Toxicological Review of NR 538 Proposed Standards

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Focus of toxicological review

- Leachate standards for Aluminum, Barium, Boron, Cobalt and Molybdenum
- Reviewed existing toxicity values used in establishing the proposed NR 538 standards based on the Chapter NR 140 Groundwater Enforcement Standards (ES) which will be compared to ASTM water leach test results to assign beneficial use categories
- Conducted literature search of publically available toxicological data, reviews, and exposure factors to determine if more recent data has become available since WDHS ES derivations

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Rationale for alternate beneficial use baseline values

- Provide health protective, alternate values based on most recent and applicable toxicity and exposure factor information based on constituent review
- Relevance of using groundwater standards for beneficial use standards considering the limitations already in place to mitigate exposures as required in NR 538
  - Prohibition for some uses in residential areas
  - Separation from groundwater tables, private and public wells
  - Setbacks and depth of fill
  - Volume limits
- Less potential for exposures with beneficial use materials as compared to groundwater standards (groundwater = drinking water in WI)

Development of alternate beneficial use baseline values

- Identified most scientifically valid toxicological study and endpoint in animals or humans with relevant health effects associated with subchronic/chronic oral exposure to constituent
- Considered appropriate uncertainty factors to derive toxicity value [(i.e., reference dose (RfD)]
- Utilized most recent exposure factors from 2014 USEPA Exposure Factors Handbook for body weights and human daily water consumption
- Determined alternate beneficial use baseline values by adjusting toxicity values with current exposure factors and relative source contribution (RSC) adjustments

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Example-Barium

- Current ES based on USEPA maximum contaminant level (MCL) of 2 mg/L based on USEPA Integrated Risk Information System (IRIS) oral reference dose (RfD) toxicity value of 0.07 mg/kg-day, assuming a body weight of 70 kg, 2 liters of drinking water consumed per day, and an assumed relative source contribution of 80%
- USEPA updated the oral RfD for barium in 2005 based on additional data to 0.2 mg/kg-day
- Agency for Toxic Substances and Disease Registry (ATSDR) derived a chronic oral minimum risk level (MRL) of 0.2 mg/kg-day similar to USEPA
- Current USEPA regional screening level (RSL) tables indicates that the RSL for barium is based on the updated USEPA IRIS oral RfD of 0.2 mg/kg-day

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Example-Barium cont'd.

- Using the updated USEPA IRIS RfD for barium of 0.2 mg/kg-day (USEPA, 2005) and the most recent USEPA exposure factors (USEPA, 2014) for human body weight and daily drinking water consumption, an alternate beneficial use baseline value for barium may be derived as follows:

$$\frac{\text{0.2 mg/kg-day X 15 kg body weight (bw)}}{\text{0.78 liters (L)/day}} = \textbf{4 mg/L}$$

- The alternate Category 1 beneficial use baseline value for barium could then be increased by an appropriate factor to determine the Category 2 standards
- The current proposed Category 1 and Category 2 standards for barium are 2 mg/L and 10 mg/L

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Example-Boron

- Toxicity value selected by WDHS for derivation of the ES of 0.2 mg/kg-day is consistent with that used by USEPA IRIS, ATSDR and other regulatory agencies and based on robust toxicological database for boron and new methodologies
- However, WDHS recommended an ES of 1 mg/L in the review conducted in 2000 and references USEPA's Lifetime Health Advisory (LHA) for the derivation
- This is not consistent with the LHA for boron provided by USEPA in the 2012 edition of the Drinking Water Standards and Health Advisories tables which lists a LHA of 6 mg/L based on the use of a 80% Relative Source Contribution (RSC) adjustment factor

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Example-Boron cont'd

- Although WDHS cites the same toxicity value as USEPA IRIS and other sources, it applies an outdated USEPA LHA to be used as the ES. The WDHS citation of 1 mg/L appears to be derived by using a RSC of 20%; this is not consistent with the current USEPA 2012 drinking water standards
- The current LHA of 6 mg/L as listed in the 2012 USEPA drinking water standards is proposed as the Category 1 alternate beneficial use baseline screening value for boron
- An appropriate factor to determine Category 2 standards could then be applied

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Example-Molybdenum

- Proposed Category 1 standard is the ES, which was established in 2005 based on the current USEPA IRIS RfD of 0.005 mg/kg-day and the USEPA LHA
- USEPA calculated a LHA of 0.04 mg/L based on a 70-kg adult consuming 2 liters of water per day and a 20% RSC (80% of exposure to chemical could come from sources other than drinking water)
- However, the human study from 1961 used to derive the oral RfD has come under scrutiny due to analytical methodological concerns, small control group and co-exposure to other environmental factors
- No other human studies show same effects noted

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Example-Molybdenum cont'd

- Institute of Medicine (2001); European Commission Scientific Committee on Food (2000) and other researchers identified a different animal study that is more scientifically valid to assess effects with molybdenum
- Based on the application of various uncertainty factors, these sources cite more appropriate toxicity values using the endpoint of the animal study from 0.009-0.03 mg/kg-day
- WDHS also re-evaluated the basis for the ES in 2013 and states:

  "Although the association between molybdenum exposure and human gout-like symptoms or increased serum uric acid levels is biologically plausible, after our literature review, we found that the concerns with the analytical protocols used in the Koval'skiy study significantly reduced our confidence in the reliability of using it as the critical study for establishing health guidelines."

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Example-Molybdenum cont'd

Source	Year	Non-Cancer Value mg/kg-day	Value Descriptor	Basis for Value
USEPA IRIS	1993	0.005	RfD	Gout-like effects
Wisconsin Scientific Support Document (SSD) RfD for ES and PAL	2005	0.005	RfD	Gout-like effects; Adopted USEPA RfD in accordance with Chapter 160
WDHS Interim Advisory Level for Individual Drinking Water Advisories	2013	0.009[a]	RfD	Reproductive and fetal effects
Vyskocil and Viau	1999	0.009	TDI	Reproductive and fetal effects
EC SCF Opinion	2000	0.01	UL	Reproductive and fetal effects
NAS IOM	2001	0.03	RfD	Reproductive and fetal effects

Example-Molybdenum cont'd

- If the 0.03 mg/kg-day toxicity value is selected based on the National Academy of Science's IOM review, an alternate beneficial use baseline value for Category 1 uses could be determined using the current USEPA exposure factors as follows:

$$\frac{0.03 \text{ mg/kg-day} \times 15 \text{ kg bw} \times 100\%}{0.78 \text{ L/day}} = \mathbf{0.58 \text{ mg/L}}$$

- It appears that WDHS used the same study and endpoint of 0.9 mg/kg-day as the other sources, but applied an uncertainty factor of 100 and adjusted the value for a 10 kg child drinking 1 liter of water a day to derive the 90 ug/L (0.09 mg/L) advisory level; this could be modified even further using a different uncertainty factor (30 instead of 100) and updated exposure factors above

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Other Examples

- Cobalt
  - WDHS Scientific Support Documentation (1997) selected a toxicity study identified by ATSDR in its 1992 Toxicological Profile of Cobalt which was since updated in 2004 by ATSDR noting that the previous study used was not appropriate.
  - Other more recent reviews and data provide different studies that are more applicable for the derivation of a toxicity value
- Aluminum
  - The study selected for the derivation of the ES has been determined to be significantly flawed and other researchers (even USEPA itself in its Provisional Peer-Reviewed Toxicity Value (PPRTV) document) have used other toxicity studies to develop a toxicity value that results in a higher standard than the NR 538 Appendix 1 value
  - Listed by USEPA as a nuisance chemical subject to secondary drinking water standards only as guidelines for aesthetic considerations
  - WDNR did not find evidence that aluminum should be included as required sampling parameter

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Conclusion

- More scientifically valid toxicological studies and assessments are available for some constituents since the original ES were established
- Updated USEPA exposure factors and more applicable relative source contributions may be considered in the derivation of alternate beneficial use baseline values
- Constituent-specific adjustment factors to establish Category 2 standards may be considered based on the available data rather than using a 5 fold factor across all constituents

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