Chemical Name: Perfluorobutyrate
CAS: 375-22-4
Synonyms: PFBA, Perfluorobutyric acid, Heptafluorobutyric acid

Acute Non-Cancer Health Risk Limit ($HRL_{\text{acute}}$) = Not Derived*

* While a developmental study is available for PFBA, a human equivalent dose (HED) forms the basis of the reference dose and assumes steady state conditions that cannot be achieved from a one-day exposure. Based on a mean human half-life of 3 days steady-state conditions would be established within ~9-15 days. At the present time the information necessary to estimate less than steady-state doses is not available. The short-term HRL assessment incorporated information regarding developmental effects.

Short-term Non-Cancer Health Risk Limit ($HRL_{\text{short-term}}$) = 7 μg/L

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

$$= \left( 0.0038 \text{ mg/kg/d} \times 0.5 \right) \times \left( 1000 \text{ μg/mg} \right) \div \left( 0.289 \text{ L/kg-d} \right)$$

$$= 6.57 \text{ rounded to 7 μg/L}$$

Toxicity value: 0.0038 mg/kg-d (laboratory animal)
Source of toxicity value: MDH 2008
Point of Departure: 3.01 mg/kg-d ($\text{BMDL}_{10}$, calculated by Butenhoff, 2007 based on NOTOX 2007a 28-day study)
Human Equivalent Dose: 3.01/8 = 0.38 mg/kg-d (factor of 8 adjusts for half-life duration of 3 days in humans versus 9.22 hours in male rats)
Total uncertainty factor: 100
UF allocation: 3 interspecies toxicodynamic differences, 10 intraspecies variability, and 3 database insufficiencies (e.g., study did not identify a NOAEL or acceptable $\text{BMDL}_{10}$ for thyroid effects. A multigeneration reproductive study has not been conducted, however the database does include an extended 1 generation developmental study.)
Critical effect(s): decreased cholesterol
Co-critical effect(s): increased relative thyroid weight, decreased serum total thyroxine (TT4) & dialysis free thyroxine (dFT4)
Additively endpoint(s): Hepatic (liver) system; Thyroid (E)
Secondary effect(s): Delayed eye opening
Subchronic Non-Cancer Health Risk Limit \((HRL_{\text{subchronic}}) = 7 \text{ \mu g/L}\)

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

\[= \frac{(0.0029 \text{ mg/kg/d}) \times (0.2) \times (1000 \text{ \mu g/mg})}{(0.077 \text{ L/kg-d})} \]

\[= 7.53 \text{ rounded to } 8 \text{ \mu g/L} \]

Toxicity value: 0.0029 mg/kg-d (laboratory animal)
Source of toxicity value: MDH 2008
Point of Departure: 6.9 mg/kg-d (NOAEL, NOTOX 2007b 90-day study)
Human Equivalent Dose: 6.9/8 = 0.86 mg/kg-d (factor of 8 adjusts for half-life duration of 3 days in humans versus 9.22 hours in male rats)
Total uncertainty factor: 300

UF allocation: 3 interspecies toxicodynamic differences, 10 intraspecies variability, and 10 database insufficiencies (e.g., assessment of thyroid effects was compromised by missing serum hormone data. A multigeneration reproductive study has not been conducted, however the database does include an extended 1 generation developmental study.)

Critical effect(s): liver weight changes, morphological changes in liver and thyroid gland, decreased TT4, and decreased red blood cells, hematocrit and hemoglobin
Co-critical effect(s): Increased relative thyroid weight, decreased serum TT4 and dFT4, decreased cholesterol, delayed eye opening
Additivity endpoint(s): Developmental; Hematologic (blood) system; Hepatic (liver) system; Thyroid (E)
Secondary effect(s): Increased liver weight and delayed vaginal opening in offspring exposed during gestation

The Subchronic HRL must be protective of short-term exposures that occur within the subchronic period and therefore, the Subchronic nHRL is set equal to the Short-term nHRL of 7 \text{ \mu g/L}. The Additivity endpoints are: Hepatic (liver) system; Thyroid (E).

Chronic Non-Cancer Health Risk Limit \((HRL_{\text{chronic}}) = 7 \text{ \mu g/L}\)

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

\[= \frac{(0.0029 \text{ mg/kg/d}) \times (0.2) \times (1000 \text{ \mu g/mg})}{(0.043 \text{ L/kg-d})} \]

\[= 13.49 \text{ rounded to } 10 \text{ \mu g/L} \]
Toxicity value: 0.0029 mg/kg-d (laboratory animal)
Source of toxicity value: MDH 2008
Point of Departure: 6.9 mg/kg-d (NOAEL, NOTOX 2007b 90-day study)
Human Equivalent Dose: 6.9/8 = 0.86 mg/kg-d (factor of 8 adjusts for half-life duration of 3 days in humans versus 9.22 hours in male rats)
Total uncertainty factor: 300
UF allocation: 3 interspecies toxicodynamic differences, 10 intraspecies variability, and 10 database insufficiencies (e.g., assessment of thyroid effects was compromised by missing serum hormone data. A multigeneration reproductive study has not been conducted, however the database does include an extended 1 generation developmental study.). A subchronic-to-chronic UF was not applied since hepatic effects (and additional hematologic effects) were observed at dose levels similar to those in 28-day study. Concerns regarding the thyroid effects are address by the database UF.
Critical effect(s): liver weight changes, morphological changes in liver and thyroid gland, decreased TT4, and decreased red blood cells, hematocrit and hemoglobin
Co-critical effect(s): Increased relative thyroid weight, decreased serum TT4 and dFT4, decreased cholesterol, delayed eye opening
Additivity endpoint(s): Developmental; Hematologic (blood) system; Hepatic (liver) system; Thyroid (E)
Secondary effect(s): Increased liver weight and delayed vaginal opening in offspring exposed during gestation

The Chronic HRL must be protective of short-term exposures that occur within the chronic period and therefore, the Chronic nHRL is set equal to the Short-term nHRL of 7 μg/L. The Additivity endpoints are: Hepatic (liver) system; Thyroid (E).

Cancer Health Risk Limit (cHRL) = Not Applicable
Cancer classification: Not available
Slope factor: Not available
Source of slope factor: Not applicable
Tumor site(s): Not applicable

Volatile: No

Summary of Guidance Value History:
The draft values for short-term, subchronic and chronic are the same as the 2008 HBV values. An acute (one-day) value of 8 μg/L had been derived in 2008. However, while a developmental study is available for PFBA, a human equivalent dose (HED) forms the basis of the reference dose and assumes steady state conditions that cannot be achieved from a one-day exposure to PFBA. Based on a mean human half-life of 3 days steady-state conditions would be established within ~ 9-15 days. At the present time the information necessary to estimate less than steady-state doses is not available. The short-term HRL assessment incorporated information regarding developmental effects.
The Additivity Endpoints associated with the HRL values above also reflect a change from 2008. Additivity Endpoints are based on the identified critical and co-critical effects. The basis of the 2008 additivity endpoints (developmental and blood system effects) are now considered secondary effects for the short-term, subchronic, and chronic based on a comparison of the HEDs at which these effects occur.

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

<table>
<thead>
<tr>
<th>Tested?</th>
<th>Endocrine</th>
<th>Immunotoxicity</th>
<th>Development</th>
<th>Reproductive</th>
<th>Neurotoxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effects?</td>
<td>Yes&lt;sup&gt;1&lt;/sup&gt;</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>Yes&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td>Secondary Observations</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
</tbody>
</table>

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. Secondary observations, including decreased T4 levels, altered hyperplasia/hypertrophy of the follicular epithelium of the thyroid, and increased thyroid weight were noted in the 28 and 90 day studies. These effects are identified as critical or co-critical effects for the short-term, subchronic and chronic duration HRLs.

2. Developmental delays were observed in offspring of mice exposed during pregnancy. This effect was observed at a human equivalent dose greater than 2-fold higher than the human equivalent dose upon which the short-term RfD is based. Developmental effects are identified as secondary effects.

3. No available neurotoxicity studies. Secondary observations reported in the 28 and 90-day studies include delayed bilateral pupillary reflex for males exposed to a dose > 10-fold higher than the BMDL used as the basis of the short-term, subchronic and chronic HRLs. Histopathological assessment of neuronal tissues (including the optic nerve) and motor activity evaluations did not reveal any treatment-related abnormalities.

**References:**


Butenhoff, JL. 2007a. E-mail correspondence conveying benchmark dose calculations conducted by 3M for liver weight and cholesterol – 28 day PFBA study. February 6, 2007.
Butenhoff, JL. 2007b. Memorandum to Helen Goeden. October 9, 2007. Subject: Data Summary for mechanistic investigation results from samples for NOTOX study no. 470677.

Butenhoff, JL. 2007c. E-mail correspondence conveying BMD estimates from Dr. Gaylor. Attachments: Benchmark Dose Calculations for Ammonium Perfluorobutyrate (PFBA) and Benchmark Dose Calculations for Ammonium Perfluorobutyrate (PFBA) based on Thyroid Hypertrophy/Hyperplasia by Dr. David W. Gaylor, Gaylor and Associates, LLC. December 13, 2007.


Butenhoff, JL. 2008b. E-mail correspondence conveying the final data summary for the thyroid hormone and thyrotropin analyses and Quantitative RT-PCR. Feb. 12, 2008.


Mariash, C. 2008. Response to review questions posed by MDH regarding thyroid effects of PFBA.


NOTOX 2008b. Morphometric analyses on thyroids form male rats treated with MTDID-8391 under NOTOX Project 484492 (Repeated dose 90-day oral toxicity study with MTDID-8391 by daily gavage in the rat, followed by a 3-week recovery period). November 20, 2008.


Rodricks, JV. 2007. Letter to Mr. John Stine with attached copy of ENVIRON’s drinking water health advisory (DWHA).


Zoeller, RT. 2008. Response to review questions posed by MDH regarding thyroid effects of PFBA.