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: Bisphenol A

CAS**: 80-05-7**

Synonyms: BPA; 4'-(1-Methylethylidene)bisphenol 4,4'-Bisphenol A; 4,4'-Isopropylidenediphenol; Phenol, 4,4'-(1-methylethylidene)bis- *p*,*p'*-isopropylidenebisphenol; 2,2-bis(4-hydroxyphenyl)propane

Acute Non-Cancer Health Risk Limit ($nHRL_{Acute}$) = Not Derived (Insufficient Data)

Short-term Non-Cancer Health Risk Limit ($nHRL_{Short\text{-}term}$) = 100 µg/L

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

$$= \frac{\text{(0.16 mg/kg/d) x (0.2*) x (1000 µg/mg)}}{\text{(0.289 L/kg-d)}}$$

= 111 rounded to **100 µg/L**

*MDH utilizes the EPA Exposure Decision Tree (EPA 2000) to select appropriate RSCs. Given the significant potential non-drinking water sources of exposure from multiple sources available for infants, an RSC of 0.2 is selected rather than the default value of 0.5 used for nonvolatile chemicals.

Reference Dose/Concentration	0.16 mg/kg-d (rat)
Source of toxicity value	MDH, 2014
Point of Departure (POD):	2.7 mg/kg-d (NOAEL, Delclos et al. 2014)
Human Equivalent Dose (MDH, 2011:	2.7 x 5.8 = 16 mg/kg-d [chemical-specific DAF for neonatal rats]
Total uncertainty factor:	100
Uncertainty factor allocation	3 for interspecies differences (for toxicodynamics), 10 for intraspecies variability, and 3 for database uncertainty (additional studies to evaluate latent effects of early life exposure, neurobehavioral, immune system, and metabolic disease are warranted)
Critical effect(s):	Developmental (decreased pup body weight), increased total T3 in male pups
Co-critical effect(s):	Developmental (decreased number and viability of offspring, pup and fetal body weight effects, delayed puberty in male and females; decreased weanling spleen and testes weights, undescended testes, seminiferous tubule hypoplasia), Female reproductive (decreased number and viability of offspring; changes in hormone ratios), Liver (changes serum liver parameters, organ weight, morphology and histology), Male reproductive effects (changes in hormone ratios, reduced

	spermatogenesis, organ weights and morphology), Renal (changes in kidney weights, morphology and histology), Thyroid (increased organ weight), Decreased maternal body weight during gestation
Additivity endpoint(s):	Developmental, Female reproductive system (E), Hepatic (liver) system, Male reproductive system (E), Renal (kidney) system, Thyroid (E)

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

(Reference Dose, mg/kg/d) x (Relative Source Contribution) x (Conversion Factor)
(Subchronic intake rate, L/kg-d)

= (0.0065 mg/kg/d) x (0.2) x (1000 µg/mg)
(0.077 L/kg-d)

= 16.9 rounded to **20 µg/L**

Reference Dose/Concentration:	0.0065 mg/kg-d (mouse)
Source of toxicity value:	MDH, 2014
Point of Departure (POD):	5.0 mg/kg-d (NOAEL, Tyl et al. 2008)
Human Equivalent Dose (MDH, 2011):	5 x 0.13 = 0.65 mg/kg-d
Total uncertainty factor:	100
Uncertainty factor allocation:	3 for interspecies differences (for toxicodynamics), 10 for intraspecies variability, and 3 for database uncertainty (additional studies to evaluate latent effects of early life exposure, neurobehavioral, immune system, and metabolic disease are warranted)
Critical effect(s):	Centrilobular hepatocyte hypertrophy; increased kidney weight
Co-critical effect(s):	Increased centrilobular hepatocyte hypertrophy, liver weight effects)
Additivity endpoint(s):	Hepatic (liver) system, Renal (kidney) system

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

(Reference Dose, mg/kg/d) x (Relative Source Contribution) x (Conversion Factor)
(Chronic intake rate, L/kg-d)

= (0.0065 mg/kg/d) x (0.2) x (1000 µg/mg)
(0.043L/kg-d)

= 30.2 rounded to 30 µg/L

Reference Dose/Concentration:	0.0065 mg/kg-d (mouse)
Source of toxicity value:	MDH, 2014
Point of Departure (POD):	5.0 mg/kg-d (NOAEL,Tyl et al. 2008)
Human Equivalent Dose (MDH, 2011):	5 x 0.13 = 0.65
Total uncertainty factor:	100

Uncertainty factor allocation:	3 for interspecies differences (for toxicodynamics), 10 for intraspecies variability, and 3 for database uncertainty (additional studies to evaluate latent effects of early life exposure, neurobehavioral, immune system, and metabolic disease are warranted)
Critical effect(s):	Centrilobular hepatocyte hypertrophy, increased kidney weight
Co-critical effect(s)	Increased centrilobular hepatocyte hypertrophy, liver weight effects
Additivity endpoint(s):	Hepatic (liver) system, Renal (kidney) system

The Chronic nHRL must be protective of the acute, short-term, and subchronic exposures that occur within the chronic period and therefore, the Chronic nHRL is set equal to the Subchronic nHRL of 20 µg/L. Additivity endpoints: Hepatic (liver) system, Renal (kidney) system

Cancer Health Risk Limit (cHRL) = Not Applicable

Cancer classification:	No cancer classification is available for bisphenol A
Slope factor:	Not applicable
Source of slope factor:	Not applicable
Tumor site(s):	Not applicable

Volatile: No

Summary of Guidance Value History:
No previous 1993/1994 HRLs exist for Bisphenol A. In 1998, a chronic noncancer Health-Based Value (nHBV) of 300 µg/L was derived. In 2012, new nHBVs were developed for acute (300 µg/L), short-term (300 µg/L) and subchronic (100 µg/L) durations and the chronic nHBV was lowered to (100 µg/L). In 2014, BPA was re-evaluated. The acute HBV was removed, the short-term value decreased to 100 µg/L and the subchronic/chronic nHBVs decreased to 20 µg/L based upon 1) a re-evaluation of the toxicity data with inclusion of more recent information, and (2) new life-stage toxicokinetic information that resulted in revised dose-adjustment factors (DAFs). In 2015, the 2014 HBVs were adopted into rule as HRLs.

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

	Endocrine	Immunotoxicity	Development	Reproductive	Neurotoxicity
Tested?	Yes	Yes	Yes	Yes	Yes
Effects?	Yes[1]	Yes[2]	Yes[3]	Yes[4]	Yes[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]Unconjugated (free) BPA is a well-known endocrine-active substance and has been extensively studied. BPA is metabolized quickly in the liver to an endocrine-inactive form (i.e., glucuronide conjugate) that is rapidly excreted in human urine. The estrogenic potency of free BPA is more than 1,000-fold lower than estrogens and BPA has a weaker binding affinity to classical hormone receptors than endogenous hormones. Estrogen, testosterone and thyroid hormone levels and hormone receptor results from laboratory animal studies at doses below 5 mg/kg-d have been inconsistent and contradictory. However, study design limitations, dose-response interpretation issues, inconsistencies in results and conflicting data in the low dose region exists. The RfDs are considered protective for endocrine effects in humans, in part, because humans and non-human primates efficiently metabolize BPA to its endocrine-inactive conjugate which is rapidly excreted in the urine. In a rodent study assessing effects resulting from early life (*in utero* and direct dosing for 3 months after birth) changes in estradiol, thyroid hormone, progesterone and prolactin levels were reported only at doses more than 3,000-fold higher than the RfDs presented above. No effects were reported on FSH or LH at doses 30,000 times higher than the subchronic RfD. Effects on serum levels of sex hormone ratios are considered as co-critical effects for the short-term duration.

[2] Immunotoxicity of BPA has not been thoroughly evaluated, but a limited number of studies evaluating either direct or *in utero* exposure to BPA using non-standard test methods suggest that BPA may interfere with immune homeostasis (cytokine activity, macrophage activity, tumor necrosis factor secretion, and T-cell activity). Several studies found no effect on adult spleen or thymus weights or histopathology of adult immune organs but one study reported spleen and thymus atrophy at a dose 4,500 times higher than the short-term RfD. BPA is a skin sensitizer in humans exposed dermally but there is no clear evidence that BPA interferes with overall immune system function. In general, doses more than 90 times higher than the short-term RfD and more than 2,000 times higher than the subchronic/chronic RfDs are required to elicit a significant immune response. A few studies reported immune-related cellular effects at lower doses, including increased IgG1, IL-4, and various splenocyte T-cell populations at doses more than 6 times higher than the subchronic RfD. Inconsistent results have been reported for IgG2a, interferon-ɣ, and splenic cell numbers. These low dose cellular-level effects have not been associated with adverse functional immune outcomes related to enhancement or suppression of response to pathogens and the biological significance is uncertain. Database limitations and uncertainties regarding available immune system data were considered in the derivation of the RfDs. The spleen, an immune system organ, was identified as a co-critical developmental additivity endpoint based on transient organ weight effects in weanling animals.

[3]The National Toxicology Program (NTP) has identified the brain, behavior, and prostate as developmental endpoints of “some concern” for fetuses, infants, and children. In other words, NTP considers there are insufficient data from human studies to support possible effects on the brain, behavior and the prostate; however, limited evidence in some animal studies cannot be dismissed. NTP concluded that the significance of the limited data from animal studies to humans is unknown at this time. See footnote #5 below for information about neurodevelopmental effects for brain and behavior. A few reports suggest that BPA exposure during gestation and infancy may increase susceptibility to prostate cancer, mammary cancer, impact mammary gland development, or contribute to metabolic diseases (e.g., obesity, diabetes) later in life; however, current data are inadequate to determine whether BPA exposure in early life leads to cancer or metabolic disease in adulthood. A statistically significant increase in mammary gland ductal hyperplasia, a potential indicator of mammary gland development, was reported in rats at a dose over 30,000 times higher than the chronic RfD. The biological significance of this finding will not be known until results from an ongoing chronic study become available. Delayed puberty in male and female animals has been reported, although a recent large-scale study in rats found no effects on pubertal onset, except for delayed testes descent reported

at a dose over 1,000 times higher than the short-term RfD. Developmental effects are considered as critical and co-critical effects for the short-term duration RfD and uncertainties related to neurobehavioral effects and metabolic disease are addressed in the derivation of the RfDs using a database uncertainty factor.

[4] Female reproductive effects, including decreased numbers of litters per breeding pair and changes in hormone ratios, are considered co-critical effects in the derivation of the short-term RfD. Estrous cycle effects were reported at doses 450 times higher than the short-term RfD and over 11,000 times higher than the subchronic/chronic RfDs. Male reproductive effects were reported in adult animals and included multinucleated giant cells in seminiferous tubules, reduced spermatogenesis in pubertal animals and various reproductive organ weight effects (testes, prostate, seminal vesicles, and epididymis). Reports of BPA effects on sperm parameters and testosterone are inconsistent. Male and female reproductive effects are considered as co-critical effects for the derivation of the short-term RfD.

[5] NTP has identified the brain and behavior as endpoints of "some concern" for fetuses, infants and children. This means that there are insufficient data from human studies, but limited evidence of potential neurotoxicity in some animal studies cannot be dismissed, although significance to humans is unknown. Experimental evidence in a well-conducted developmental neurotoxicity study in rats does not support brain developmental neuropathological changes in offspring exposed via maternal dietary doses up to 700 times higher than the short-term RfD. Low dose (defined as doses < 5 mg/kg-d) gestational and/or neonatal exposures have been reported to cause various neurodevelopmental effects in offspring in a variety of studies. Some studies suggest possible effects of early life exposure on various sexually dimorphic behaviors, changes in maternal behaviors nursing and nesting behaviors, anxiety, aggression and learning performance resulting from doses below the short-term RfD; however, there has been a lack of consistency, reproducibility and a variety of study design or reporting limitations in existing data. Several brain morphology studies with various methodological flaws and/or using routes of exposure that are not relevant for evaluating the oral route (e.g., injection studies) have reported effects on various biochemical and neurotransmitter gene expression changes in brain tissues. Developmental neurobehavioral endpoints were identified as areas of data uncertainty in the derivation of acute and short-term RfDs/HRLs.

Acute or short-term exposure to adult animals has resulted in nervous system effects in some studies including piloerection, decreased locomotor activity, sedation, lethargy, arched back, and vocalization. These effects occurred at high gavage doses that were over 700 times higher than the short-term RfD. One study reported decreased serum cholinesterase in female rats exposed to a dose that was about 900 times higher than the short-term RfD, but this effect has not been evaluated in other studies and the biological significance is unknown.

References:

Anjum, S., S. Rahman, M. Kaur, F. Ahmad, H. Rashid, R. A. Ansari, et al. (2011). Melatonin ameliorates bisphenol A-induced biochemical toxicity in testicular mitochondria of mouse. *Food and chemical toxicology : an international journal published for the British Industrial Biological Research Association* 49(11): 2849-2854.

Arase, S., K. Ishii, K. Igarashi, K. Aisaki, Y. Yoshio, A. Matsushima, et al. (2011). Endocrine disrupter bisphenol A increases *in situ* estrogen production in the mouse urogenital sinus. *Biology of reproduction* 84(4): 734-742.

Arnich, N., M. C. Canivenc-Lavier, M. Kolf-Clauw, H. Coffigny, J. P. Cravedi, K. Grob, et al. (2011). Conclusions of the French Food Safety Agency on the toxicity of bisphenol A. *International journal of hygiene and environmental health* 214(3): 271-275.

Ashby, J., H. Tinwell, P. A. Lefevre, R. Joiner and J. Haseman (2003). The effect on sperm production in adult Sprague-Dawley rats exposed by gavage to bisphenol A between postnatal days 91-97. *Toxicological sciences : an official journal of the Society of Toxicology* 74(1): 129-138.

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_%20200809.pdf.

Ayyanan, A., O. Laribi, S. Schuepbach-Mallepell, C. Schrick, M. Gutierrez, T. Tanos, et al. (2011). Perinatal exposure to bisphenol a increases adult mammary gland progesterone response and cell number. *Molecular endocrinology* 25(11): 1915-1923.

Basavarajappa, M., C. Chang, T. Han, J. C. Fuscoe, B. K. Delclos and L. Camacho (2014). Effects of bisphenol A (BPA) on transcription in male and female rat mammary glands (meeting abstract). *The Toxicologist: Supplement to Toxicological Sciences* 138(1): 447.

Betancourt, A. M., I. A. Eltoum, R. A. Desmond, J. Russo and C. A. Lamartiniere (2010). *In utero* exposure to bisphenol A shifts the window of susceptibility for mammary carcinogenesis in the rat. *Environmental health perspectives* 118(11): 1614-1619.

Bloom, M. S., D. Kim, F. S. Vom Saal, J. A. Taylor, G. Cheng, J. D. Lamb, et al. (2011b). Bisphenol A exposure reduces the estradiol response to gonadotropin stimulation during *in vitro* fertilization (abstract). *Fertility and sterility* 96(3): 672-677 e672.

Bloom, M. S., F. S. Vom Saal, D. Kim, J. A. Taylor, J. D. Lamb and V. Y. Fujimoto (2011a). Serum unconjugated bisphenol A concentrations in men may influence embryo quality indicators during *in vitro* fertilization (abstract). *Environmental toxicology and pharmacology* 32(2): 319-323.

Braniste, V., A. Jouault, E. Gaultier, A. Polizzi, C. Buisson-Brenac, M. Leveque, et al. (2010). Impact of oral bisphenol A at reference doses on intestinal barrier function and sex differences after perinatal exposure in rats. *Proceedings of the National Academy of Sciences of the United States of America* 107(1): 448-453.

Braun, J. M. and R. Hauser (2011a). Bisphenol A and children's health. *Current opinion in pediatrics* 23(2): 233-239.

Braun, J. M., A. E. Kalkbrenner, A. M. Calafat, K. Yolton, X. Ye, K. N. Dietrich, et al. (2011b). Impact of early-life bisphenol a exposure on behavior and executive function in children. *Pediatrics* 128(5): 873-882.

Brucker-Davis, F., P. Ferrari, M. Boda-Buccino, K. Wagner-Mahler, P. Pacini, J. Gal, et al. (2011). Cord blood thyroid tests in boys born with and without cryptorchidism: correlations with birth parameters and *in utero* xenobiotics exposure. *Thyroid : official journal of the American Thyroid Association* 21(10): 1133-1141.

Cagen, S. Z., J. M. Waechter, Jr., S. S. Dimond, W. J. Breslin, J. H. Butala, F. W. Jekat, et al. (1999b). Normal reproductive organ development in Wistar rats exposed to bisphenol A in the drinking water. *Regulatory toxicology and pharmacology : RTP* 30(2 Pt 1): 130-139.

Calafat, A. M., J. Weuve, X. Ye, L. T. Jia, H. Hu, S. Ringer, et al. (2009). Exposure to bisphenol A and other phenols in neonatal intensive care unit premature infants. *Environmental health perspectives* 117(4): 639-644.

California State Water Resources Control Board (2010). Monitoring Strategies for Chemicals of Emerging Concern (CECs) in Recycled Water. Recommendations of a Science Advisory Panel.

California Water Resources Control Board. (2008). "Water Quality Limits for Consituents and Parameters." from http://www.waterboards.ca.gov/water_issues/programs/water_quality_goals/docs/limit_tables_2008.pdf.

Camacho, L., C. Chang, M. Basavarajappa, T. Han, J. C. Fuscoe, S. Lewis, et al. (2014). Effect of oral bisphenol a (BPA) and ethinyl estradiol (EE2) on genome-wide gene expression in prostates from 4-day old rats (meeting abstract). *The Toxicologist: Supplement to Toxicological Sciences* 138(1): 447.

Cantonwine, D., J. D. Meeker, H. Hu, B. N. Sanchez, H. Lamadrid-Figueroa, A. Mercado-Garcia, et al. (2010). Bisphenol a exposure in Mexico City and risk of prematurity: a pilot nested case control study (abstract reviewed). *Environmental health : a global access science source* 9: 62.

Cardoso, N., M. Pandolfi, J. Lavalle, S. Carbone, O. Ponzo, P. Scacchi, et al. (2011). Probable gamma-aminobutyric acid involvement in bisphenol A effect at the hypothalamic level in adult male rats. *Journal of physiology and biochemistry* 67(4): 559-567.

Carwile, J. L. and K. B. Michels (2011). Urinary bisphenol A and obesity: NHANES 2003-2006. *Environmental research* 111(6): 825-830.

Chapin, R. E., J. Adams, K. Boekelheide, L. E. Gray, Jr., S. W. Hayward, P. S. Lees, et al. (2008). NTP-CERHR expert panel report on the reproductive and developmental toxicity of bisphenol A. *Birth defects research. Part B, Developmental and reproductive toxicology* 83(3): 157-395.

Chou, W. C., J. L. Chen, C. F. Lin, Y. C. Chen, F. C. Shih and C. Y. Chuang (2011). Biomonitoring of bisphenol A concentrations in maternal and umbilical cord blood in regard to birth outcomes and adipokine expression: a birth cohort study in Taiwan. *Environmental health : a global access science source* 10: 94.

Churchwell, M. I., L. Camacho, M. M. Vanlandingham, N. C. Twaddle, E. Sepehr, K. B. Delclos, et al. (2014). Comparison of life-stage-dependent internal dosimetry for bisphenol A, ethinyl estradiol, a reference estrogen, and endogenous estradiol to test an estrogenic mode of action in Sprague Dawley rats. *Toxicological sciences : an official journal of the Society of Toxicology* 139(1): 4-20.

Clayton, E. M., M. Todd, J. B. Dowd and A. E. Aiello (2011). The impact of bisphenol A and triclosan on immune parameters in the U.S. population, NHANES 2003-2006 (reviewed abstract only). *Environmental health perspectives* 119(3): 390-396.

Cox, K. H., J. D. Gatewood, C. Howeth and E. F. Rissman (2010). Gestational exposure to bisphenol A and cross-fostering affect behaviors in juvenile mice. *Hormones and behavior* 58(5): 754-761.

D'Cruz, S. C., R. Jubendradass and P. P. Mathur (2012). Bisphenol A induces oxidative stress and decreases levels of insulin receptor substrate 2 and glucose transporter 8 in rat testis. *Reproductive sciences* 19(2): 163-172.

Delclos, K. B., L. Camacho, S. M. Lewis, M. M. Vanlandingham, J. R. Latendresse, G. R. Olson, et al. (2014). Toxicity evaluation of bisphenol A administered by gavage to Sprague Dawley rats from gestation day 6 through postnatal day 90. *Toxicol Sci* 139(1): 174-197.

Della Seta, D., I. Minder, V. Belloni, A. M. Aloisi, F. Dessi-Fulgheri and F. Farabollini (2006). Pubertal exposure to estrogenic chemicals affects behavior in juvenile and adult male rats. *Hormones and behavior* 50(2): 301-307.

Della Seta, D., I. Minder, F. Dessi-Fulgheri and F. Farabollini (2005). Bisphenol-A exposure during pregnancy and lactation affects maternal behavior in rats. *Brain research bulletin* 65(3): 255-260.

Dobrzynska, M. M. and J. Radzikowska (2012) Genotoxicity and reproductive toxicity of bisphenol A and X-ray/bisphenol A combination in male mice. *Drug and chemical toxicology* DOI: 10.3109/01480545.2011.644561.

Doerge, D. R., N. C. Twaddle, M. Vanlandingham, R. P. Brown and J. W. Fisher (2011a). Distribution of bisphenol A into tissues of adult, neonatal, and fetal Sprague-Dawley rats. *Toxicology and applied pharmacology* 255(3): 261-270.

Doerge, D. R., N. C. Twaddle, M. Vanlandingham and J. W. Fisher (2010a). Pharmacokinetics of bisphenol A in neonatal and adult Sprague-Dawley rats. *Toxicology and applied pharmacology* 247(2): 158-165.

Doerge, D. R., N. C. Twaddle, M. Vanlandingham and J. W. Fisher (2011b). Pharmacokinetics of bisphenol A in neonatal and adult CD-1 mice: inter-species comparisons with Sprague-Dawley rats and rhesus monkeys. *Toxicology letters* 207(3): 298-305.

Doerge, D. R., N. C. Twaddle, M. Vanlandingham and J. W. Fisher (2012). Pharmacokinetics of bisphenol A in serum and adipose tissue following intravenous administration to adult female CD-1 mice. *Toxicology letters* 211(2): 114-119.

Doerge, D. R., N. C. Twaddle, K. A. Woodling and J. W. Fisher (2010b). Pharmacokinetics of bisphenol A in neonatal and adult rhesus monkeys. *Toxicology and applied pharmacology* 248(1): 1-11.

Doerge, D. R., M. Vanlandingham, N. C. Twaddle and K. B. Delclos (2010c). Lactational transfer of bisphenol A in Sprague-Dawley rats. *Toxicology letters* 199(3): 372-376.

Edginton, A. N. and L. Ritter (2009). Predicting plasma concentrations of bisphenol A in children younger than 2 years of age after typical feeding schedules, using a physiologically based toxicokinetic model. *Environmental health perspectives* 117(4): 645-652.

EFSA (European Food Safety Authority) (2006). Opinion of the Scientific Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food on a request from the commission related to 2,2-bis(4-hydroxyphenyl)propane. EFSA Journal. 428: 1-75.

EFSA (European Food Safety Authority) (2008). Toxicokinetics of Bisphenol A. Scientific Opinion of the Panel on Food additives, Flavourings, Processing aids and Materials in Contact with Food (AFC). Adopted on 9 July 2008. EFSA Journal. 759: 1-10.

EFSA (European Food Safety Authority) (2010). Scientific Opinion on Bisphenol A: evaluation of a study investigating its neurodevelopmental toxicity, review of recent scientific literature on its toxicity and advice on the Danish risk assessment of Bisphenol A. EFSA Journal. 8: 1829.

EFSA (European Food Safety Authority) (2014). Endorsed for Public Consultation Draft Scientific Opinion. Draft Scientific Opinion on the risks to public health related to the presence of bisphenol A (BPA) in foodstuffs. *EFSA Journal* volume:(issue): 1-532.

Ema, M., S. Fujii, M. Furukawa, M. Kiguchi, T. Ikka and A. Harazono (2001). Rat two-generation reproductive toxicity study of bisphenol A. *Reproductive toxicology* 15(5): 505-523.

European Chemicals Agency (ECHA). (2011). "Information on Registered Substances, Summary documents for SVHC candidates, Consultations for proposed SVCH candidates." from http://www.echa.europa.eu/home_en.asp.

European Union (2010). European Union Risk Assessment Report: 4,4'-Isopropylidenediphenol (Bisphenol-A) CAS No. 80-05-7, EINECS No: 201-245-8; Risk Assessment.

FAO/WHO (Food and Agriculture Organization and World Health Organization) (2010a). Joint FAO/WHO Expert Meeting to Review Toxicological and Health Aspects of Bisphenol A. Summary Report including Report of Stakeholder Meeting on Bisphenol A. Ottawa, Canada.

FAO/WHO (Food and Agriculture Organization and World Health Organization) (2010b). Background Paper on Carcinogenicity of Bisphenol A presented at FAO/WHO Expert Meeting on Bisphenol A (BPA). Prepared by Dr. John R. Bucher. Ottawa, Canada, 2-5 November 2010.

FAO/WHO (Food and Agriculture Organization and World Health Organization) (2010c). Background Paper on BPA Biomonitoring and Biomarker Studies presented at the FAO/WHO Expert Meeting on Bisphenol A (BPA). Prepared by Dr. Antonia Calafat. Ottawa, Canada, 2-5 November 2010.

FAO/WHO (Food and Agriculture Organization and World Health Organization) (2010d). Background Paper on Genotoxicity of Bisphenol A. Presented that the FAO/WHO Expert Meeting on Bisphenol A (BPA). Prepared by Dr. John R. Bucher. Ottawa, Canada, 2-5 November 2010.

Fenichel, P., H. Dechaux, C. Harthe, J. Gal, P. Ferrari, P. Pacini, et al. (2012). Unconjugated bisphenol A cord blood levels in boys with descended or undescended testes. *Human reproduction* 27(4): 983-990.

Ferguson, S. A., C. D. Law, Jr. and J. S. Abshire (2011). Developmental treatment with bisphenol a or ethinyl estradiol causes few alterations on early preweaning measures. *Toxicological sciences : an official journal of the Society of Toxicology* 124(1): 149-160.

Ferguson, S. A., C. D. Law and G. E. Kissling (2014). Developmental Treatment with Ethinyl Estradiol, but not Bisphenol A, Causes Alterations in Sexually Dimorphic Behaviors in Male and Female Sprague Dawley Rats. *Toxicological sciences : an official journal of the Society of Toxicology* DOI: 10.1093/toxsci/kfu077.

Fisher, J. W., N. C. Twaddle, M. Vanlandingham and D. R. Doerge (2011). Pharmacokinetic modeling: prediction and evaluation of route dependent dosimetry of bisphenol A in monkeys with extrapolation to humans. *Toxicology and applied pharmacology* 257(1): 122-136.

Golub, M. S., K. L. Wu, F. L. Kaufman, L. H. Li, F. Moran-Messen, L. Zeise, et al. (2010). Bisphenol A: developmental toxicity from early prenatal exposure. *Birth defects research. Part B, Developmental and reproductive toxicology* 89(6): 441-466.

Goncalves, C. R., R. W. Cunha, D. M. Barros and P. E. Martinez (2010). Effects of prenatal and postnatal exposure to a low dose of bisphenol A on behavior and memory in rats. *Environmental toxicology and pharmacology* 30(2): 195-201.

Goodman, J. E., E. E. McConnell, I. G. Sipes, R. J. Witorsch, T. M. Slayton, C. J. Yu, et al. (2006). An updated weight of the evidence evaluation of reproductive and developmental effects of low doses of bisphenol A. *Critical reviews in toxicology* 36(5): 387-457.

Goodman, J. E., R. J. Witorsch, E. E. McConnell, I. G. Sipes, T. M. Slayton, C. J. Yu, et al. (2009). Weight-of-evidence evaluation of reproductive and developmental effects of low doses of bisphenol A. *Critical reviews in toxicology* 39(1): 1-75.

Gray, G., JT Cohen, G Cunha, C Hughes, EE McConnell, L Rhomberg, I Glenn Sipes, D Mattison, (2004). Weight of the Evidence of Low-Dose Reproductive and Developmental Effects of Bisphenol A. *Human and Ecological Risk Assessment* 10: 875-921.

Haighton, L., J. W. Card, B. Lynch and A. Roberts (2012). Bisphenol a and infant neonatal neurobehavior. *Environmental health perspectives* 120(3): a102.

Hanioka, N., H. Oka, K. Nagaoka, S. Ikushiro and S. Narimatsu (2011). Effect of UDP-glucuronosyltransferase 2B15 polymorphism on bisphenol A glucuronidation. *Archives of toxicology* 85(11): 1373-1381.

Hao, J., J. Wang, W. Zhao, L. Ding, E. Gao and W. Yuan (2011 (English abstract)). [Effect of bisphenol A exposure on sex hormone level in occupational women]. *Wei sheng yan jiu = Journal of hygiene research* 40(3): 312-314, 319.

Health Canada (2008). Health Risk Assessment of Bisphenol A from Food Packaging Applications. Bureau of Chemical Safety Food Directorate Health Products and Food Branch.

Hengstler, J. G., H. Foth, T. Gebel, P. J. Kramer, W. Lilienblum, H. Schweinfurth, et al. (2011). Critical evaluation of key evidence on the human health hazards of exposure to bisphenol A. *Critical reviews in toxicology* 41(4): 263-291.

Howdeshell, K. L., J. Furr, C. R. Lambright, V. S. Wilson, B. C. Ryan and L. E. Gray, Jr. (2008). Gestational and lactational exposure to ethinyl estradiol, but not bisphenol A, decreases androgen-dependent reproductive organ weights and epididymal sperm abundance in the male

long evans hooded rat. *Toxicological sciences : an official journal of the Society of Toxicology* 102(2): 371-382.

Iso, T., T. Watanabe, T. Iwamoto, A. Shimamoto and Y. Furuichi (2006). DNA damage caused by bisphenol A and estradiol through estrogenic activity. *Biological & pharmaceutical bulletin* 29(2): 206-210.

Jain, S., C. H. Kumar, U. D. Suranagi and P. K. Mediratta (2011). Protective effect of N-acetylcysteine on bisphenol A-induced cognitive dysfunction and oxidative stress in rats. *Food and chemical toxicology : an international journal published for the British Industrial Biological Research Association* 49(6): 1404-1409.

Jasarevic, E., P. T. Sieli, E. E. Twellman, T. H. Welsh, Jr., T. R. Schachtman, R. M. Roberts, et al. (2011). Disruption of adult expression of sexually selected traits by developmental exposure to bisphenol A. *Proceedings of the National Academy of Sciences of the United States of America* 108(28): 11715-11720.

Jenkins, S., N. Raghuraman, I. Eltoum, M. Carpenter, J. Russo and C. A. Lamartiniere (2009). Oral exposure to bisphenol a increases dimethylbenzanthracene-induced mammary cancer in rats. *Environmental health perspectives* 117(6): 910-915.

Jenkins, S., J. Wang, I. Eltoum, R. Desmond and C. A. Lamartiniere (2011). Chronic Oral Exposure to Bisphenol A Results in a Non-Monotonic Dose Response in Mammary Carcinogenesis and Metastasis in MMTV-erbB2 Mice. *Environmental health perspectives*.

Jones, B. A., J. J. Shimell and N. V. Watson (2011). Pre- and postnatal bisphenol A treatment results in persistent deficits in the sexual behavior of male rats, but not female rats, in adulthood. *Hormones and behavior* 59(2): 246-251.

Jones, B. A. and N. V. Watson (2012). Perinatal BPA exposure demasculinizes males in measures of affect but has no effect on water maze learning in adulthood. *Hormones and behavior* 61(4): 605-610.

Kabil, A., E. Silva and A. Kortenkamp (2008). Estrogens and genomic instability in human breast cancer cells--involvement of Src/Raf/Erk signaling in micronucleus formation by estrogenic chemicals. *Carcinogenesis* 29(10): 1862-1868.

Kandaraki, E., A. Chatzigeorgiou, S. Livadas, E. Palioura, F. Economou, M. Koutsilieris, et al. (2011). Endocrine disruptors and polycystic ovary syndrome (PCOS): elevated serum levels of bisphenol A in women with PCOS (abstract). *The Journal of clinical endocrinology and metabolism* 96(3): E480-484.

Kararli, T. T. (1995). Comparison of the gastrointestinal anatomy, physiology, and biochemistry of humans and commonly used laboratory animals. *Biopharmaceutics & drug disposition* 16(5): 351-380.

Kass, L., G. A. Altamirano, V. L. Bosquiazzo, E. H. Luque and M. Munoz-de-Toro (2012). Perinatal exposure to xenoestrogens impairs mammary gland differentiation and modifies milk composition in Wistar rats. *Reproductive toxicology* 33(3): 390-400.

Kawamoto, Y., W. Matsuyama, M. Wada, J. Hishikawa, M. P. Chan, A. Nakayama, et al. (2007). Development of a physiologically based pharmacokinetic model for bisphenol A in pregnant mice. *Toxicology and applied pharmacology* 224(2): 182-191.

Kim, J. C., H. C. Shin, S. W. Cha, W. S. Koh, M. K. Chung and S. S. Han (2001). Evaluation of developmental toxicity in rats exposed to the environmental estrogen bisphenol A during pregnancy. *Life sciences* 69(22): 2611-2625.

Kim, M. E., H. R. Park, E. J. Gong, S. Y. Choi, H. S. Kim and J. Lee (2011). Exposure to bisphenol A appears to impair hippocampal neurogenesis and spatial learning and memory. *Food and chemical toxicology : an international journal published for the British Industrial Biological Research Association* 49(12): 3383-3389.

Kobayashi, K., K. Ohtani, H. Kubota and M. Miyagawa (2010). Dietary exposure to low doses of bisphenol A: effects on reproduction and development in two generations of C57BL/6J mice. *Congenital anomalies* 50(3): 159-170.

Kunz, N., E. J. Camm, E. Somm, G. Lodygensky, S. Darbre, M. L. Aubert, et al. (2011). Developmental and metabolic brain alterations in rats exposed to bisphenol A during gestation and lactation. *International journal of developmental neuroscience : the official journal of the International Society for Developmental Neuroscience* 29(1): 37-43.

Kwon, S., D. B. Stedman, B. A. Elswick, R. C. Cattley and F. Welsch (2000). Pubertal development and reproductive functions of Crl:CD BR Sprague-Dawley rats exposed to bisphenol A during prenatal and postnatal development. *Toxicological sciences : an official journal of the Society of Toxicology* 55(2): 399-406.

Lakind, J. S., M. Goodman and D. R. Mattison (2014). Bisphenol A and indicators of obesity, glucose metabolism/type 2 diabetes and cardiovascular disease: A systematic review of epidemiologic research. *Critical reviews in toxicology* 44(2): 121-150.

Lang, I. A., T. S. Galloway, A. Scarlett, W. E. Henley, M. Depledge, R. B. Wallace, et al. (2008). Association of urinary bisphenol A concentration with medical disorders and laboratory abnormalities in adults. *JAMA : the journal of the American Medical Association* 300(11): 1303-1310.

LaRocca, J., A. Boyajian, C. Brown, S. D. Smith and M. Hixon (2011). Effects of *in utero* exposure to Bisphenol A or diethylstilbestrol on the adult male reproductive system. *Birth defects research. Part B, Developmental and reproductive toxicology* 92(6): 526-533.

Lawson, C., M. Gieske, B. Murdoch, P. Ye, Y. Li, T. Hassold, et al. (2011). Gene expression in the fetal mouse ovary is altered by exposure to low doses of bisphenol A. *Biology of reproduction* 84(1): 79-86.

Li, D. K., Z. Zhou, M. Miao, Y. He, J. Wang, J. Ferber, et al. (2011). Urine bisphenol-A (BPA) level in relation to semen quality. *Fertility and sterility* 95(2): 625-630 e621-624.

Li, M., Y. Bi, L. Qi, T. Wang, M. Xu, Y. Huang, et al. (2012). Exposure to bisphenol A is associated with low-grade albuminuria in Chinese adults. *Kidney international* 81(11): 1131-1139.

Lind, P. M. and L. Lind (2011). Circulating levels of bisphenol A and phthalates are related to carotid atherosclerosis in the elderly. *Atherosclerosis* 218(1): 207-213.

Liu, Y. M., Y. P. Shen, H. Liang, Y. Wang, X. M. Luo, Z. J. Shen, et al. (2011). [A correlative study on Bisphenol A and recurrent spontaneous abortion] (English abstract only reviewed). *Zhonghua yu fang yi xue za zhi [Chinese journal of preventive medicine]* 45(4): 344-349.

Lopez-Casas, P. P., S. C. Mizrak, L. A. Lopez-Fernandez, M. Paz, D. G. de Rooij and J. del Mazo (2012). The effects of different endocrine disruptors defining compound-specific alterations of gene expression profiles in the developing testis. *Reproductive toxicology* 33(1): 106-115.

Martini, M., D. Miceli, S. Gotti, C. Viglietti-Panzica, E. Fissore, P. Palanza, et al. (2010). Effects of perinatal administration of Bisphenol A on the neuronal nitric oxide synthase expressing system in the hypothalamus and limbic system of CD1 mice. *Journal of neuroendocrinology* 22(9): 1004-1012.

Meeker, J. D., A. M. Calafat and R. Hauser (2010b). Urinary bisphenol A concentrations in relation to serum thyroid and reproductive hormone levels in men from an infertility clinic. *Environmental science & technology* 44(4): 1458-1463.

Meeker, J. D., S. Ehrlich, T. L. Toth, D. L. Wright, A. M. Calafat, A. T. Trisini, et al. (2010a). Semen quality and sperm DNA damage in relation to urinary bisphenol A among men from an infertility clinic. *Reproductive toxicology* 30(4): 532-539.

Meeker, J. D. and K. K. 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 Examination Survey (NHANES) 2007-2008. *Environmental health perspectives* 119(10): 1396-1402.

Melzer, D., L. Harries, R. Cipelli, W. Henley, C. Money, P. McCormack, et al. (2011). Bisphenol a exposure is associated with *in vivo* estrogenic gene expression in adults. *Environmental health perspectives* 119(12): 1788-1793.

Melzer, D., N. J. Osborne, W. E. Henley, R. Cipelli, A. Young, C. Money, et al. (2012). Urinary bisphenol A concentration and risk of future coronary artery disease in apparently healthy men and women. *Circulation* 125(12): 1482-1490.

Mendoza-Rodriguez, C. A., M. Garcia-Guzman, N. Baranda-Avila, S. Morimoto, M. Perrot-Applanat and M. Cerbon (2011). Administration of bisphenol A to dams during perinatal period modifies molecular and morphological reproductive parameters of the offspring. *Reproductive toxicology* 31(2): 177-183.

Miao, M., W. Yuan, Y. He, Z. Zhou, J. Wang, E. Gao, et al. (2011a). *In utero* exposure to bisphenol-A and anogenital distance of male offspring. *Birth defects research. Part A, Clinical and molecular teratology* 91(10): 867-872.

Miao, M., W. Yuan, G. Zhu, X. He and D. K. Li (2011b). *In utero* exposure to bisphenol-A and its effect on birth weight of offspring. *Reproductive toxicology* 32(1): 64-68.

Midoro-Horiuti, T., R. Tiwari, C. S. Watson and R. M. Goldblum (2010). Maternal bisphenol a exposure promotes the development of experimental asthma in mouse pups. *Environmental health perspectives* 118(2): 273-277.

Mielke, H. and U. Gundert-Remy (2009). Bisphenol A levels in blood depend on age and exposure. *Toxicology letters* 190(1): 32-40.

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.

Miodovnik, A., S. M. Engel, C. Zhu, X. Ye, L. V. Soorya, M. J. Silva, et al. (2011 (abstract reviewed)). Endocrine disruptors and childhood social impairment. *Neurotoxicology* 32(2): 261-267.

Morrissey, R. E., J. D. George, C. J. Price, R. W. Tyl, M. C. Marr and C. A. Kimmel (1987). The developmental toxicity of bisphenol A in rats and mice. *Fundamental and applied toxicology : official journal of the Society of Toxicology* 8(4): 571-582.

Morrissey, R. E., J. C. t. Lamb, R. W. Morris, R. E. Chapin, D. K. Gulati and J. J. Heindel (1989). Results and evaluations of 48 continuous breeding reproduction studies conducted in mice. *Fundamental and applied toxicology : official journal of the Society of Toxicology* 13(4): 747-777.

Nagel, S. C., F. S. vom Saal, K. A. Thayer, M. G. Dhar, M. Boechler and W. V. Welshons (1997). Relative binding affinity-serum modified access (RBA-SMA) assay predicts the relative *in vivo* bioactivity of the xenoestrogens bisphenol A and octylphenol. *Environmental health perspectives* 105(1): 70-76.

Nakajima, Y., R. M. Goldblum and T. Midoro-Horiuti (2012). Fetal exposure to bisphenol A as a risk factor for the development of childhood asthma: an animal model study. *Environmental health : a global access science source* 11: 8.

Ning, G., Y. Bi, T. Wang, M. Xu, Y. Xu, Y. Huang, et al. (2011). Relationship of urinary bisphenol A concentration to risk for prevalent type 2 diabetes in Chinese adults: a cross-sectional analysis. *Annals of internal medicine* 155(6): 368-374.

NTP (National Toxicology Program -Center for the Evaluation of Risks to Human Reproduction) (2007). NTP-CERHR Expert Panel Report on the Reproductive and Developmental Toxicity of Bisphenol A.

NTP (National Toxicology Program). (1982). "Carcinogenesis Bioassay of Bisphenol A (CAS No. 80-05-7) in F344 Rats and B6C3F1 Mice (Feed Study)." from http://ntp-apps.niehs.nih.gov/ntp_tox/index.cfm

NTP (National Toxicology Program). (1985a). "Teratologic Evaluation of Bisphenol A: (CAS No. 80-05-7) Administered to CD Rats on Gestational Days 6 through 15." NTIS# PB85-205110/AS, from http://ntp-apps.niehs.nih.gov/ntp_tox/index.cfm

NTP (National Toxicology Program). (1985b). "Teratologic Evaluation of Bisphenol A (CAS NO. 80-05-7) Administered to CD-1 Mice on Gestational Days 6 through 15." NTIS # PB85-205102/AS from http://ntp-apps.niehs.nih.gov/ntp_tox/index.cfm.

NTP (National Toxicology Program). (1985c). "Bisphenol A: (CAS No. 80-05-7) Reproduction and Fertility Assessment in CD-1 Mice When Administered in the Feed." NTP Report # RACB84080 and NTIS #PB86103207, from http://ntp.niehs.nih.gov/index.cfm?objectid=071C89F0-F76A-D393-446C76E3F5AC28EA.

OEHHA (California Office of Environmental Health Hazard Assessment). (2009a). "Evidence on the Developmental and Reproductive Toxicity of Bisphenol A. October 2009.", from http://oehha.ca.gov/prop65/CRNR_notices/state_listing/data_callin/pdf/BPAd050109.pdf.

OEHHA (California Office of Environmental Health Hazard Assessment). (2009b). "Developmental and Reproductive Toxicant Identification Committee Meeting Transcript, July 15, 2009." from http://oehha.ca.gov/prop65/public_meetings/pdf/DARTICTranscript71509.pdf.

OEHHA (California Office of Environmental Health Hazard Assessment). (2011). "Chemical for CIC Consultation: Bisphenol A. July 2011.", from http://oehha.ca.gov/prop65/public_meetings/CIC101211/101211Bisphenol_CIC.pdf.

Okuda, K., M. Takiguchi and S. Yoshihara (2010). *In vivo* estrogenic potential of 4-methyl-2,4-bis(4-hydroxyphenyl)pent-1-ene, an active metabolite of bisphenol A, in uterus of ovariectomized rat. *Toxicology letters* 197(1): 7-11.

Palanza, P. L., K. L. Howdeshell, S. Parmigiani and F. S. vom Saal (2002). Exposure to a low dose of bisphenol A during fetal life or in adulthood alters maternal behavior in mice. *Environmental health perspectives* 110 Suppl 3: 415-422.

Patterson, T. A., N. C. Twaddle, C. S. Roegge, R. J. Callicott, J. W. Fisher and D. R. Doerge (2013). Concurrent determination of bisphenol A pharmacokinetics in maternal and fetal rhesus monkeys. *Toxicology and applied pharmacology* 267(1): 41-48.

Prins, G. S., S. H. Ye, L. Birch, S. M. Ho and K. Kannan (2011). Serum bisphenol A pharmacokinetics and prostate neoplastic responses following oral and subcutaneous exposures in neonatal Sprague-Dawley rats. *Reproductive toxicology* 31(1): 1-9.

Qiao, L., L. Zheng and D. Cai (2010). Study on the levels of the bisphenol A, octylphenol, 4-nonylphenol in serum of precocious girls. (English abstract only reviewed). *Wei sheng yan jiu = Journal of hygiene research* 39(1): 9-12.

Quignot, N., M. Arnaud, F. Robidel, A. Lecomte, M. Tournier, C. Cren-Olive, et al. (2012). Characterization of endocrine-disrupting chemicals based on hormonal balance disruption in male and female adult rats. *Reproductive toxicology* 33(3): 339-352.

Rashid, H., F. Ahmad, S. Rahman, R. A. Ansari, K. Bhatia, M. Kaur, et al. (2009). Iron deficiency augments bisphenol A-induced oxidative stress in rats. *Toxicology* 256(1-2): 7-12.

Ryan, B. C., A. K. Hotchkiss, K. M. Crofton and L. E. Gray, Jr. (2010a). In utero and lactational exposure to bisphenol A, in contrast to ethinyl estradiol, does not alter sexually dimorphic

behavior, puberty, fertility, and anatomy of female LE rats. *Toxicological sciences : an official journal of the Society of Toxicology* 114(1): 133-148.

Ryan, B. C. and J. G. Vandenbergh (2006). Developmental exposure to environmental estrogens alters anxiety and spatial memory in female mice. *Hormones and behavior* 50(1): 85-93.

Ryan, K. K., A. M. Haller, J. E. Sorrell, S. C. Woods, R. J. Jandacek and R. J. Seeley (2010b). Perinatal exposure to bisphenol-a and the development of metabolic syndrome in CD-1 mice. *Endocrinology* 151(6): 2603-2612.

Salian, S., T. Doshi and G. Vanage (2009). Perinatal exposure of rats to Bisphenol A affects the fertility of male offspring. *Life sciences* 85(21-22): 742-752.

Sathyanarayana, S., J. M. Braun, K. Yolton, S. Liddy and B. P. Lanphear (2011). Case report: high prenatal bisphenol a exposure and infant neonatal neurobehavior. *Environmental health perspectives* 119(8): 1170-1175.

Shankar, A. and S. Teppala (2011). Relationship between urinary bisphenol A levels and diabetes mellitus. *The Journal of clinical endocrinology and metabolism* 96(12): 3822-3826.

Shankar, A. and S. Teppala (2012a). Urinary bisphenol A and hypertension in a multiethnic sample of US adults. *Journal of environmental and public health* 2012: 481641.

Shankar, A., S. Teppala and C. Sabanayagam (2012b). Bisphenol A and Peripheral Arterial Disease: Results from the NHANES. *Environmental health perspectives* 120(9): 1297-1300.

Schug, T. T., J. J. Heindel, L. Camacho, K. B. Delclos, P. Howard, A. F. Johnson, et al. (2013). A new approach to synergize academic and guideline-compliant research: the CLARITY-BPA research program. *Reproductive toxicology* 40: 35-40.

Silver, M. K., M. S. O'Neill, M. R. Sowers and S. K. Park (2011). Urinary Bisphenol A and Type-2 Diabetes in U.S. Adults: Data from NHANES 2003-2008. *PloS one* 6(10): e26868.

Snyder, S., RA Trenholm, EM Snyder, GM Bruce, RC Pleus, and JDC Hemming, (2008). Toxicological Relevance of EDCs and Pharmaceuticals in Drinking Water. AWWA Research Foundation.

Spanier, A. J., R. S. Kahn, A. R. Kunselman, R. Hornung, Y. Xu, A. M. Calafat, et al. (2012). Prenatal exposure to bisphenol A and child wheeze from birth to 3 years of age. *Environmental health perspectives* 120(6): 916-920.

Stump, D. G., M. J. Beck, A. Radovsky, R. H. Garman, L. L. Freshwater, L. P. Sheets, et al. (2010). Developmental neurotoxicity study of dietary bisphenol A in Sprague-Dawley rats. *Toxicological sciences : an official journal of the Society of Toxicology* 115(1): 167-182.

Tang-Peronard, J. L., H. R. Andersen, T. K. Jensen and B. L. Heitmann (2011). Endocrine-disrupting chemicals and obesity development in humans: a review. *Obesity reviews : an official journal of the International Association for the Study of Obesity* 12(8): 622-636.

Taylor, J. A., F. S. Vom Saal, W. V. Welshons, B. Drury, G. Rottinghaus, P. A. Hunt, et al. (2011). Similarity of bisphenol A pharmacokinetics in rhesus monkeys and mice: relevance for human exposure. *Environmental health perspectives* 119(4): 422-430.

Teeguarden, J. G., A. M. Calafat, X. Ye, D. R. Doerge, M. I. Churchwell, R. Gunawan, et al. (2011). Twenty-four hour human urine and serum profiles of bisphenol a during high-dietary exposure. *Toxicological sciences : an official journal of the Society of Toxicology* 123(1): 48-57.

Teeguarden, J., S. Hanson-Drury, J. W. Fisher and D. R. Doerge (2013). Are typical human serum BPA concentrations measurable and sufficient to be estrogenic in the general population? *Food and chemical toxicology : an international journal published for the British Industrial Biological Research Association* 62: 949-963.

Tharp, A. P., M. V. Maffini, P. A. Hunt, C. A. VandeVoort, C. Sonnenschein and A. M. Soto (2012). Bisphenol A alters the development of the rhesus monkey mammary gland. *Proceedings of the National Academy of Sciences of the United States of America* 109(21): 8190-8195.

Thayer, K. A., J. J. Heindel, J. R. Bucher and M. A. Gallo (2012). Role of environmental chemicals in diabetes and obesity: a National Toxicology Program workshop review. *Environmental health perspectives* 120(6): 779-789.

Tian, Y. H., J. H. Baek, S. Y. Lee and C. G. Jang (2010). Prenatal and postnatal exposure to bisphenol a induces anxiolytic behaviors and cognitive deficits in mice. *Synapse* 64(6): 432-439.

Tinwell, H., J. Haseman, P. A. Lefevre, N. Wallis and J. Ashby (2002). Normal sexual development of two strains of rat exposed *in utero* to low doses of bisphenol A. *Toxicological sciences : an official journal of the Society of Toxicology* 68(2): 339-348.

Tiwari, D., J. Kamble, S. Chilgunde, P. Patil, G. Maru, D. Kawle, et al. (2012). Clastogenic and mutagenic effects of bisphenol A: an endocrine disruptor. *Mutation research* 743(1-2): 83-90.

Tyl, R. W., C. B. Myers, M. C. Marr, C. S. Sloan, N. P. Castillo, M. M. Veselica, et al. (2008). Two-generation reproductive toxicity study of dietary bisphenol A in CD-1 (Swiss) mice. *Toxicological sciences : an official journal of the Society of Toxicology* 104(2): 362-384.

Tyl, R. W., C. B. Myers, M. C. Marr, B. F. Thomas, A. R. Keimowitz, D. R. Brine, et al. (2002). Three-generation reproductive toxicity study of dietary bisphenol A in CD Sprague-Dawley rats. *Toxicological sciences : an official journal of the Society of Toxicology* 68(1): 121-146.

U.S. Environmental Protection Agency - IRIS. (1993). "Bisphenol A (CASRN 80-05-7)." from http://www.epa.gov/iris/subst/0356.htm.

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. (2010). "Bisphenol A Action Plan (CASRN 80-05-7)." from http://www.epa.gov/oppt/existingchemicals/pubs/actionplans/bpa.html.

U.S. Environmental Protection Agency. (2002). "A Review of the Reference Dose and Reference Concentration Processes. Risk Assessment Forum. EPA/630/P-02/002F."

U.S. Food and Drug Administration (FDA) (2007). Compact Summary of Bisphenol A (BPA) Pharmacokinetics, Memorandum from William Roth and Vanee Komolprasert to Michelle Twarowski, June 1, 2007.

U.S. Food and Drug Administration (FDA) (2012). Indirect Food Additives: Polymers. Final Rule. Federal Register, Vol. 77, No. 137, Tuesday, July 17, 2012. 21 CFR Part 177. Docket No. FDA-2012-F-0031: pp. 41899-41902.

U.S. National Institutes of Environmental Health Sciences (NIEHS). (2012, Last Update: March 14, 2014). "Bisphenol A Controlled Exposure Study, NCT 01573429." Retrieved 4/4/14, from http://clinicaltrials.gov/ct2/show/record/NCT01573429.

Ulutas, O. K., N. Yildiz, E. Durmaz, M. A. Ahbab, N. Barlas and I. Cok (2011). An *in vivo* assessment of the genotoxic potential of bisphenol A and 4-tert-octylphenol in rats. *Archives of toxicology* 85(8): 995-1001.

Viberg, H., A. Fredriksson, S. Buratovic and P. Eriksson (2011). Dose-dependent behavioral disturbances after a single neonatal Bisphenol A dose. *Toxicology* 290(2-3): 188-195.

Volkel, W., M. Kiranoglu and H. Fromme (2008). Determination of free and total bisphenol A in human urine to assess daily uptake as a basis for a valid risk assessment. *Toxicology letters* 179(3): 155-162.

Volkel, W., M. Kiranoglu and H. Fromme (2011). Determination of free and total bisphenol A in urine of infants. *Environmental research* 111(1): 143-148.

vom Saal, F. S., P. S. Cooke, D. L. Buchanan, P. Palanza, K. A. Thayer, S. C. Nagel, et al. (1998). A physiologically based approach to the study of bisphenol A and other estrogenic chemicals on the size of reproductive organs, daily sperm production, and behavior. *Toxicology and industrial health* 14(1-2): 239-260.

Wang, T., M. Li, B. Chen, M. Xu, Y. Xu, Y. Huang, et al. (2012). Urinary bisphenol A (BPA) concentration associates with obesity and insulin resistance. *The Journal of clinical endocrinology and metabolism* 97(2): E223-227.

Weber Lozada, K. and R. A. Keri (2011). Bisphenol A increases mammary cancer risk in two distinct mouse models of breast cancer. *Biology of reproduction* 85(3): 490-497.

Wei, J., Y. Lin, Y. Li, C. Ying, J. Chen, L. Song, et al. (2011). Perinatal exposure to bisphenol A at reference dose predisposes offspring to metabolic syndrome in adult rats on a high-fat diet. *Endocrinology* 152(8): 3049-3061.

Weinhouse, C., O. S. Anderson, I. L. Bergin, D. J. Vandenbergh, J. P. Gyekis, M. A. Dingman, et al. (2014) Dose-Dependent Incidence of Hepatic Tumors in Adult Mice following Perinatal Exposure to Bisphenol A. *Environmental health perspectives* DOI: 10.1289/ehp.1307449.

WHO (2005). Chemical-Specific Adjustment Factors for Interspecies Differences and Human Variability: Guidance Document for Use of Data in Dose/Concentrations-Response Assessment. Harmonization Project Document No. 2. World Health Organization.

Willhite, C. C., G. L. Ball and C. J. McLellan (2008). Derivation of a bisphenol A oral reference dose (RfD) and drinking-water equivalent concentration. *Journal of toxicology and environmental health. Part B, Critical reviews* 11(2): 69-146.

Wolstenholme, J. T., J. A. Taylor, S. R. Shetty, M. Edwards, J. J. Connelly and E. F. Rissman (2011). Gestational exposure to low dose bisphenol A alters social behavior in juvenile mice. *PloS one* 6(9): e25448.

Wu, J. H., X. R. Jiang, G. M. Liu, X. Y. Liu, G. L. He and Z. Y. Sun (2011). Oral exposure to low-dose bisphenol A aggravates testosterone-induced benign hyperplasia prostate in rats. *Toxicology and industrial health* 27(9): 810-819.

Xi, W., C. K. Lee, W. S. Yeung, J. P. Giesy, M. H. Wong, X. Zhang, et al. (2011). Effect of perinatal and postnatal bisphenol A exposure to the regulatory circuits at the hypothalamus-pituitary-gonadal axis of CD-1 mice. *Reproductive toxicology* 31(4): 409-417.

Xu, X., L. Tan, T. Himi, M. Sadamatsu, S. Tsutsumi, M. Akaike, et al. (2011b). Changed preference for sweet taste in adulthood induced by perinatal exposure to bisphenol A-A probable link to overweight and obesity. *Neurotoxicology and teratology* 33(4): 458-463.

Xu, X., D. Tian, X. Hong, L. Chen and L. Xie (2011a). Sex-specific influence of exposure to bisphenol-A between adolescence and young adulthood on mouse behaviors. *Neuropharmacology* 61(4): 565-573.

Xu, X. H., Y. M. Wang, J. Zhang, Q. Q. Luo, Y. P. Ye and Q. Ruan (2010a). Perinatal exposure to bisphenol-A changes N-methyl-D-aspartate receptor expression in the hippocampus of male rat offspring. *Environmental toxicology and chemistry / SETAC* 29(1): 176-181.

Xu, X. H., J. Zhang, Y. M. Wang, Y. P. Ye and Q. Q. Luo (2010b). Perinatal exposure to bisphenol-A impairs learning-memory by concomitant down-regulation of N-methyl-D-aspartate receptors of hippocampus in male offspring mice. *Hormones and behavior* 58(2): 326-333.

Yang, M., J. H. Ryu, R. Jeon, D. Kang and K. Y. Yoo (2009). Effects of bisphenol A on breast cancer and its risk factors. *Archives of toxicology* 83(3): 281-285.

Yang, X., D. R. Doerge and J. W. Fisher (2013). Prediction and evaluation of route dependent dosimetry of BPA in rats at different life stages using a physiologically based pharmacokinetic model. *Toxicology and applied pharmacology* 270(1): 45-59.

Yang, Y. J., Y. C. Hong, S. Y. Oh, M. S. Park, H. Kim, J. H. Leem, et al. (2009). Bisphenol A exposure is associated with oxidative stress and inflammation in postmenopausal women. *Environmental research* 109(6): 797-801.

Yolton, K., Y. Xu, D. Strauss, M. Altaye, A. M. Calafat and J. Khoury (2011). Prenatal exposure to bisphenol A and phthalates and infant neurobehavior. *Neurotoxicology and teratology* 33(5): 558-566.

You, L., X. Zhu, M. J. Shrubsole, H. Fan, J. Chen, J. Dong, et al. (2011). Renal function, bisphenol A, and alkylphenols: results from the National Health and Nutrition Examination Survey (NHANES 2003-2006). *Environmental health perspectives* 119(4): 527-533.