

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.

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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)

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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

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Minnesota Department of Health
Post Office Box 64975
St. Paul, MN 55164-0975

ATTACHMENT
(Corrected March 9, 2007)

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