HEALTH-BASED DRINKING WATER VALUE RECOMMENDATIONS FOR PFAS IN MICHIGAN

MPART SCIENCE ADVISORY WORKGROUP

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Presentation Outline

- Charge of the Science Advisory Workgroup
- Variability in Chemical Risk Assessments
- Development of Health-Based Drinking Water Values
  - Point of Departure
  - Uncertainty Factors
  - Relative Source Contribution
  - Water Intake Rates
- Results MPART Science Advisory Workgroup

Charge of the MPART SAW

- Identify PFAS listed under USEPA Method 537.1 with available risk assessments
- Identify key studies and points of departure from which to derive toxicity values
- Apply appropriate uncertainty factors, RSC, and intake rates to derive health-based drinking water values
- Consider class-based approaches

Preamble

On March 26, 2019, Governor Gretchen Whitmer directed the Michigan PFAS Action Response Team (MPART) to further protect public health and the environment, by forming a Science Advisory Workgroup to "review both existing and proposed health-based drinking water standards from around the nation to inform the rule making process for appropriate Maximum Contaminant Levels for Michigan..." Toward this objective, the Science Advisory Workgroup shall make numeric recommendation(s) to MPART for those per- and polyfluoroalkyls substances (PFAS) for which adequate information exists.

Charge

The Science Advisory Workgroup shall:

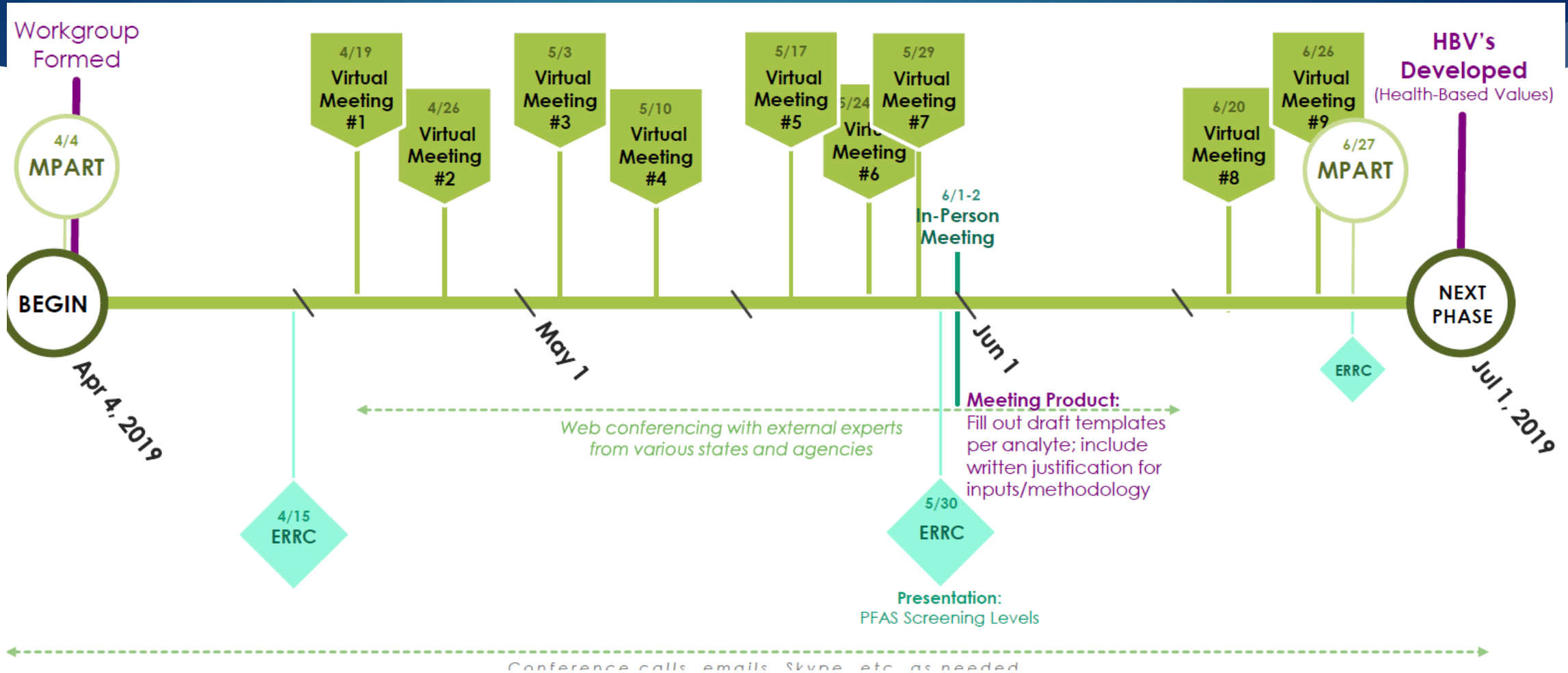
1. For the PFAS listed in USEPA Method 537.1, review all existing and proposed national- and state-derived PFAS drinking water standards and identify the most scientifically defensible non-cancer or cancer-based public health toxicity values available for each individual PFAS chemical family member, or combination thereof, for which the Science Advisory Workgroup determines that adequate information exists. Provide written justification that shall include, but not be limited to, the basis for the selection of the primary studies, critical effect identification, point of departure determination, evaluation of all uncertainty and/or modification factors applied, and the non-cancer or cancer-based toxicity value derivation. Consider the extent of corroborating evidence from other pertinent studies, including both toxicology and epidemiology.

2. Review all existing and proposed national- and state-derived PFAS drinking water standards and identify the most scientifically defensible exposure assessment and risk evaluation methodology for each individual PFAS chemical family member, or combination thereof, for which the Science Advisory Workgroup determines that adequate information exists. Provide written justification that shall include, but not be limited to, selection of the most appropriate receptor(s) and identification of all appropriate exposure assumptions for the receptor(s).

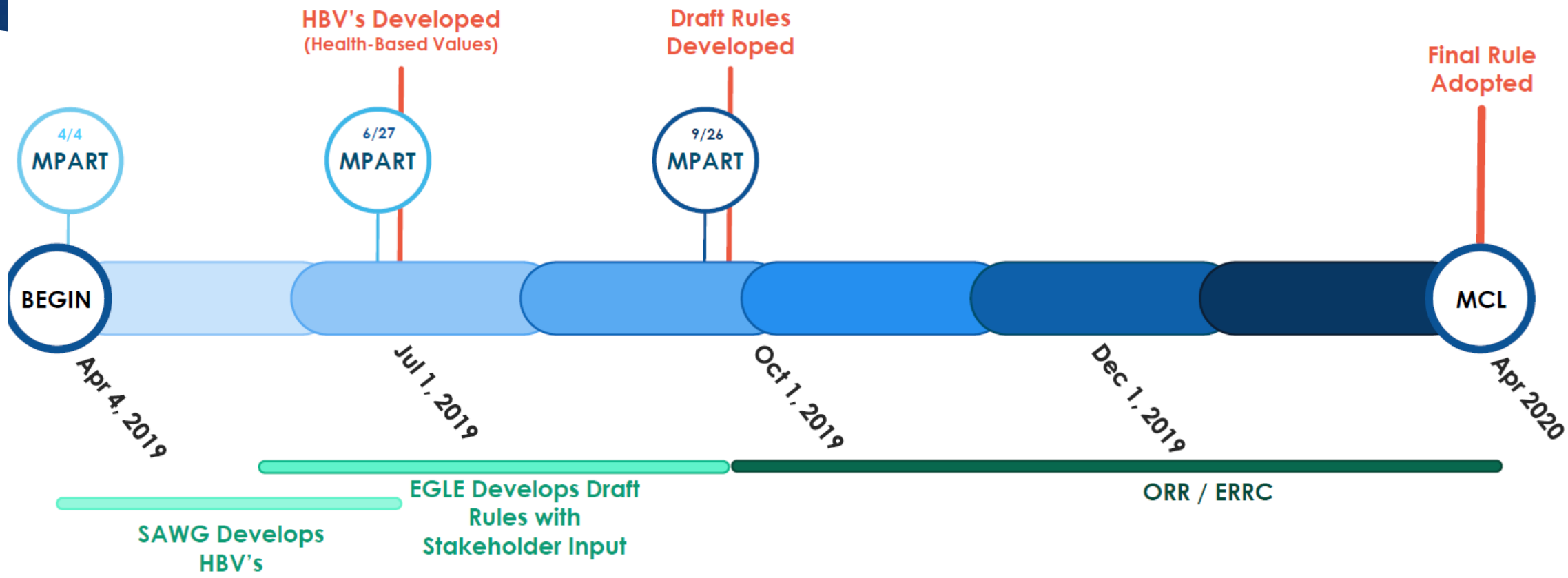
3. Identify the most appropriate and scientifically defensible combination of each specific PFAS toxicity value and exposure assessment and risk evaluation methodology, including consideration of relative source contribution, from which to derive a health-based drinking water value for each individual PFAS chemical family member, or combination thereof, for which the Science Advisory Workgroup determines that adequate information exists.

4. Provide to MPART no later than July 1, 2019, a report recommending scientifically-defensible numeric health-based values to inform the rulemaking process for Maximum Contaminant Levels for each individual PFAS chemical family member, or combination thereof, with written justification for the calculation

Timeline for the MPART SAW



Timeline for MCL Development Process



Select PFAS assessments (adapted from Post, 2019)

	PFOA	PFOS	PFNA	PFHxS	PFHpA	PFDA	TOTAL	PFBA	PFBS	GenX
EPA	70	70	-	-	-	-	Yes	-	-	-
CT	70	70	70	70	70	-	Yes	-	-	-
MA*	20	20	20	20	20	20	Yes	-	2000	-
VT	20	20	20	20	20	-	Yes	-	-	-
MN	35	15	-	47	-	-	No	7000	2000	-
NH*	38	70	23	85	-	-	No	-	-	-
NJ	14*	13*	13	-	-	-	No	-	-	-
NY*	10	10	-	-	-	-	No	-	-	-
NC	-	-	-	-	-	-	No	-	-	140

*Proposed, recommended or draft values (all values are in ng/L (PPT))

Risk Assessment Process

Step 1: Chemical of Interest Identified

Step 2:
- Hazard Assessment
- Exposure Assessment
- Dose Response Assessment
- Risk Characterization

Step 3: Internal Peer Review

Step 4: External Peer Review

Step 5: Publication of Assessments

Adapted from National Academy of Science, 1983

Variability in Risk Assessments

- Risk assessments involve many decision points that may significantly impact the final values
- Regulatory Framework/Problem Formulation
  - What issue is the assessor is trying to understand? What are the guidelines/regulations the risk assessor is having to follow?
- New Data
  - How old is the risk assessment? Were there new data that were selected for the key study/critical effect?

Variability in Risk Assessments

- Professional/Scientific Judgment
  - Selection of key study/critical effect, disagreement on the adversity of a particular finding
  - Different approaches for dose/response assessment
  - Selection of uncertainty factors
- Exposure Assessment
  - What exposures routes/populations are being considered in the risk assessment?
  - Selection of Relative Source Contribution (drinking water)
- Different scientists, even when using the same risk assessment guidelines and toxicity data, may come to different conclusions

Development of Health-Based Values

- Toxicity Values
  - Identification of Key Study, Critical Effect(s), Point of Departure
  - Toxicokinetic adjustment to Human Equivalent Dose
  - Uncertainty Factors
- Relative Source Contribution
- Exposure Parameters
  - Identification of sensitive population
  - Minnesota Department of Health (MDH) Toxicokinetic Model

Derivation of Toxicity Values

- $Toxicity\ Value =$

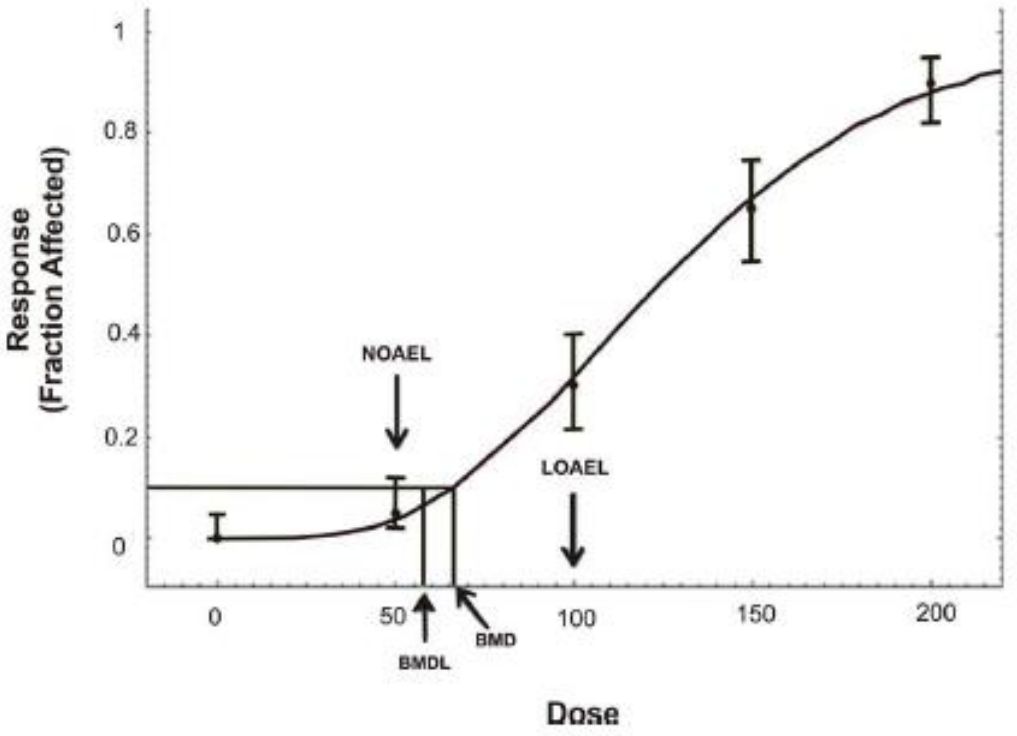
$$\frac{Point\ of\ Departure\ (e.g.,\ NOAEL,\ LOAEL,\ BMDL,\ serum\ level)}{Uncertainty\ factors}$$

- An amount of chemical (estimate with uncertainty) that is thought to cause minimal risk of harm for exposures lasting up to a lifetime (e.g. EPA RfD)

Derivation of Toxicity Values

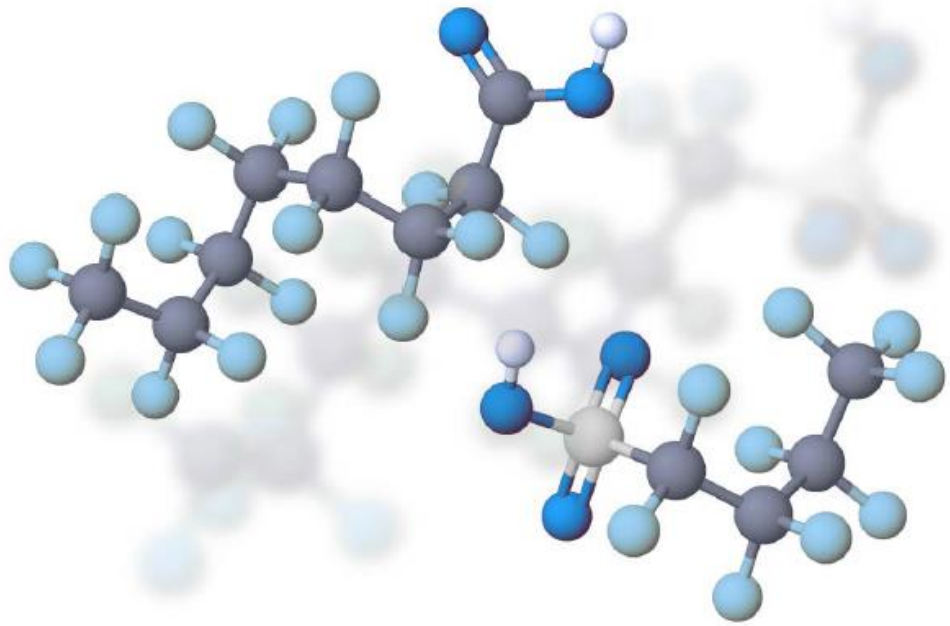
- Critical Effect: The first adverse effect, or its known precursor, that occurs to the most sensitive species as the dose rate of an agent increases.

- Point of Departure: Dose from the animal study used as the "starting point".
  - NOAEL – Highest dose not causing an adverse effect
  - LOAEL – Lowest dose causing adverse effect
  - Benchmark Dose (BMD/BMDL) – Model to predict dose causing specific minimal change (e.g. 10% response)



Examples of Critical Effects for PFAS

- Hepatic toxicity (increased liver weight/necrosis)
- Renal toxicity (hyperplasia)
- Immune system suppression
- Changes in thyroid hormone levels
- Developmental effects
  - Decreased weight gain
  - Delayed ossification (hardening of bones)
  - Accelerated puberty
  - Delayed mammary gland development



Derivation of Toxicity Values

- Laboratory animal dose or serum level is converted to a human equivalent dose or serum level
  - Dosimetric adjustment factors (body weight scaling or use of animal and human half-life)
  - Human-specific information on clearance rates (occupational and non-occupational)
- Example: A **1 mg/kg/day** PFOA dose in mice resulting in a serum concentration of 38 mg/L corresponds to a human equivalent dose of **0.0053 mg/kg/day** (Lau et al., 2006; USEPA, 2016)

		Rat	Human
PFOA	Male	4-6 days	2.1-3.8 years
	Female	2-4 hours	
PFOS	Male	38-41 days	3.4-5.0 years
	Female	62-71 days	

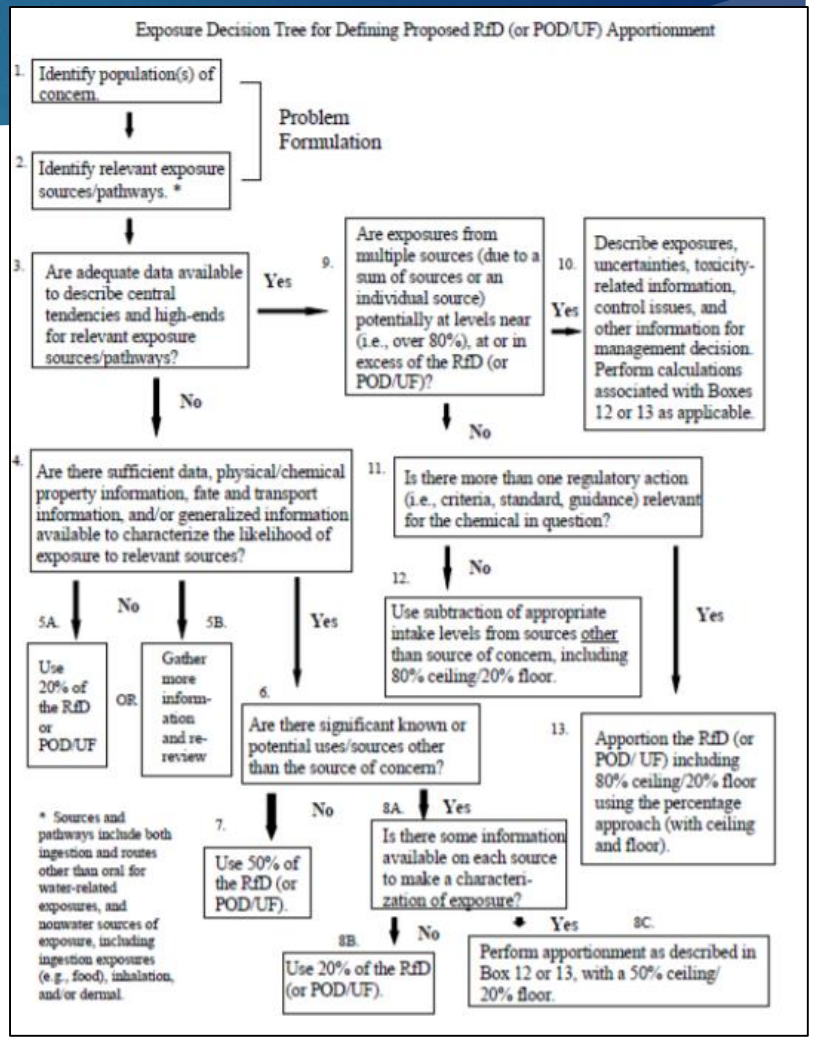
Serum half-life estimates (adapted from Lau, 2015)

Derivation of Toxicity Values

- Uncertainty Factors (1x, 3x ($10^{0.5}$), 10x)
  - Intraspecies extrapolation – Accounts for variations in chemical sensitivity among individuals in a species
  - Interspecies extrapolation – Accounts for variations in chemical sensitivity between experimental animals
  - Exposure duration – Allows for extrapolation of experimental results from subchronic to chronic exposure
  - Use of LOAEL rather NOAEL – Accounts for the uncertainty in using a RfD derived from LOAEL
  - Lack of Database Completeness – Accounts for the absence of data for specific toxic endpoints (e.g. developmental)

Relative Source Contribution

- An amount of a person's exposure to a chemical that is attributed to drinking water
- Consideration of background exposures
- Decision framework provided by US EPA (20 to 80%)
  - Default is 20%



Relative Source Contribution – Subtraction method

- Subtract all non-drinking water exposures (i.e. background) from the Toxicity value to determine the amount of the Toxicity value available for drinking water exposure
- Determine what percentage of the Toxicity value that remainder represents
- NHANES or local biomonitoring information (if available)

Exposure: Intake Rates and Body Weights

- Upper percentile water intake (protect high-intake consumers)
- Connection between body weight (age) and water intake
  - 95th percentile of water intake with average body weight
  - US EPA Exposure Factors Handbook (2011, 2019)
- Infants are the population likely to have the highest water intake in relation to their body weight

Derivation of Drinking Water Values

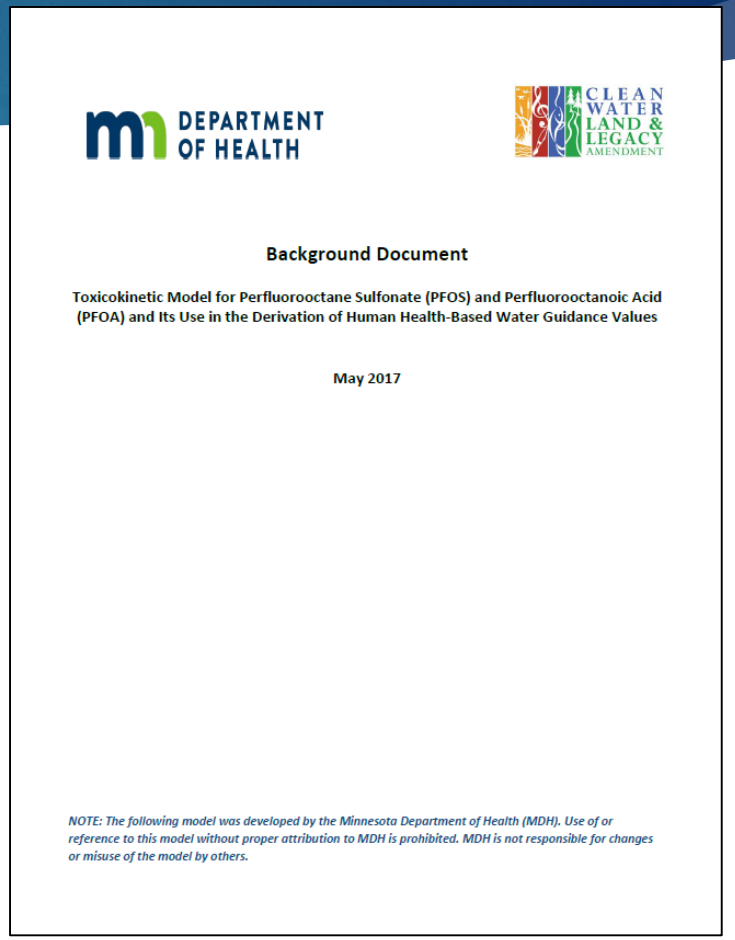
- Standard equation:

$$Health\text{-}Based\ Drinking\ Water\ Value = \frac{\text{toxicity value} * relative\ source\ contribution * body\ weight}{water\ intake}$$

- Minnesota Department of Health (MDH) Toxicokinetic Model:
  - Accounts for prenatal (maternal serum and placental transfer) exposure along with exposure through breastmilk (maternal serum and transfer to breastmilk)

Minnesota Toxicokinetic Model

- "However, PFOS and PFOA have unique characteristics that are not adequately addressed when using this traditional approach."
- "PFOA and PFOS bioaccumulate in serum, cross the placenta, and are excreted into breastmilk."
- Reviewers of the model and recently published for PFOA (Goeden et al., 2019)



DEPARTMENT OF HEALTH

CLEAN WATER LAND & LEGACY AMENDMENT

Background Document

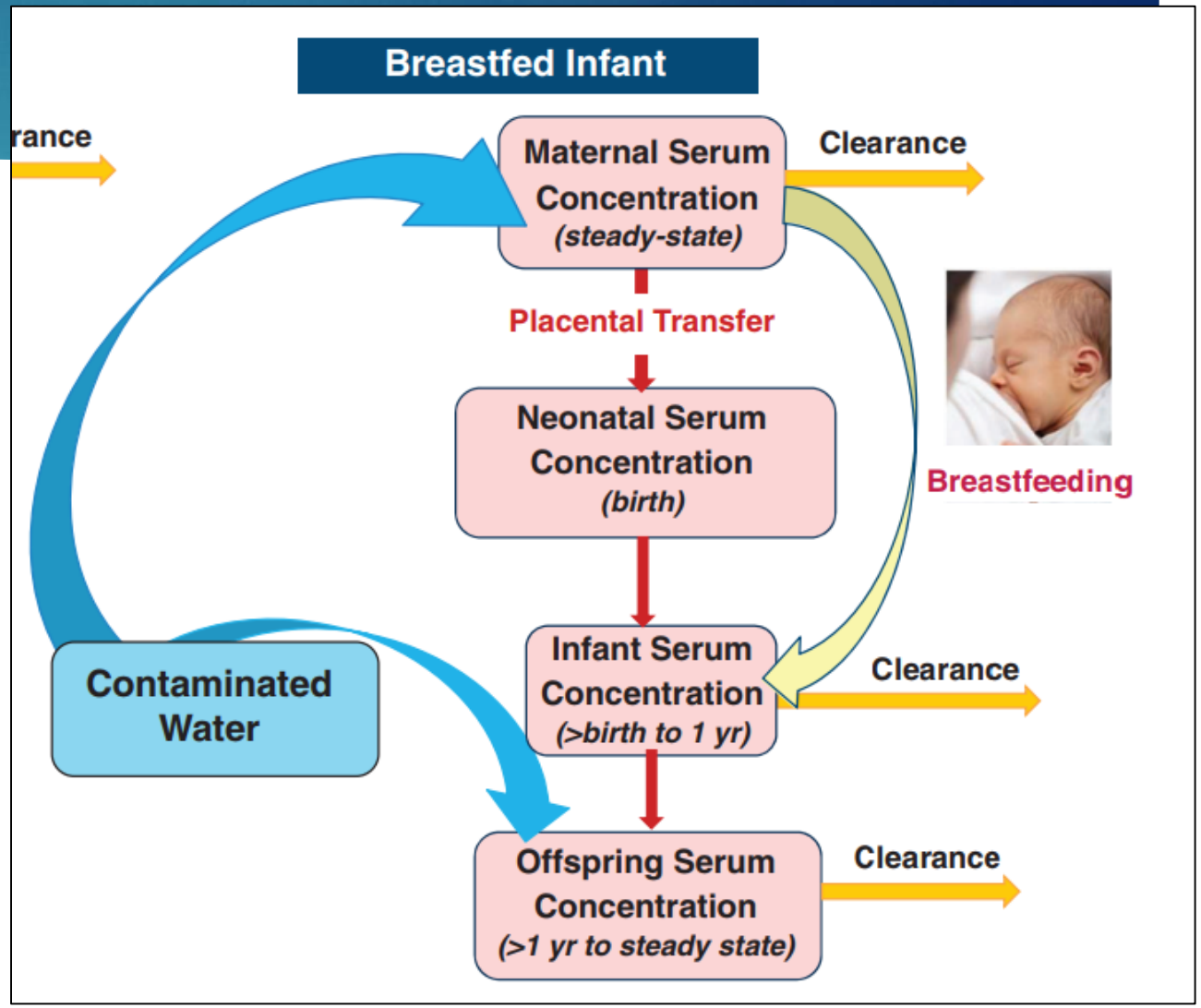
Toxicokinetic Model for Perfluorooctane Sulfonate (PFOS) and Perfluorooctanoic Acid (PFOA) and Its Use in the Derivation of Human Health-Based Water Guidance Values

May 2017

NOTE: The following model was developed by the Minnesota Department of Health (MDH). Use of or reference to this model without proper attribution to MDH is prohibited. MDH is not responsible for changes or misuse of the model by others.

Minnesota Toxicokinetic Model

- One-compartment model to predict serum concentrations of PFOS and PFOA from birth through attainment of steady-state conditions



Toxicity values used in Minnesota model

- Serum levels for PFNA, PFOA, PFOS, and PFHxS levels at the selected points of departure were divided by the uncertainty factors resulting in the serum level associated with the toxicity value

- Example: Average serum concentration at the PFNA point of departure (1 mg/kg/day) was estimated to be 6.8 mg/L. Divide by total UF of 300x results in a reference serum concentration of 0.023 mg/L.

- Serum levels used in development of the Health-Based Values are not meant to indicate a level where health effects are likely
  - These serum levels are calculated to be at a point where no or minimal risk exists for people drinking water with a certain PFAS

Selected PFAS for HBVs

- PFAS selected from USEPA Method 537.1 for development of individual Health-Based Values
  - PFNA
  - PFOA
  - PFHxA
  - PFOS
  - PFHxS
  - PFBS
  - GenX

METHOD 537.1

DETERMINATION OF SELECTED PER- AND POLYFLUORINATED ALKYL SUBSTANCES IN DRINKING WATER BY SOLID PHASE EXTRACTION AND LIQUID CHROMATOGRAPHY/TANDEM MASS SPECTROMETRY (LC/MS/MS)

1. SCOPE AND APPLICATION

1.1. This is a solid phase extraction (SPE) liquid chromatography/tandem mass spectrometry (LC/MS/MS) method for the determination of selected per- and polyfluorinated alkyl substances (PFAS) in drinking water. Accuracy and precision data have been generated in reagent water and drinking water for the compounds listed in the table below.

Analyte[a]	Acronym	Chemical Abstract Services Registry Number (CASRN)
Hexafluoropropylene oxide dimer acid	HFPO-DA	13252-13-6[b]
N-ethyl perfluorooctanesulfonamidoacetic acid	NEtFOSAA	2991-50-6
N-methyl perfluorooctanesulfonamidoacetic acid	NMeFOSAA	2355-31-9
Perfluorobutanesulfonic acid	PFBS	375-73-5
Perfluorodecanoic acid	PFDA	335-76-2
Perfluorododecanoic acid	PFDoA	307-55-1
Perfluoroheptanoic acid	PFHpA	375-85-9
Perfluorohexanesulfonic acid	PFHxS	355-46-4
Perfluorohexanoic acid	PFHxA	307-24-4
Perfluorononanoic acid	PFNA	375-95-1
Perfluorooctanesulfonic acid	PFOS	1763-23-1
Perfluorooctanoic acid	PFOA	335-67-1
Perfluorotetradecanoic acid	PFTA	376-06-7
Perfluorotridecanoic acid	PFTrDA	72629-94-8
Perfluoroundecanoic acid	PFUnA	2058-94-8
11-chloroeicosafluoro-3-oxaundecane-1-sulfonic acid	11Cl-PF3OUdS	763051-92-9[c]
9-chlorohexadecafluoro-3-oxanone-1-sulfonic acid	9Cl-PF3ONS	756426-58-1[d]
4,8-dioxa-3H-perfluorononanoic acid	ADONA	919005-14-4[e]

[a] Some PFAS are commercially available as ammonium, sodium and potassium salts. This method measures all forms of the analytes as anions while the counterion is inconsequential. Analytes may be purchased as acids or as any of the corresponding salts (see Section 7.2.3 regarding correcting the analyte concentration for the salt content).
[b] HFPO-DA is one component of the GenX processing aid technology.
[c] 11Cl-PF3OUdS is available in salt form (e.g. CASRN of potassium salt is 83329-89-9).
[d] 9Cl-PF3ONS analyte is available in salt form (e.g. CASRN of potassium salt is 73606-19-6)
[e] ADONA is available as the sodium salt (no CASRN) and the ammonium salt (CASRN is 958445-448).

Proposed Health-Based Values

PFAS	Health-Based Value (ng/L or PPT)	MDHHS Screening Levels (ng/L or PPT)	Key Difference(s)
PFNA	6	9	Serum half-life (1417 v. 900)
PFOA	8	9	Vd (0.17 v. 0.2)
PFHxA	400,000	-	-
PFOS	16	8	Immunotoxicity endpoint v. Developmental endpoint
PFHxS	51	84	New information used (NTP, 2018; MDH, 2019)
PFBS	420	1,000	New information used (Feng et al., 2017; USEPA, 2018)
Gen X	370	-	-

PFNA

NH DES proposed MCL (2018)
- Water intake for a woman who is breast-feeding
- NH RfD
- Daily exposure
- 50% Relative Source Contribution

ATSDR Environmental Media Evaluation Guide for children (2018)
- Water intake for children less than 1 year old
- ATSDR MRL
- Daily exposure
- No Relative Source Contribution

Proposed MPART SAW HBV
- MDH toxicokinetic model (2019)
- Water intake varies by age
- ATSDR (2018), NJDEP (2015)
- Daily exposure
- 50% Relative Source Contribution

78 ppt

23 ppt

21 ppt

13 ppt

6 ppt

ATSDR Environmental Media Evaluation Guide for adults only (2018)
- Adult drinking water intake
- ATSDR MRL
- Daily exposure
- No Relative Source Contribution

New Jersey DEP (2015)
- Adult drinking water intake
- NJ developed target serum level
- 200:1 ratio between PFNA serum levels and drinking water concentrations, which is meant to represent a central tendency estimate
- 50% Relative Source Contribution

PFOA

US EPA Lifetime Health Advisory, for PFOA individually or in combination with PFOS (2016)
- Water intake for a woman who is breast-feeding
- US EPA RfD
- Daily exposure
- 20% Relative Source Contribution

78 ppt

70 ppt

ATSDR Environmental Media Evaluation Guide for adults only (2018)
- Adult drinking water intake
- ATSDR MRL
- Daily exposure
- No Relative Source Contribution

NH DES proposed MCL (2018)
- Water intake for a woman who is breast-feeding
- NH RfD
- Daily exposure
- 40% Relative Source Contribution

38 ppt

35 ppt

Minnesota Dept of Health, protective of breast-feeding infants, both from exposure they may receive prenatally and while breast-feeding (2018)
- Water intake varies by age
- US EPA RfD
- Daily exposure
- 50% Relative Source Contribution

ATSDR Environmental Media Evaluation Guide for children (2018)
- Water intake for children less than 1 year old
- ATSDR MRL
- Daily exposure
- No Relative Source Contribution

21 ppt

14 ppt

New Jersey DEP (2017)
- Adult drinking water intake
- NJ RfD
- Daily exposure
- 20% Relative Source Contribution

Proposed MPART SAW HBV
- MDH toxicokinetic model (2019)
- Water intake varies by age
- ATSDR (2018)
- Daily exposure
- 50% Relative Source Contribution

8 ppt

NY Proposed MCL: 10 ppt (not all details are available yet)

PFHxA

Proposed MPART SAW HBV
- Adult drinking water intake
- Luz et al. (2019) Point of Departure
- Total Uncertainty (300x)
- Daily exposure
- 20% Relative Source Contribution

400,000 ppt

- PFHxA selected by Workgroup for development of individual health-based value based on sufficient toxicity data as well as reported detections within Michigan drinking water
- Luz et al. (2019) published risk assessment of PFHxA in *Regulatory Toxicology and Pharmacology* identifying a PoD_{HED} of 24.8 mg/kg-day based on renal tubular degeneration and renal papillary necrosis in rats
- Toxicokinetic adjustment of PoD based on body weight scaling
  - human β phase half-life comparable to animals (Buck and Gannon, 2017)
- Workgroup recommended an increase for the database uncertainty from 3x to 10x for a total UF of 300x

PFOS

NH DES proposed MCL (2018)
- Water intake for a woman who is breast-feeding
- NH RfD
- Daily exposure
- 50% Relative Source Contribution

ATSDR Environmental Media Evaluation Guide for adults only (2018)
- Adult drinking water intake
- ATSDR MRL
- Daily exposure
- No Relative Source Contribution

Proposed MPART SAW HBV
- MDH toxicokinetic model (2019)
- NJDEP (2018), MDH (2019)
- Water intake varies by age
- Daily exposure
- 50% Relative Source Contribution

ATSDR Environmental Media Evaluation Guide for children (2018)
- Water intake for children less than 1 year old
- ATSDR MRL
- Daily exposure
- No Relative Source Contribution

70 ppt

52 ppt

16 ppt

15 ppt

14 ppt

13 ppt

US EPA Lifetime Health Advisory, for PFOS individually or in combination with PFOA (2016)
- Water intake for a woman who is breast-feeding
- US EPA RfD
- Daily exposure
- 20% Relative Source Contribution

Minnesota Dept of Health, protective of breast-feeding infants, both from exposure they may receive prenatally and while breast-feeding (2019)
- Water intake varies by age
- MDH RfD
- Daily exposure
- 50% Relative Source Contribution

New Jersey DEP (2017)
- Adult drinking water intake
- NJ RfD
- Daily exposure
- 20% Relative Source Contribution

NY Proposed MCL: 10 ppt (not all details are available yet)

PFHxS

ATSDR Environmental Media Evaluation Guide for children (2018)
- Water intake for children less than 1 year old
- ATSDR MRL
- Daily exposure
- No Relative Source Contribution

Proposed MPART SAW HBV
- MDH toxicokinetic model (2019)
- Water intake varies by age
- MDH (2019)
- Daily exposure
- 50% Relative Source Contribution
- Small variations in model parameters compared to MDH (2019)

520 ppt

140 ppt

85 ppt

51 ppt

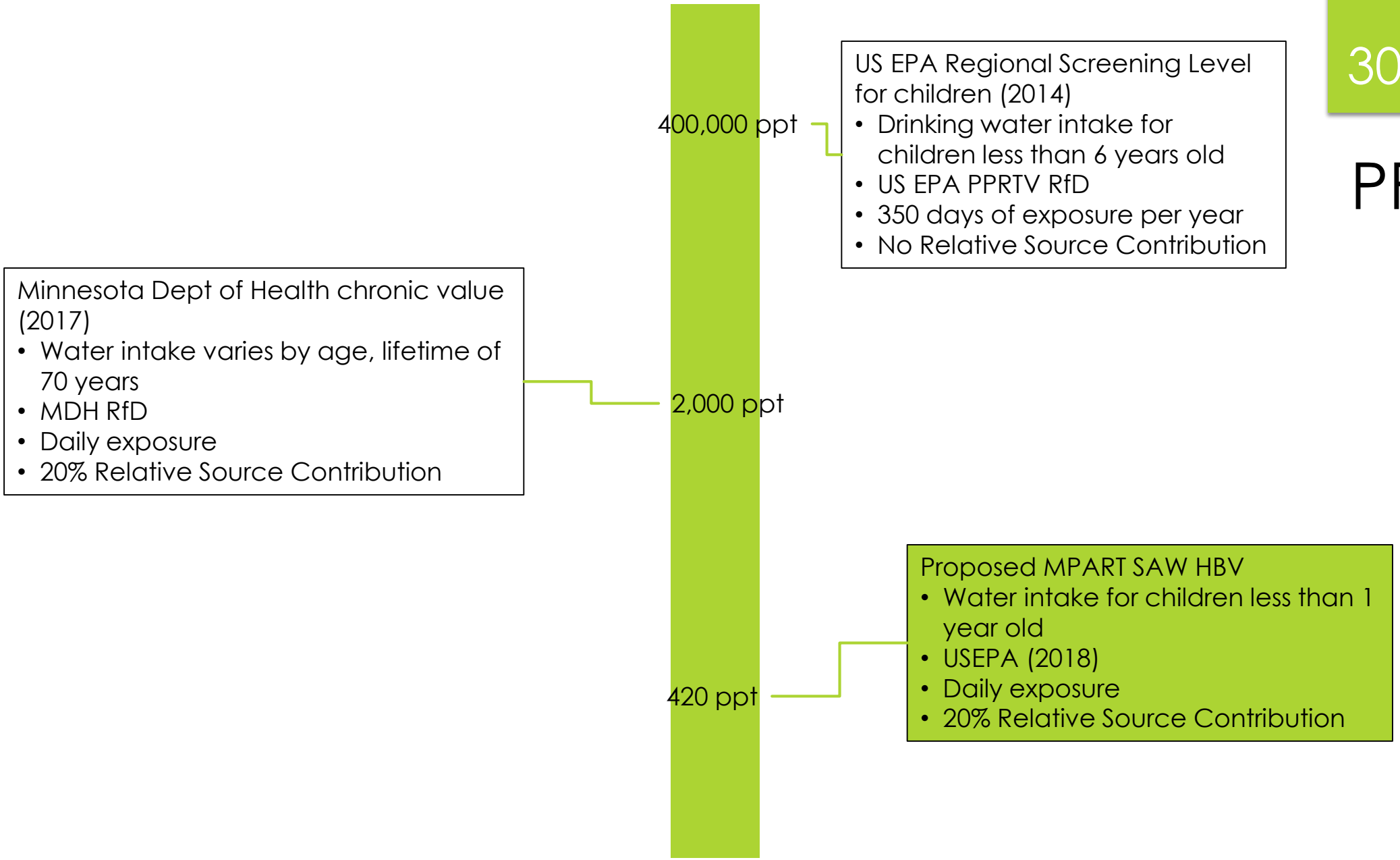
47 ppt

ATSDR Environmental Media Evaluation Guide for adults only (2018)
- Adult drinking water intake
- ATSDR MRL
- Daily exposure
- No Relative Source Contribution

NH DES proposed MCL (2018)
- Water intake for a woman who is breast-feeding
- NH RfD
- Daily exposure
- 50% Relative Source Contribution

Minnesota Dept of Health, protective of breast-feeding infants, both from exposure they may receive prenatally and while breast-feeding (2019)
- Water intake varies by age
- MDH RfD
- Daily exposure
- 50% Relative Source Contribution

PFBS


400,000 ppt
US EPA Regional Screening Level for children (2014)
• Drinking water intake for children less than 6 years old
• US EPA PPRTV RfD
• 350 days of exposure per year
• No Relative Source Contribution
Minnesota Dept of Health chronic value (2017)
• Water intake varies by age, lifetime of 70 years
• MDH RfD
• Daily exposure
• 20% Relative Source Contribution
2,000 ppt
420 ppt
Proposed MPART SAW HBV
• Water intake for children less than 1 year old
• USEPA (2018)
• Daily exposure
• 20% Relative Source Contribution

GenX

North Carolina DHHS (2017)
- Water intake for children less than 1 year old
- NC DHHS RfD (total UF 1000x)
- Daily exposure
- 20% Relative Source Contribution

Proposed MPART SAW HBV
- Adult drinking water intake
- USEPA (2018) (total UF 300x)
- Daily exposure
- 20% Relative Source Contribution

Screening Levels for Long-Chain PFAS

- No scientific consensus on which PFAS should be grouped or the basis of such grouping
  - Proposed Health-Based Drinking Water Values are to be applied individually to the specific PFAS
- Stronger scientific consensus on the similar toxicity profiles for long-chain PFAS
  - Long-Chain defined as ≥C6 for sulfonates and ≥C8 for carboxylates
- Recommending the use of the HBV for PFNA (6 ppt) as screening level for all other long-chain PFAS listed in USEPA Method 537.1 for which an individual HBV was not derived
  - The screening level should not be used to evaluate risk but as a tool for EGLE/public water supplies to use for decision making

Conclusions / Future Directions

- Workgroup commends the State of Michigan for addressing PFAS concerns
- Further research is needed to better elucidate the mode of action for PFAS toxicity as well as further assess endpoints such as endocrine disruption, immunotoxicity and neurodevelopmental effects
- It should be recognized that the science of PFAS is constantly evolving and new information may arise that requires a re-evaluation of the Health-Based Values presented today

Special thanks to the following individuals:

Dr. David Savitz
Mr. Steve Sliver
Dr. Jennifer Gray
Ms. Chelsea Dickerson
Dr. Jamie DeWitt
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Timeline for MCL Development Process