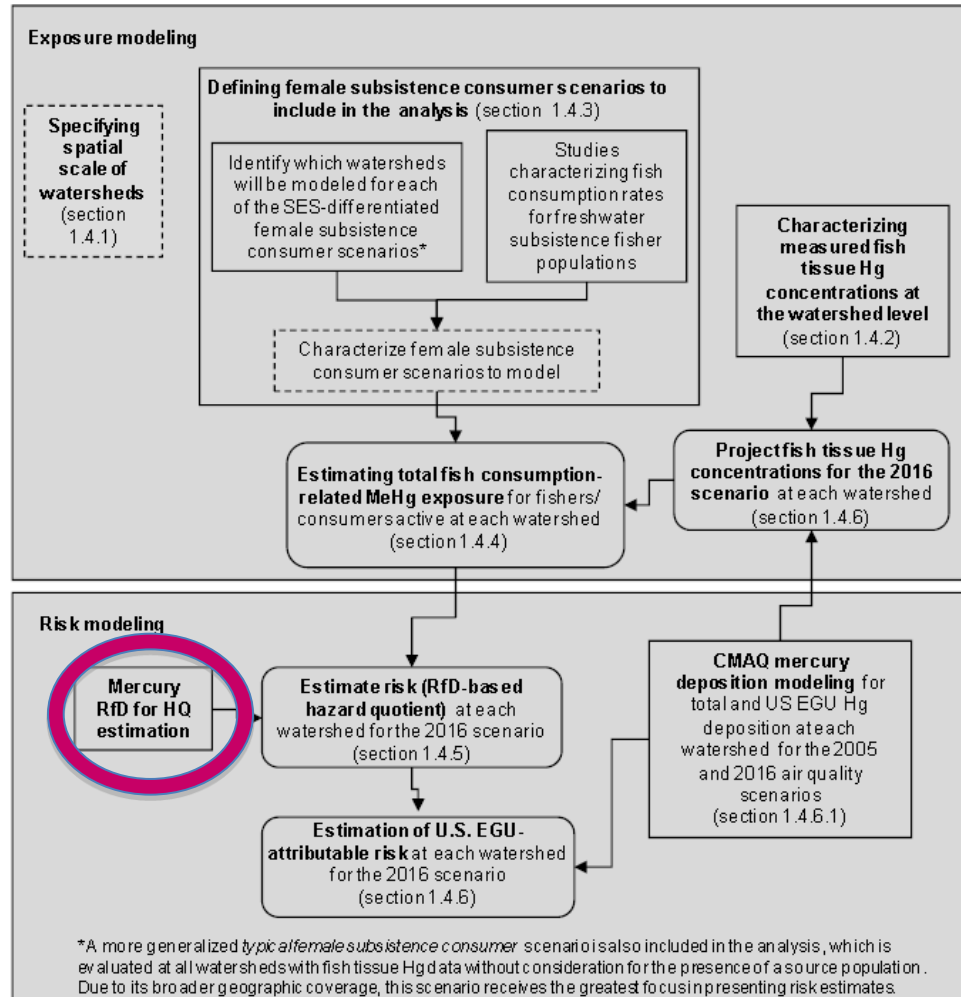
*“The National Institute of Environmental Health Sciences shall conduct, ... a study to determine the threshold level of mercury exposure below which adverse human health effects are not expected to occur. Such study shall include a threshold for mercury concentrations in the tissue of fish which may be consumed (including consumption by sensitive populations) without adverse effects to public health.”*

- CAA 112 (n)(1)(C)





- Policies: Overall guidance used in rule, and many CEH-specific policies in IRIS review setting mercury reference dose (RfD)



KEY:

decision

data input

analysis step



- Impact: A large part of the rationale for writing the rule – Appropriate and Necessary Finding – is based on the fetal neurodevelopmental sensitivity to Hg exposure and children’s sensitivities to other hazardous air pollutants
- The standards themselves are technology-based, set by what is considered to be maximum achievable control technology, not set by health



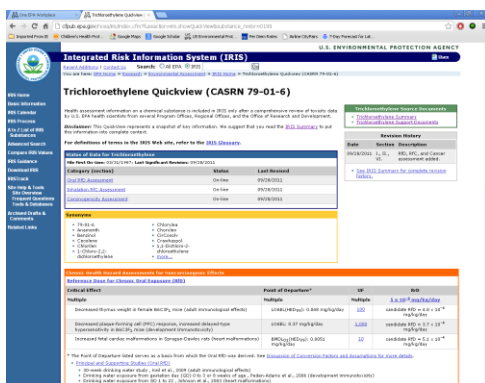
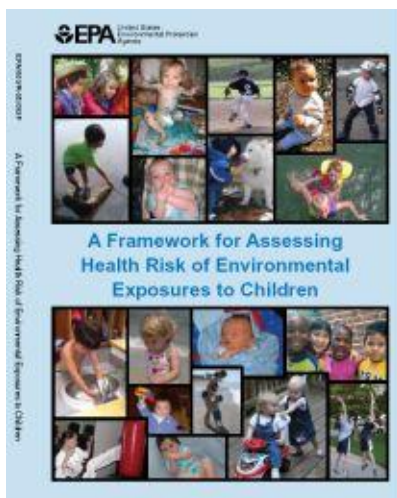
# Overview of IRIS Toxicological Reviews



- Statute: None – IRIS isn't regulatory, but various EPA program offices need the toxicological reviews in order to fulfill their statutory requirements

- Policies: IRIS Reviews draw on many relevant policies:

- Guidelines for developmental toxicity risk assessment (1991)
- Guidelines for reproductive toxicity risk assessment (1996)
- Guidelines for neurotoxicity risk assessment (1998)
- A review of the reference dose (RfD) and reference concentration (RfC) processes (2002)
- Guidance on selecting age groups for monitoring and assessing childhood exposures to environmental contaminants (2005)
- Supplemental guidance for assessing susceptibility from early-life exposure to carcinogens (2005)
- A framework for assessing health risk of environmental exposures to children (2006)
- Child-specific exposure factors handbook (2008)
- Recommended use of body weight 3/4 as the default method in derivation of the oral reference dose (2011)



- Each IRIS review has sections on: reproductive and developmental toxicity, susceptible populations and lifestages, and application of ADAFs



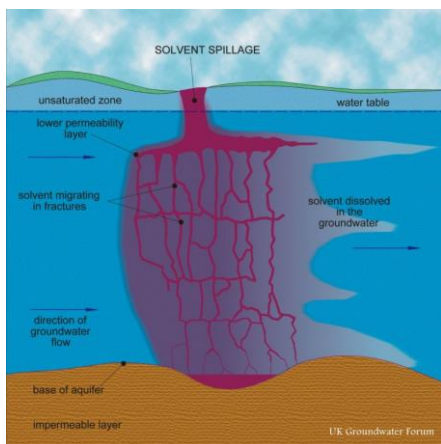


# Toxicological Review of TCE 2011

- Science (noncarcinogenic effects): TCE affects developing fetus and other organs and systems
  - “...TCE poses a potential human health hazard for noncancer toxicity to the CNS, kidney, liver, immune system, male reproductive system, and developing fetus.”
  - “...overall, ... it can be concluded that TCE exposure poses a potential hazard for congenital malformations, including cardiac defects, in offspring.”

- Toxicological Review of TCE (EPA 2011)

- Science (carcinogenicity): TCE carcinogenic by all routes of exposure, causal for kidney and liver cancer, and non-Hodgkin Lymphoma, and suggestive for numerous cancers and childhood leukemia, with a mutagenic mode of action for kidney



- Impact (noncarcinogenic effects): Two of three candidate RfDs and one of two candidate RfC are based on developmental endpoints.

Reference Dose for Chronic Oral Exposure (RfD)

Critical Effect	Point of Departure*	UF	RfD
<b>Multiple</b>	<b>Multiple</b>	<b>Multiple</b>	<b><math>5 \times 10^{-4}</math> mg/kg/day</b>
Decreased thymus weight in female B6C3F1 mice (adult immunological effects)	LOAEL(HED99): 0.048 mg/kg/day	<u>100</u>	candidate RfD = $4.8 \times 10^{-4}$ mg/kg/day
Decreased plaque-forming cell (PFC) response, increased delayed type hypersensitivity in B6C3F1 mice (development Immunotoxicity)	LOAEL: 0.37 mg/kg/day	<u>1,000</u>	candidate RfD = $3.7 \times 10^{-4}$ mg/kg/day
Increased fetal cardiac malformations in Sprague-Dawley rats (heart malformations)	BMDL01(HED99): 0.0051 mg/kg/day	<u>10</u>	candidate RfD = $5.1 \times 10^{-4}$ mg/kg/day

[http://cfpub.epa.gov/ncea/iris/index.cfm?fuseaction=iris.showQuickView&substance\\_nmbr=0199](http://cfpub.epa.gov/ncea/iris/index.cfm?fuseaction=iris.showQuickView&substance_nmbr=0199) \*The Point of Departure listed serves as a basis from which the Oral RfD was derived.

- Impact (carcinogenicity): ADAFs applied for kidney cancer (mutagenic mode of action) in the cancer oral slope factor and inhalation unit risk estimate, but only a small portion of the total cancer risk, so little impact overall.

“...application of the default ADAFs to the kidney cancer inhalation unit risk and oral slope factor estimates for TCE is likely to have minimal impact on the total cancer risk except when exposure is primarily during early life.”

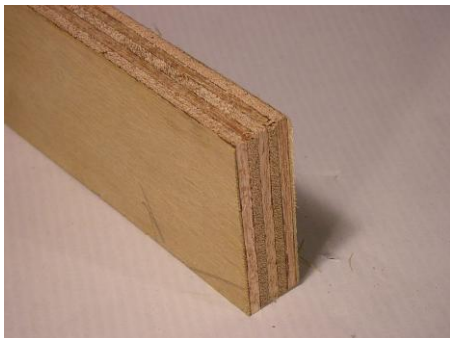
- Toxicological Review of TCE (EPA 2011)



# Toxicological Review of Formaldehyde Inhalation Toxicity draft 2010



- Science (noncarcinogenic effects): Effects at portal of entry (eye irritation, respiratory tract morbidity), in immune, nervous and reproductive systems, and in developmental stages for onset and severity of asthma and allergies.
- Science (carcinogenicity): carcinogenic for upper respiratory tract and possibly causal for lymphohematopoietic cancers, with multiple modes of action, including mutagenic.







- Impact (noncarcinogenic effects): Of the candidate RfCs, three include focus on children's health, and one is related to reproductive health

Table 6-1: Summary of candidate reference concentrations (RFC) for co-critical studies

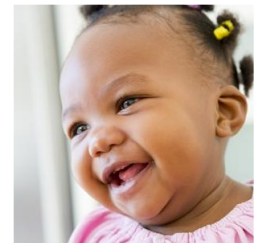
Endpoint	Study	Study size	Homes	Children	POD (ppb)	Application of study-specific UF			cRfC <sup>1</sup> (ppb)
						UF <sub>L</sub>	UF <sub>S</sub>	UF <sub>H</sub>	
<b>Respiratory effects / asthma and sensitization</b>									
Reduction of PEFr in children (10%)	Krzyzanowski et al. (1990)	208	Yes	Yes	BMCL <sub>10</sub> = 17	1	1	3	5.6
Asthma prevalence	Rumchev et al. (2002)	192	Yes	Yes	NOAEL = 33	1	3	Alternative A	
								3	3.3
Asthma, atopy and severity of allergic sensitization	Garrett et al. (1999)	148	Yes	Yes	LOAEL = 28	3	1	Alternative A	
								3	2.8
								1	9.3

Notes: 1: The final RfC will be rounded to one significant digit per EPA policy. Since the Candidate RfC is an interim calculation, two-significant digits are retained as is common practice in mathematics (i.e. one significant digit more than the final result, to avoid rounding errors compounding across multiple mathematical manipulations).

- Impact (carcinogenicity): Applying ADAFs changes inhalation unit risk estimate for total cancer incidence from 0.081 per ppm to 0.13 per ppm (62% higher)



- The unique vulnerabilities and susceptibilities of children mean that children's environmental health comes up in numerous contexts at EPA
- Depending upon the statute, some EPA regulations specifically draw upon children's environmental health, for others it is important context
- Health outcomes during development are often most sensitive, and can directly affect IRIS hazard reviews and subsequent regulatory actions
- Better understanding of children's environmental health, paired with continued attention to all relevant policies may ensure that EPA's actions continue to address children's health





Thank You!  
Any Questions?

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