Risk assessment of chemical contaminants in drinking water

Stephen Robjohns CRCE Chilton - September 2013
Contents of talk

- Regulatory limits & WHO drinking water Guideline values
- Risk assessment of threshold and non-threshold chemicals
- Risk from endocrine disrupters in drinking water
- Risk from disinfection by-products
- DWI monitoring study of pharmaceuticals in drinking water
Drinking water Regulations

- The European Directive (98/83/EC) sets concentration limits for chemicals present in drinking water in EU countries.
- The Private water regulations 2009 regulate private water supply in England & Wales (boreholes & private water supplies of mainly rural and isolated/remote properties e.g. farms & some B&Bs).
WHO drinking water Guideline values

- Most EU and UK drinking water regulatory limits are based on WHO drinking water Guideline Values (WHO GV).
- A WHO Guideline value (GV) represents the concentration of a chemical in drinking water that does not result in a significant risk to the health of the general population over a lifetime of consumption.
- Often based on toxicological risk assessment [but some are based on aesthetic effects (taste/odour/discolouration) & practical achievability]
Examples of chemicals with regulatory limits in UK drinking water

<table>
<thead>
<tr>
<th>Chemical</th>
<th>Regulatory Limit (micrograms/litre)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arsenic</td>
<td>10</td>
</tr>
<tr>
<td>Lead</td>
<td>25 (10 – from 25/12/2013)</td>
</tr>
<tr>
<td>Fluoride</td>
<td>1500 (1.5 mg/L)</td>
</tr>
<tr>
<td>Individual pesticides</td>
<td>0.1</td>
</tr>
<tr>
<td>Total pesticides</td>
<td>0.5</td>
</tr>
<tr>
<td>Total trihalomethanes (disinfection by-products)</td>
<td>100</td>
</tr>
<tr>
<td>Nitrate</td>
<td>50000 (50 mg/L)</td>
</tr>
</tbody>
</table>
Examples of chemicals with regulatory limits in UK drinking water

<table>
<thead>
<tr>
<th>Health based</th>
<th>Aesthetic reasons (taste &amp; discolouration)</th>
<th>Technological achievability (ALARP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Copper (2 mg/L)</td>
<td>Iron (0.2 mg/L)</td>
<td>Arsenic (10 microg/L)</td>
</tr>
<tr>
<td>Nitrate (50 mg/L)</td>
<td>Manganese (0.050 mg/L)</td>
<td>Lead (25 microg/L)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pesticides (individual 0.1 &amp; total 0.5 micrograms/L)</td>
</tr>
</tbody>
</table>
Approaches to prevent potential health effects from contaminants

- Monitoring and compliance with regulatory limits
- Water must be ‘wholesome’ (a ‘catch all’ phrase where a substance must not be present at a concentration on its own or combination that will present a danger to health)
- Testing and approval of products contacting or used in drinking water treatment
- DWI research projects into potential health threats e.g. disinfection by-products, pharmaceuticals & endocrine disrupters
Stages of Toxicological Risk Assessment

Hazard Identification

Hazard characterisation

Exposure Assessment

Risk Characterisation
Dose response relationship – generally the higher the dose the greater the response
A: Chemical has no threshold, there is some risk at any level of exposure. Cannot estimate a ‘safe’ level at which there is no adverse health effects.

B: Chemical has a threshold below which adverse effects are not discernible. Can estimate a ‘safe’ level (TDI) at which there is no adverse health effects.
Decision ‘tree’ – threshold chemicals

- Is conc. …
  - < UK standard?
    - < WHO GV?
      - < TDI?
        - [Result: No sig. risk to health expected]
        - [Result: No sig. risk to health expected]
        - [Result: No sig. risk to health expected]
      - [Result: May still not cause sig. risk to health. Compare intake to TDI. Consider endpoints, dose response curve]
Risk assessment approach

For any chemical detected in drinking water:

• Estimate the intake/exposure from the detected concentration
• Compare the intake with a toxicological reference point (i.e. point of departure (POD))
  
  e.g.

  No observed adverse Effect Level (NOAEL)

  Lowest observed adverse effect level (LOAEL)

  Benchmark dose (from mathematical modelling of dose-response data)
Derivation of a WHO health based Guidance value - for threshold chemicals

In many cases a Tolerable Daily Intake (TDI) has been derived.

- This is a daily intake in milligrams per kilogram of body weight (mg/kg body weight/day) averaged over a lifetime that provides no risk to health

\[
TDI = \text{Toxicological reference point (point of departure)}^* \\
\text{Uncertainty Factor (default = 100)}
\]

*POD = NOAEL or LOAEL or BMDL
Derivation of a WHO health based guideline value for threshold chemicals

\[ GV \text{ (mg/L)} = TDI^* \times \text{body weight (60kg)} \times \text{allocation (0.2)} \times \text{Consumption (2L/day)} \]

Usual default values:

- Body weight = 60 kg
- Consumption = 2 litres per day
- Allocation = 20% (default)

(*TDI = Tolerable Daily intake or ADI = Acceptable Daily Intake)
What is the intake?

Amount of the chemical that gets into the body

- **Adult**: 60kg; 2L per day
- **Child**: 10kg; 1L per day
- **Infant**: 5kg; 0.75L per day

Intake = mg/kg body weight/day
Example threshold substance – Bisphenol A

Bisphenol A can migrate into water at low concentrations from plastic or resin type materials i.e. under laboratory test conditions:

Bisphenol A is known as an ‘endocrine disrupter’ i.e. at sufficiently high doses it can cause adverse effects on the endocrine (hormone system).

The WHO have not derived a drinking water GV.

However, as this substance can occur in food at low levels, the European Food Safety Authority (EFSA) has derived a TDI.
Example threshold substance – Bisphenol A

For example, if a migration test gave a concentration of 3 micrograms per litre (3 µg L$^{-1}$).

Then, for an adult, child and infant consuming water containing (3 µg L$^{-1}$), the approximate intake would be 0.1, 0.3 and 0.45 micrograms per kilogram of body weight (µg kg$^{-1}$ bw day$^{-1}$).

This is below the European Food Safety Authority (EFSA) TDI of 50 µg kg$^{-1}$ bw day$^{-1}$.

Therefore there would be no risk to health.

• Chemicals that produce adverse effects by damaging genetic material (DNA) – genotoxic substances
• ‘one-hit’ theory that one molecule can interact with DNA resulting in a heritable mutation that could subsequently lead to cancer
• Assume that genotoxic substances are human carcinogens.
• Any exposure is associated with an increased risk, although this may be very small.
• Exposure should be as low as practically achievable (ALARP)
Risk assessment approach to non-threshold substances

For non-threshold chemicals e.g. genotoxic carcinogens and the developmental neurotoxic chemical lead:

• Cannot derive a TDI or a level of exposure without risk
• Therefore, compare intake to that associated with minimal risk
• Keep exposure to as low as reasonably practicable (ALARP)
Deriving the Margin of Exposure

The magnitude of the MOE reflects magnitude of risk

larger the MOE = smaller the risk

POD = BMDL or NOAEL or T25
<table>
<thead>
<tr>
<th>MOE based on BMDL\textsubscript{10}</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;10,000</td>
<td>May be a concern</td>
</tr>
<tr>
<td>10,000 – 1,000,000</td>
<td>Unlikely to be a concern</td>
</tr>
<tr>
<td>&gt;1,000,000</td>
<td>Highly unlikely to be a concern</td>
</tr>
</tbody>
</table>
Example non-threshold carcinogen - dibromoacetronitrile

Dibromoacetronitrile is nitrogenous a disinfection by-product that has been detected in drinking water e.g. 8 micrograms/litre.

The International Agency for Research on Cancer (IARC 2012) indicate that this substance is genotoxic and carcinogenic and therefore has no threshold for adverse effects.

Animal studies gave a cancer benchmark dose of 5 – 11 mg/kg body weight/day (a POD = BMDL10).

The estimated intake is 19,000 to 40,000 below the POD.

Therefore, there is unlikely to be a risk to health according to the COC banding.
Endocrine disrupting chemicals

The WHO/IPCS definition on an endocrine disrupter:

An *endocrine disruptor* is an exogenous substance or mixture that alters function(s) of the endocrine system and consequently causes adverse health effects in an intact organism, or its progeny, or (sub)populations.

[Must cause pathology or impairment of function - i.e. not just a change in the levels of a particular hormone].
Endocrine disrupting chemicals

The DWI commissioned a research project on endocrine disrupters by the Institute of Environment & Health (IEH) – published in 2012.

• This modelled estimated ‘worst-case’ drinking water concentrations for a number of prioritised chemicals - selected on the basis of potential exposure and potential to cause adverse endocrine disrupting effects.
Endocrine disrupting chemicals

- Estimated intakes were compared with available authoritative health criteria values (e.g. TDIs) or against calculated chemical specific exposures limits.

- These comparisons were reassuring and did not indicate a significant concern for health.
Disinfection by-products

- Disinfection of drinking water is an important public health measure and UK public water suppliers are required to disinfect the water supply by law.
- Chlorination is the most commonly used method of disinfection in the UK and is intended to protect human health from microbial contaminants.
- Disinfection of drinking water is fundamental to preventing the spread of waterborne diseases, such as cholera.
Disinfection by-products

- Chlorination can produce a range of disinfection by-products (DBPs) by reaction between chlorine and natural organic matter (NOM) present in surface waters.
- The main DBPs are the four trihalomethanes (THMs):
- Chloroform, bromodichloromethane (BDCM), dibromochloromethane (DBCM), and bromoform.
Disinfection of drinking water

- Regulated in the UK by specifying a maximum concentration of 100 micrograms/litre for the sum of THMs (TTHMs).
- Bromate – regulatory limit of 10 micrograms/litre
- Haloacetic acids (HAAs) and other DBPs are not regulated directly.

- Removal of precursor organic compounds before chlorination is commonly practised in the UK to reduce TTHM concentrations. This is also considered to indirectly reduce the formation of HAAs and other DBPs.

[i.e. TTHM concentrations are often regarded as a marker for total DBPs]
Disinfection of drinking water

- Adverse reproductive/developmental effects and cancer have been reported to be associated with chlorination DBPs in some human epidemiological studies
- This led to an evaluation of the available evidence for such effects by the UK expert Committees on Toxicity (COT) and Carcinogenicity (COC)
Disinfection of drinking water – reproductive effects

- The COT in 2008 concluded that:
  - Human studies (epidemiological studies) showed no consistent relationship between chlorinated drinking-water and adverse pregnancy effects.
  - In animal studies, effects mainly seen at high doses (associated with maternal toxicity – secondary effect) and these are not considered to be predictive of effects in humans exposed to far lower levels.

Centre for Radiation, Chemical & Environmental Hazards (CRCE)
Disinfection of drinking water – cancer risk

- The COC in 2008 concluded from epidemiological studies “that the evidence for a causal association between cancer and exposure to DBPs is limited and any such association is unlikely to be strong.”
- An increased risk of bladder cancer has been seen in some studies, but only for males, not females, which is difficult to explain.
- Some studies have also shown an association between DBPs and colon cancer, but other studies have shown no association.
Disinfection of drinking water – advice

• Overall the expert advice regarding DBPs in drinking water is that:
• Efforts should be made to minimise exposure to DBPs, but without compromising effective disinfection of drinking water.

[There are common difficulties in interpreting epidemiological studies on DBPs, which include: small relative risks; the possibility of residual confounding; and difficulties with exposure assessment e.g. using concentrations of DBPs in water zones i.e. the estimated exposure is on a group basis, which is not ideal for assessing individual exposure].
Pharmaceuticals in drinking water

• The DWI has commissioned studies to investigate the potential risk to health from pharmaceuticals that may enter the public water supply e.g. from water sewage treatment works.

• There are approximately over 3,000 active pharmaceuticals in use. It is impossible to monitor for all.

• From initial desk based exposure modelling and other selection/prioritisation criteria (e.g. usage rates & potential hazard) a number of candidate/representative pharmaceuticals were selected for monitoring.
Selected compounds

- atenolol
- benzoylecgonine
- caffeine
- carbamazepine
- carbamazepine epoxide
- cocaine
- cyclophosphamide
- Diclofenac
- fluoxetine
- furosemide
- ibuprofen
- ketoprofen
- naproxen
- norfluoxetine
- Orlistat
- simvastatin
- trimethoprim
Pharmaceuticals detected in source river water

- Ten of the 17 study compounds were detected in untreated source waters (derived from rivers) at sub-micrograms/L concentrations. These were:

- Atenolol, diclofenac, furosemide, trimethoprim, caffeine, carbamazepine, carbamazepine epoxide, ibuprofen, naproxen and benzoylecgonine
# Pharmaceuticals detected in river water

<table>
<thead>
<tr>
<th>Pharmaceutical</th>
<th>Maximum river water concentration (nanograms/litre)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atenolol</td>
<td>114</td>
</tr>
<tr>
<td>caffeine</td>
<td>441</td>
</tr>
<tr>
<td>carbamazepine</td>
<td>555</td>
</tr>
<tr>
<td>Carbamazepeine epoxide</td>
<td>25</td>
</tr>
<tr>
<td>diclofenac</td>
<td>76</td>
</tr>
<tr>
<td>furosemide,</td>
<td>63</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>38</td>
</tr>
<tr>
<td>Naproxen</td>
<td>44</td>
</tr>
<tr>
<td>trimethoprim</td>
<td>26</td>
</tr>
<tr>
<td>benzoylecgonine</td>
<td>16</td>
</tr>
</tbody>
</table>
Pharmaceuticals detected in final treated drinking water

- Six of these compounds were detected in final treated drinking water generally - at nanograms/litre concentrations. These were:

- Caffeine, carbamazepine, carbamazepine epoxide, ibuprofen, naproxen and benzoylecgonine.
Pharmaceuticals detected in final treated drinking water

<table>
<thead>
<tr>
<th>Pharmaceutical</th>
<th>Median drinking water concentration (ng/L)</th>
<th>Maximum drinking water concentration (ng/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>caffeine</td>
<td>11</td>
<td>79</td>
</tr>
<tr>
<td>carbamazepine</td>
<td>2</td>
<td>148</td>
</tr>
<tr>
<td>Carbamazepeine epoxide</td>
<td>5</td>
<td>17</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>&lt;2</td>
<td>3</td>
</tr>
<tr>
<td>Naproxen</td>
<td>&lt;1</td>
<td>3</td>
</tr>
<tr>
<td>benzoylecgonine</td>
<td>&lt;1</td>
<td>4</td>
</tr>
</tbody>
</table>
Pharmaceuticals in final treated drinking water

- Toxicological information and health based exposure guidelines are not generally available for pharmaceuticals (unlike environmental chemicals).
- Such data is likely to be commercial in-confidence. Thus, in general, therapeutic doses are used in the risk assessment, rather than toxicological points of departure, e.g. NOAELs/LOAELs or BMDs.
- The margin of exposure (MoE) between the lowest therapeutic dose and estimated intakes from the maximum concentration was typically in excess of a million.
Pharmaceuticals in final treated drinking water - conclusions

- Concentrations of pharmaceuticals in drinking waters are generally significantly lower than those seen in surface waters. This indicates that treatment is effective at removing these contaminants.

- Intakes of the compounds detected in drinking water are many orders of magnitude lower than levels therapeutic doses.

- Estimated exposures for most of the detected compounds are at least thousands of times below doses seen to produce adverse effects in animals and hundreds of thousands below human therapeutic doses.

- Thus, the detected pharmaceuticals are unlikely to present a risk to health.
Summary – this talk covered

• The basis for drinking water regulatory limits
• The derivation of WHO Guideline values
• Risk assessment of threshold and non-threshold chemicals
• Risk from endocrine disrupters in drinking water
• Risk from disinfection by-products
• DWI monitoring study of pharmaceuticals in drinking water

Recommended further reading:

• WHO Guidelines for Drinking water quality, Chapter 8 (chemical aspects) & Chapter 12 (chemical factsheets)
• Drinking Water Inspectorate (DWI) website/research