Risk Assessment of Chemicals in Drinking Water and Associated Uncertainties

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Outline

- Risk assessment of chemicals in drinking water
- Bioaccessibility/bioavailability (concept)
- Development of Public Health Goals (PHGs)
- Petroleum related chemicals
- (Benzene, ethylbenzene, toluene, BaP)
- Use of PHGs and reference values
- Data gaps
- Uncertainties
- Decisions in face of uncertainty-
- MTBE, perchlorate
- Research needs

Risk Assessment

- Hazard identification
- Dose-response assessment
- Exposure assessment (bioaccessibility/bioavailability)
- Risk characterization

- Associated uncertainties
- How can research help to reduce uncertainties
- Improve information supporting risk assessment

Bioaccessibility/bioavailability

- Bioaccesibility
- If a chemical is not within the zone/medium of bioaccessibility, it is not a source of significant exposure and risk (e.g., soil, water, food, air)

- Bioavailability
- If a chemical is not bioavailable to the organism even if it may reside in the bioaccessible medium, it is not a source of significant risk (e.g., from soil to blood stream)

Public Health Goals (PHGs)

- Definition – conc. in water not anticipated to result in adverse health effects after long-term exposure
- Authority – Ca Safe Drinking Water Act 1996, amended 1999
- Nature - Advisory / guidance
- Primary use – Health basis for regulatory standards, MCLs

PHGs

- A. First set of PHGs:
- For all chemicals w state MCLs
- Non-regulatory in nature
- Health basis for regulated chemicals

- B. New PHGs:
- Required by law
- For newly regulated chemicals
- Requested by DHS

PHGs vs. MCLs

PHGs

Non-regulatory

- Health based
- Chemicals w state MCLs
- State

By OEHHA, Cal/EPA

- Higher, same, or lower than State/Fed MCLs
- PHGoals

MCLs

Regulatory

- Health, cost, technology
- Chemicals w fed MCLs
- Fed and state
- By DHS
- State, same or lower than Fed MCL
- MCLGoals eq

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PHG development process -1

- Prioritization
- Initiation of risk assessment
- Literature search, review, evaluation
- Draft technical support document
- Internal review
- External peer review
- Public comment period (web posting)
- Public workshop

PHG development process –2

- Revision
- Second web posting
- Second public comment period
- Revision
- Final posting

Chemical	PHG ppb	MCL ppb CA	MCL ppb USEPA	Oral Ref Value PDD mg/kg-d	Health endpoint
BaP	0.004	0.2	0.2	1×10^{-7} (diet)	Cancer
Benzene	0.15	1	5	0.01 (inh)	Cancer
Ethyl-benzene	300	300	700	0.049 (inh)	Liver tox (hypertrophy, necrosis, hepatic syncytia altertion)
Toluene	150	150	1,000	.022 (dr water)	Inc. liver wt. $Immunotox_{10}$

Chemical	PHG ppb	MCL ppb CA	MCL ppb USEPA	Oral ref value PDD mg/kg-d	Health Endpoint
Xylene	1,800	1,750	10,000	.25 (inh)	Neuro tox (anxiety, inability to concentrate, forgetfulness, poor appetite, reduced muscle power in extremities)
Lead	2	-	-		Neuro-developmental
MTBE	13	-	-	0.37 (gav, inh)	Cancer
Perchlorate	6 Preg	-	-	0.0185 (dr water)	Inhibition of iodide update by thyroid

Uncertainty

- Definition
- A lack of precise knowledge as to what the truth is, whether qualitative or quantitative

- Existence of uncertainty
- Results of -
- Information gaps in health assessment
- Results in –
- Use of defaults and extrapolation assumptions

Assumptions

- Assumptions, cost, uncertainty

- Complete study specific data, no assumptions
- - higher cost, lower uncertainty

- No data, all assumptions
- - lower cost, high uncertainty

Extrapolations/Assumptions

- Animal to human prediction
- Adjustment of differences between animals and humans (bioavailability)
- Sensitive animal species
- Body scaling factor
- High to low dose prediction
- MTD
- Data based on route of exposure

Sources of uncertainty

- Use of NOAEL/LOAEL
- (route, absorption)
- Uncertainty factors
- (pharmacokinetics, pharmacodynamics)

Calculation of PHG

- $$C = \frac{NOAEL \times BW \times RSC}{UF \times CR}$$

- where,

- NOAEL = no-observed-adverse-effect-level;
- BW = adult body weight, a default of 70 kg for adults;
- RSC = relative source contribution (a default of 20 percent to 80 percent);
- ;

Calculation of PHG- 2

- UF = combined uncertainty factor (typical defaults of 10 each for intra- and inter-species extrapolation, 10 if necessary to extrapolate from a LOAEL to a NOAEL, and possibly other factors for data deficiencies or particularly serious toxic effects); and
- CR = L_{eqs}/day = adult daily water consumption rate, 2 L/day.

Parameters affected by bioavailability data

- $C = \frac{NOAEL \times BW \times RSC}{UF \times CR}$
- Chemicals with adequate bioavailability data useful for RA (?)

Decisions in face of uncertainty

- MTBE
- Perchlorate

MTBE

- **Issue**
- Use - gasoline additive, synthetic solvent, primarily as an oxygenate in unleaded gasoline
- Nov 1979 - first allowed use as gasoline additive, 7% (v/v) or less
- Contaminant of groundwater, incl sources of drinking water
- No national drinking water standard
- What is the potential health hazards associated with consumption of, and contact with, drinking water containing MTBE?

MTBE

- **Concern and uncertainty**
- 91-99, discussion re human carcinogenic potential
- Uncertainty & difference of opinion as to the relevance to human cancer causation for each of the tumor types

MTBE

- **Evaluation activities**
- 5 of 6 assays in 3 studies were positive, showing tumors in two species, in both sexes, by oral and inhalation exposures
- Cal EPA concluded MTBE an animal carcinogen. PHG based on carcinogenic risk

MTBE

- **Evaluation activities -2**

- 1997, the Office of Water at USEPA developed a Drinking Water Advisory based upon the organoleptic (taste and odor) characteristics of MTBE
- USEPA has not developed a Reference Dose or performed a cancer risk assessment for MTBE, although in December 1998, it was said to be undergoing (re)assessment

MTBE

- **Implementation**
- USEPA Office of Water concluded –
- available data not adequate to estimate potential health risks of MTBE at low exposure levels in drinking water, but that the data support the conclusion that MTBE is a potential human carcinogen at high doses.

MTBE

- **Impact, outcome**
- Two environmental agencies, seemingly different determination on carcinogenicity potential at low exposure levels, but in agreement at high doses
- Difference of opinion had minimal impact in practice. Roughly comparable advisory levels for drinking water (13 ppb vs. 20-40 ppb).

Perchlorate

Oxidizer in solid propellants for rockets and missiles since mid-1940s

Found in soil and aquifers for drinking water sources

Perchlorate

No MCLs, or drinking water regulations/standards

2000 - DHS action level 18 µg/L (ppb)

Early 2002 - draft RA by U.S. EPA DL, DHS action level 4 µg/L (ppb)

2004 - PHG 6 ppb

2004 - CA drinking water action level now 6 ppb

Several states have action levels in the range of 1-20 ppb

Perchloarete

Animal and human studies – reduce or inhibit thyroidal iodide uptake

iodine is necessary for normal thyroid function and brain development,

Iodide is a key ingredient of thyroid hormones and perchlorate inhibits iodide absorption by the thyroid, depending on dosage, perchlorate can reduce the production of
thyroid hormones and disrupt thyroid-pituitary homeostasis

Perchlorate

Compete with iodide for transport protein called NIS

NIS present in the placenta and lactating mammary glands

Perchlorate can impact the NIS in these tissues and reduce the iodine supply to fetuses and breast-fed infants

Since breast milk is the sole source of iodine for some infants and adequate level of iodine in breast milk is vital to the well-being of breastfed infants

Furthermore, if there were a reduction in thyroidal iodide uptake, neonates are less capable to maintain normal thyroid hormone production by using the iodide stored in the thyroid.

Perchlorate

Dietary iodine intake and thyroidal iodide uptake vary among individuals

Intake affected by the type of food one eats (some food is rich in iodine while others contain goitrogens), smoking habits (tobacco smoke contains goitrogens), and exposure to environmental contaminants (such as nitrate, polychlorinated biphenyls and dioxins)

Preliminary results showed perchlorate in some foods
A low level detected in a single sample of human breast milk
Studies are underway to quantify perchlorate levels in various food types.

Perchlorate

Four sensitive subpopulations:

1. pregnant women and their fetuses, especially those who are getting less than a sufficient amount of iodine

2. lactating women, especially those who are getting less than a sufficient amount of iodine

3. Infants

4. Individuals with thyroid problems

Research needs -1

- In absence of data, use default assumptions to fill data gaps
- Defaults themselves need to be supported by best available data
- <u>Research to develop and refine defaults</u>

Research needs -2

- Need good available specific data (chemical-, medium-, site-specific, other)
- Research to reduce uncertainties in RA by understanding and elucidating the fundamental **determinants of exposure and dose** and the basic biological changes that follow exposure to an agent
- Cumulative risk