Regulating PFAS in Drinking Water a Subgroup Approach

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presentation to

NC Science Advisory Board

April 5, 2021

Outline

- MA PFAS regulatory overview
- Challenges for regulating PFAS
- MassDEP approach for addressing
  - Limited toxicity values
  - Exposure to a PFAS mixture
- Supporting evaluations
  - Read across
  - Relative potency exploration
  - Dose addition

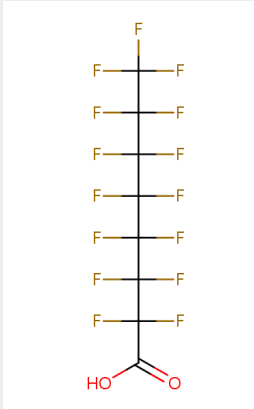
Challenges for Regulating PFAS

- Test method EPA 537 identifies 14 PFAS
- Increasing number of PFAS identified in media
- Multiple PFAS are found in drinking water samples
- People are exposed to different combinations or mixtures of PFAS in water and other media
- Toxicity information for PFAS that may be detected in drinking water samples is variable and often limited

PFAS: Per- and Polyfluoroalkyl Substances

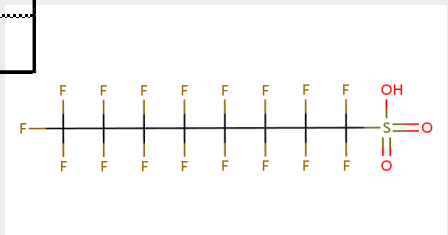
Subgroup of Longer Chain PFAS

# Carbons	EPA Method 537 Analytes	
4	PFBS	Perfluorobutanesulfonic acid
6	PFHxA	Perfluorohexanoic acid
6	PFHxS	Perfluorohexanesulfonic acid
7	PFHpA	Perfluoroheptanoic acid
8	PFOA	Perfluorooctanoic acid
8	PFOS	Perfluorooctanesulfonic acid
9	PFNA	Perfluorononanoic acid
10	PFDA	Perfluorodecanoic acid
11	NMeFOSAA	2-(N-Methylperfluorooctanesulfonamido)acetic acid
11	PFUnA	Perfluoroundecanoic acid
12	NEtFOSAA	2-(N-Ethylperfluorooctanesulfonamido)acetic acid
12	PFDoA	Perfluorododecanoic acid
13	PFTrDA	Perfluorotridecanoic acid
14	PFTA	Perfluorotetradecanoic acid



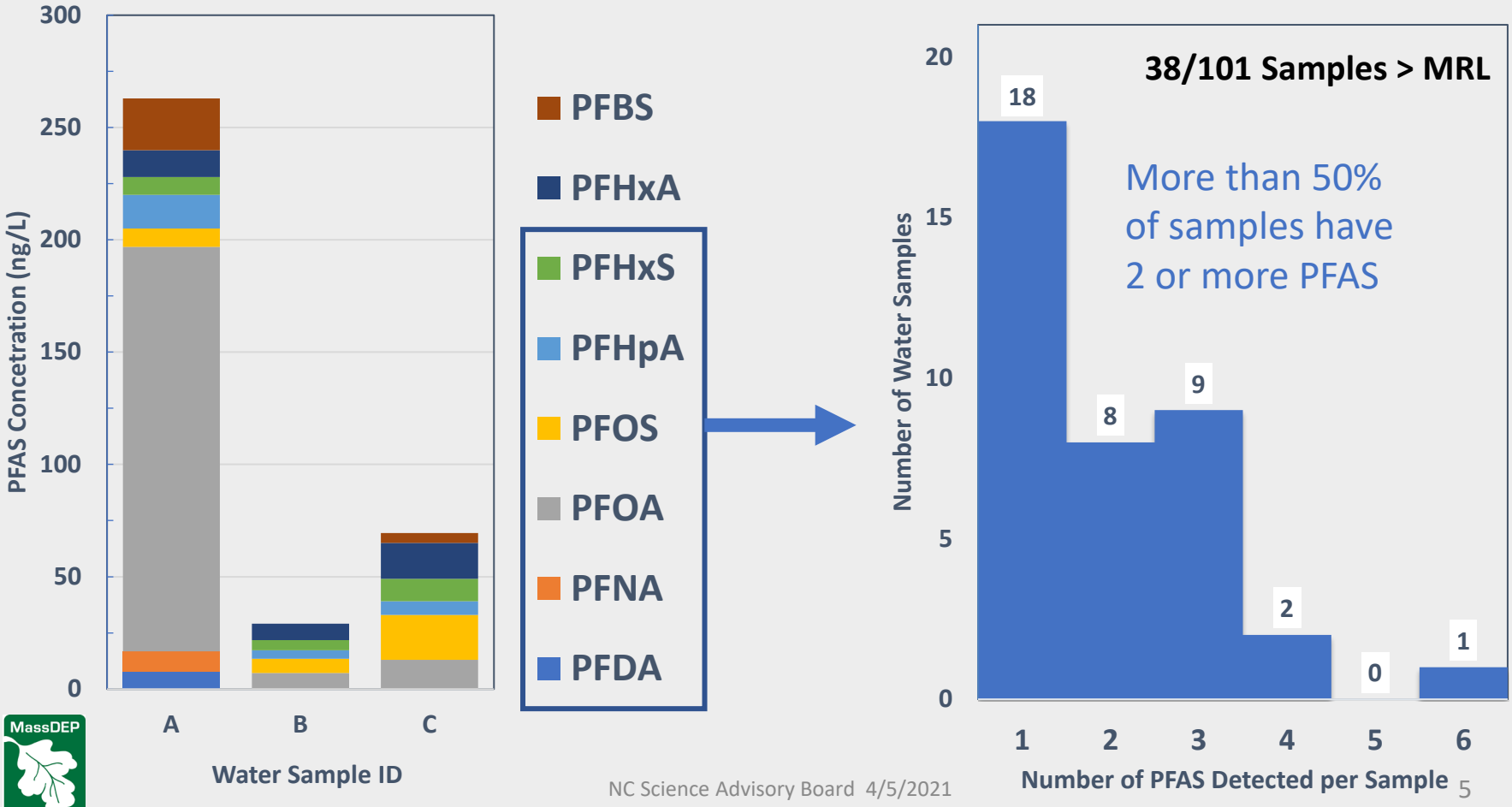
PFOA

PFOS



PFAS Co-occur in Drinking Water

MA drinking water shown here from early subset of DW samples



MassDEP Approach

- Reviewed USEPA RfD for PFOA and PFOS
- Extended USEPA Health Advisory and RfD approach for PFOA and PFOS ----> surrogate toxicity values
- Address as a subgroup of PFAS rather than one by one
- Applied individually and to the sum of any one or more together ----> dose addition

MassDEP Drinking Water Values

- 2018 - established DW Guideline (ORSG) of 70 ppt (ng/L) for 5 PFAS - PFOA, PFOS, PFNA, PFHxS and PFHpA
- January 2020 – revised ORSG to 20 ppt (ng/L) for 6 PFAS - PFOA, PFOS, PFNA, PFHxS, PFHpA and PFDA
- September 2020 – MCL of 20 ppt (ng/L) for 6 PFAS (PFAS6) - PFOA, PFOS, PFNA, PFHxS, PFHpA and PFDA

(ORSG – Office of Research and Standards Guideline)

MassDEP Approach - Estimating Toxicity for Chemicals with Limited Data

- Look to similar chemicals with toxicity data – surrogate chemicals → PFOA and PFOS
- How is "similar" determined?
  - Read Across - approach used to organize and evaluate what is known about chemicals that might be related
  - Relative potency evaluation – a quantitative measure of difference between the dose required to cause a specific response.
- Determining similarity or difference – consider variability and uncertainty in the available data

MassDEP Approach – Read Across

The PFAS in this subgroup have similar:

- Structures 8 ± 2 carbons
- Organ systems affected
  - Liver
  - Thyroid
  - Development and Reproduction
- Serum concentrations at LOAELs range 5-77 mg/L
- Have long half-lives

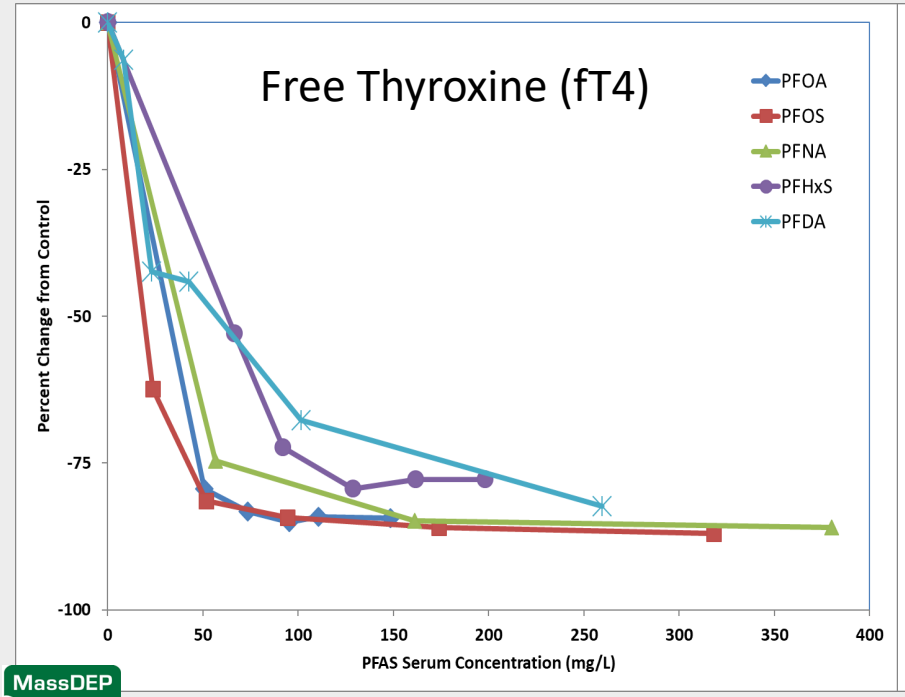
Half-life estimates in humans (years)				
PFOA	PFOS	PFNA	PFHxS	PFDA
2.3 – 2.9	1.9 - 18	1.7 – 3.2	5.3 – 15.5	4 – 7

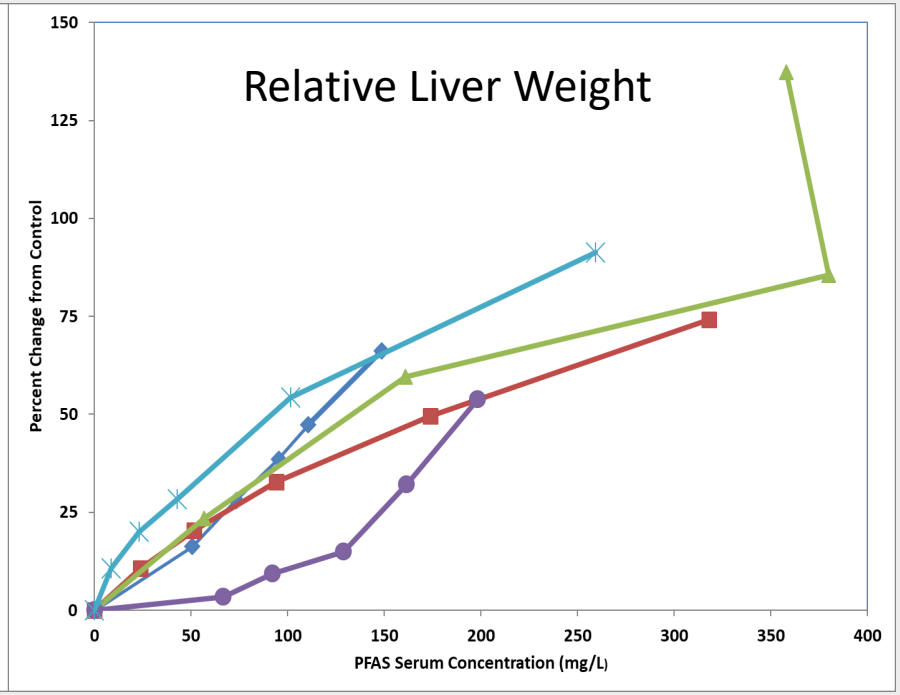
Relative Potency Evaluation

- Quantitative approach for evaluating differences in potency for groups of similarly acting chemicals
- Structurally related congeners, sensitive effect with similar toxicity and mechanistic rationale,
  - PAH Relative Potency Factors (RPF) for carcinogenicity
- Special case – common well-known mechanism of action, applies across all effects and exposures,
  - Dioxin-like PCBs Toxicity Equivalency Factors (TEF)

NTP (2018) 28-day Bioassay

- Male rats equal or higher internal PFAS concentration (mg/L) and more sensitive to effects than female
- Most sensitive endpoints – free thyroxine and relative liver weight





Benchmark Dose Estimates

NTP (2018) 28-day male rat bioassay data

End Point	Free T4	Relative Liver Wt	Free T4	Relative Liver Wt
Exposure Metric	Serum (mg/L)		HED (mg/kg-day)	
BMR	20%	5%	20%	5%
PFOA	18	13	0.0018	0.0013
PFOS	6.7	13	0.0005	0.0009
PFNA	5.6	13	0.0009	0.0021
PFHxS	36	82	0.0023	0.0053
PFDA	13	7	0.0012	0.0006

- Dose metric- internal dose PFAS serum concentration
- Adjust to human equivalent dose (HED) estimated using USEPA (2016) clearance equation and ATSDR (2018) volume of distribution and half-life values
- Model Average of 7 D-R models Bayesian Benchmark Dose Software

Calculation of Relative Potency

$$RPF_i = \frac{\text{Index Chemical}}{\text{Chemical}_i}$$

$$RPF_{fT4} = \frac{PFOA}{PFOS} = \frac{18}{6.7} = 3 \qquad RPF_{liver} = \frac{PFOA}{PFOS} = \frac{13}{13} = 1$$

RPF = 1	Same potency
RPF > 1	Chemical more potent than Index chemical
RPF < 1	Chemical less potent than Index chemical

How big does the RPF need to be to be considered different?

Dioxin-like PCBs – 1/2 an order of magnitude (3)

- Special case – common well-known mechanism of action, applies across all effects and exposures

PAH - one order of magnitude (10)

- Structurally related congeners, sensitive effect with similar toxicity and mechanistic rationale

PFAS - ??

- Structurally related, similar toxicity across several endpoints, mechanism(s) unknown

Potency Relative to PFOA

NTP (2018) 28-day male rat bioassay data

End Point	Free T4	Relative Liver Wt	Free T4	Relative Liver Wt
Exposure Metric	Serum (mg/L)		HED (mg/kg-day)[a]	
BMR	20%	5%	20%	5%
PFOA	1	1	1	1
PFOS	3	1	4	1
PFNA	3	0.9	2	0.6
PFHxS	0.5	0.2	0.8	0.2
PFDA	1	2	2	2

- All RPF within factor of five (5)
- Most within factor of two (2)

Limitations of RPF Exploration

- Low dose portion of D-R curve poorly characterized for thyroid hormone response
- Potential for interference by PFAS in methods used to measure thyroid hormone
- Uncertainty in serum concentration to represent consistent measure of exposure
- Uncertainty in HED
- Limited number of endpoints

Conclusions: RPF Exploration

- All five of the longer-chain subgroup of PFAS - PFOA, PFOS, PFNA, PFHxS and PFDA - caused dose-dependent effects in the liver and thyroid.
- Serum concentrations associated with sensitive responses in animals are generally within 1-2-fold of PFOA, all within 5-fold.
- Exposure expressed as HED yielded similar relationship as serum to PFOA.
- NTP 2018 data support similarity of potencies among these 5 PFAS in rats.

MassDEP Approach – Additivity

PFAS co-occur in water and other media

Long half-lives mean internal exposure is to a mixture even if not exposed at the same time

Consistent with previous approaches for regulating a mixture, e.g., polycyclic aromatic hydrocarbons (PAH), dioxins, disinfection by products (DBP), total petroleum hydrocarbons (TPH)

Assuming additivity is health protective

Acceptance of additivity by EFSA 2020 report on PFAS in food

MassDEP Approach – Conclusions

PFAS in this subgroup –

Co-occur in drinking water and in human serum samples

Effect multiple organ systems, at similar internal concentrations

Available data support similar potencies and do not demonstrate significant differences

PFOA and PFOS have the most extensive data and can serve as surrogates for PFNA, PFHxS, PFHpA and PFDA toxicity values

Assuming additivity of the dose is health protective and consistent with approaches used for regulating mixtures

Acknowledgements

Massachusetts Department of Environmental Protection

- Office of Research and Standards

Tsedash Zewdie

- Drinking Water Program

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