New Jersey Drinking Water Maximum Contaminant Levels for PFOA, PFOS, and PFNA

Gloria B. Post & Brian Pachkowski, NJ Dept. of Environmental Protection; Jessie A. Gleason, NJ Dept. of Health

Abstract

Long-chain PFAAs such PFOA, PFOS, and PFNA are of concern in drinking water because of their widespread occurrence, extreme environmental persistence, long human half-lives, multiple toxicological effects, and associations of low exposures with human health effects. Unlike other well-known PBT contaminants (e.g. dioxins and PCBs), drinking water is an important exposure route for these PFAAs; low levels in drinking water can overwhelm exposures from other sources (e.g. food, consumer products) prevalent in the general population. NJDEP has adopted a drinking water standard (MCL) for PFNA of 13 ng/L, and it has proposed MCLs for PFOA of 14 ng/L and PFOS of 13 ng/L. In the national USEPA UCMR3 study, these three PFAAs occurred more frequently in NJ public water systems than in the U.S. as a whole. The quantitative basis of the risk assessments (i.e. Health-based MCLs) is animal toxicology data, with associations of human health effects with low exposures providing support for a protective approach. Both non-cancer and cancer effects were evaluated, and a detailed mode of action analysis was performed to evaluate human relevance of toxicological effects in animals. Interspecies comparisons were based on internal dose (blood serum PFAA levels) to account for the much longer half-lives of these PFAAs in humans versus laboratory animals. For PFOA, a stringent Health-based MCL of 0.77 ng/L for delayed mammary gland (MG) development in mice was considered to be scientifically valid but was not proposed, primarily because of lack of precedent for use of this effect as the primary basis for risk assessment or health-based standards. The Health-based MCL of 14 ng/L for PFOA for increased liver weight in mice incorporates a database uncertainty factor of 10 for more sensitive effects such as delayed MG development. The Health-based MCL for PFNA is also based on increased liver weight in mice, and the Health-based MCL for PFOS is based on decreased immune response in mice. Analytical considerations (Practical Quantitation Levels) and availability of treatment removal technologies did not limit achievement of the Health-based MCLs. Therefore, the MCLs are identical to the Health-based MCLs.

Current Regulatory Status of NJDEP PFAS MCLs

PFNA – 13 ng/L (adopted - September 2018).

- First MCL in the nation for any PFAS.
- Quarterly monitoring by public water systems has begun:
  - 2019: Small groundwater systems; nontransient noncommunity systems (e.g. schools, factories).
    - Most are also voluntarily reporting PFOA & PFOS.
  - 1st quarter, 2019: ~10% of systems detected 1 or more PFAS above MCL.
  - 2020: Large groundwater systems; all surface water systems.

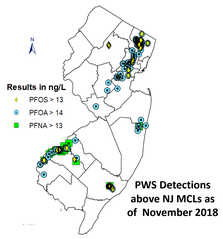
PFOA (14 ng/L) and PFOS (13 ng/L):

- Proposed rule (April 2019):
- In NJ, rule adoptions must occur within one year of rule proposal.

PFAS Occurrence in NJ Public Water Systems (PWS)

PWS Detections: 2013-15
USEPA Unregulated Contaminated Monitoring Rule 3

PFAS	Reporting Level (ng/L)	New Jersey		U.S. other than NJ	
		Detects	%	Detects	%
PFOA	20	19/175	**10.9%**	98/4745	**2.1%**
PFNA	20	4/175	**2.3%**	10/4745	**0.2%**
PFOS	40	6/175	**3.4%**	89/4745	**1.9%**
PFHxS	30	2/175	1.1%	53/4745	1.1%
PFBS	90	0/175	0%	8/4745	0.2%
PFHpA	10	6/175	3.4%	80/4745	1.7%



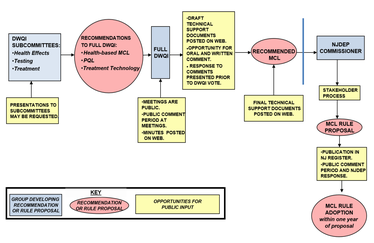
PWS Detections above NJ MCLs as of November 2018

NJ Drinking Water Quality Institute & NJDEP MCL Development Process

- **Drinking Water Quality Institute (DWQI):** Advisory body established in NJ Safe Drinking Water Act to recommend MCLs to NJDEP Commissioner.
- **DWQI Subcommittees** determine:
  - **Health-based MCL**
    - Non-carcinogens: No health effects expected from lifetime exposure.
    - Carcinogens: 1-in-1 million lifetime cancer risk.
  - **Practical Quantitation Level (PQL)**
    - Level that can be reliably measured by drinking water laboratories.
  - Capability of available **treatment removal technology.**
- PFAS MCLs were not limited by analytical or treatment factors and were set at Health-based MCLs.

(Units: ng/L)	Health-based MCL	Analytical PQL	Treatment Removal	Recommended MCL
PFOA	14	6	Not limiting	14
PFOS	13	4.2	Not limiting	13
PFNA	13	5	Not limiting	13

NJDEP MCL DEVELOPMENT PROCESS



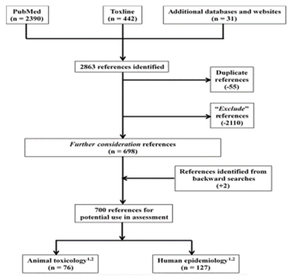
PFAS Health-based Maximum Contaminant Levels

Overview

- Primary basis is **animal toxicology data**.
- **Multiple human health effects** associated with low exposures support protective approach.
- **Animal-to-human comparison** based on blood serum PFAS levels.
  - Half-life in humans much longer than in animals.
- **Non-cancer effects:**
  - Most sensitive effects that are well-established, adverse/can progress to adverse, and relevant to humans.
- **Cancer risk:**
  - PFOA and PFOS: "Suggestive evidence of carcinogenicity."
    - PFOA: MCLs for non-cancer and cancer effects are identical.
    - PFOS: Too uncertain for basis; estimated risk at MCL is close to 1-in-1 million.
  - PFNA: No studies of cancer effects.

Literature Review Strategy – Example: PFOS

More than 2000 citations identified and screened.



Reference Dose Development Process

Serum Level Point of Departure (POD) from end of dosing period in animal study *(ng/ml; BMDL, NOAEL, or LOAEL)*

↓ *Apply Uncertainty Factors*

Target Human Serum Level (ng/L)

↓ *Apply Clearance Factor*:*
Target Human Serum Level (ng/L) x ***Clearance Factor (L/kg/day)***
= Reference Dose (ng/kg/day)

Reference Dose (ng/kg/day)

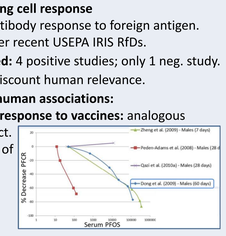
**CL (L/kg/day) = Volume of Distribution (L) x (ln 2 ÷ Half-life [days])*

Health-based MCL (ng/L) = Reference Dose (ng/kg/day) x Relative Source Contribution (%) ÷ Water Ingestion Rate (L/kg/day)

	PFOA		PFOS	PFNA
Toxicological Endpoint	**Delayed mammary gland development** (mouse, Macon et al., 2011)	**↑ liver weight** (mouse, Loveless et al., 2006)	**↓ plaque forming cell response** (mouse, Dong et al., 2009)	**↑ liver weight** (mouse, Das et al., 2015)
Point of Departure	**$BMDL_{10\%}$ - 23 ng/ml**	**$BMDL_{10\%}$ - 4350 ng/ml**	**NOAEL - 674 ng/ml**	**$BMDL_{10\%}$ - 4900 ng/ml**
Uncertainty Factors	**Total - 30** 10 - Intra-human 3 - Animal-to-human	**Total - 300** 10 - Intra-human 3 - Animal-to-human 10 - Database (more sensitive effects - mammary gland & other low-dose developmental)	**Total - 30** 10 - Intra-human 3 - Animal-to-human	**Total - 1000** 10 - Human variation 3 - Animal-to-human 10 - Less-than-chronic duration 3 – Incomplete database; liver necrosis at lower doses but numerical serum PFNA data not provided.
Target Human Serum Level	**0.8 ng/ml**	**14.5 ng/ml**	**22.5 ng/ml**	**4.9 mg/ml**
Animal-to-Human	**Clearance factor - 1.4 x 10^{-4} L/kg/day**		**Clearance Factor - 8.1 x 10^{-5} L/kg/day**	**200:1 serum: drinking water ratio**
Reference Dose	**0.11 ng/kg/day**	**2 ng/kg/day**	**1.8 ng/kg/day**	*Not applicable*
Water Ingestion Rate	***Health-based MCL not recommended - No precedent for endpoint as basis for risk assessment***	**Default adult - 0.029 L/kg/day (70 kg body wt.; 2 L/day)**		
Relative Source Contribution		**20%** (Default adult; Partially accounts for ↑ exposures of young infants from breastmilk/prepared formula, since substantial exposure from other sources is unlikely)		**50 %** (Subtraction - based on 95th percentile from NHANES)
Health-based MCL		**14 ng/L**	**13 ng/L**	**13 ng/L**

Rationale for Choice of Toxicological Endpoints

PFOA			PFOS	PFNA
Delayed Mammary Gland Development	***Increased Liver Weight***	***Mode of Action for Hepatic Effects***	***Decreased Plaque Forming Cell Response***	***Summary***
• **Well established** - 9 mouse studies; from gestational and/or lactational exposure. • Only 1 negative study, which has problematic issues. • Differing strain susceptibility consistent with toxicokinetic differences. • **Adverse** - Structural changes persist until adulthood. • **Human relevance** – No reason to discount based on mode of action. • **Human studies –** PFOA associated with ↓ breastfeeding duration.	• **Well established** in non-human primates and rodents. • Most **sensitive effect** with serum data needed for dose-response analysis, except mammary gland delay. • **Co-occurred with and/or progressed** to more severe hepatic effects. • Reversibility **not relevant** to chronic exposure duration of MCLs.	• Primary issues: • Human relevance of rodent effects. • Role of PPAR-α in **non-carcinogenic** hepatic effects. • Review of data from: • Non-human primates. • Standard rodent strains. • PPAR-alpha null mice. • Mice with humanized PPAR-α. • Human tissues. • In vitro studies. Example of Approach Used • **Overall conclusion: Non-carcinogenic hepatic effects of PFOA are relevant to humans for the purposes of risk assessment.**	• Immunotoxicity is also basis for other recent PFOS RfDs (MI, MN, NH, NY). • **↓ plaque forming cell response** • Measures antibody response to foreign antigen. • Basis for other recent USEPA IRIS RfDs. • **Well established:** 4 positive studies; only 1 neg. study. • No reason to discount human relevance. • Supported by **human associations:** • **↓ antibody response to vaccines:** analogous human effect. • **↑ incidence of infectious disease.**	• Toxicity (hepatic, developmental, immune, male reproductive) and mode of action generally **similar to PFOA** but: – **Longer half-life.** – Effects at **lower doses.** – More **severe** effects (e.g. delayed offspring growth persists to adulthood). • Human half-life estimated to be twice that of PFOA based on rodent data and limited human data.



Increases in Serum PFOA & PFOS Predicted at NJ MCLs & USEPA Health Advisories (70 ng/L)

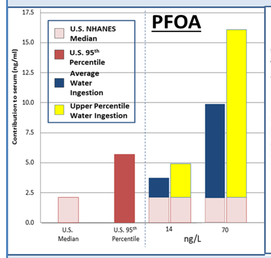
- **Clearance factor** (CL, L/kg/day) = Volume of Distribution (L) x (ln 2 ÷ Half-life [days])

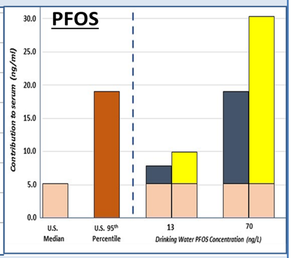
Dose (µg/kg/day) = Serum Conc. (µg/L) x CL (L/kg/day)

Dose (µg/kg/day) = Drinking Water Conc. (µg/L) x Ingestion Rate (L/kg/day)

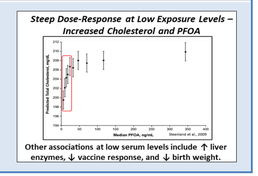
$$\textit{Serum:Drinking Water Ratio} = \frac{\textit{Serum Conc. (µg/L)}}{\textit{Drinking Water Conc. (µg/L)}} = \frac{\textit{Ingestion Rate (L/kg/day)}}{\textit{CL (L/kg/day)}}$$

- **PFOA** - Predicted serum: drinking water ratios:
  - ***114:1*** *- average water consumption;* ***200:1*** *- upper percentile water consumption.*
- Ratio of **>100:1 supported by empirical data** from several studies.
- **Higher ratios** predicted for PFOS, PFNA & other PFAAs with longer half-lives.





"NJ Drinking Water Quality Institute Health Effects Subcommittee concludes that these [blood serum PFAS] increases [at 70 ng/L] **are not desirable and may not be protective of public health.**"



Other associations at low serum levels include ↑ liver enzymes, ↓ vaccine response, and ↓ birth weight.

NJ, USEPA, ATSDR, & European Food Safety Authority Toxicity Factors & Drinking Water Guidelines

PFOA

Agency	Species	Basis	Toxicity Factor (ng/kg/day)	Drinking Water Guideline (ng/L)*
New Jersey DEP	Animal	Delayed mammary gland development (mouse)	0.11	*(0.77)*
		Not recommended due to lack of precedent as basis for risk assessment.		
		↑ liver weight (rat): With uncertainty factor of 10 for more sensitive effects (e.g. mammary gland)	2	14
		Cancer (rat testicular tumors)	---	14
USEPA		Developmental: Delayed bone development & earlier puberty in males (mouse)	20	70**
ATSDR		Developmental: Behavioral & skeletal changes (mouse)	3	--
EFSA	Human	↑ cholesterol (also ↑ liver enzyme ALT, ↓ birth wt.)	0.8	---

PFOS

Agency	Species	Basis	Toxicity Factor (ng/kg/day)	Drinking Water Guideline (ng/L)*
NJDEP	Animal	Immune system suppression (mouse)	1.8	13
USEPA		Developmental: ↓ offspring body weight (rat)	20	70**
ATSDR		↓ offspring body wt.; immune system suppression	2	--
EFSA	Human	↑ cholesterol; ↓ vaccine response; ↓ birth wt.	1.8	---

***Exposure Assumptions:** NJ – default adult; USEPA – lactating woman.
***Applies to total of PFOA & PFOS.*

For Additional Information

NJ Drinking Water Quality Institute website:
https://www.state.nj.us/dep/watersupply/g_boards_dwqi.html

Contact: gloria.post@dep.nj.gov