Health Based Guidance for Water
Health Risk Assessment Unit, Environmental Health Division
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Toxicological Summary for: Boron

CAS: **7440-42-8**

The 2008 MDH SONAR directs the Health Risk Assessment unit (HRA) to develop guidance values that are protective of all humans, including sensitive populations such as infants, children, and pregnant women. In the case of boron, HRA calculated an initial value of 2000 µg/L that was protective of pregnant women, in utero exposures, children, and adults. This was further adjusted downward to 500 µg/L by use of a database uncertainty factor to address the unknown toxicity and exposures of bottle-fed infants. Therefore, 2000 µg/L is protective to all persons except bottle-fed infants, for which 500 µg/L is protective.

Acute Non-Cancer Risk Assessment Advice ($nRAA_{Acute}$) = Not Derived (Insufficient Data)

Short-term Non-Cancer Risk Assessment Advice ($nRAA_{Short\text{-}term}$) = 500 µg/L

$$\frac{\text{(Reference Dose, mg/kg-d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Short-term Intake Rate, L/kg-d)}}$$

$$= \frac{\text{(0.047 mg/kg-d) x (0.5)}^{*} \text{ x (1000 µg/mg)}}{\text{(0.043 L/kg-d)}^{**}}$$

= 547 rounded to **500 µg/L**

*Relative Source Contribution: MDH 2008, Section IV.E.1 and US EPA 2011. MDH applied an RSC of 0.5, by using the subtraction method, instead of the default 0.2 for pregnant women. Food is the only other major source of boron exposure; comprising approximately half of the RfD, leaving the other half for water ingestion exposures (Rainey, 2002).

**Intake Rate: MDH 2008, Section IV.E.1. and US EPA 2011, Table 3-3. The RfD is based on decreased fetal body weight that occurred *in utero*; therefore, the intake rate for a pregnant woman is used rather than the default infant intake rate as described in the 2008 SONAR (p. 46). No related postnatal effects were reported in available studies.

Reference Dose/Concentration:	HED/Total UF = 2.81/60 = 0.047 mg/kg-d*** (Sprague-Dawley rats)
Source of toxicity value:	Determined by MDH in 2017
Point of Departure (POD):	9.37 mg/kg-d (administered dose $BMDL_{05}$, Heindel 1992/Price 1996b)
Dose Adjustment Factor (DAF):	0.30; MDH-derived Chemical-Specific Toxicokinetic Adjustment, applicable only for pregnant rats and humans: $(CL_H \times F_R \times BW_R)/(CL_R \times F_H \times BW_H) = 0.30$; where CL_H = human renal clearance; CL_R = rat renal clearance; F_H = human oral bioavailability; F_R = rat

	oral bioavailability (using data from US EPA 2014 and Dourson 1998).
Human Equivalent Dose (HED):	POD x DAF = 9.37 mg/kg-d x 0.30 = 2.81 mg/kg-d
Total uncertainty factor (UF):	60
Uncertainty factor allocation:	3 for interspecies differences (for toxicodynamics), 3 for human intraspecies variability in toxicodynamics, 2 for human intraspecies variability in toxicokinetics****, and 3 for database uncertainty (lack of adequate multigenerational reproductive and immunotoxicity studies, and uncertainty regarding sensitivity for the neonatal period)
Critical effect(s):	Decreased fetal weight
Co-critical effect(s):	Fetal skeletal malformations
Additivity endpoint(s):	Developmental

*** MDH added a data base uncertainty factor due to the ambiguity surrounding neonatal exposure to boron and uncertainty regarding the sensitivity of the neonatal period. This resulted in a water concentration of 500 µg/L. MDH considers the short-term RAA to be protective of infants.

****The uncertainty factor (UF) for human intraspecies variability in toxicokinetics is based on chemical-specific data showing dependence of boron kinetics on kidney glomerular filtration rate (GFR). As GFR increases during pregnancy, the UF was based on data characterizing glomerular filtration rates among pregnant women (Dourson 1998, EPA 2014).

Subchronic Non-Cancer Risk Assessment Advice ($nRAA_{Subchronic}$) = 500 µg/L

$$\frac{\text{(Reference Dose, mg/kg-d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Subchronic Intake Rate, L/kg-d)}}$$

$$= \frac{(0.047 \text{ mg/kg-d})^{\#} \times (0.5)^{*} \times (1000 \text{ µg/mg})}{(0.043 \text{ L/kg-d})^{**}}$$

= 547 rounded to **500 µg/L**

[#] The calculated Subchronic RfD (0.21 mg/kg-d) is higher than the Short-term RfD (0.047 mg/kg-d), which is based on developmental effects. The Subchronic RfD must be protective of all types of adverse effects that could occur as a result of subchronic exposure, including short-term effects (MDH 2008, page 34). Therefore, the Short-term RfD is used in place of the calculated Subchronic RfD.

[*] Relative Source Contribution: MDH 2008, Section IV.E.1. See (*) footnote in short-duration.

[**] Intake Rate: MDH 2008, Section IV.E.1. and US EPA 2011, Table 3-3. See (**) footnote in short-duration.

Chronic Non-Cancer Risk Assessment Advice ($nRAA_{Chronic}$) = 500 µg/L

$$\frac{\text{(Reference Dose, mg/kg-d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Chronic Intake Rate, L/kg-d)}}$$

$$= \frac{(0.047^{\#} \text{ mg/kg-d}) \times (0.5)^{*} \times (1000 \text{ µg/mg})}{(0.043 \text{ L/kg-d})^{**}}$$

= 547 rounded to **500 µg/L**

[#] The calculated Chronic RfD (0.17 mg/kg-d) is higher than the Short-term RfD (0.047 mg/kg-d), which is based on developmental effects. The Chronic RfD must be protective of all types of adverse effects that could occur as a

result of chronic exposure, including short-term effects (MDH 2008, page 34). Therefore, the Short-term RfD is used in place of the calculated Chronic RfD.

*Relative Source Contribution: MDH 2008, Section IV.E.1. See (*) footnote in short-duration.

** Intake Rate: MDH 2008, Section IV.E.1. and US EPA 2011, Table 3-3. See (**) footnote in short-duration.

Cancer Risk Assessment Advice (cRAA) = Not Applicable

Cancer classification: Data are inadequate for assessment (US EPA 2014)
Slope factor (SF): Not Applicable
Source of cancer slope factor (SF): Not Applicable
Tumor site(s): Not Applicable

Volatile: No

Summary of Guidance Value History: A non-cancer HRL of 600 µg/L (based on effects of the male reproductive system) was derived for boron, by MDH, in 1993/1994. In 2008, updated Risk Assessment Advice (RAA) was provided by MDH (1,000 µg/L) based on the EPA RfD of 0.20 mg/kg-d for developmental effects, and the 2001 National Academy of Science's estimate of boron ingestion that is safe for adults. In 2017, MDH derived an RAA of 500 µg/L for boron. The guidance value changed as a result of: 1) using MDH's most recent risk assessment methodology; 2) incorporation of a boron-specific DAF for pregnant women (the sensitive population) in the short-term duration; 3) an uncertainty factor of 2 instead of the default of 3 for toxicokinetic variability of the glomerular filtration rate of pregnant women in the short-term duration; and 4) application of a database uncertainty factor. MDH's guidance is categorized as RAA due to the ambiguity surrounding infant neonatal exposure to boron and uncertainty regarding the sensitivity of the neonatal period.

Summary of toxicity testing for health effects identified in the Health Standards Statute (144.0751):

Even if testing for a specific health effect was not conducted for this chemical, information about that effect might be available from studies conducted for other purposes. MDH has considered the following information in developing health protective guidance.

	Endocrine	Immunotoxicity	Development	Reproductive	Neurotoxicity
Tested for specific effect?	Yes	Yes	Yes	Yes	Yes
Effects observed?	Yes[1]	Yes[2]	Yes[3]	Yes[4]	Yes[5]

Comments on extent of testing or effects:

[1] Changes in hormone levels in rats exposed to boron have been observed. Boron exposures 150-300 times higher than the short-term reference dose resulted in increased follicular stimulating hormone (FSH) and luteinizing hormone (LH) levels, as well as decreased basal testosterone levels. However, at extremely high boron exposure (approximately 2,000 times higher), there was no change in serum levels of LH, FSH, thyroid stimulating hormone, or prolactin. In rats dosed with boron at levels 400 times higher than the short-term reference dose, weight changes in the adrenal gland occurred. At boron levels 250 times higher than the short-term reference dose, structural changes in the adrenal glands occurred in beagles. Histological and weight changes in the thyroid began occurring at levels 350 times higher than the short-term reference dose in beagles and rats. In humans, one study reported that nutritional supplementation with boron tablets was reported to affect 17β-estradiol and testosterone concentrations.

[2]There are currently very few immune studies in animals. At boron levels 250 times higher than the short-term reference dose, there was a reduced T-cell response in mice. At levels 150 times higher than the short-term reference dose, mice experienced lymphoid depletion and increased blood cell production in the spleen.

[3]The short-term reference dose is based on developmental effects in rats (reduced fetal weight). Doses 90-fold higher than the short-term reference dose resulted in fetal skeletal variations, whereas doses 600-fold higher resulted in pregnancy resorptions. These effects were also observed in mice and rabbits, beginning at levels 200-fold and 400-fold, respectively, higher than the short-term reference dose. One human epidemiology study associated high boron exposure during the 3rd trimester of pregnancy with shorter and lighter newborns at birth.

[4]Aside from resorptions in the pregnant female mouse, rat, and rabbit occurring at boron levels between 200 to 600 times higher than the short-term reference dose, reproductive effects occurred primarily in the male. These effects in mice and rats include reduced organ weights (testes, prostate, and epididymis), organ atrophy (testes and seminiferous tubules), enzymatic changes in the testes; shrunken scrotum, and reduced fertility and pregnancy rates beginning at levels 150 times higher than the short-term reference dose. At boron levels 300 times higher than the short-term reference dose, sperm defects appeared. At levels 500 times higher than the short-term reference dose, the process of producing sperm ceased. To date, there are no epidemiological studies that confirm fertility loss in humans exposed to high amounts of boron.

[5]Brain chemistry changes occurred in rats dosed with boron at levels 100 times higher than the short-term reference dose. In rats dosed with boron at levels 200 times higher than the short-term reference dose, structural changes in the brain occurred. Additional neurotoxicity studies have not been reported for boron.

Resources Consulted During Review:

Agency for Toxic Substances and Disease Registry - U.S. Department of Health and Human Services. (2010). *Toxicological Profile for Boron*. Atlanta, Georgia. Retrieved from https://www.atsdr.cdc.gov/toxprofiles/tp26.pdf

Allen, B. C., Strong, P. L., Price, C. J., Hubbard, S. A., & Daston, G. P. (1996). Benchmark dose analysis of developmental toxicity in rats exposed to boric acid. *Fundam Appl Toxicol, 32*(2), 194-204.

Baker, M. D., & Bogema, S. C. (1986). Ingestion of boric acid by infants. *Am J Emerg Med, 4*(4), 358-361.

California Environmental Protection Agency - State Water Resources Control Board. Water Quality Goals - Boron. Retrieved from http://www.waterboards.ca.gov/water_issues/programs/water_quality_goals/search.shtml

Cherrington, J. W., & Chernoff, N. (2002). Periods of vertebral column sensitivity to boric acid treatment in CD-1 mice in utero. *Reprod Toxicol, 16*(3), 237-243.

Curry, P. (2012a). *Evaluation of the Potential Immunogenic Activity of Boric Acid Using the Sheep Red Cell Plaque Forming Assay in Mice. Project number: 2328/002.* Unpublished Report. IIT Research Institute, Chicago, IL.

Curry, P. (2012b). *Evaluation of the Potential Immunogenic Activity of Boric Acid Using the Sheep Red Cell Plaque Forming Assay in Mice. Project number: 2337/001.* Unpublished report. IIT Research Institute, Chicago, IL.

Dieter, M. P. (1994). Toxicity and carcinogenicity studies of boric acid in male and female B6C3F1 mice. *Environ Health Perspect, 102 Suppl 7*, 93-97.

Dixon, R. L., Lee, I. P., & Sherins, R. J. (1976). Methods to assess reproductive effects of environmental chemicals: studies of cadmium and boron administered orally. *Environ Health Perspect, 13*, 59-67.

Dixon, R. L., Sherins, R. J., & Lee, I. P. (1979). Assessment of environmental factors affecting male fertility. *Environ Health Perspect, 30*, 53-68.

Dourson, M., Maier, A., Meek, B., Renwick, A., Ohanian, E., & Poirier, K. (1998). Boron tolerable intake: re-evaluation of toxicokinetics for data-derived uncertainty factors. *Biol Trace Elem Res, 66*(1-3), 453-463.

EBA Consortium. (2004). *Sodium Tetraborate. Subchronic and chronic studies. Section 6.5. Annex Point IIA6.3/ 6.4/6.5.* Retrieved from http://dissemination.echa.europa.eu/Biocides/ActiveSubstances/0029-08/Data_007.pdf

Fail, P. A., George, J. D., Seely, J. C., Grizzle, T. B., & Heindel, J. J. (1991). Reproductive toxicity of boric acid in Swiss (CD-1) mice: assessment using the continuous breeding protocol. *Fundam Appl Toxicol, 17*(2), 225-239.

Frisbie, S. H., Mitchell, E. J., & Sarkar, B. (2015). Urgent need to reevaluate the latest World Health Organization guidelines for toxic inorganic substances in drinking water. *Environ Health, 14*, 63.

Harari, F., Ronco, A. M., Concha, G., Llanos, M., Grander, M., Castro, F., . . . Vahter, M. (2012). Early-life exposure to lithium and boron from drinking water. *Reprod Toxicol, 34*(4), 552-560.

Hasegawa, R., Hirata-Koizumi, M., Dourson, M. L., Parker, A., Ono, A., & Hirose, A. (2013). Safety assessment of boron by application of new uncertainty factors and their subdivision. *Regul Toxicol Pharmacol, 65*(1), 108-114.

Health Canada. (2014, June 2015). Guidelines for Canadian Drinking Water Quality - Summary Table. Retrieved from http://www.hc-sc.gc.ca/ewh-semt/pubs/water-eau/sum_guide-res_recom/index-eng.php

Health Canada - Natural Health Products Directorate. (2007). *Boron as a Medicinal Ingredient in Oral Natural Health Products*. Ottawa, Ontario. Retrieved from http://www.hc-sc.gc.ca/dhp-mps/alt_formats/hpfb-dgpsa/pdf/pubs/boron-bore-eng.pdf.

Health Canada - Pest Management Regulatory Agency. (2012). *Proposed Re-evaluation Decision. Boric Acid and its Salts (Boron).* Ottawa, Ontario. Retrieved from http://publications.gc.ca/collections/collection_2012/sc-hc/H113-27-2012-3-eng.pdf.

Health Canada - Pest Management Regulatory Agency. (2016). *Boric Acid and its Salts (Boron) Re-evaluation Decision*. Ottawa, Ontario. Retrieved from http://www.hc-sc.gc.ca/cps-spc/alt_formats/pdf/pubs/pest/_decisions/rvd2016-01/rvd2016-01-eng.pdf.

Heindel, J. J., Price, C. J., Field, E. A., Marr, M. C., Myers, C. B., Morrissey, R. E., & Schwetz, B. A. (1992). Developmental toxicity of boric acid in mice and rats. *Fundam Appl Toxicol, 18*(2), 266-277.

Heindel, J. J., Price, C. J., & Schwetz, B. A. (1994). The developmental toxicity of boric acid in mice, rats, and rabbits. *Environ Health Perspect, 102 Suppl 7*, 107-112.

Hubbard, S. A., Sullivan, F.M. (1996). Toxicological effects of inorganic boron compounds in animals: A review of the literature. *The Journal of Trace Elements in Experimental Medicine, 9*(4), 165-173.

Hunt, C. D., Friel, J. K., & Johnson, L. K. (2004). Boron concentrations in milk from mothers of full-term and premature infants. *Am J Clin Nutr, 80*(5), 1327-1333.

Igra, A. M., Harari, F., Lu, Y., Casimiro, E., & Vahter, M. (2016). Boron exposure through drinking water during pregnancy and birth size. *Environ Int, 95*, 54-60.

Ku, W. W., Chapin, R. E., Wine, R. N., & Gladen, B. C. (1993). Testicular toxicity of boric acid (BA): relationship of dose to lesion development and recovery in the F344 rat. *Reprod Toxicol, 7*(4), 305-319.

Lee, I. P., Sherins, R. J., & Dixon, R. L. (1978). Evidence for induction of germinal aplasia in male rats by environmental exposure to boron. *Toxicol Appl Pharmacol, 45*(2), 577-590.

Linder, R. E., Strader, L. F., & Rehnberg, G. L. (1990). Effect of acute exposure to boric acid on the male reproductive system of the rat. *J Toxicol Environ Health, 31*(2), 133-146.

Lopez-Garcia, I., Vinas, P., Romero-Romero, R., Hernandez-Cordoba, M. (2009). Preconcentration and determination of boron in milk, infant formula, and honey samples by solid phase extraction-electrothermal atomic absorption spectrometry. *Spectrochimica Acta Part B, 64*, 179-183.

Minnesota Department of Health (MDH). (2008). Statement of Need and Reasonableness (SONAR), July 11, 2008. Support document relating to Health Risk Limits for Groundwater Rules. Retrieved from http://www.health.state.mn.us/divs/eh/risk/rules/water/hrlsonar08.pdf

Minnesota Department of Health (MDH). (2017). MDH Health Risk Assessment Methods to Incorporate Human Equivalent Dose Calculations into Derivation of Oral Reference Doses (May 2011, revised 2017). Retrieved from http://www.health.state.mn.us/divs/eh/risk/guidance/hedrefguide.pdf

Naghii, M. R., & Samman, S. (1997). The effect of boron supplementation on its urinary excretion and selected cardiovascular risk factors in healthy male subjects. *Biol Trace Elem Res, 56*(3), 273-286.

Narotsky, M. G., Wery, N., Hamby, B.T., Best, D.S., Pacico, N., Picard, J.J., Gofflot, F., Kavlock, R.J. (2003). Effects of boric acid on Hox gene expression and the axial skeleton in the developing rat. In E. J. Massaro, J.M. Rogers, (Ed.), *The skeleton: biochemical, genetic and molecular interactions in development and homeostasis.* Totowa, NJ: Humana Press.

National Academy of Sciences - Institute of Medicine - Food and Nutrition Board. (2001). *Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc.* Retrieved from Washington, D.C.: https://fnic.nal.usda.gov/sites/fnic.nal.usda.gov/files/uploads/vitamin_a_full_report.pdf

National Health and Medical Research Council - Australia. (2011). *Australian Drinking Water Guidelines Paper 6 National Water Quality Management Strategy*. Commonwealth of Australia, Canberra. Retrieved from https://www.nhmrc.gov.au/_files_nhmrc/file/publications/nhmrc_adwg_6_february_2016.pdf.

O'Sullivan, K., & Taylor, M. (1983). Chronic boric acid poisoning in infants. *Arch Dis Child, 58*(9), 737-739.

Pizzorno, L. (2015). Nothing Boring About Boron. *Integr Med (Encinitas), 14*(4), 35-48.

Price, C. J., Marr, M. C., Myers, C. B., Seely, J. C., Heindel, J. J., & Schwetz, B. A. (1996a). The developmental toxicity of boric acid in rabbits. *Fundam Appl Toxicol, 34*(2), 176-187.

Price, C. J., Strong, P. L., Marr, M. C., Myers, C. B., & Murray, F. J. (1996b). Developmental toxicity NOAEL and postnatal recovery in rats fed boric acid during gestation. *Fundam Appl Toxicol, 32*(2), 179-193.

Price, C. J., Strong, P. L., Murray, F. J., & Goldberg, M. M. (1997). Blood boron concentrations in pregnant rats fed boric acid throughout gestation. *Reprod Toxicol, 11*(6), 833-842.

Rainey, C. J., Nyquist, L. A., Coughlin, J. R., & Downing, R. G. (2002). Dietary Boron Intake in the United States: CSFII 1994-1996. *Journal of Food Composition and Analysis, 15*, 237-250.

Robbins, W. A., Wei, F., Elashoff, D. A., Wu, G., Xun, L., & Jia, J. (2008). Y:X sperm ratio in boron-exposed men. *J Androl, 29*(1), 115-121.

Sayli, B. S., Tuccar, E., & Elhan, A. H. (1998). An assessment of fertility in boron-exposed Turkish subpopulations. *Reprod Toxicol, 12*(3), 297-304.

Schroeder, H. A., & Mitchener, M. (1975). Life-term effects of mercury, methyl mercury, and nine other trace metals on mice. *J Nutr, 105*(4), 452-458.

Scialli, A. R., Bonde, J. P., Bruske-Hohlfeld, I., Culver, B. D., Li, Y., & Sullivan, F. M. (2010). An overview of male reproductive studies of boron with an emphasis on studies of highly exposed Chinese workers. *Reprod Toxicol, 29*(1), 10-24.

Seal, B. S., & Weeth, H. J. (1980). Effect of boron in drinking water on the male laboratory rat. *Bull Environ Contam Toxicol, 25*(5), 782-789.

Settimi, L., Elovaara, E., & Savolainen, H. (1982). Effects of extended peroral borate ingestion on rat liver and brain. *Toxicol Lett, 10*(2-3), 219-223.

Toccalino, P. L., Norman, J.E., Booth, N.L., Thompson, J.L., & Zogorski, J.S. (2012, June 2014). Health-based screening levels: benchmarks for evaluating water-quality data. U.S. Geological Survey, National Water-Quality Assessment Program. Retrieved from http://water.usgs.gov/nawqa/HBSL

Treinen, K. A., & Chapin, R. E. (1991). Development of testicular lesions in F344 rats after treatment with boric acid. *Toxicol Appl Pharmacol, 107*(2), 325-335.

U.S. Department of Health and Human Services - National Toxicology Program. (1987). *Toxicology and Carcinogenesis Studies of Boric Acid in B6C3F1 Mice*. Research Triangle Park, NC: National Institutes of Health. Retrieved from https://ntp.niehs.nih.gov/ntp/htdocs/lt_rpts/tr324.pdf.

U.S. Department of Health and Human Services - National Toxicology Program. (1990). Final Report on the Reproductive Toxicity of Boric Acid in CD-1-Swiss Mice. Obtained from NTIS #PB90-253808.

U.S. Environmental Protection Agency (EPA) - Office of Research and Development. (2011). Exposure Factors Handbook: 2011 Edition. Retrieved from https://cfpub.epa.gov/ncea/risk/recordisplay.cfm?deid=236252

U.S. Environmental Protection Agency - IRIS. (2004a). *Boron and Compounds - Chemical Assessment Summary*. Washington, D.C. Retrieved from https://cfpub.epa.gov/ncea/iris/iris_documents/documents/subst/0410_summary.pdf.

U.S. Environmental Protection Agency - IRIS. (2004b). *Toxicological Review of Boron and Compounds*. Washington, D.C. Retrieved from https://cfpub.epa.gov/ncea/iris/iris_documents/documents/toxreviews/0410tr.pdf.

U.S. Environmental Protection Agency - Office of Chemical Safety and Pollution Prevention. (2015). *Boric Acid/Sodium Salts of Boric Acid. Human Health Draft Risk Assessment for Registration Review.* Washington, D.C. Retrieved from https://www.regulations.gov/document?D=EPA-HQ-OPP-2009-0306-0024.

U.S. Environmental Protection Agency - Office of Drinking Water. (2012). 2012 Edition of the Drinking Water Standards and Health Advisories. Retrieved from https://www.epa.gov/sites/production/files/2015-09/documents/dwstandards2012.pdf

U.S. Environmental Protection Agency - Office of Prevention, Pesticides, and Toxic Substances. (2006). *Boric Acid/Sodium Borate Salts: HED Chapter of the Tolerance Reassessment Eligibility Decision Document (TRED).* Washington, D.C.

U.S. Environmental Protection Agency - Office of Research and Development. (1988). Recommendations for and Documentation of Biological Values for Use in Risk Assessment. Retrieved from http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=34855

U.S. Environmental Protection Agency - Office of Science and Technology and the Office of Water. (2008). *Drinking Water Health Advisory for Boron*. Washington, D.C. Retrieved from https://www.epa.gov/sites/production/files/2014-09/documents/drinking_water_health_advisory_for_boron.pdf.

U.S. Environmental Protection Agency - Office of the Science Advisor. (2011). Recommended Use of Body Weight¾ as the Default Method in Derivation of the Oral Reference Dose. Retrieved from http://www.epa.gov/raf/publications/pdfs/recommended-use-of-bw34.pdf

U.S. Environmental Protection Agency - Office of the Science Advisor. (2014). *Guidance for Applying Quantitative Data to Develop Data-Derived Extrapolation Factors for Interspecies and Intraspecies Extrapolation.* Washington, D.C. Retrieved from https://www.epa.gov/sites/production/files/2015-01/documents/ddef-final.pdf.

U.S. Environmental Protection Agency - Office of Water. (2008). *Health Effects Support Document for Boron*. Washington, D.C. Retrieved from https://www.epa.gov/nscep.

Weir, R. J., Jr., & Fisher, R. S. (1972). Toxicologic studies on borax and boric acid. *Toxicol Appl Pharmacol, 23*(3), 351-364.

Wong, L. C., Heimbach, M. D., Truscott, D. R., & Duncan, B. D. (1964). Boric Acid Poisoning: Report of 11 Cases. *Can Med Assoc J, 90*, 1018-1023.

World Health Organization. (2011). *Guidelines for Drinking-water Quality - Fourth Edition*. Retrieved from http://apps.who.int/iris/bitstream/10665/44584/1/9789241548151_eng.pdf