

Memo



Date: February 26, 2007

To: John Stine, Environmental Health Division Director *JS*

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

From: Helen Goeden, Health Risk Assessment Unit staff *Helen Goeden*

Subject: Health Based Values for Perfluorooctanoic acid (PFOA)

In 2002 the Minnesota Department of Health (MDH) developed a HBV of 7 ppb for PFOA. 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 PFOA be lowered to 0.5 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>
PFOA	335-67-1	hepatic (liver) system, hemotopoietic (blood) system, developmental, and immune system	0.00014	0.5	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 un-promulgated 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.

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ATTACHMENT

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

Chemical Name: Perfluorooctanoic Acid (PFOA)

CAS: 335-67-1(acid)

3825-26-1 (ammonium salt, APFO)

2395-00-8 (potassium salt)

335-95-5 (sodium salt)

Non-Cancer Health Based Value (HBV) = 0.5 ug/L

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

$$= \frac{(0.00014 \text{ mg/kg/d}) \times (0.2) \times (1000 \text{ ug/mg})}{(0.053 \text{ L/kg/day})}$$

$$= 0.5 \text{ ug/L}$$

Toxicity value:	0.00014 mg/kg-d (Cynomolgus monkeys)
Source of toxicity value:	MDH 2007 (RfD derived by MDH)
Point of Departure:	LOAEL, 3 mg/kg-d
Dose Metric Adjustment:	70 (to adjust for half-life duration of 3.8 years in humans versus 20 days in male Cynomolgus monkeys)
Total uncertainty factor:	300
UF allocation:	3 interspecies toxicodynamic differences, 10 intraspecies variability; and 10 LOAEL-to-NOAEL (for lack of a no effect dose in the critical study)
Critical effect(s)*:	Increased relative liver weight
Co-critical effect(s)*:	Reduced number of erythrocytes, reduced body weight and body weight gain, developmental effects (decreased weight gain, delayed developmental progress, hypoactive response in nicotine-induced behavior test), suppressed IgM titers
Additivity endpoint(s):	Hepatic (liver) system, hematopoietic (blood) system, developmental, immune system
Secondary effect(s)*:	Decreased postnatal survival, increase in the incidence of full litter resorptions, altered mammary gland development, decreased thyroid hormones (T4 & T3), disruption of spontaneous behavior, changes in the adrenal cortex

* 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 70-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:

PFOA, 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 PFOA 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 PFOA the time to steady-state would be approximately 19 years (5 x human half-life of 3.8 years). The intake rate selected for the revised HBV was a time-weighted average intake of an upper-end consumer over the first 19 years of life (0.053 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:

Delayed development and growth deficits in the offspring of females mice exposed during pregnancy have been reported at dose levels similar to the LOAEL of the critical study (3 mg/kg-d). Studies have shown that the developmental effects are mainly due to exposure during pregnancy rather than after birth. Possible HBVs, based on protection of a pregnant woman and her fetus, were also calculated. Two scenarios were evaluated: 1) a long-term exposure – exposure to the mother from birth to age 19 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 0.053 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 higher 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	Unclear 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 Hormonal perturbations (e.g., decreased thyroxine (T4) and triiodothyronine (T3) levels) have been observed in laboratory animals at dose levels approximately 3-fold higher than the LOAEL and have been identified as secondary effects.

² Short-term immunotoxicity studies have shown that PFOA exposure suppresses humoral immunity and may adversely affect cell mediated immunity at doses similar to the critical study LOAEL. These effects have been identified as co-critical effects.

³ Developmental delays, lower body weight/weight gain and behavior in offspring have been observed at dose levels similar to the LOAEL. These effects have been identified as co-critical effects. At doses 3-fold higher than the LOAEL additional developmental effects (decreased pup viability, delays in eye opening, increased incidence of full-litter resorption, alterations in mammary gland development) are observed. Effects occurring at doses approximately 3 fold higher have been identified as secondary effects.

⁴ The results of the 2-generational study indicate that fertility is not affected by treatment. Full-litter resorption was observed at dose levels 3-fold higher than the LOAEL, however, it is unclear whether this resulted from maternal toxicity or a direct effect on the developing organism. Altered mammary gland development during the lactational period was observed in mice exposed to dose levels slightly higher than the critical study LOAEL during pregnancy. Increased incidence of full-litter resorption and alterations in mammary gland development have been identified as a secondary effects.

⁵ Hypoactive response to nicotine has been observed in neonatal mice and has been included in the list of co-critical effects. A dose-related increase in ataxia in the female rats was reported in the chronic 2 year study at dose levels greater than the LOAEL, however, this effect was not observed in males with higher body burdens or in 90 day studies utilizing higher doses. Disruption of spontaneous behavior following acute neonatal exposure to doses approximately 3-fold higher than the critical study LOAEL have been observed and are identified as a secondary effect. The SAB has recommended additional neurological testing.

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