



# PFAS Water Quality Standards: Toxicological Summary Information

*Modified from presentation to the Environmental Management Commission on Nov 9, 2023*

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# *Topics Covered*

1. Review of Groundwater Quality and Surface Water Quality Standards Calculation
2. Proposed PFAS Chemicals for Standards Development
3. Available Toxicological Values

# *Review of Groundwater Quality Standards Calculation*

# *Groundwater Quality Standards Rule*

## **Title 15A NCAC Subchapter 02L –Groundwater Classifications and Standards**

Section .0100: General Considerations

Section .0200: Classifications and Groundwater Quality Standards

.0201 Groundwater Classifications

.0202 Groundwater Quality Standards

# Groundwater Standards Calculation (15A NCAC 02L .0202 (d)(1))

## 1. Noncancer/systemic

$$GWQS = \frac{RfD \times BW \times RSC}{WCR}$$

## 2. Cancer

$$GWQS = \frac{RL \times BW}{CPF \times WCR}$$

RL = Risk Level =  $1 \times 10^{-6}$

## Toxicity benchmarks

RfD = Chronic Oral Reference Dose

CPF = Carcinogen Potency Factor  
or Cancer Slope Factor (CSF)

## Exposure factors

RSC = Relative Source Contribution  
(0.1 for inorganics; 0.2 for organics)

BW = Body Weight = 70 kg (adult)

WCR = Water Consumption Rate =  
2 L/day (adults)

# *Review of Surface Water Quality Standards Calculation*

# *Surface Water Human Health Criteria*

- Human health criteria protect for fish consumption & water supply uses
- Standards determined using human health criteria calculations
- Calculations consider current toxicological information and exposure factors
- Calculation per 15A NCAC 02B .0208 (a)(2):

$$WQS = RfD \times RSC \times \frac{BW}{WCR + (FCR \times BCF)}$$

**\*\*\*Exposure factors highlighted in red\*\*\***

**WQS** = Water Quality Standard

**RfD** = Reference Dose

**RSC** = Relative Source Contribution

**BW** = Body Weight

**WCR** = Water Consumption Rate

**FCR** = Fish Consumption Rate

**BCF** = Bioconcentration Factor

# *Fish Consumption Standard Calculation*

## *15A NCAC 02B .0208 (a)(2)*

Fish tissue consumption only (all waters)

Noncancer

$$WQS = (RfD \times RSC) \times \frac{BW}{FCR \times BCF}$$

Cancer

$$WQS = \frac{RL}{CPF} \times \frac{BW}{FCR \times BCF}$$

RL = Risk Level =  $1 \times 10^{-6}$

WQS = Water Quality Standard

### **Toxicity benchmarks**

RfD = Oral Reference Dose

CPF = Carcinogen Potency Factor  
or Cancer Slope Factor (CSF)

### **Exposure Factors**

RSC = Relative Source Contribution

BW = Body Weight = 80 kg

FCR = Fish Consumption Rate =  
22.0 g/person-day

BCF = Bioconcentration Factor or  
Bioaccumulation Factor (BAF), if  
available



# Water Supply Standard Calculation

## 15A NCAC 02B .0208 (a)(2)

Water + Fish consumption (Water Supply waters)

### Noncancer

$$WQS = RfD \times RSC \times \frac{BW}{WCR + (FCR \times BCF)}$$

### Cancer

$$WQS = \frac{RL}{CPF} \times \frac{BW}{WCR + (FCR \times BCF)}$$

RL = Risk Level =  $1 \times 10^{-6}$

WQS = Water Quality Standard

### **Toxicity benchmarks**

RfD = Oral Reference Dose

CPF = Carcinogen Potency Factor  
or Cancer Slope Factor (CSF)

### **Exposure Factors**

RSC = Relative Source Contribution

BW = Body Weight = 80 kg (adult)  
or 10 kg (child)

WCR = Water Consumption Rate =  
2.4 L/day (adults) or 1 L/day (child)

FCR = Fish Consumption Rate =  
22.0 g/person-day

BCF = Bioconcentration Factor or  
Bioaccumulation Factor (BAF), if  
available

# *Proposed PFAS Chemicals for Standards Development*

## *PFAS Proposed for Standards Development*

1. Perfluorooctane sulfonic acid (**PFOS**)
2. Perfluorooctanoic acid (**PFOA**)
3. Hexafluoropropylene Oxide Dimer Acid (HFPO-DA; **GenX**)
4. Perfluorobutane Sulfonic Acid (**PFBS**)
5. Perfluorobutanoic Acid (**PFBA**)
6. Perfluorohexanoic Acid (**PFHxA**)
7. Perfluorononanoic acid (**PFNA**)
8. Perfluorohexanesulfonic acid (**PFHxS**)
9. ~~Perfluoropropanoic Acid (**PFPrA**)~~
  - To be examined in the future as EPA develops a test method for this compound

## *Why these PFAS Compounds?*

1. All compounds have a significant literature base so health effects can be determined.
2. Literature bases for all compounds have been evaluated by a federal agency.
3. All compounds have health effects data to support development of a reference dose or cancer slope factor.
4. All compounds have been detected in NC's environmental media.
5. Final test method of these chemicals in different environmental media are to be released by EPA.

# *Summary of Available Toxicological Values*

# *Toxicological Values for Standards Calculations*

## 1. Reference Dose (RfD)

An estimate of a daily exposure to the human population that is likely to be without an appreciable risk of deleterious effects during a lifetime

## 2. Cancer Slope/Potency Factor (CSF or CPF)

The cancer risk (proportion affected) per unit of dose and can be used to compare the relative potency of different chemical substances.

## 3. Bioaccumulation Factor (BAF) *(Surface Water Standards Only)*

The amount of a chemical taken up from water plus the contribution of chemical in the diet of the organism.

# *Toxicological Values for Proposed PFAS*

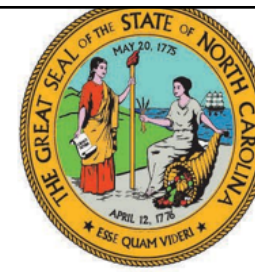
PFAS	RfD (mg/kg-day)	Source	Burkhard EPA 2021 BAF
PFOS	0.0000001; (CSF = 39.5)	EPA Human Health Toxicity Assessment (draft until Dec 2023)	1514
PFOA	0.00000003; (CSF=0.00000000293)		8.5
PFBA	0.001	EPA IRIS Assessment (2022)	3
PFBS	0.0003	EPA Human Health Toxicity Assessment (2021)	22
HPFO-DA	0.000003	EPA Human Health Toxicity Assessment (2021)	4.1
PFHxA	0.0005	EPA IRIS Assessment (2023)	1.6
PFNA	0.000003	ATSDR Minimal Risk Level (2021); EPA MCLG Summary (2023)	144
PFHxS	0.000002	ATSDR Minimal Risk Level (2021); EPA MCLG Summary (2023)	20

# *Bioaccumulation Factor (BAF) Sources*

## 1. EPA Critical Review Publication (Burkhard 2021)

- PFOS
- PFOA
- GenX
- PFBS
- PFBA
- PFHxA
- PFNA
- PFHxS





NORTH CAROLINA  
Environmental Quality

ROY COOPER  
Governor

ELIZABETH S. BISER  
Secretary

## Secretaries' Science Advisory Board Official Recommendation

**Subject:** Use of EPA's Bioaccumulation Factors (BAF) in North Carolina's waterbodies

**Date:** June 7, 2023

## *BAF Source Accuracy*

NCSSAB evaluated both DEQ's and EPA's data and concluded that the values from the datasets are similar and determined that using either is appropriate and scientifically sound to represent NC waterbodies.

PFAS	EPA Aquatic Life Data	Burkhard EPA 2021	NCDEQ Cape Fear River Data
PFOS	1585	1514	1539
PFOA	10	8.5	36



The EPA Critical Review (Burkhard 2021) presents BAFs for many PFAS compounds and has been filtered for quality of studies and appropriate species.

## *BAF Source Accuracy*

PFAS	EPA Aquatic Life Data	Burkhard EPA 2021	Cape Fear River Data
PFOS	1585	1514	1539
PFOA	10	8.5	36
PFBA	Not included in Aquatic Life Criteria documents	3	54
PFBS		155	No accumulation observed in study
GenX		4.1	
PFHxA		1.6	
PFNA		144	
PFHxS		20	39
PFPPrA		Not examined	Not examined

# *Toxicological Values for Proposed PFAS*

PFAS	RfD (mg/kg-day)	Source	Burkhard EPA 2021 BAF
PFOS	0.0000001; (CSF = 39.5)	EPA Human Health Toxicity Assessment (draft until Dec 2023)	1514
PFOA	0.00000003; (CSF=0.0000000293)		8.5
PFBA	0.001	EPA IRIS Assessment (2022)	3
PFBS	0.0003	EPA Human Health Toxicity Assessment (2021)	22
HPFO-DA	0.000003	EPA Human Health Toxicity Assessment (2021)	4.1
PFHxA	0.0005	EPA IRIS Assessment (2023)	1.6
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PFHxS	0.000002	ATSDR Minimal Risk Level (2021); EPA MCLG Summary (2023)	20

*CSF (CPF)  
Source  
Confidence*

1. EPA Office of Water (OW) Toxicity Assessment  
PFAS compounds

- PFOS –
  - **High**; listed as carcinogenic in 2023 by EPA, the CSF denoted carcinogenicity to a much lower degree than PFOA.
- PFOA –
  - **High**; listed as a carcinogenic compound from previous EPA assessments, many studies report carcinogenic observations.

## *RfD Source Confidence*

1. EPA Office of Water Toxicity Assessment PFAS compounds
  - PFOS, PFOA, GenX, PFBS
    - High** – EPA based the proposed national drinking water standards (or MCLs) on these RfDs
2. EPA Integrated Risk Information System (IRIS) Assessments
  - PFBA, PFHxA
    - High** – IRIS is the most rigorous review process the EPA conducts
3. Agency for Toxic Substance and Disease Registry (ATSDR); EPA MCLGs
  - PFNA, PFHxS
    - High** – Values vetted by 2 federal agencies, and used in EPA's drinking water proposal; used in proposed national drinking water standards (or MCLs)

## *Question to the Board*

- We need to understand the difference in rigor and quality between the IRIS and other EPA Program Assessments.
- How can DEQ provide the details of these assessments for your review of these metrics?



*Thank you*



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# *Individual PFAS Compounds and Associated Toxicological Values*

PFAS	Source	Health Effects	RfD or CSF	BAF (# studies)	POD	Total UF	UF Components
PFAS	Source Document	Critical health effects used to derive RfD or CSF	#	# (n=#)	Value in critical study that the RfD or CSF is derived from	Total uncertainty value used to calculate RfD	Types of uncertainty



# *PFOS Toxicity Information*

*(non-carcinogenic)*

PFAS	Source	RfD (mg/kg-d)	BAF (# studies)
PFOS	EPA OW Human Health Toxicity Assessment (draft until Dec 2023)	$1 \times 10^{-7}$	1514 (n=155)

Notes: BAF = bioaccumulation factor. POD = point of departure, UF = uncertainty factor; BAF determined by critical EPA review (Burkhard 2021); \*from Wikstrom et al., 2020; Dong et al., 2019; ^ from Butenhoff et al 2012.

Health Effects	POD <sub>HED</sub> (mg/kg-day)	Total UF	UF Components	RfD (mg/kg-d)
Developmental and Cardiovascular - low birth weight and increased total cholesterol*	0.0000013	10	10 for interspecies extrapolation	0.0000001

Notes: POD = point of departure, POD<sub>HED</sub> = human equivalency dose; UF = uncertainty factor; \*from Wikstrom et al., 2020; Dong et al., 2019.

# PFOS Toxicity Information

(carcinogenic)

PFAS	Source	CSF (mg/kg-d)	BAF (# studies)
PFOS	EPA OW Human Health Toxicity Assessment (draft until Dec 2023)	39.5	1514 (n=155)

Notes: BAF = bioaccumulation factor. POD = point of departure, UF = uncertainty factor; BAF determined by critical EPA review (Burkhard 2021); \*from Wikstrom et al., 2020; Dong et al., 2019; ^ from Buttenhoff et al 2012.

Health Effects	POD (internal dose)	Human Clearance value	POD <sub>HED</sub> (mg/kg-day)	BMR	CSF (mg/kg-d)
Hepatocellular adenomas and carcinomas in female rats <sup>^</sup>	19.8 mg/L	0.128 mL/kg-d	0.00253	10%	39.5

Notes: Human clearance value = calculated from half-life and volume of distribution;  $Cl = V_d * \ln(2)/t_{1/2}$ ; BMR = Benchmark Response, lower 95% confidence interval for 10% change; ^ from Buttenhoff et al 2012.

# *PFOA Toxicity Information*

*(non-carcinogenic)*

PFAS	Source	RfD (mg/kg-d)	BAF (# studies)
PFOA	EPA OW Human Health Toxicity Assessment (draft until Dec 2023)	$3 \times 10^{-8}$	8.5 (n=98)

Notes: BAF = bioaccumulation factor. POD = point of departure, UF = uncertainty factor; BAF determined by critical EPA review (Burkhard 2021); \*from Budtz-Jorgensen and Grandjean, 2018; Wikstrom et al., 2020; Dong et al., 2019; ^ from Shearer et al 2021.

Health Effects	POD <sub>HED</sub> (mg/kg-day)	Total UF	UF Components	RfD (mg/kg-d)
Immune, Developmental and Cardiovascular – decreased vaccine response, low birth weight and increased total cholesterol*	0.0000000275	10	10 for interspecies extrapolation	0.000000003

# *PFOA Toxicity Information*

*(carcinogenic)*

PFAS	Source	CSF (mg/kg-d)	BAF (# studies)
PFOA	EPA OW Human Health Toxicity Assessment (draft until Dec 2023)	<b><math>2.93 \times 10^{-8}</math></b>	<b>8.5 (n=98)</b>

Notes: BAF = bioaccumulation factor. POD = point of departure, UF = uncertainty factor; BAF determined by critical EPA review (Burkhard 2021); \*from Budtz-Jorgensen and Grandjean, 2018; Wikstrom et al., 2020; Dong et al., 2019; ^ from Shearer et al 2021.

Health Effects	POD (internal dose)	Human Clearance value	POD <sub>HED</sub> (mg/kg-day)	BMR	CSF (ng/kg-d)
Renal cell carcinomas <sup>^</sup>	0.00352	0.120	NA- human epidemiology study		<b>0.0293</b>

Notes: Human clearance value = calculated from half-life and volume of distribution;  $Cl = Vd * \ln(2)/t_{1/2}$ ); BMR = Benchmark Response, lower 95% confidence interval for 10% change; ^ from Shearer et al. 2021.

# PFBA Toxicity Information

(non-carcinogenic)

PFAS	Source	RfD (mg/kg-day)	BAF (L/kg) (# studies)
PFBA	EPA IRIS Assessment (2022)	$1 \times 10^{-3}$	3 (n=40)

Notes: BAF = bioaccumulation factor; BAF determined by critical EPA review (Burkhard 2021); \* from Butenhoff et al., 2012.

Health Effects	POD <sub>HED</sub> (mg/kg-day)	Total UF	UF Components	RfD (mg/kg-d)
Hepatic and Thyroid: Increased hepatocellular hypertrophy and decreased total T4*	1.27	1000	<ul style="list-style-type: none"> <li>• 10 for human variation,</li> <li>• 3 for interspecies extrapolation,</li> <li>• 10 for duration extrapolation,</li> <li>• 3 for database deficiencies</li> </ul>	0.001

Notes: POD = point of departure, POD<sub>HED</sub> = human equivalency dose; UF = uncertainty factor; \*from Butenhoff et al. 2012.

# PFBS Toxicity Information

(non carcinogenic)

PFAS	Source	RfD (mg/kg-day)	BAF (L/kg) (# studies)
PFBS	EPA OW Human Health Toxicity Assessment (2021)	$3 \times 10^{-4}$	22 (n=40)

Notes: BAF = bioaccumulation factor. BAF determined by critical EPA review (Burkhard 2021); \* from Feng et al 2017.

Health Effects	POD (mg/kg-day)	Total UF	UF Components	RfD (mg/kg-day)
Thyroid- decreased T4 in mice*	0.095	300	<ul style="list-style-type: none"> <li>• 10 for variation in the human population,</li> <li>• 3 for interspecies extrapolation,</li> <li>• 1 for duration extrapolation,</li> <li>• 10 for database deficiencies</li> </ul>	0.0003

Notes: POD = point of departure,  $POD_{HED}$  =human equivalency dose; UF = uncertainty factor; \* from Feng et al., 2017

# GenX Toxicity Information

(non-carcinogenic)

PFAS	Source	RfD (mg/kg-day)	BAF (L/kg) (# studies)
GenX	EPA OW Human Health Toxicity Assessment (2021)	$3 \times 10^{-6}$	4.1 (n=1)

Notes: BAF = bioaccumulation factor. POD = point of departure, UF = uncertainty factor; BAF determined by critical EPA review (Burkhard 2021); \* from DuPont, 2010.

Health Effects	POD (mg/kg-day)	Total UF	UF Components	RfD (mg/kg-day)
Reproductive and Developmental liver toxicity study in mice*	0.01	3000	<ul style="list-style-type: none"> <li>• 10 for human variation,</li> <li>• 3 for interspecies extrapolation,</li> <li>• 10 for duration extrapolation,</li> <li>• 10 for database deficiencies</li> </ul>	0.000003

Notes: POD = point of departure, POD<sub>HED</sub> = human equivalency dose; UF = uncertainty factor; \* from DuPont, 2010).

# *PFHxA Toxicity Information*

*(non-carcinogenic)*

PFAS	Source	RfD (mg/kg-day)	BAF (L/kg) (# studies)
PFHxA	EPA IRIS Assessment (2023)	$5 \times 10^{-4}$	1.6 (n=25)

Notes: BAF = bioaccumulation factor. POD = point of departure, UF = uncertainty factor; BAF determined by critical EPA review (Burkhard 2021); \* from Loveless et al, 2009.

Health Effects	POD (mg/kg-day)	Total UF	UF Components	RfD (mg/kg-day)
Developmental effects observed in a gestational 12-day oral exposure study in rodents*	0.048	100	<ul style="list-style-type: none"> <li>10 for human variation,</li> <li>3 for interspecies extrapolation,</li> <li>1 for duration extrapolation,</li> <li>3 for database deficiencies</li> </ul>	0.0005

Notes: POD = point of departure,  $POD_{HED}$  =human equivalency dose; UF = uncertainty factor; \* from Loveless et al, 2009.



# PFNA Toxicity Information

(non-carcinogenic)

PFAS	Source	RfD (mg/kg-day)	BAF (L/kg) (# studies)
PFNA	ATDSR Assessment (2021) EPA MCLG Summary (2023)	$3 \times 10^{-6}$	144 (n=79)

Notes: BAF = bioaccumulation factor. POD = point of departure, UF = uncertainty factor; BAF determined by critical EPA review (Burkhard 2021); \* from Das et al. 2015.

Health Effects	POD (mg/kg-day)	Total UF	UF Components	RfD (mg/kg-day)
Developmental delays and decreased body weight in mice*	0.001	300	<ul style="list-style-type: none"> <li>10 for human variation,</li> <li>3 for interspecies extrapolation,</li> <li>10 for database deficiencies</li> </ul>	0.000003

Notes: POD = point of departure,  $POD_{HED}$  =human equivalency dose; UF = uncertainty factor ;\* from Das et al. 2015.

# *PFHxS Toxicity Information*

*(non-carcinogenic)*

PFAS	Source	RfD (mg/kg-day)	BAF (L/kg) (# studies)
PFHxS	ATDSR Assessment (2021) EPA MCLG Summary (2023)	$2 \times 10^{-6}$	20 (n=47)

Notes: BAF = bioaccumulation factor. POD = point of departure, UF = uncertainty factor; BAF determined by critical EPA review (Burkhard 2021); \* from Butenhoff et al., 2009.

Health Effects	POD (mg/kg-day)	Total UF	UF Components	RfD (mg/kg-day)
Thyroid follicular epithelial hypertrophy/ hyperplasia in rats*	0.0047	3000	<ul style="list-style-type: none"> <li>• 10 for human variation,</li> <li>• 3 for interspecies extrapolation,</li> <li>• 10 for duration extrapolation,</li> <li>• 10 for database deficiencies</li> </ul>	0.000002

Notes: POD = point of departure, POD<sub>HED</sub> = human equivalency dose; UF = uncertainty factor; \* from Butenhoff et al., 2009.