Minnesota Department of Health

Health Based Guidance for Water
Health Risk Assessment Unit, Environmental Health Division
651-201-4899

Adopted as Rule: November 2015

Toxicological Summary for: Dibutyl Phthalate

CAS: **84-74-2**

Synonyms: DBP; Di-n-butyl phthalate; 1,2-Benzenedicarboxylic acid, dibutyl ester; Dibutyl 1,2-benzenedicarboxylate

Acute Non-Cancer Health Risk Limit ($nHRL_{Acute}$) = 20 µg/L

$$= \frac{\text{(Reference Dose, mg/kg/d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Acute intake rate, L/kg/d)}}$$

$$= \frac{\text{(0.023 mg/kg/d) x (0.2)}^{*} \text{ x (1000 µg/mg)}}{\text{(0.289 L/kg-d)}}$$

= 15.9 rounded to **20 µg/L**

*MDH utilizes the EPA Exposure Decision Tree (EPA 2000) to select appropriate Relative Source Contributions (RSCs) (MDH 2008, Appendix K). Typically an RSC of 0.5 is utilized for nonvolatile contaminants for the acute and short-term durations. However, there is evidence that there are significant known or potential sources other than ingestion of water. Therefore, a 0.2 RSC was selected rather than the default value of 0.5 for nonvolatile contaminants.

Reference Dose/Concentration	0.023 mg/kg-d (Sprague-Dawley rats)
Source of toxicity value	MDH 2012
Point of Departure (POD)	10 mg/kg-d (NOAEL from Lehmann et al 2004 and Boekelheide et al., 2009)
Human Equivalent Dose (MDH, 2011):	10 x 0.23 = 2.3 mg/kg-d (MDH 2011)
Total uncertainty factor:	100
Uncertainty factor allocation:	3 for interspecies extrapolation, 10 for intraspecies variability, and 3 for database uncertainties (additional study is warranted for potential thyroid and immunological effects)
Critical effect(s):	Decreased fetal testosterone, decreased testicular cell number and testes size
Co-critical effect(s):	Decreased fetal testosterone, Sertoli cell atrophy, decreased total cell number and number of seminiferous tubules
Additivity endpoint(s):	Development (E) (male reproductive system)

Short-term Non-Cancer Health Risk Limit ($nHRL_{Short\text{-}term}$) = 20 µg/L

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

$$= \frac{(0.023 \text{ mg/kg/d}) \times (0.2)^{*} \times (1000 \text{ µg/mg})}{(0.289 \text{ L/kg-d})}$$

= 15.9 rounded to **20 µg/L**

* Rationale for selecting an RSC of 0.2 - same explanation as that provided for the acute duration (see above).

Reference Dose/Concentration	0.023 mg/kg-d (Sprague-Dawley rats)
Source of toxicity value	MDH 2012
Point of Departure (POD)	10 mg/kg-d (NOAEL from Lehmann et al 2004 and Boekelheide et al., 2009)
Human Equivalent Dose (MDH, 2011):	10 x 0.23 = 2.3 mg/kg-d (MDH 2011)
Total uncertainty factor:	100
Uncertainty factor allocation:	3 for interspecies extrapolation, 10 for intraspecies variability, and 3 for database uncertainties (additional study is warranted for potential thyroid and immunological effects)
Critical effect(s):	Decreased fetal testosterone, decreased testicular cell number and testes size
Co-critical effect(s):	Decreased fetal testosterone, Sertoli cell atrophy, decreased total cell number and number of seminiferous tubules
Additivity endpoint(s):	Development (E) (male reproductive system)

Subchronic Non-Cancer Health Risk Limit ($nHRL_{Subchronic}$) = Short-term nHRL = 20 µg/L

$$= \frac{(\text{Reference Dose, mg/kg/d}) \times (\text{Relative Source Contribution}) \times (\text{Conversion Factor})}{(\text{Subchronic intake rate, L/kg/d})}$$

$$= \frac{(0.023 \text{ mg/kg/d}) \times (0.2) \times (1000 \text{ µg/mg})}{(0.077 \text{ L/kg-d})}$$

= 59.7 rounded to 60 µg/L

Reference Dose/Concentration: Use the Short-term RfD**

** The calculated Subchronic RfD (0.13 mg/kg-d) is higher than the Short-term RfD (0.023 mg/kg-d), which is based on male reproductive 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 Subchronic RfD is set to the Short-term RfD.

The Subchronic nHRL must be protective of the acute and short-term exposures that occur within the subchronic period and therefore, the Subchronic nHRL is set equal to the Short-term nHRL of 20 µg/L. Additivty endpoints: Developmental (E) (male reproductive system).

Chronic Non-Cancer Health Risk Limit ($nHRL_{Chronic}$) = Short-term nHRL = 20 µg/L

$$= \frac{(\text{Reference Dose, mg/kg/d}) \times (\text{Relative Source Contribution}) \times (\text{Conversion Factor})}{(\text{Chronic intake rate, L/kg/d})}$$

$$= \frac{(0.023\ mg/kg/d) \times (0.2) \times (1000\ \mu g/mg)}{(0.043 L/kg\text{-}d)}$$

= 107 rounded to **100 µg/L**

Reference Dose/Concentration: Use the Short-term RfD**

**The calculated Chronic RfD (0.043 mg/kg-d) is higher than the Short-term RfD (0.023 mg/kg-d), which is based on male reproductive 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 Chronic RfD is set to the Short-term RfD.

The Chronic nHRL must be protective of the acute and short-term exposures that occur within the chronic period and therefore, the Chronic nHRL is set equal to the Short-term nHRL of 20 µg/L. Additivity endpoints: Developmental (E) (male reproductive system).

Cancer Health Risk Limit (cHRL) = "Not Applicable"

Cancer Classification: Group D (not classifiable)
Source: US EPA IRIS 1993

Volatile: Yes (Low)

Summary of Guidance Value History:
The 2012 HBVs (20 µg/L) are 35-fold lower than the 1993 HRL value (700 µg/L) as the result of: 1) utilization of more recent toxicity information resulting in a 4-fold lower RfD; 2) utilization of more recent intake rates which incorporate higher intake rates during early life; and 3) rounding to one significant digit. Health-Based Values (HBVs) developed in 2014 were adopted into rule as HRLs in November 2015.

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

	Endocrine	Immunotoxicity	Development	Reproductive	Neurotoxicity
Tested?	Yes	No[2]	Yes	Yes	Yes
Effects?	Yes[1]	-	Yes[3]	Yes[4]	No[5]

Note: 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. Most chemicals have been subject to multiple studies in which researchers identify a dose where no effects were observed, and the lowest dose that caused one or more effects. A toxicity value based on the effect observed at the lowest dose across all available studies is considered protective of all other effects that occur at higher doses.

Comments on extent of testing or effects:

[1] Some epidemiology studies have identified associations between phthalate exposure and changes in thyroid and reproductive hormones. However, these effects were not consistently observed and studies were generally accompanied by multiple confounding factors such that it is not possible to draw conclusions.

In vitro studies evaluating pituitary cell proliferation and thyroid receptor interactions suggest that DBP may impact thyroid function. The relevance of the *in vitro* effects to *in vivo* is unclear. Potential DBP thyroid effects following *in vivo* exposure have not been evaluated. Changes in thyroid

hormone serum levels were identified as sensitive effects following butyl benzyl phthalate exposure in laboratory animals. The lack of thyroid studies on DBP is part of the rationale for incorporating a database uncertainty factor into the derivation of the RfD.

In studies conducted in laboratory animals changes in FSH, LH and PRL have also been reported but effects were not consistent across doses or time points of evaluation. Disruption of fetal testes steroidogenesis was been identified as a sensitive effect and forms the basis for the RfD.

[2] Several mechanistic toxicological studies and epidemiological studies have been conducted, mainly on other phthalates (e.g., DEHP). The mechanistic studies typically utilized topical or subcutaneous injection as the route of exposure. Epidemiological studies have suggested an association with PVC-related exposure and asthma.

Laboratory animal studies on DEHP suggest immunological effects at doses of similar magnitude to those causing male reproductive developmental effects. The need for immunological study of DBP is part of the rationale for incorporating a database uncertainty factor into the derivation of the RfD.

[3] Some epidemiology studies have identified an association between phthalate exposure and male reproductive and neurobehavioral development. However, effects were not consistently observed and results from these studies are generally accompanied by multiple confounding factors such that it is not possible to draw definite conclusions.

Studies in laboratory animals have identified a variety of developmental effects following exposure to DBP. Disruption of fetal testicular development has been identified as a sensitive effect. Increased malformations and decreased offspring viability were observed at higher doses, doses ~10 to 20-fold higher than those associated with fetal testicular development. The sensitive effects of fetal testicular development and steroidogenesis form the basis of the RfD.

[4] Some epidemiology studies have identified an association between phthalate exposure and male reproductive effects. However, effects were not consistently observed and these studies are generally accompanied by multiple confounding factors such that it is not possible to draw conclusions.

Studies in laboratory animals have identified a variety of male reproductive effects, including testicular effects and decreased fertility. The fetal male reproductive system is more sensitive than the mature male reproductive system following exposure to DBP. Fetal male reproductive effects form the basis of the RfD.

[5] Some epidemiological studies have identified an association between phthalate exposure and changes in neurobehavioral development. However, these studies are generally accompanied by multiple confounding factors such that it is not possible to draw definitive conclusions.

Neurodevelopmental studies have been conducted in laboratory animals. Neurobehavioral impairment was not observed.

References:

Agency for Toxic Substances and Disease Registry (2001). Toxicological Profile for Di-n-Butyl Phthalate.

Australian Guidelines- Natural Resource Management Ministerial Council; Environmental Protection and Heritage Council; and National Health and Medical Research Council. (2008). "Augmentation of Drinking Water Supplies." from http://www.ephc.gov.au/sites/default/files/WQ_AGWR_GL__ADWS_Corrected_Final_%202008

09.pdf.

Aylward LL, SM Hays, M Gagne and K Krishnan (2009). Derivation of Biomonitoring Equivalents for di-n-butyl phthalate (DBP), benzylbutyl phthalate (BzBP), and diethyl phthalate (DEP). *Regulatory Toxicology and Pharmacology* 55: 259-267.

Bao AM, SM Man, XJ Guo, HB Dong, FQ Wang, H Sun, et al. (2011). Effects of di-n-butyl phthalate on male rat reproduction following pubertal exposure. *Asian J Androl* 13: 702-709.

Benson R (2009). Hazard to the developing male reproductive system from cumulative exposure to phthalate esters - dibutyl phthalate, diisobutyl phthalate, butylbenzyl phthalate, diethylhexyl phthalate, dipentyl phthalate, and diisononyl phthalate. *Regulatory Toxicology and Pharmacology* 53: 90-101.

Boekelheide K, E Kleymenova, K Liu, C Swanson and K Gaido (2009). Dose-dependent effects on cell proliferation, seminiferous tubules, and male germ cells in the fetal rat testis following exposure to di(n-butyl) phthalate. *Microscopy Res Tech* 72: 629-638.

California Environmental Protection Agency - OEHHA Proposition 65. "Most Current Proposition 65 No Significant Risk Levels (NSRLs) Maximum Allowable Dose Levels (MADLs)." from http://www.oehha.ca.gov/prop65/getNSRLs.html.

Center for Disease Control (2009). Fourth National Report on Human Exposure to Environmental Chemicals.

Cho SC, SY Bhang, YC Hong, MS Shin, BN Kim, JE Kim, et al. (2010). Relationship between Environmental Phthalate Exposure and the Intelligence of School-Age Children. *Env Health Perspect* 118(7): 1027-1032.

Clewell RA, JJ Kremer, CC Williams, JL Campbell, MA Sochaski, ME Andersen, et al. (2009). Kinetics of selected di-n-butyl phthalate metabolites and fetal testosterone following repeated and single administration in pregnant rats. *Toxicology* 255: 80-90.

Clewell RA, JJ Kremer, CC Williams, JL Campbell Jr, ME Andersen and SJ Borghoff (2008). Tissue exposures to free and glucuronidated monobutylphthalate in the pregnant and fetal rat following exposure to di-n-butylphthalate: evaluation with a PBPK model. *Toxicol Sci* 103(2): 241-259.

Corton JC and PF Lapinskas (2005). Peroxisome Proliferator-Activated Receptors: Mediators of Phthalate Ester-Induced Effects in the Male Reproductive Tract? *Tox Sci* 83: 4-17.

Dobrzynska MM, EJ Tyrkiel and KA Pachocki (2011). Developmental toxicity in mice following paternal exposure to Di-n-butyl phthalate (DBP). *Biomed Environ Sci* 24(5): 569-578.

Engel SM, A Miodovnik, RL Canfield, C Zhu, MJ Silva, AM Calafat, et al. (2010). Prenatal Phthalate Exposure Is Associated with Childhood Behavior and Executive Functioning. *Environ Health Perspect* 118: 565-571.

European Chemical Agency (2008c). Support Document for Identification of Dibutyl Phthalate (DBP) as a Substance of Very High Concern. from http://echa.europa.eu/documents/10162/13638/svhc_supdoc_dibutylphthalate_publication_en.pdf

European Chemical Agency (2011). Annex XV Report. Proposal for a Restriction. Bis(2-ethylhexyl)phthalate (DEHP), Benzyl butyl phthalate (BBP), Dibutyl phthalate (DBP), Diisobutyl phthalate (DIBP). from http://echa.europa.eu/documents/10162/13641/restriction_report_phthalates_en.pdf

European Chemical Bureau (2004). European Union Risk Assessment Report, with addendum 2004, Dibutyl phthalate; CAS No: 84-74-2, EINECS No: 201-557-4 29.

European Chemicals Bureau (2007). European Union Risk Assessment Report. CAS: 85-68-7. Benzyl butyl phthalate (BBP). 76. from http://www.bbp-facts.com/upload/documents/document3.pdf

European Food Safety Authority (EFSA) (2005a). Opinion of the Scientific Panel on Food Additives, Flavourings, Process Aids and Materials in Contact with Food (AFC) on request from the Commission related to Di-Butylphthalate (DBP) for use in food contact materials. from http://www.efsa.europa.eu/en/efsajournal/doc/242.pdf

Foster PMD (2006). Disruption of reproductive development in male rat offspring following in utero exposure to phthalate esters. *Int J Androl* 29: 140-147.

Gaido KW, JB Hensley, D Liu, DG Wallace, S Borghoff, KJ Johnson, et al. (2007). Fetal mounse phthalate exposure shows that gonocyte multinucleation is not associated with decreased testicular testosterone. *Tox Sci* 97(2): 491-503.

Hines EP, AM Calafat, MJ Silva, P Mendola and SE Fenton (2009). Concentrations of Phthalate Metabolites in Milk, Urine, Saliva, and Serum of Lactating North Carolina Women. *Environ Health Perspect* 117: 86-92.

Hoshi H and T Ohtsuka (2009). Adult rats exposed to low-doses of di-n-butyl phthalate during gestation exhibit decreased grooming behavior. *Bull Environ Contam Toxicol* 83: 62-66.

Howdeshell KL, CV Rider, VS Wilson and LE Gray (2008b). Mechanisms of action of phthalate esters, individually and in combination, to induce abnormal reproductive development in male laboratory rats. *Env Res* 108: 168-176.

Howdeshell KL, VS Wilson, J Furr, CR Lambright, CV Rider, CR Blystone, et al. (2008a). A Mixture of Five Phthalate Esters Inhibits Fetal Testicular Testosterone Production in the Sprague-Dawley Rat in a Cumulative, Dose-Additive Manner. *Tox Sci* 105: 153-165.

Huang PC, PL Kuo, YL Guo, PC Liao and CC Lee (2007). Associations between urinary phthalate monoesters and thyroid hormones in pregnant women. *Human Reproduction* 22(10): 2715-2722.

Huang PC, PL Kuo, YY Chou, SJ Lin and CC Lee (2009). Association between prenatal exposure to phthalates and the health of newborns. *Env Intl* 35: 14-20.

Jaakkola JJK and TL Knight (2008). The Role of Exposure to Phthalates from Polyvinyl Chloride Products in the Development of Asthma and Allergies: A Systematic Review and Meta-analysis. *Environ Health Perspect* 116: 845-853.

Johnson K, Heger NE and Boekelheide K (2012). Of mice and men (and rats): phthalate-induced fetal testis endocrine disruption is species-dependent. *Tox Sci* Ahead of Print. June 14, 2012.

doi:10.1093/toxsci/kfs206

Kim Y, EH Ha, EJ Kim, H Park, M Ha, JH Kim, et al. (2011). Prenatal Exposure to Phthalates and Infant Development at 6 Months: Prospective Mothers and Chidren's Environmental Health (MOCEH) Study. *Environ Health Perspect* 119: 1495-1500.

Kolarik B, K Naydenov, M Larsson, CG Bornehag and J Sundell (2008). The association between phthalates in dust and allergic diseases among Bulgarian children. *Env Health Perspect* 116(1): 98-103.

Kwack SJ, KB Kim, HS Kim and BM Lee (2009). Comparative toxicological evaluation of phthalate diesters and metabolites in Sprague-Dawley male rats for risk assessment. *J Tox Env Health, Part A* 72: 1446-1454.

Lee KY, M Shibutani, H Takagi, N Kato, S Takigami, C Uneyama, et al. (2004). Diverse developmental toxicity of di-n-butyl phthalate in both sexes of rat offspring after maternal exposure during teh period from late gestation through lactation. *Toxicology* 203: 221-238.

Lehmann KP, S Phillips, M Sar, PMD Foster and KW Gaido (2004). Dose-dependent alterations in gene expression and testosterone synthesis in the fetal testes of male rats exposed to di(n-butyl) phthalate. *Tox Sci* 81: 60-68.

Lhuguenot JC (2009). Review: Recent European Food Safety Authority toxicological evalautions of major phthalates used in food contact materials. *Mol. Nutr. Food Res.* 53: 1063-1070.

Li S, J Dai, L Zhang, J Zhang, Z Zhang and B Chen (2011). An association of elevated serum prolactin with phthalate exposure in adult men. *Biomed Environ Sci* 24(1): 31-39.

Li Y, M Zhaung, T Li and N Shi (2009). Neurobehavioral toxicity study of dibutyl phthalae on rats following *in utero* and lactational exposure. *J Appl Tox* 29: 603 - 611.

Li Y, T Li, M Zhuang, K Wang, J Zhang and N Shi (2010). High-dose dibutyl phthalate improves performance of F1 generation male rats in spatial learning and increases hippocampal BDNF expression independent of p-CREB immunocontent. *Env Tox Pharm* 29: 32-38.

Lyche JL, AC Gutleb, A Bergman, GS Eriksen, ATJ Murk, E Ropstad, et al. (2009). Reproductive and Developmental Toxicity of Phthalates. *J of Toxicol Env Health, Part B* 12: 225-249.

M Ghisari, E. B.-J. (2009). Effect of plasticizers adn their mixtures on estrogen receptor and thyroid hormone functions. *Tox Letters* 189: 67-77.

Mahood IK, HB Scott, R Brown, N Hallmark, M Walker and RM Sharpe (2007). In utero exposure to di(n-butyl) phthalate adn testicular dysgenesis: comparison of fetal and adult end points and their dose sensitivity. *Envrion Health Perspect* 115 (suppl 1): 55-61.

Main KM, GK Mortensen, MM Kaleva, KA Boisen, IN Damgaart, M Chellakooty, et al. (2006). Human Breast Milk Contamination with Phthalates and Alterations of Endogenous Reproductive Hormones in Infants Three Months of Age. *Env Health Perspect* 114: 270-276.

Marsee K, TJ Woodruff, DA Axelrad, AM Calafat and SH Swan (2006). Estimated Daily Phthalate Exposures in a Population of Mothers of Male Infants Exhibiting Reduced Anogenital Distance.

Envrion Health Perspect 114: 805-809.

Matsumoto M, M Hirata-Koizumi and M Ema (2008). Potential adverse effects of phthalic acid esters on human health: A review of recent studies on reproduction. *Regulatory Toxicology and Pharmacology* 50: 37-49.

McKinnell C, RT Mitchell, M Walker, K Morris, CJH Kelner, WH Wallace, et al. (2009). Effect of fetal or neonatal exposure to monobutyl phthalate (MBP) on testicular development and function in the marmoset. *Human Reproduction* 24(9): 2244-2254.

Meeker JD and KK Ferguson (2011). Relationship between Urinary Phthalate and Bisphenol A Concentrations and Serum Thyroid Measures in U.S. Adults and Adolescents from the National Health and Nutrition Survey (NHANES) 2007-2008. *Environ Health Perspect* 119: 1396-1402.

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

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

Mylchreest E, DG Wallace, RC Cattley and PMD Foster (2000). Dose-dependent alterations in androgen-regulated male reproductive development in rats exposed to di(n-butyl) phthalate during late gestation. *Tox Sci* 55: 143-151.

National Research Council (2008). Phthalates and Cumulative Risk Assessment The Task Ahead.

National Toxicology Progam (2003). NTP-CERHR Monograph on the Potential Human Reproductive and Developmental Effects of Butyl Benzyl Phthalate (BBP).

National Toxicology Program (1995). NTP Technical Report on Toxicity Studies of Dibutyl Phthalate (CAS No. 84-74-2) Administered in Feed to F344/N Rats and B6C3F1 Mice.

National Toxicology Program (2003). NTP-CERHR Monograph on the Potential Human Reproductive and Developmental Effects of Di-n-Butyl Phthalate (DBP).

Pant N, AB Pant, M Shukla, N Mathur, YK Gupta and DK Saxena (2010). Environmental and experimental exposure of phthalate esters: The toxicological consequence on human sperm. *Human and Exper Tox* 30(6): 507-514.

Shi SW, X Hu, F Zhang, G Hu, Y Hao, X Zhang, et al. (2012). Occurrence of thyroid hormone activities in drinking water from Eastern China: Contributions of phthalate esters. *Env Sci Tech* 46: 1811-1818.

Snijder CA, N Roeleveld, E te Velde, EAP Steefers, H Raat, A Hofman, et al. (2012). Occupational exposure to chemicals and fetal growth: the Generation R Study. *Human Reproduction* Advance Access doi:10.1093/humrep/der437.

Stahlhut RW, E van Wijngaarden, TD Dye, S Cook and SH Swan (2007). Concentrations of Urinary Phthalate Metabolites Are Associated with Increased Waist Circumference and Insulin

Resistance in Adult U.S. Males. *Env Health Perspect* 115: 876-882.

Swan SH, F Liu, M Hines, RL Kruse, C Wang, JB Redmon, et al. (2010). Prenatal phthalate exposure and reduced masculine play in boys. *Int J Androl* 33: 259-269.

Tranfo G, L Caporossi, E Paci, C Aragona, D Romanzi, C De Carolis, et al. (2012). Urinary phthalate monoesters concentration in couples with infertility problems. *Tox Letters* doi:10.1016/j.toxlet.2011.11.033.

U.S. Consumer Product Safety Commission (2010a). Toxicity Review of Benzyl-n-butyl Phthalate. from http://www.cpsc.gov/about/cpsia/toxicityBBP.pdf

U.S. Consumer Product Safety Commission (2010b). Toxicity Review of Di-n-butyl Phthalate. from http://www.cpsc.gov/about/cpsia/toxicityDBP.pdf

U.S. Environmental Protection Agency - IRIS. "Integrated Risk Information Systems (IRIS) A-Z List of Substances." from http://cfpub.epa.gov/ncea/iris/index.cfm?fuseaction=iris.showSubstanceList.

U.S. Environmental Protection Agency - Office of Drinking Water. (2011). "2011 Edition of the Drinking Water Standards and Health Advisories." from http://water.epa.gov/action/advisories/drinking/drinking_index.cfm#dw-standards.

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

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." from http://www.epa.gov/raf/publications/pdfs/recommended-use-of-bw34.pdf.

U.S. Environmental Protection Agency - Regional Screening Tables. "Mid-Atlantic Risk Assessment - Regional Screening Table." from http://www.epa.gov/reg3hwmd/risk/human/rb-concentration_table/Generic_Tables/index.htm

U.S. Environmental Protection Agency (2000). Methodology for Deriving Ambient Water Quality Criteria for the Protection of Human Health (2000), U.S. Environmental Protection Agency.

U.S. Environmental Protection Agency (2006a). External Peer Review Draft. Toxicological Review of Dibutyl Phthalate (Di-n-Butyl Phthalate) (CAS No. 84-74-2). In Support of Summary Information on the Integrated Risk Information System (IRIS).

U.S. Environmental Protection Agency (2006b). External Peer Review of Summary for the DiButyl Phthalate Human Health Assessment. Final Report. from http://cfpub.epa.gov/ncea/iris_drafts/recordisplay.cfm?deid=155707

U.S. Environmental Protection Agency (2009b). An Approach to Using Toxicogenomic Data In U.S. EPA Human Health Risk Assessments: A Dibutyl Phthalate Case Study.

Whyatt RM, S Liu, VA Rauh, AM Calafat, AC Just, L Hoepneer, et al. (2011). Maternal Prenatal Urinary Phthalate Metabolite Concentrations and Child Mental, Psychomotor and Behavioral Development at Age Three Years. *Environ Health Perspect* Advance Access

http://dx.doi.org/10.1289/ehp.1103705.

Wine RN, LH Li, LH Barnes, DK Gulati and RE Chapin (1997). Reproductive toxicity of di-n-butylphthalate in a continuous breeding protocol in Sprague-Dawley rats. *Env Health Perspect* 105(1): 102-107.

Wisconsin Department of Health Services (2009). Scientific Support Documentation for CYCLE 9 Revisions of NR 140.10. Groundwater Enforcement Standards & Preventative Action Limit Recommendations. from http://www.sej.org/sites/default/files/WiscTechnicalInfo2009.pdf

Wittassek M, J Angerer, M Kolossa-Gehring, SD Schafer, W Klockenbusch, L Dobler, et al. (2009). Fetal exposure to phthalates - a pilot study. *Int J Hyg Environ Health* 212(5): 492-498.

Wolff MS, SM Engel, GS Berkowitz, X Ye, MJ Silva, C Zhu, et al. (2008). Prenatal Phenol and Phthalate Exposure and Birth Outcomes. *Environ Health Perspect* 116: 1092-1097.

Yolton K, Y Xu, D Strauss, M Altaye, AM Calafat and J Khoury (2011). Prenatal exposure to bisphenol A and phthalates and infant neurobehavior. *Neurotox Teratol* 33: 558-566.

Zhang Y, X Jiang and B Chen (2004). Reproductive and developmental toxicity in F1 Sprague-Dawley male rats exposed to di-n-butyl phthalate in utero and during lactation and determination of its NOAEL. *Reproductive Toxicology* 18: 669-676.