

Memo



Date: February 26, 2007

To: John Stine, Environmental Health Division Director

Via: Larry Gust, Environmental Surveillance and Assessment Section Manager
Pamela Shubat, Health Risk Assessment Unit Supervisor

From: Helen Goeden, Health Risk Assessment Unit staff

Subject: Health Based Values for Perfluorooctane Sulfonate (PFOS)

In 2002 the Minnesota Department of Health (MDH) developed a HBV of 1 ppb for PFOS. Since 2002 additional toxicity data, toxicokinetic data, and reviews of preexisting data have been produced. After a careful review of this information the Health Risk Assessment Unit staff recommends that the HBV for PFOS be lowered to 0.3 ug/L (ppb).

The following information was utilized in generating the revised HBV:

<u>Chemical</u>	<u>CAS #</u>	<u>Endpoint</u>	<u>RfD (mg/kg-d)</u>	<u>HBV (ug/L)</u>	<u>Source</u>
PFOS	1763-23-1	hepatic (liver) system and thyroid	0.000075	0.3	MDH 2007

More detailed information, supporting the development of the HBV, is attached. Please be advised that, although we believe that this number will provide an adequate level of protection, there is a degree of uncertainty associated with all HBVs, and they should be considered provisional. Professional judgment should be used in implementing this HBV. MDH will review this HBV if and when additional studies have been conducted.

The MDH's authority to promulgate health risk limits under the Groundwater Protection Act is limited to situations where degradation has already occurred. Similarly, health-based values, which are unpromulgated exposure values, serve as interim advice issued for specific sites where a contaminant has been detected. As such, neither health risk limits nor health-based values are developed for the purpose of providing an upper limit for degradation.

cc: Larry Gust, MDH
Pam Shubat, MDH
Rita Messing, MDH
Cathy Villas-Horns, MDA
Shelley Burman, MPCA
Paul Hoff, MPCA
Doug Wetzstein, MPCA

ATTACHMENT

DATA FOR DERIVATION OF GROUND WATER HEALTH BASED VALUE (HBV)

Chemical Name: Perfluorooctane Sulfonate (PFOS)

CAS: 1763-23-1 (acid)

29081-56-9 (ammonium salt)

70225-14-8 (diethanolamine salt)

2795-39-3 (potassium salt)

29457-72-5 (lithium salt)

Non-Cancer Health Based Value (HBV) = 0.3 ug/L

$$= \frac{(\text{toxicity value, mg/kg/d}) \times (\text{relative source contribution}) \times (1000 \text{ ug/mg})}{(\text{intake rate, L/kg-d})}$$

$$= \frac{(0.000075 \text{ mg/kg/d}) \times (0.2) \times (1000 \text{ ug/mg})}{(0.048 \text{ L/kg/day})}$$

$$= 0.3 \text{ ug/L}$$

Toxicity value:	0.000075 mg/kg-d (Cynomolgus monkeys)
Source of toxicity value:	MDH 2007 (RfD derived by MDH)
Point of Departure:	minimal LOAEL, 0.15 mg/kg-d
Dose Metric Adjustment:	20 (to adjust for half-life duration of 5.4 years in humans versus 110 - 132 days in Cynomolgus monkeys)
Total uncertainty factor:	100
UF allocation:	3 interspecies toxicodynamic differences, 10 intraspecies variability; and 3 LOAEL-to-NOAEL (for the lack of a no effect dose in the critical study. A value of 3 rather than 10 is utilized because the effect observed at the LOAEL was considered to be of minimal severity)
Critical effect(s)*:	Decreased HDL and T3
Co-critical effect(s)*:	None
Additivity endpoint(s):	Hepatic (liver) system, Thyroid (E)
Secondary effect(s)*:	Developmental (decreased body weight/weight gain, decreased total T4), decreased gestation length, immune system alterations

* for explanation of terms see Glossary located at: <http://www.health.state.mn.us/divs/eh/groundwater/hrlgw/glossary.html>

Cancer Health Risk Limit (HRL) = N/A

Volatile: No

Summary of changes since 2002 HBV:**Toxicity Value (RfD):**

Improved toxicokinetic (e.g., half-life) information allowed for the incorporation of a 20-fold dose-metric adjustment based on half-life differences between humans and monkeys and a 10-fold decrease in the total UF. In 2002 a 30-fold factor (3 interspecies extrapolation + 10 subchronic-to-chronic) was used to address uncertainties around toxicokinetics.

Intake rate:

PFOS, unlike most ground water contaminants, has a long half-life and therefore will accumulate in the body if repeated exposure occurs over long-periods of time. Eventually the internal concentration of PFOS will reach a plateau (steady-state). The length of time to reach steady state conditions is equivalent to approximately 5 half-lives. In the case of PFOS the time to steady-state would be approximately 27 years (5 x human half-life of 5.4 years). The intake rate selected for the revised HBV was a time-weighted average intake of an upper-end consumer over the first 27 years of life (0.048 L/kg-d). This intake rate incorporates the higher intake rates early in life (i.e., infants and children) as well as the accumulation of the chemical over time.

Consideration of Sensitive Populations:

Growth deficits, alterations in thyroid hormone levels (T4 and T3), increased liver weights, and delays in development have been reported in offspring exposed during development. These effects were observed at doses approximately 3 to 7 times higher than the critical study minimal LOAEL. Potential health-based values based on protection of a pregnant woman and her fetus were evaluated. Two scenarios were evaluated: 1) a long-term exposure – exposure to the mother from birth to age 27 years, and 2) a short-term exposure – exposure to an infant. The long-term exposure scenario incorporated accumulation over time and utilized a time-weighted intake rate 0.048 L/kg-d. The short-term exposure scenario did not incorporate accumulation over time but did utilize a young infant intake rate of 0.221 L/kg-d. The resulting potential HBVs for both scenarios were not lower (i.e., more restrictive) than the HBV based on the selected critical study in monkeys.

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

	Endocrine	Immunotoxicity	Development	Reproductive	Neurotoxicity
Tested?	Sec. Observations ¹	Yes	Yes	Yes	Yes
Effects?	Yes	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 may 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:

¹Thyroid hormonal perturbations have been observed in laboratory animals at dose levels similar to the critical study LOAEL. Alterations in thyroid hormone levels have been identified as critical effect.

²Short-term immunotoxicity studies have shown that PFOS exposure alters several immunologic parameters (suppression of SRBC-specific IgM production and T-cell proliferation, increased natural killer cell activity) at levels below the critical study LOAEL. The biological significance of these effects

is not entirely clear. Further study is needed to determine whether PFOS poses potential health risks to humans as a result of alterations in immune function, however, the MDH will include immune system as a secondary effect at this time.

³ Lower body weight in offspring, decreased T4, increased sternal defects and decreased gestation length have been reported at levels approximately 3-fold higher than the critical study LOAEL. These effects have been identified at secondary effects. At doses approximately 10-fold higher than the LOAEL additional developmental effects (decreased pup viability, developmental delays) are observed.

⁴ A male reproductive study reported decreases in sperm count and increases in sperm deformities at levels 10-fold higher than the critical study LOAEL.

⁵ Hypoactive responses to nicotine has been observed in neonatal mice acutely exposed to levels 75-fold higher than the critical study LOAEL but these effects were not observed at levels 5-fold higher.

Convulsions, severe rigidity and body trembling have been observed in Rhesus monkeys subchronically exposed to levels approximately 30-fold higher than the critical study LOAEL.

The following sources were reviewed in the preparation of the HBV:

Andersen, ME, et. al., 2006 Pharmacokinetic Modeling of Saturable, Renal Resorption of Perfluoroalkylacids in Monkeys – Probing the Determinants of Long Plasma Half-Lives. Toxicology (on-line) doi:10.1016/j.tox.2006.08.004

Austin et al., Neuroendocrine Effects of Perfluorooctane Sulfonate in Rats. Env Health Perspect 111(12)1485-1489, 2003

Bondy G, I Curran, L Coady, C Armstrong, M Parenteau, V Liston, L Hierlihy, J Shenton. Immunomodulation by perfluorooctanesulfonate (PFOS) in a 28-day rat feeding study. The Toxicologist, Abstract #101, 2006.

Butenhoff et al, Perfluorooctane Sulfonate-Induced Perinatal Mortality in Rat Pups is Associated with a Steep Dose-Response. The Toxicologist 66(1): 25 (Abstract 120), 2002.

Butenhoff et al, Thyroid hormone status in adult female rats after an oral dose of perfluorooctanesulfonate (PFOS). The Toxicologist, Abstract #1740, 2005.

Curran et al., Perfluorooctanesulfonate (PFOS) Toxicity in the Rat: A 28-Day Feeding Study. The Toxicologist Abstract #102, 2006

Fan YO, Jin YH, Ma YX, Zhang YH 2005. [Effects of perfluorooctane sulfonate on spermiogenesis function of male rats] [Article in Chinese] Wei Sheng Yan Jiu. Jan;34(1):37-9. (accessed at: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=15862018)

Food Standards Agency, Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment. Second Draft Working Paper on the Tolerable Daily Intake for Perfluorooctane Sulfonate (May 2006).

Food Standards Agency (a United Kingdom Government Agency), Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment. Minutes of the July 11, 2006 meeting.

Food Standards Agency, Committee on Toxicity (COT) of Chemicals in Food, Consumer Products and the Environment. COT Statement on the Tolerable Daily Intake for Perfluorooctane Sulfonate (November 2006).

Fuentes S, MT Colomina, J Rodriguez, P Vicens, JL Domingo. Interactions in developmental toxicology: concurrent exposure to perfluorooctane sulfonate (PFOS) and stress in pregnant mice. Toxicology Letters 164:81-89, 2006.

German Ministry of Health Drinking Water Commission. Provisional evaluation of PFT in drinking water with the guide substances perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS) as examples. July 13, 2006. <http://www.umweltbundesamt.de/uba-info-presse-e/hintergrund/pft-in-drinking-water.pdf>

- Grasty et al, Critical Period for Increased Neonatal Mortality Induced by Perfluorooctane Sulfonate (PFOS) in the Rat. *The Toxicologist* 66(1): 25 (Abstract 118), 2002.
- Grasty et al., Perfluorooctane Sulfonate (PFOS) Alters Lung Development in the Neonatal Rat. *The Toxicologist*, Abstract # 1916, 2004.
- Hu Wen yue, PD. Jones, W DeCoen, L King, P Fraker, J Newsted and JP Giesy 2003. Alterations in cell membrane properties caused by perfluorinated compounds. *Comparative Biochemistry & Physiology Part C* 135:77-88.
- Hu Wen yue, PD. Jones, T Celius and JP Giesy 2005. Identification of genes responsive to PFOS using gene expression profiling. *Environmental Toxicology and Pharmacology Jan* (Vol 19, Issue 1): 57-70.
- Johansson, N, et al., 2006. Neonatal exposure to perfluorooctane sulfonate (PFOS) and perfluorooctanoic acid (PFOA) causes deranged behaviour and increased susceptibility of the cholinergic system in adult mice. *The Toxicologist* Abstract # 1458
- Keil DE, T Mehlman, L Butterworth, MM Peden-Adams. Gestational exposure to PFOS suppresses immunological function in F1 mice. *The Toxicologist* Abstract #882, 2005.
- Lau, et al., 2003. Exposure to Perfluorooctane Sulfonate during Pregnancy in Rat and Mouse. II. Postnatal Evaluations. *Tox Sci* 74: 382-392.
- Lau, et al., 2004. The developmental toxicity of perfluoroalkyl acids and their derivatives. *Tox Appl Pharm* 198:231-241.
- Lau et al, 2006. Evaluation of Perfluorooctane Sulfonate (PFOS) in Rat Brain. *The Toxicologist* Abstract #576.
- Lieder PH, PE Noker, GS Gorman, SC Tanaka, JL Butenhoff. 2006. Elimination Pharmacokinetics of a Series of Perfluorinated Alkyl Carboxylate and Sulfonates (C4, C6 and C8) in Male and Female Cynomolgus Monkeys. Poster presentation at the 2006 European SETAC meeting in Den Hague, Netherlands.
- Logan MN, JR Thibodeaux, RG Hanson, M Strynar, A Lindstrom, C Lau. 2004. Effects of perfluorooctane sulfonate (PFOS) on thyroid hormone status in adult and neonatal rats. *The Toxicologist* Abstract #1917
- Luebker, D. et al., Two-generation reproduction and cross-foster studies of perfluorooctanesulfonate (PFOS) in rats. *Toxicology* 215:126-148, 2005a.
- Luebker, D. et al., Neonatal mortality from in utero exposure to perfluorooctanesulfonate (PFOS) in Sprague-Dawley rats: Dose-response, and biochemical and pharmacokinetic parameters. *Toxicology* 215:149-169, 2005b.

- Karrman A, I Ericson, B van Bavel, PO Darnerud, M Aune, A Glynn, S Lignell and G Lindstrom. 2006. Exposure of Perfluorinated Chemicals through Lactation – Levels of Matched Human Milk and Serum and a Temporal Trend, 1996 – 2004, in Sweden. EHP Online November 2006.
- Maras, M et al., 2006. Estrogen-like properties of fluorotelomer alcohols as revealed by MCF-7 breast cancer cell proliferation. *Env Hlth Perspec* 114(1):100-105.
- Olsen et al, 2005 Evaluation of the half-life ($t_{1/2}$) of elimination of perfluorooctanesulfonate (PFOS), perfluorohexanesulfonate (PFHS) and perfluorooctanoate (PFOA) from human serum. FLUOROS: International Symposium on Fluorinated Alky Organics in the Environment, TOX017)
- Organization for Economic Co-operation and Development (OECD) Nov. 21, 2002. Hazard Assessment of Perfluorooctane Sulfonate (PFOS) and Its Salts.
http://www.oecd.org/document/58/0,2340,en_2649_37465_2384378_1_1_1_37465,00.html#3
 (Accessed Nov. 2002)
- Peden-Adams, et al., Oral Exposure to PFOS for 28 Days Suppresses Immunological Function in B6C3F1 Mice. *The Toxicologist Abstract* #573, 2006.
- Seacat et al., Subchronic Toxicity Studies on Perfluorooctanesulfonate Potassium Salt in Cynomolgus Monkeys. *Tox Sci* 68:249-264, 2002
- Takacs ML and BD Abbot. 2007. Activation of Mouse and Human Peroxisome Proliferator-Activated Receptors (α , β/δ , γ) by Perfluorooctanoic Acid and Perfluorooctane Sulfonate *Toxicological Sciences* 95(1), 108–117.
- Tanaka et al., 2005. Thyroid hormone status in adult rats given oral doses of perfluorooctanesulfonate. FLUOROS: International Symposium on Fluorinated Alky Organics in the Environment, TOX018)
- Tanaka, S, et al. 2006 Effects of Perfluorooctanesulfonate on ^{125}I Elimination in Rats after a Single Intravenous Dose of ^{125}I -Labeled Thyroxine. *The Toxicologist Abstract* #573
- Thayer, K. 2002. Environmental Working Group: Perfluorinated chemicals: Justification for inclusion of this chemical class in the national report on human exposure to environmental chemicals.
http://www.ewg.org/reports/pfcworld/pdf/EWG_CDC.pdf
- Thibodeaux, et al., Exposure to Perfluorooctane Sulfonate during Pregnancy in Rat and Mouse. I. Maternal and Prenatal Evaluations. *Tox Sci* 74: 369-381, 2003.
- Thomford, P. 2002 Final Report: 104 Week Dietary Chronic Toxicity and Carcinogenicity Study with Perfluorooctane Sulfonic Acid Potassium Salt (PFOS: T-6295) in Rats. (Abstract only).
- 3M 2002. Personal communication from Dr. John Butenhoff. Nov 25, 2002. Benchmark doses from the 6-month oral dosing study in monkeys developed by Dr. Gaylor.
- 3M 2003. Environmental and Health Assessment of Perfluorooctane Sulfonic Acid and Its Salts.

UK Environmental Agency 2004. Environmental Risk Evaluation Report: Perfluorooctanesulphonate (PFOS).

U.S. EPA 2003. Toxicological Review of Perfluorooctane Sulfonate (PFOS) In Support of Summary Information on the Integrated Risk Information System (IRIS). September 2003. External Peer Review Draft.

Stevens, Jeff

From: Helen Goeden [Helen.Goeden@state.mn.us]
Sent: Tuesday, March 13, 2007 10:23 AM
To: Seale.Terry@DORSEY.com; John Stine; Larry Gust; Pamela Shubat; Rita Messing; John Butenhoff; Cathy Villas-Horns; Wetzstein, Doug; Paul.Hoff@state.mn.us; Shelley.Burman@state.mn.us; lloreton@steptoe.com; Stevens, Jeff; jbritt@terra1.com
Cc: Helen Goeden; James Kelly; Rick Kipp; Laura Solem
Subject: correction to the PFOS HBV Attachment

Attachments: Corrected PFOS ATTACHMENT.pdf



Corrected
ATTACHMENT

An error in the Uncertainty Factor (UF) Allocation statement within the Attachment to the PFOS HBV memo was found. A corrected version is attached to this e-mail.

If you have any questions, please feel free to contact me.

Thank you.

Helen

Helen Goeden, Ph.D.
Research Scientist 3
helen.goeden@health.state.mn.us
Phone: (651)201- 4904
FAX number: 651-201-4606

Street Address:
625 North Robert Street
St. Paul, MN 55155

Mailing Address:
Environmental Health Division
Minnesota Department of Health
Post Office Box 64975
St. Paul, MN 55164-0975

ATTACHMENT
(Corrected March 9, 2007)

DATA FOR DERIVATION OF GROUND WATER HEALTH BASED VALUE (HBV)

Chemical Name: Perfluorooctane Sulfonate (PFOS)

CAS: 1763-23-1 (acid)

29081-56-9 (ammonium salt)

70225-14-8 (diethanolamine salt)

2795-39-3 (potassium salt)

29457-72-5 (lithium salt)

Non-Cancer Health Based Value (HBV) = 0.3 ug/L

$$= \frac{(\text{toxicity value, mg/kg/d}) \times (\text{relative source contribution}) \times (1000 \text{ ug/mg})}{(\text{intake rate, L/kg-d})}$$

$$= \frac{(0.000075 \text{ mg/kg/d}) \times (0.2) \times (1000 \text{ ug/mg})}{(0.048 \text{ L/kg/day})}$$

$$= 0.3 \text{ ug/L}$$

Toxicity value:	0.000075 mg/kg-d (Cynomolgus monkeys)
Source of toxicity value:	MDH 2007 (RfD derived by MDH)
Point of Departure:	minimal LOAEL, 0.15 mg/kg-d
Dose Metric Adjustment:	20 (to adjust for half-life duration of 5.4 years in humans versus 110 - 132 days in Cynomolgus monkeys)
Total uncertainty factor:	100
UF allocation:	3 interspecies toxicodynamic differences, 10 intraspecies variability; and 3 LOAEL-to-NOAEL (a value of 3 was applied to the study LOAEL rather than using the NOAEL or the default UF of 10 because the effect observed at the LOAEL was considered to be of minimal severity)
Critical effect(s)*:	Decreased HDL and T3
Co-critical effect(s)*:	None
Additivity endpoint(s):	Hepatic (liver) system, Thyroid (E)
Secondary effect(s)*:	Developmental (decreased body weight/weight gain, decreased total T4), decreased gestation length, immune system alterations

* for explanation of terms see Glossary located at:
<http://www.health.state.mn.us/divs/eh/groundwater/hrlgw/glossary.html>

Cancer Health Risk Limit (HRL) = N/A

Volatile: No

Summary of changes since 2002 HBV:**Toxicity Value (RfD):**

Improved toxicokinetic (e.g., half-life) information allowed for the incorporation of a 20-fold dose-metric adjustment based on half-life differences between humans and monkeys and a 10-fold decrease in the total UF. In 2002 a 30-fold factor (3 interspecies extrapolation + 10 subchronic-to-chronic) was used to address uncertainties around toxicokinetics.

Intake rate:

PFOS, unlike most ground water contaminants, has a long half-life and therefore will accumulate in the body if repeated exposure occurs over long-periods of time. Eventually the internal concentration of PFOS will reach a plateau (steady-state). The length of time to reach steady state conditions is equivalent to approximately 5 half-lives. In the case of PFOS the time to steady-state would be approximately 27 years (5 x human half-life of 5.4 years). The intake rate selected for the revised HBV was a time-weighted average intake of an upper-end consumer over the first 27 years of life (0.048 L/kg-d). This intake rate incorporates the higher intake rates early in life (i.e., infants and children) as well as the accumulation of the chemical over time.

Consideration of Sensitive Populations:

Growth deficits, alterations in thyroid hormone levels (T4 and T3), increased liver weights, and delays in development have been reported in offspring exposed during development. These effects were observed at doses approximately 3 to 7 times higher than the critical study minimal LOAEL. Potential health-based values based on protection of a pregnant woman and her fetus were evaluated. Two scenarios were evaluated: 1) a long-term exposure – exposure to the mother from birth to age 27 years, and 2) a short-term exposure – exposure to an infant. The long-term exposure scenario incorporated accumulation over time and utilized a time-weighted intake rate 0.048 L/kg-d. The short-term exposure scenario did not incorporate accumulation over time but did utilize a young infant intake rate of 0.221 L/kg-d. The resulting potential HBVs for both scenarios were not lower (i.e., more restrictive) than the HBV based on the selected critical study in monkeys.

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

	Endocrine	Immunotoxicity	Development	Reproductive	Neurotoxicity
Tested?	Sec. Observations ¹	Yes	Yes	Yes	Yes
Effects?	Yes	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 may 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 Thyroid hormonal perturbations have been observed in laboratory animals at dose levels similar to the critical study LOAEL. Alterations in thyroid hormone levels have been identified as critical effect.

² Short-term immunotoxicity studies have shown that PFOS exposure alters several immunologic parameters (suppression of SRBC-specific IgM production and T-cell proliferation, increased natural killer cell activity) at levels below the critical study LOAEL. The biological significance of these effects

is not entirely clear. Further study is needed to determine whether PFOS poses potential health risks to humans as a result of alterations in immune function, however, the MDH will include immune system as a secondary effect at this time.

³ Lower body weight in offspring, decreased T4, increased sternal defects and decreased gestation length have been reported at levels approximately 3-fold higher than the critical study LOAEL. These effects have been identified at secondary effects. At doses approximately 10-fold higher than the LOAEL additional developmental effects (decreased pup viability, developmental delays) are observed.

⁴ A male reproductive study reported decreases in sperm count and increases in sperm deformities at levels 10-fold higher than the critical study LOAEL.

⁵ Hypoactive responses to nicotine has been observed in neonatal mice acutely exposed to levels 75-fold higher than the critical study LOAEL but these effects were not observed at levels 5-fold higher.

Convulsions, severe rigidity and body trembling have been observed in Rhesus monkeys subchronically exposed to levels approximately 30-fold higher than the critical study LOAEL.

The following sources were reviewed in the preparation of the HBV:

Andersen, ME, et. al., 2006 Pharmacokinetic Modeling of Saturable, Renal Resorption of Perfluoroalkylacids in Monkeys – Probing the Determinants of Long Plasma Half-Lives. Toxicology (on-line) doi:10.1016/j.tox.2006.08.004

Austin et al., Neuroendocrine Effects of Perfluorooctane Sulfonate in Rats. Env Health Perspect 111(12):1485-1489, 2003

Bondy G, I Curran, L Coady, C Armstrong, M Parenteau, V Liston, L Hierlihy, J Shenton. Immunomodulation by perfluorooctanesulfonate (PFOS) in a 28-day rat feeding study. The Toxicologist, Abstract #101, 2006.

Butenhoff et al, Perfluorooctane Sulfonate-Induced Perinatal Mortality in Rat Pups is Associated with a Steep Dose-Response. The Toxicologist 66(1): 25 (Abstract 120), 2002.

Butenhoff et al, Thyroid hormone status in adult female rats after an oral dose of perfluorooctanesulfonate (PFOS). The Toxicologist, Abstract #1740, 2005.

Curran et al., Perfluorooctanesulfonate (PFOS) Toxicity in the Rat: A 28-Day Feeding Study. The Toxicologist Abstract #102, 2006

Fan YO, Jin YH, Ma YX, Zhang YH 2005. [Effects of perfluorooctane sulfonate on spermiogenesis function of male rats] [Article in Chinese] Wei Sheng Yan Jiu. Jan;34(1):37-9. (accessed at: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=15862018)

Food Standards Agency, Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment. Second Draft Working Paper on the Tolerable Daily Intake for Perfluorooctane Sulfonate (May 2006).

Food Standards Agency (a United Kingdom Government Agency), Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment. Minutes of the July 11, 2006 meeting.

Food Standards Agency, Committee on Toxicity (COT) of Chemicals in Food, Consumer Products and the Environment. COT Statement on the Tolerable Daily Intake for Perfluorooctane Sulfonate (November 2006).

Fuentes S, MT Colomina, J Rodriguez, P Vicens, JL Domingo. Interactions in developmental toxicology: concurrent exposure to perfluorooctane sulfonate (PFOS) and stress in pregnant mice. Toxicology Letters 164:81-89, 2006.

German Ministry of Health Drinking Water Commission. Provisional evaluation of PFT in drinking water with the guide substances perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS) as examples. July 13, 2006. <http://www.umweltbundesamt.de/uba-info-presse-e/hintergrund/pft-in-drinking-water.pdf>

Grasty et al, Critical Period for Increased Neonatal Mortality Induced by Perfluorooctane Sulfonate (PFOS) in the Rat. *The Toxicologist* 66(1): 25 (Abstract 118), 2002.

Grasty et al., Perfluorooctane Sulfonate (PFOS) Alters Lung Development in the Neonatal Rat. *The Toxicologist*, Abstract # 1916, 2004.

Hu Wen yue, PD. Jones, W DeCoen, L King, P Fraker, J Newsted and JP Giesy 2003. Alterations in cell membrane properties caused by perfluorinated compounds. *Comparative Biochemistry & Physiology Part C* 135:77-88.

Hu Wen yue, PD. Jones, T Celius and JP Giesy 2005. Identification of genes responsive to PFOS using gene expression profiling. *Environmental Toxicology and Pharmacology* Jan (Vol 19, Issue 1): 57-70.

Johansson, N, et al., 2006. Neonatal exposure to perfluorooctane sulfonate (PFOS) and perfluorooctanoic acid (PFOA) causes deranged behaviour and increased susceptibility of the cholinergic system in adult mice. *The Toxicologist* Abstract # 1458

Keil DE, T Mehlman, L Butterworth, MM Peden-Adams. Gestational exposure to PFOS suppresses immunological function in F1 mice. *The Toxicologist* Abstract #882, 2005.

Lau, et al., 2003. Exposure to Perfluorooctane Sulfonate during Pregnancy in Rat and Mouse. II. Postnatal Evaluations. *Tox Sci* 74: 382-392.

Lau, et al., 2004. The developmental toxicity of perfluoroalkyl acids and their derivatives. *Tox Appl Pharm* 198:231-241.

Lau et al, 2006. Evaluation of Perfluorooctane Sulfonate (PFOS) in Rat Brain. *The Toxicologist* Abstract #576.

Lieder PH, PE Noker, GS Gorman, SC Tanaka, JL Butenhoff. 2006. Elimination Pharmacokinetics of a Series of Perfluorinated Alkyl Carboxylate and Sulfonates (C4, C6 and C8) in Male and Female Cynomolgus Monkeys. Poster presentation at the 2006 European SETAC meeting in Den Hague, Netherlands.

Logan MN, JR Thibodeaux, RG Hanson, M Strynar, A Lindstrom, C Lau. 2004. Effects of perfluorooctane sulfonate (PFOS) on thyroid hormone status in adult and neonatal rats. *The Toxicologist* Abstract #1917

Luebker, D. et al., Two-generation reproduction and cross-foster studies of perfluorooctanesulfonate (PFOS) in rats. *Toxicology* 215:126-148, 2005a.

Luebker, D. et al., Neonatal mortality from in utero exposure to perfluorooctanesulfonate (PFOS) in Sprague-Dawley rats: Dose-response, and biochemical and pharmacokinetic parameters. *Toxicology* 215:149-169, 2005b.

Karrman A, I Ericson, B van Bavel, PO Darnerud, M Aune, A Glynn, S Lignell and G Lindstrom. 2006. Exposure of Perfluorinated Chemicals through Lactation – Levels of Matched Human Milk and Serum and a Temporal Trend, 1996 – 2004, in Sweden. *EHP Online* November 2006.

Maras, M et al., 2006. Estrogen-like properties of fluorotelomer alcohols as revealed by MCF-7 breast cancer cell proliferation. *Env Hlth Perspec* 114(1):100-105.

Olsen et al, 2005 Evaluation of the half-life ($t_{1/2}$) of elimination of perfluorooctanesulfonate (PFOS), perfluorohexanesulfonate (PFHS) and perfluorooctanoate (PFOA) from human serum. FLUOROS: International Symposium on Fluorinated Alky Organics in the Environment, TOX017)

Organization for Economic Co-operation and Development (OECD) Nov. 21, 2002. Hazard Assessment of Perfluorooctane Sulfonate (PFOS) and Its Salts.

http://www.oecd.org/document/58/0,2340,en_2649_37465_2384378_1_1_1_37465,00.html#3
(Accessed Nov. 2002)

Peden-Adams, et al., Oral Exposure to PFOS for 28 Days Suppresses Immunological Function in B6C3F1 Mice. *The Toxicologist Abstract* #573, 2006.

Seacat et al., Subchronic Toxicity Studies on Perfluorooctanesulfonate Potassium Salt in Cynomolgus Monkeys. *Tox Sci* 68:249-264, 2002

Takacs ML and BD Abbot. 2007. Activation of Mouse and Human Peroxisome Proliferator-Activated Receptors (α , β/δ , γ) by Perfluorooctanoic Acid and Perfluorooctane Sulfonate *Toxicological Sciences* 95(1), 108-117.

Tanaka et al., 2005. Thyroid hormone status in adult rats given oral doses of perfluorooctanesulfonate. FLUOROS: International Symposium on Fluorinated Alky Organics in the Environment, TOX018)

Tanaka, S, et al. 2006 Effects of Perfluorooctanesulfonate on ^{125}I Elimination in Rats after a Single Intravenous Dose of ^{125}I -Labeled Thyroxine. *The Toxicologist Abstract* #573

Thayer, K. 2002. Environmental Working Group: Perfluorinated chemicals: Justification for inclusion of this chemical class in the national report on human exposure to environmental chemicals.
http://www.ewg.org/reports/pfcworld/pdf/EWG_CDC.pdf

Thibodeaux, et al., Exposure to Perfluorooctane Sulfonate during Pregnancy in Rat and Mouse. I. Maternal and Prenatal Evaluations. *Tox Sci* 74: 369-381, 2003.

Thomford, P. 2002 Final Report: 104 Week Dietary Chronic Toxicity and Carcinogenicity Study with Perfluorooctane Sulfonic Acid Potassium Salt (PFOS: T-6295) in Rats. (Abstract only).

3M 2002. Personal communication from Dr. John Butenhoff. Nov 25, 2002. Benchmark doses from the 6-month oral dosing study in monkeys developed by Dr. Gaylor.

3M 2003. Environmental and Health Assessment of Perfluorooctane Sulfonic Acid and Its Salts.

UK Environmental Agency 2004. Environmental Risk Evaluation Report: Perfluorooctanesulphonate (PFOS).

U.S. EPA 2003. Toxicological Review of Perfluorooctane Sulfonate (PFOS) In Support of Summary Information on the Integrated Risk Information System (IRIS). September 2003. External Peer Review Draft.