Disinfection By-Products and Drinking Water

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Environmental Health Section
• What are disinfection by-products (DBPs)?
• What are some of the challenges around interpreting the evidence base?
• How can we best use the evidence base to manage DBPs in drinking water?
NHMRC has responsibility for the Australian Drinking Water Guidelines (ADWG, 2011)

• Framework for managing safe and good quality drinking water

• Guidance on managing microbial and chemical risks

• Not regulatory, but relied upon by states and territories in their water regulatory systems

• Expert committee provides advice to NHMRC on water quality issues
Derivation of drinking water guideline values

Guideline value (threshold chemicals) =

animal dose x human weight x proportion of intake from water
volume of water consumed x safety factor

Animal dose = NOEL or LOEL
Human weight = 70 kg (adult) or 13 kg (2 year-old child)
Proportion of intake from water = default 10%
Volume of water consumed = default 2 L
Safety factor/uncertainty factor = 10 (interspecies) x 10 (intraspecies)
Disinfection By-Products

**Guideline values in the Australian Drinking Water Guidelines**
- Trihalomethanes (1996) chloroform, bromoform, dibromochloromethane and bromodichloromethane
- Haloacetic acids (1996)
- Chlorophenols (1996)
- Bromate (1996)
- N-Nitrosodimethylamine (2011)

**Data inadequate to set guideline values**

*Action to reduce DBPs is encouraged but must not compromise disinfection as non-disinfected water poses significantly greater risk.*
In early 2016 NHMRC established the Disinfection By-Products Advisory Committee to:

- Consider the quality of the published epi and tox studies on DBP and potential association with adverse health effects
- Advise NHMRC if the Australian Drinking Water Guidelines for DBPs require revision

https://kirstyevidence.files.wordpress.com/2012/11/evidence-literate.jpg
Different types of evidence for different purposes

• establish an association (or strength of evidence for an association)
• plausibility/mode of action
• set a safe level
Other regulatory reviews - trihalomethanes

Epidemiological evidence:
• Potential association with bladder cancer (men)
• Potential association with reproductive/developmental endpoints (?)
• Genotypic differences in metabolism (?)

Toxicological evidence
• Tox studies on some DBPs
• Uncertainties in translating these into potential human outcomes – e.g. no evidence of bladder cancer in animals
In considering evidence base other regulators have considered:

- consistency
- strength and specificity of association
- exposure precedes outcome (temporality)
- dose response relationship (biological gradient)
- biological plausibility
- coherence with multiple lines of evidence
- In addition USEPA considered reliability of exposure data, statistical power and significance and freedom from bias and confounding.
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</thead>
<tbody>
<tr>
<td>Chloroform</td>
<td></td>
<td>0.3</td>
<td>MCLG = 0.07</td>
<td></td>
<td>1999: Group 2B (pos carcinogenic)</td>
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<tr>
<td>Dog 7.5 yr</td>
<td></td>
<td>UF=25 Alloc. 75%</td>
<td>UF=1000 Alloc. 20%</td>
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<tr>
<td>DBCM</td>
<td></td>
<td>0.1</td>
<td>MCLG = 0.06</td>
<td></td>
<td>1991: Group 3 (not classifiable)</td>
</tr>
<tr>
<td>Rat 90 day</td>
<td></td>
<td>UF=1000 Alloc. 20%</td>
<td>UF=1000 Alloc. 80%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rat 104 wk</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>BDCM</td>
<td></td>
<td>0.06&lt;sup&gt;b&lt;/sup&gt;</td>
<td>MCLG = 0</td>
<td>MAC = 0.016 10&lt;sup&gt;-5&lt;/sup&gt; to 10&lt;sup&gt;-6&lt;/sup&gt; cancer risk</td>
<td>1991: Group 2B</td>
</tr>
<tr>
<td>Rat 2yr</td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>Mouse 102 wks</td>
<td></td>
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<td>Bromoform</td>
<td></td>
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<td>Rat 104 wks</td>
<td></td>
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<tr>
<td>Total THMs</td>
<td>0.25</td>
<td>Ratio of each THM to GLV should not exceed 1</td>
<td>MCL = 0.08 Based on best available technology considerations</td>
<td>HBT=0.08, MAC=0.1 80% (2100)</td>
<td></td>
</tr>
</tbody>
</table>
Exposure issues for epi studies

• TTHM used widely as surrogates for all DBPs although the correlation is variable
• Monthly or annual average or often used. Other DBPs occasionally also measured
• Oral, dermal and inhalation exposures considered (showering, bathing, washing dishes by hand, swimming)
• Individual water consumption may or may not be taken into account
• Length of exposure (bladder cancer)
• Residences in same water treatment areas grouped or measurements taken at individual homes
• Address at delivery (repro/devo studies)
• Drinking water source, surface water treatment used to group cases/controls
• Use of biomarkers to indicate exposure (urine, blood)
Comparing ADWG guideline value to exposure in epi studies looking at bladder cancer

ADWG: TTHM 250 µg/L (fluctuating occasionally 1 mg/L for 1-2 days annually)

• some water utilities struggle to meet this at certain times of year

Evaluating evidence for association of human bladder cancer with drinking water chlorination disinfection by-products
### TABLE 3. Comparison of Risk Estimates (ORs) of Bladder Cancer for King and Marrett (1996): Original Analysis Versus Reanalysis (Amy et al. 2006)

<table>
<thead>
<tr>
<th>Duration of exposure</th>
<th>Cases/controls</th>
<th>Original analysis, peak THM4 &gt;50 µg/L</th>
<th>Cases/controls</th>
<th>Reanalysis, mean THM4 &gt;40 µg/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤10 years</td>
<td>253/650</td>
<td>1.0 (reference)</td>
<td>593/1310</td>
<td>1.0 (reference)</td>
</tr>
<tr>
<td>10–19 years</td>
<td>226/519</td>
<td>1.10 (0.87–1.38)</td>
<td>23/51</td>
<td>1.21 (0.71–2.05)</td>
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<tr>
<td>20–34 years</td>
<td>163/297</td>
<td>1.36 (1.05–1.76)</td>
<td>30/68</td>
<td>1.01 (0.63–1.60)</td>
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<tr>
<td>≥35 years</td>
<td>54/79</td>
<td>1.63 (1.08–2.46)</td>
<td>43/65</td>
<td>1.36 (0.90–2.07)</td>
</tr>
</tbody>
</table>

### TABLE 4. Bladder Cancer Odds Ratio in Relation to Residential THM4 Exposure (Villaneuva et al. 2007)

<table>
<thead>
<tr>
<th>Average THM measure</th>
<th>Cases/controls</th>
<th>Odds ratio (95% CI)</th>
<th>p Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤8 µg/L</td>
<td>137/172</td>
<td>1.0 (reference)</td>
<td></td>
</tr>
<tr>
<td>&gt;8.0–26.0 µg/L</td>
<td>140/158</td>
<td>1.53 (0.95–2.48)</td>
<td></td>
</tr>
<tr>
<td>&gt;26.0–49 µg/L</td>
<td>183/160</td>
<td>2.34 (1.36–4.03)</td>
<td></td>
</tr>
<tr>
<td>&gt;49 µg/L</td>
<td>158/180</td>
<td>2.53 (1.23–5.20)</td>
<td>p &lt; .01</td>
</tr>
</tbody>
</table>
“As long as associations are large enough to be demonstrated, epidemiological study results suffering from exposure misclassification or quantitative inaccuracy can still provide useful evidence towards an evaluation of consistency of association and potentially for informing causal inference.

“However, from the perspective of those who must regulate exposures to minimise potential health risks in drinking water, quantitatively inaccurate exposure assessment has serious implications if used for quantitative risk assessment to inform regulation.”

Hrudey et al 2015
There is a clear policy need for assessments in which benefits are balanced against risks.
WHAT DO WE WANT?
EVIDENCE-BASED CHANGE
WHEN DO WE WANT IT?
AFTER PEER REVIEW
Possible directions

• Continue chemical-by-chemical approach to guideline development as new data becomes available

• Provide guidance intended to reduce overall risk (modelling approaches)

• Promote/encourage actions to reduce organic matter in source water

• Investigate use of surrogate measures e.g. AoX (total absorbable organic halogens), AoCl, AoBr, AoI and correlations with known DBPs and treatment processes
Final thoughts
Thank you

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