MICHIGAN PFAS ACTION RESPONSE TEAM
AGENDA

Friday, September 27, 2019, 11:00 a.m. – 12:30 p.m.

Michigan Department of Environment, Great Lakes, and Energy
Constitution Hall, Lee Walker Conference Room, Atrium Level North
525 West Allegan Street, Lansing, Michigan 48933

MPART Members Attending:

Kevin Besey, MDARD	Liesl Clark, EGLE	Joneigh Khaldun, MDHHS
Tammy Newcomb, MDNR	Mike Price, DMVA	Kevin Sehlmeyer, LARA
Steve Sliver (Chair)	Mike Trout, MDOT	

Clerk:

Candra Wilcox

1. Welcome
   Liesl Clark, EGLE Director
2. MPART Roll Call
   Candra Wilcox, Clerk
3. Approval of Agenda
   Steve Sliver, MPART Chair
4. Approval of MPART Minutes from meeting of June 27, 2019
   Steve Sliver, MPART Chair
5. Summary and conclusions of input received on the Recommended Health-Based Values for PFAS in Drinking Water.
   Steve Sliver, MPART Chair
   Kory Groetsch, DHHS
   Eric Wildfang, EGLE
   Jennifer Gray, DHHS
6. MPART members vote to accept the summary and conclusions of input received on the Recommended Health-Based Values for PFAS in Drinking Water.
7. Update on the development of state drinking water standards for PFAS.
   George Krisztian, EGLE
8. Report on the Citizens Advisory Workgroup.
   Steve Sliver, Chair
9. MPART members vote to form the Citizens Advisory Workgroup with the citizens registered to participate.
10. Public Comment
11. Adjourn

Environmental Rules Review Committee (ERRC)
Michigan PFAS Action Response Team (MPART)
Constitution Hall, Lansing, Michigan
1:00-3:00 p.m.
June 27, 2019

MEETING MINUTES

MPART Members Present:
Kevin Besey, MDARD
Dan Eichinger, MDNR Director
Joneigh Khaldun, MDHHS
Steve Sliver, MDEQ, MPART Executive Director
Mike Trout, MDOT
Kevin Sehlmeyer, LARA
Jim Shay, DMVA

ERRC Members Present:
Janet Barlow
Tyler Ernst
Mark Fowler
Dave Maness
Fadi Mourad
Robert Nederhood
Jeremy Orr
Eric Pessell
Nickolas Ramos
Helen Taylor
Grant Trigger

ERRC Members Absent: John Myers

Welcome and Introduction of MART Members
Liesl Clark, EGLE Director, welcomed the MPART/ERRC members and audience for attending.

Roll Call
The clerk Heather Feuerstein took roll call. Both MPART and the ERRC had a quorum. Steve Sliver also made comments on the run of show. The meeting materials will be made available online at Michigan.gov/PFASResponse

Approval of Agenda
Both MPART and ERRC voted to accept the agenda.

Approval of ERRC Minutes from April 15 and May 30, 2019
The ERRC approved the minutes from the April 15 and May 30, 2019 meetings.

Approval of MPART Minutes from the April 4, 2019
MPART approved the minutes from the April 4, 2019 meeting.

Presentation: Recommended Health-Based Values for PFAS in Drinking Water
Kevin Cox, a member of the MPART Science Advisory Workgroup presented the Workgroup's recommended health-based values for PFAS in drinking water to MPART and the ERRC.

Motion: Dan Eichinger moved to accept the health-based value recommendations. The motion passed with all ayes.

Public Comment:
John Dulmes made comment on behalf of the Michigan Chemistry Council.

Adjourn
The meeting was adjourned at 2:35 p.m.

TO: MPART Members

FROM: Steve Sliver, Executive Director, MPART

SUBJECT: Public Input on Health Based Values for PFAS in Drinking Water

DATE: September 27, 2019

This memorandum is to make you aware of multiple meeting requests from both state- and national-level stakeholders regarding Michigan's efforts to establish drinking water maximum contaminant levels (MCLs) for PFAS supported by the health-based values (HBVs) recommended by the Science Advisory Workgroup (SAWG) and accepted by MPART members on June 27, 2019.

During development of the MCL rulemaking, the Department of Environment, Great Lakes, and Energy (EGLE) has been focused on feasibility and other factors related to whether the MCLs should be higher or lower than the HBVs. Any comments they received relative to the development of the HBVs themselves were directed to MPART.

In response, MPART technical staff and I met informally with representatives of industry, the regulated community, and environmental organizations this summer to listen to and discuss their respective comments and concerns. These conversations were primarily focused on the content of the SAWG report, but also crossed over into the EGLE rulemaking process and subsequent implementation of the MCLs. It is anticipated that each of these groups will submit formal written comments as part of the MCL rule making public comment process.

<u>Summary</u>

While the individual stakeholder groups brought different perspectives to the discussion table, there were common conversational themes among all three groups. These included:

- The transparency of the State's process used to convene the SAWG and the details of this group's actions to establish the recommended PFAS drinking water health-based values;
- Concern regarding speed with which the process occurred and whether that may have affected the relevant information considered and quality of the outcome; and
- Opportunities for stakeholder input in the MCL process.

Brief summaries of the three separate meetings are provided below. Comments on the details of the HBVs were not included here.

- On July 18, 2019, scientists from 3M walked through the many specific chemical inputs, methods and scientific conclusions considered by the SAWG members for five of the PFAS for which HBVs were recommended. In general, this group provided alternative interpretation of the scientific data considered by the SAWG members that would result in slightly different outcomes.

- On August 20, 2019, a conversation took place with representatives of both the American Chemistry Council and Michigan Chemistry Council. This discussion was primarily focused on the MCL rule making process, implementation of the MCLs, and possible downstream impacts of the MCLs on other EGLE regulatory standards.

- On August 23, 2019, there was a conversation with representatives from the NRDC, Sierra Club, Ecology Center, and concerned Michigan citizen groups. The consistent message from these groups was that Michigan should not squander this opportunity to lead the nation in protecting the public from PFAS by regulating these chemicals as a class rather than individually.

Conclusion

The subject matter of the above comments was discussed to some degree by the SAWG members where it fell within their charge. In many cases these considerations were documented in the final SAWG report. While it's clear that the cross-section of stakeholders involved in these discussions each brought their specific agendas to the conversation, we were not presented with information from any of these groups that would significantly challenge the scientific recommendations put forth by the SAWG.

The scientific database related to human health effects of PFAS exposure is not expected to remain static. This is reflected in the changing landscape of PFAS drinking water values put forth by different states. MPART and EGLE will likely have to develop a strategy to accommodate such information updates in the future. In the meantime, the SAWG report and the recommendations therein are considered transparent, data-driven, and defensible.

cc: Kory Groetsch, DHHS
Jennifer Gray, DHHS
Eric Wildfang, EGLE

MPART Citizens Advisory Workgroup Charter

Draft 9/20/19

OVERVIEW

Per- and polyfluoroalkyl substances (PFAS) are a class of man-made chemicals that are pervasive and persistent in the environment. Some have been associated with adverse health effects. The Michigan PFAS Action Response Team (MPART) was established under Governor Gretchen Whitmer's Executive Order 2019-03 "…to address the threat of PFAS contamination in Michigan, protect public health, and ensure the safety of Michigan's land, air, and water, while facilitating inter-agency coordination, increasing transparency, and requiring clear standards to ensure accountability."

Under the Executive Order, MPART is charged, among other things, with the following outreach duties and responsibilities:

- "Develop routine communication and information-sharing protocols between all members and stakeholders."
- "Perform outreach to ensure all stakeholders in impacted areas are informed, educated, and empowered."
- "Perform outreach to ensure the general public is informed about PFAS contamination and the work of MPART."

The Executive Order also enables MPART to form advisory workgroups to assist it in performing its duties and responsibilities. MPART may adopt, reject, or modify any recommendations proposed by an advisory workgroup.

A Citizens Advisory Workgroup (hereafter "workgroup") is formed to assist MPART with fulfilling its outreach duties and responsibilities and its mandate to address PFAS threats with transparency and accountability. This MPART Citizens Advisory Workgroup Charter (Charter) reflects the thoughtful input from two focus groups of engaged residents in communities impacted by PFAS contamination across Michigan.

PURPOSE

It is a fundamental purpose of this workgroup to advise and assist MPART to partner proactively with PFAS-impacted citizens and communities throughout Michigan, recognizing that the ideas and perspectives of an engaged and empowered citizenry are essential to MPART in fulfilling its duty to protect public health and ensure the safety of Michigan's land, air, and water.

The workgroup will: (1) advise MPART on performing outreach and establishing a dialogue with interested parties to ensure that all community stakeholders in impacted areas are informed, educated, and fully empowered to provide input to MPART regarding PFAS contamination and all non-confidential aspects of the work of MPART; and (2) work with MPART to ensure that the general public is informed in a timely and coordinated manner.

SCOPE

The workgroup will address MPART's communication and information sharing methods and protocols between members and stakeholders, including how it engages with and empowers impacted communities, the methods and timeliness of MPART responses to those communities' inquiries, and how it informs the general public of PFAS-related developments.

The workgroup is encouraged to provide non-binding stakeholder and community input to MPART regarding all non-confidential aspects of MPART's work and may also be asked from time-to-time for input on key communications with statewide implications prior to release.

The workgroup is not intended for technical or regulatory review and input on site-specific investigations and responses, nor is it intended to address specific MPART communications with responsible parties, other agencies, and elected officials. However, workgroup members may make non-binding suggestions as to how modifying existing communications with responsible parties, other agencies, and elected officials might improve the overall effectiveness of MPART's mandate.

Concerns about site-specific investigations and responses should be raised at a local level first, involving the local project team that includes MPART staff and local officials. Should the community feel those concerns are not adequately addressed at the local level, this workgroup may consider how and why those concerns were not adequately addressed and work with either the local project team or MPART to find a solution.

While the workgroup is not a decision-making body, it will be helpful for its members to understand the decision-making process for items not within its scope so they can make recommendations on how best to communicate that information to the public and to help the public understand how they can effectively participate in decisions that impact them. MPART will help workgroup members to understand the current decision-making process.

The workgroup will not be engaged in the review of any personally identifiable information or information that is considered confidential, enforcement-related, and/or attorney/client privileged.

GOALS AND OBJECTIVES

The workgroup will develop a schedule to provide recommendations to MPART under two main goals.

1. How to engage impacted communities:

    a. Review existing protocols.
    b. Recommend new protocols.
    c. Recommend types and timing of public forums and formats for those forums.
    d. Identify gaps in information.
    e. Recommend how to empower community members and stakeholders to provide input on any MPART action or response and to pose questions to MPART regarding those actions or responses, recognizing the inherent value of strong partnerships with communities.
    f. Identify community expectations as to nature, format, and timing of MPART responses to communities.
    g. Recommend how to improve awareness of the public health risk and the response.
    h. Other objectives requested by MPART.

2. How to engage the general public on PFAS and MPART's efforts:

    a. Comment on the MPART Web page and proposed Web updates and provide suggestions for same.
    b. Provide recommendations on how impacted communities and the general public can stay informed via routine updates from MPART.
    c. Provide recommendations as to how public inquiries and comments might be addressed by MPART so as to inform and empower the interested public.
    d. Provide recommendations on potential outreach materials and information.
    e. Provide comment on outreach material.
    f. Other objectives requested by MPART.

COMPOSITION

The workgroup will consist of residents from impacted communities, subject to the following:

- An impacted community is generally defined as any city, township, or village that has at least one official MPART PFAS site within its boundaries. An official MPART PFAS site is defined as a location with a groundwater result over 70 parts per trillion (ppt) PFOS+PFOA or a result exceeding any Michigan maximum contaminant level (MCL) for any PFAS constituent, once promulgated. MPART may determine a community is impacted even if it does not have an official MPART PFAS site.
- Interested residents must register to be a member. The content of the registration form is contained in Attachment 1. MPART will notify residents as necessary of the opportunity to register through various electronic media, including but not limited to GovDelivery, news releases, and other email distribution lists.
- MPART will appoint two members from an impacted community. When making the appointment, MPART may consult with other workgroup members, the applicants, and local leaders. (Other applicants not appointed will still be encouraged to participate in an unofficial capacity.)
- Member appointments are for terms of two years with no limitation on reappointment.
- The members may elect a Chairperson and Vice Chairperson for terms not to exceed two years to help lead the workgroup and coordinate with MPART.
- Employees of the State of Michigan or federal government, individuals acting in the sole interest of an industry, and officials of state or national associations are not eligible to be members. Representatives of organizations intended primarily for citizen engagement on PFAS are not excluded. MPART will consult with other workgroup members on any exception to these guidelines.
- An appointment may be rescinded in writing by MPART for cause.

EXPECTATIONS OF MEMBERS

Members are expected to engage the workgroup to the extent possible and consistent with the following:

- Read and adhere to this workgroup Charter.
- Actively participate in scheduled meetings.
- Provide timely follow up to action items, such as submitting written comments on meeting materials.

- Be a representative of the workgroup in his or her community and keep the residents informed.
- Respect requests to not disclose information that is draft deliberative, such as an embargoed news release where MPART is seeking workgroup input.
- Value and respect diversity.
- Act with integrity.

Members are volunteers with multiple demands for their time. The demands for the workgroup should be reasonable given their other personal and professional obligations.

MEETINGS

The workgroup will meet routinely:

- Meetings will be scheduled with the appointed members.
- Meetings will be open to other interested residents.
- The meeting frequency will be monthly, except as adjusted by MPART and the members.
- The meetings will typically be held on a weeknight, Monday–Friday, from 6:00 p.m. to 7:30 p.m.
- All meeting formats will be a web conference to enable remote participation.
- The meetings will be broadcast from Constitution Hall in Lansing, except MPART will endeavor to broadcast one meeting on a quarterly basis from a community impacted by PFAS contamination.
- An agenda will be provided prior to each meeting and generally include:
  - Items recommended from a previous meeting.
  - MPART update on key state initiatives (e.g., MCLs) and site developments.
  - Development of recommendations for items under review by the workgroup.
  - Questions, comments, and updates from members.
  - MPART responses to prior questions, comments, and updates from members not fully answered in prior meetings.
- Every effort will be made to get input from all appointed members during the meeting. As time permits, other residents who are participating in the meeting will also be given an opportunity for comments, questions, and input. If time does not permit other residents to participate, those residents will be given an opportunity to submit their comments, questions, and input in writing to be considered at the next workgroup meeting.
- The meetings are not subject to the Open Meetings Act.

COMMUNICATIONS

MPART will facilitate communications for the workgroup:

- MPART will maintain an email distribution list.
- MPART will post workgroup information on the Web.
- The web conferences are recorded and will be made available online.
- The GovDelivery email notification system will be available for key messaging from the workgroup.

SUPPORT

MPART will provide logistical, administrative, and technical support to the workgroup:

- Schedule workgroup meetings after consultation with the workgroup.
- Prepare workgroup agendas after receipt of workgroup input and subject to the approval of the workgroup.
- Facilitate workgroup meetings.
- Prepare workgroup meeting summaries.
- Provide routine updates to the workgroup.
- Respond to workgroup comments, inquiries, and input in a timely fashion.
- Provide support as resources from all MPART agencies as needed.
- Maintain current information on the MPART Web site.

Citizens Advisory Workgroup Registrations
9/20/19

Community/Site	First Name	Last Name	City
Belmont-House St.	Jennifer	Carney	Belmont
Belmont-House St.	Sandy	Wynn-Stelt	Belmont
Camp Grayling	Gary	Pettyjohn	Northville
Central Sanitary LDF	Daniel	Buyze	Pierson
Gordie Howe Bridge	Connie	Boris	Grosse Pointe Farms
Gordie Howe Bridge	Theresa	Landrum	Detroit
GR Ford Airport	Patti	Baldwin	Grand Rapids
Muskegon	Lea	Dyga	East Lansing
Muskegon	Matthew	Farrar	Muskegon
Robinson Twp	Jeffrey	Dutton	Grand Haven
Rockford Tannery	A.J.	Birkbeck	Ada
Rockford Tannery	Kenneth	Harvey	Rockford
Van Ettan Lake	Tony	Spaniola	Troy
Van Ettan Lake	David	Winn	Shelby Twp
Wurtsmith AFB	Aaron	Weed	Oscoda
NA	Kate	Gislason	Williamston
NA	Shellene	Thurston	Saginaw
NA	William	Barnett	Cadillac
NA	David	Lipscomb	Traverse City
NA - Huron River Watershed	Daniel	Brown	Ann Arbor
NA - Huron River Watershed	William	Creal	Whitmore Lake
NA - Huron River Watershed	Elizabeth	Hauptman	Brighton
NA - Huron River Watershed	Robert	Potocki	Brighton
NA - Menasha	Pam	McQueer	Otsego

Review of Michigan Science Advisory Workgroup (MI SAW) Health-Based Drinking Water Value Recommendations for PFAS

Geary Olsen, DVM, PhD
Sue Chang, PhD

3M Company

July 18, 2019

Current Recommended Health-Based Drinking Water Value by Michigan Science Advisory Workgroup

		PFOS	PFOA	PFHxS	PFBS	PFHxA
Reference Study		Dong et al. 2009	Onishchenko et al. 2011; Koskela et al. 2016	NTP, 2018 (unpublished data)	Feng et al. 2017	Klaunig et al. 2015
Critical effect(s)		↓ Plaque forming cells ↑ liver weight	Neurobehavioral effects Skeletal alteration	↓ Free T4	↓ Total T4	↑ Renal tubular hyperplasia ↑ Renal papillary necrosis
Species		Rats	Mice	Rats	Mice	Rats
Serum Elimination Toxicokinetics (TK)	Rodent $T_{1/2}$	40 - 60 days	~ 7 days	~ 30 days	~0.08 day	~ 0.08 day
	Human $T_{1/2}$	1241 days	840 days	1935 days	27.7 days	32 days
TK adjustment sought by MI SAW?		Yes	Yes	Yes	Yes	No
Relative Source of Contribution		50%	50%	50%	20%	20%
Exposure Scenario for drinking water		MDH breast milk model	MDH breast milk model	MDH breast milk model	7.8-kg child; 1.106 L/day	80-kg adult; 3.353 L/day
Recommended Health-Based Drinking Water Value (ng/L)		16	8	51	420	400,000

PFOS

2019 MI SAW Recommended Health-Based Drinking Water Value for PFOS

Reference Study		Mouse immunotoxicity (Dong et al., 2009)
Effects		↓ Plaque forming cell response and ↑ liver weight
Basis		NOAEL
POD (serum PFOS level)		0.674 mg/L
Human Equivalent Dose (HED)		0.0000866 mg/kg-d (= POD x V_d x 0.693 / $T_{1/2}$ = 0.674 x 0.23 x 0.693 / 1241)
Uncertainty Factor (UF)	Interspecies	3
	Intraspecies	10
	Database	1
Toxicity Value		2.89 ng/kg-d (=HED / UF = 0.0000866 x 10^6 / 30)
RSC (%)		50%
Water consumption (L/kg/day)		Varied (sum of life stages based on MDH breast milk model)
Water guidance value (ng/L)		16

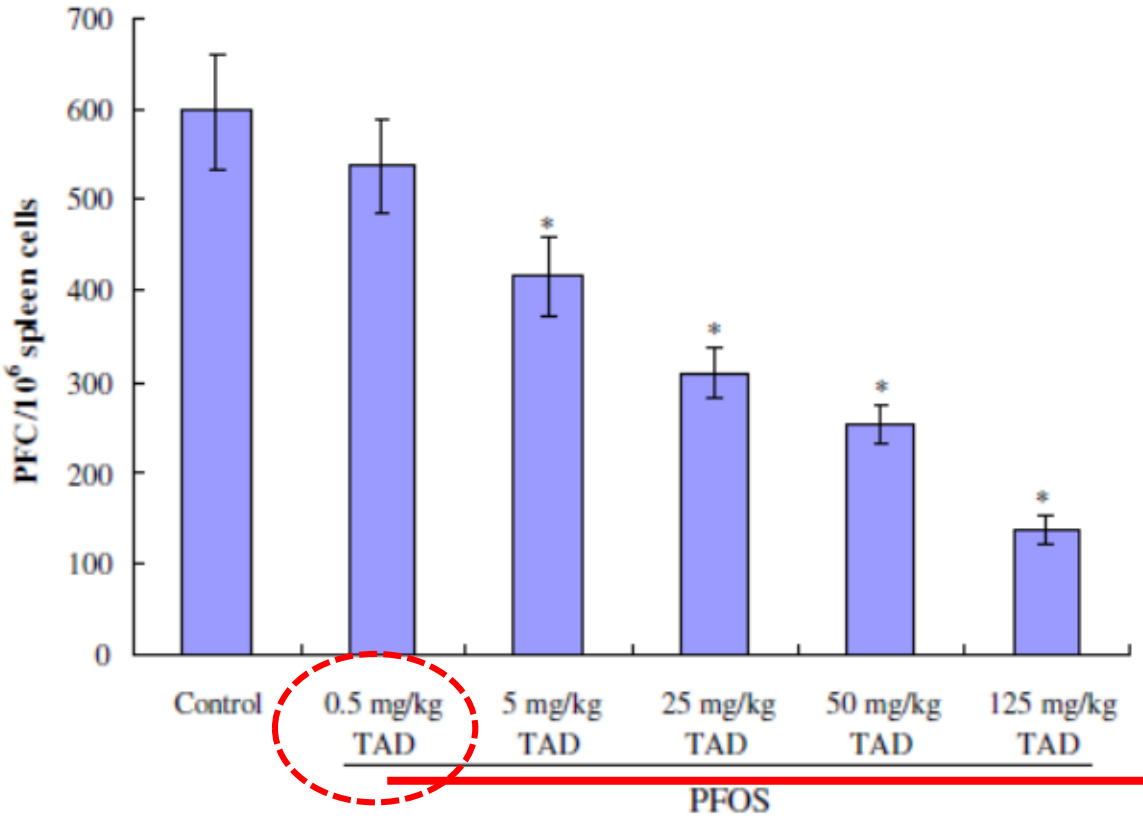
Arch Toxicol (2009) 83:805–815
DOI 10.1007/s00204-009-0424-0

ORGAN TOXICITY AND MECHANISMS

Chronic effects of perfluorooctanesulfonate exposure on immunotoxicity in adult male C57BL/6 mice

Guang-Hui Dong · Ying-Hua Zhang · Li Zheng ·
Wei Liu · Yi-He Jin · Qin-Cheng He

Source: Dong et al 2009 Arch Toxicol 83 805-15



PFOS (mg/kg TAD)	*n*	PFOS concentration in serum (mg/l)
Control	10	0.048 ± 0.014
0.5	10	0.674 ± 0.166*
5	10	7.132 ± 1.039*
25	10	21.638 ± 4.410*
50	10	65.426 ± 11.726*
125	10	120.670 ± 21.759*

Fig. 7 Sheep red blood cell (SRBC)-specific IgM plaque forming cell (*PFC*) response was measured using the Cunningham modification of the Jerne plaque assay in adult male C57BL/6 mice following oral exposure to PFOS for 60 days. Data are presented as mean ± SEM. *Significantly different from control ($P \leq 0.05$). PFC data were log transformed for statistical analysis; $n = 10$ in each group. *TAD* total administered dose over the course of 60 days

HEALTH-BASED MAXIMUM CONTAMINANT LEVEL SUPPORT DOCUMENT: PERFLUOROOCTANE SULFONATE (PFOS)

(CAS #: 1763-23-1; Chemical Formula: $C_8HF_{17}O_3S$)

New Jersey Drinking Water Quality Institute
Health Effects Subcommittee

June 5, 2018

Subcommittee Members:
Jessie A. Gleason, M.S.P.H., Chair
Keith R. Cooper, Ph.D.
Judith B. Klotz, M.S., Dr.P.H.
Gloria B. Post, Ph.D., D.A.B.T.
George Van Orden, Ph.D.

From NJDWQI, 2018, page 236

"Note that the plaque-forming cell response data were reported graphically in Dong et al. (2009, Figure 7 therein). The study authors provided the actual numerical data (mean ± standard error of the mean), which for the control group to the highest dose group were: 597±64, 538±52, 416±43, 309±27, 253±21, and 137±16 (personal communication with G. Dong, 2016). "

Environmental Research 171 (2019) 452–469

Contents lists available at ScienceDirect

Environmental Research

journal homepage: www.elsevier.com/locate/envres

Review article

The derivation of a Reference Dose (RfD) for perfluorooctane sulfonate (PFOS) based on immune suppression

Brian Pachkowski*, Gloria B. Post, Alan H. Stern

Bureau for Risk Analysis, Division of Science, Research and Environmental Health, New Jersey Department of Environmental Protection, Trenton, NJ, USA

Source: Pachowski et al. 2019 Eviron Res 171 452-469

3.1. Exposure-response modeling

When possible, the POD is derived from the exposure-response data through benchmark dose modeling (USEPA, 2012). We attempted benchmark dose modeling of the data for the decreased PFC response dendpoint from the Dong et al. (2009) study using USEPA benchmark dose software (BMD software, ver. 2.6.0.1). Using all six data points for PFC response from Dong et al. (2009), none of the available benchmark dose models gave an acceptable fit. This was due, in part, to a disproportionally large decrease in PFC response at the highest dose that was possibly indicative of a stress response (e.g., increased serum corticosterone) and/or splenic cytotoxicity (data not shown). Therefore, benchmark dose modeling was attempted with the omission of the highest dose. Although several models gave ostensibly acceptable fits to these data, the BMDS software identified that these data did not meet the criteria for an assumption of constant variance. In addition, the software was unable to calculate a BMDL under the assumption of nonconstant variance. This was likely due to the steepness of the dose-response in the vicinity of the BMD (DWQI, 2018).

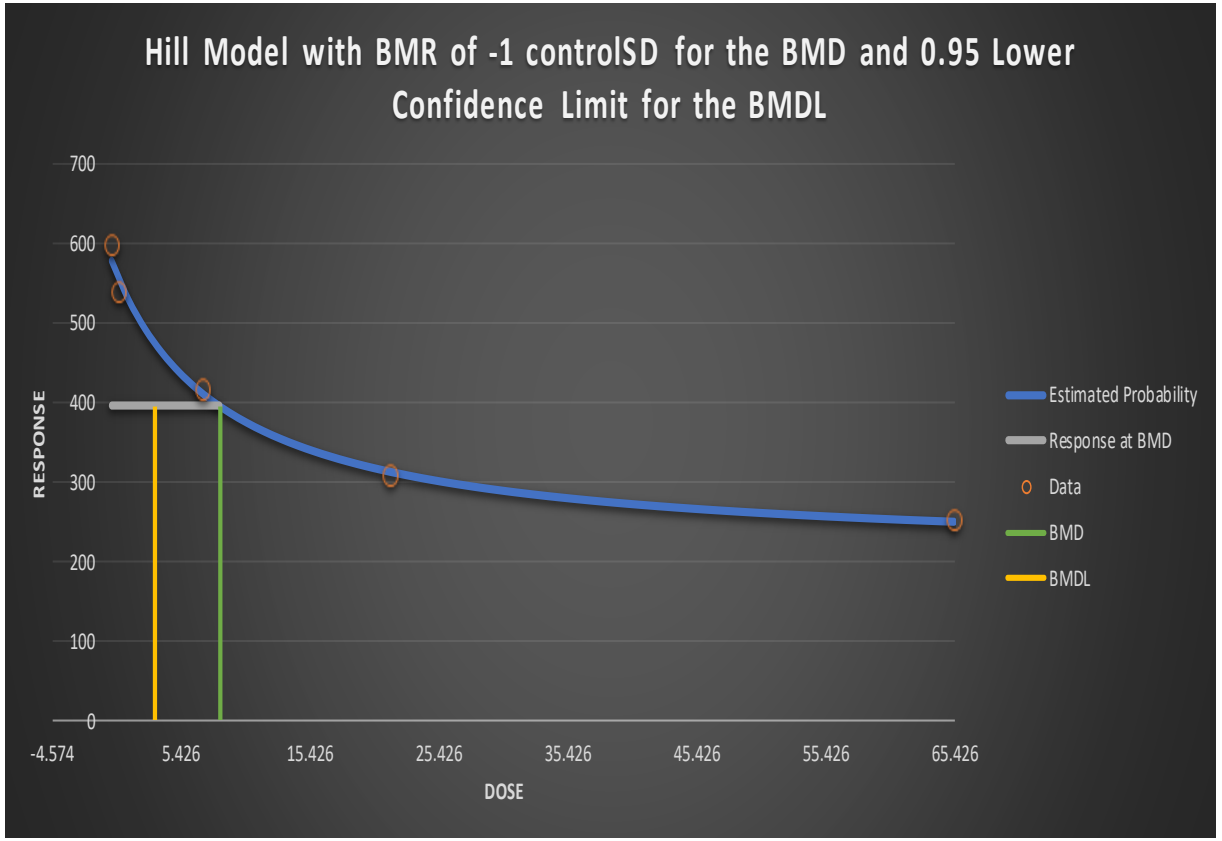
When no BMDL can be derived, a NOAEL or LOAEL is used as the POD (USEPA, 2012). We identified the NOAEL serum concentration of 674 ng/ml for decreased PFC response from Dong et al. (2009) as the POD.

- **Standard deviation values (SD) are required for BMDS, not standard error of the mean (SEM)**

- **$SD = SEM \times (\text{sample size})^{0.5}$**

- **Using the adjusted dataset (mean ± SD), plaque-forming cell response and serum [PFOS] reported by Dong et al. 2009 can be modeled by BMDS 3.1**

Using the adjusted data as mean ± SD, plaque-forming cell response and serum [PFOS] reported by Dong et al. 2009 yielded a $BMDL_{1SD}$ at 3.4 mg/L (3,400 ng/mL)



Model	RiskType	BMD (mg/L)	BMDL (mg/L)	BMDU (mg/L)	Test 4 P-Value	AIC	BMDS Recommendation
Exponential 4 (NCV)	Std. Dev.	10.03	5.10	24.02	0.74	626.74	Viable - Alternate
Exponential 5 (NCV)	Std. Dev.	9.98	5.09	24.02	0.74	626.74	Viable - Alternate
Hill (NCV)	*Std. Dev.*	*8.43*	*3.40*	*25.59*	*0.78*	*626.65*	*Viable - Recommended*

2019 MI SAW Recommended Health-Based Drinking Water Value for PFOS

Reference Study		Mouse immunotoxicity (Dong et al., 2009)
Effects		↓ Plaque forming cell response and ↑ liver weight
Basis		NOAEL
POD (serum PFOS level)		~~0.674~~ 3.4 mg/L
Human Equivalent Dose (HED)		~~0.0000866~~ 0.000437 mg/kg-d (= POD x V_d x 0.693 / $T_{1/2}$ = ~~0.674~~ 3.4 x 0.23 x 0.693 / 1241)
Uncertainty Factor (UF)	Interspecies	3
	Intraspecies	10
	Database	1
Toxicity Value		~~2.89~~ 14.6 ng/kg-d (=HED / UF = ~~0.0000866~~ 0.000437 x 10^6 / 30)
RSC (%)		50%
Water consumption (L/kg/day)		Varied (sum of life stages based on MDH breast milk model)
Water guidance value (ng/L)		~~16~~ 80

- MPART SAW should have performed their own BMD analysis

Page 19 of MPART SAW Report:

"The Workgroup noted that the Benchmark Dose approach is preferred over the use of a NOAEL/LOAEL."

- $BMDL_{1SD}$ = 3.4 mg/L (5X ↑ than NOAEL)

- What does "Reasonable Maximum Exposure (RME) Mean?

Exposure assumptions in the MDH human breast milk model

(Source: Goeden 2019 J Expo Sci Environ Epi 29 183-195)

Table 2 Selection of different central (e.g., mean) and upper (e.g., 95th percentile) parameter values for alternative scenario evaluation

Scenario	Intake rate	Breastfeeding duration	Half-life	Transfer rates	Volume of distribution (V_d)	V_d adjustment factor
MDH RME	Upper	Upper	Central	Central	Central	Central
Alternative 1	Central	Central	Upper	Upper	Central	Central
Alternative 2	Upper	Central	Upper	Central	Central	Central
Alternative 3	Central	Upper	Upper	Central	Central	Central

See Table 1 for actual numerical values used for each parameter

Please note:
This model was for PFOA; the same assumptions were used for PFOS and PFHxS models

What does "Upper" Mean for Exposure in MDH Breast Milk Model?

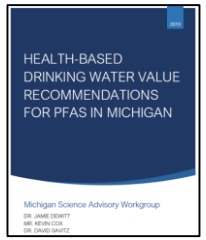
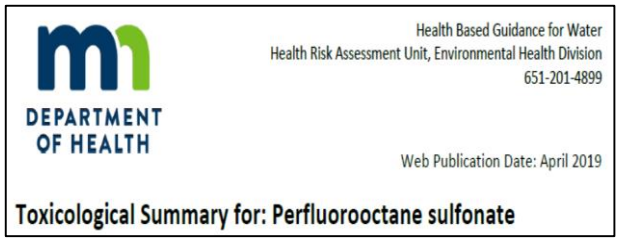
	Mom's water intake (before, during, and after pregnancy)	Duration of babies that are exclusively breast fed for one year	Child post-weaning water intake (1 – 50 yrs old)	Theoretical population assumed to be exposed at this percentile (%)
Exposure Scenarios	95th percentile*			0.01%
	90th percentile			0.1%
	85th percentile			0.33%
	80th percentile			0.8%
	75th percentile			1.6%

*From Goeden et al. (2019): intake assumptions

"American Academy of Pediatrics recommends exclusively breastfeeding for the first 6 months, with continued breastfeeding alongside introduction of complementary food for at least 12 months. The Center for Disease Control (CDC) Breastfeeding Report Card for 2016 reports nearly 66% of mothers in Minnesota report breastfeeding at 6 months, with 31.4% exclusively breastfeeding. At 12 months, 41% of mothers reported breastfeeding. Central tendency: exclusively a breastfed intake rates used from birth to 6 months of age. From 6 to 12 months, breastfeeding is phased out and water intake is phased in. Upper percentile: exclusively breastfed intake rates used from birth to 12 months of age. At 12 months, breastfeeding ends and water intake begins."

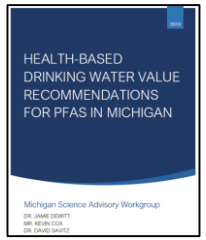
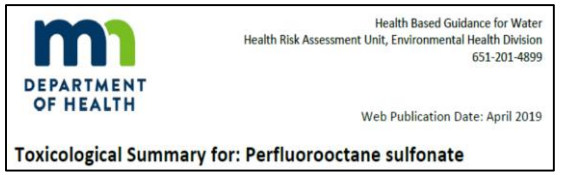
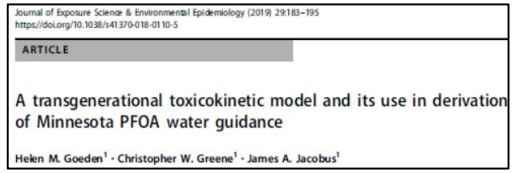
Inconsistencies in the Breast Milk Model Parameters

(Sources: MI SAW, 06/2019; MDH / MDHHS, 04/2019)

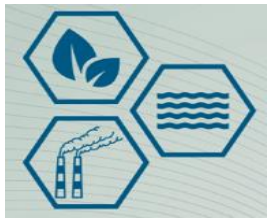
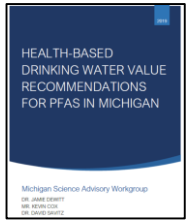
 MI SAW (06/2019)	 Minnesota Department of Health (04/2019)
Page 17: PFOS Exposure parameters for drinking water HBV	Page 3: Toxicokinetic Model Description
Breast-fed infant, which is also protective of a formula-fed infant Placental transfer of 43% (MDHHS 2019) Breastmilk transfer of 1.3% (MDHHS 2019) Human serum half-life of 1241 days (3.2 years) (Li et al. 2018) Volume of distribution of 0.23 L/kg (Thompson et al. 2010)	In both scenarios the simulated individuals began life with a pre-existing body burden through placental transfer of PFOS (maternal serum concentration x 40%) based on average cord to maternal serum concentration ratios reported in the literature. The serum concentration of the mother at delivery was assumed to be at steady-state and was calculated by using the equation above with a time-weighted 95th percentile intake from birth to 30 years of age (0.047 L/kg-d). During lactation a 95th percentile water intake rate of 55 mL/kg-d and a body weight of 65.2 kg ((USEPA 2011), Table 3-3) was used to calculate daily maternal serum concentrations. Consistent with MDH methodology, 95th percentile water intake and upper percentile breastmilk intake rates were used to simulate a reasonable maximum exposed individual. A PFOS breastmilk transfer factor of 1.7%, based on average breastmilk to maternal serum concentration ratios reported in the literature, was used to calculate breastmilk concentration.

Inconsistencies in the Breast Milk Model Parameters

(Sources: MI SAW, 06/2019; MDH / MDHHS, 04/2019)

 MI SAW (06/2019)	 Minnesota Department of Health  Goeden et al. 2019
Page 17: PFOS Exposure parameters for drinking water HBV	Table 1: Exposure and chemical-specific toxicokinetic parameters used in modeling PFOA serum concentrations
95th percentile drinking water intake, consumers only, from birth to more than 21 years old (Goeden et al. [2019]) Upper percentile (mean plus two standard deviations) breast milk intake rate (Goeden et al. [2019]) Time-weighted average water ingestion rate from birth to 30-35 years of age (to calculate maternal serum concentration at delivery) (Goeden et al. [2019])	**For calculation of maternal serum concentration at time of delivery, a time-weighted average water intake rate was calculated from birth to 30–35 years of age,** resulting in a mean and **95th percentile water intake rate** of 18 and **47 mL/kg per day,** respectively**.** (final model parameter for calculation of the PFOA HBGVs shown in **bold**)

Inconsistencies in the Parameter Recommendation by Michigan Science Advisory Workgroup (MI SAW)

	 **ATSDR Toxicological Profile for Perfluoroalkyls (*draft*) June 2018**	 **MI SAW Drinking Water Recommendation June 2019** (sponsored by MPART; Michigan EGLE; Michigan HHS)
Reviewers or Workgroup Members	Jamie DeWitt David Savitz Deborah Cory-Slechta Edward Emmitt	Jamie DeWitt David Savitz Kevin Cox
Recommended PFAS serum elimination half-lives in human to calculate guidance values	PFOS → 2000 days (5.4 years)[1] PFOA → 1400 days (3.8 years)[1] PFHxS → 3100 days (8.5 years)[1]	PFOS → 1241 days (3.4 years)[2] PFOA → 840 days (2.3 years)[3] PFHxS → 1935 days (5.3 years)[2]

1. Olsen et al. 2007 Environ Health Perspect 115 1298-1305
2. Li et al. 2018 Occup Environ Med 75 46-51
3. Bartell et al. 2010 Environ Health Perspect 118 222-228

PFOA

2019 MI SAW Recommended Health-Based Drinking Water Value for PFOA

Reference Study		Mouse Developmental Studies (Onishchenko et al. (2011) and Koskela et al. (2016))
Effects		Neurobehavioral effects and skeletal alteration
Basis		LOAEL
POD (serum PFOA level)		8.29 mg/L
Human Equivalent Dose (HED)		0.001163 mg/kg-d (= POD x V_d x 0.693 / $T_{1/2}$ = 8.29 x 0.17 x 0.693 / 840)
Uncertainty Factor (UF)	LOAEL-to-NOAEL	3
	Interspecies	3
	Intraspecies	10
	Database	3
Toxicity Value		3.9 ng/kg-d (=HED / UF = 0.001163 x 10^6 / 300)
RSC (%)		50%
Water consumption (L/kg/day)		Varied (sum of life stages based on MDH breast milk model)
Water guidance value (ng/L)		8

Toxicological relevance of endpoints: Non-standardized testing methods

Only single dose was used in the study (D-R relationship not possible to evaluate)

- What does "Reasonable Maximum Exposure (RME) Mean?

Minnesota also weighed in on ATSDR's selection of PFOA studies

(Source: https://www.regulations.gov/document?D=ATSDR-2015-0004-0057)

DEPARTMENT OF HEALTH

Protecting, Maintaining and Improving the Health of All Minnesotans

August 17, 2018

Ms. Susan Ingber
Agency for Toxic Substances and Disease Registry
Division of Toxicology and Human Health Sciences
1600 Clifton Road NE, MS F-57
Atlanta, GA 30329

Sincerely,

Paul Allwood, PhD, MPH, RS
Assistant Commissioner
P.O. Box 64975
St. Paul, MN 55164-0975

Comments on PFOA Draft MRL:

Both critical studies selected by ATSDR (Onishchenko et al and Koskela et al) used only one dose level and a small number of animals, making dose response analysis impossible. In addition, ATSDR appears to have automatically applied a full 10 LOAEL-to-NOAEL uncertainty factor without discussion of severity of the effects observed at the LOAEL.

Authors in Onishchenko, described the neurobehavioral outcome (changes in exploratory behavior and global activity) as mild alterations in motor function. The effects reported in Koskela et al 2016 at the single dose evaluated were apparently considered adverse by ATSDR even though no impact on biomechanical properties were observed and the morphological changes were considered mild. A discussion regarding the magnitude and application of the LOAEL-to-NOAEL uncertainty factor should be included.

A human half-life of 1400 days (~3.8 years) was used to calculate HEDs; however, more recent studies on exposed general populations suggest a shorter half-life. See General Toxicology Comments above.

PFOA Drinking Water Value: USEPA vs. MDH

		2009 USEAP PHA	USEPA (2016)	MDH (2018)
Reference Study		Mouse Developmental Study (Lau et al., 2006)		
Effects		↑ Liver weight	↓ limb ossification ↑puberty onset in male pups	↓ Limb ossification; ↓ trend in pup body weight ↑ Puberty onset in male pups ↑ Dam liver weight
Basis		$BMDL_{10}$ (dose)	LOAEL (serum)	LOAEL (serum)
Point of Departure		0.46 mg/kg-d	38 mg/L	38 mg/L
TK Adjustment Factor (kg-d/L)		0.0124 (= CL_{human} /CL_{mouse} = 17 / 1387)	0.00014 (=V_d x 0.693 / $T_{1/2}$= 0.17 x 0.693 / 839.5)	7142 (=1/V_d x 0.693 / $T_{1/2}$= 1/0.00014)
Human Equivalent Dose, HED (mg/kg-d)		0.0057 (= 0.46 x 0.0124)	0.0053 (=38 x 0.00014)	0.0053 (=38/7142)
Uncertainty Factor (UF)	Interspecies TD	3	3	3
	Intraspecies	10	10	10
	LOAEL-to-NOAEL	1	10	3
	Database uncertainly	1	1	3
Reference Dose, RfD (mg/kg-d)		0.00019 (= 0.0057/30)	0.00002 (=0.0053/300)	0.000018 (=0.0053/300)
Relative Source of Contribution (RSC)		0.2	0.2	0.5
Water Consumption (L/kg/d)		0.1 (10 kg child)	0.054 (Lactating women)	Varied (sum of life stages via breast milk model)
Water Guidance Level (ng/L)		400	70	35

PFHxS

2019 MI SAW Recommended Health-Based Drinking Water Value for PFHxS

Reference Study		Rat 28-day study (NTP, 2018)
Effects		↓ Free T4
Basis		$BMDL_{20}$
POD (serum PFHxS level)		32.4 mg/L
Human Equivalent Dose (HED)		0.00292 mg/kg-d (= POD x V_d x 0.693 / $T_{1/2}$ = 32.4 x 0.25 x 0.693 / 1935)
Uncertainty Factor (UF)	Interspecies	3
	Intraspecies	10
	Database	10
Toxicity Value		9.7 ng/kg-d (=HED / UF = 0.00292 x 10^6 / 300)
RSC (%)		50%
Water consumption (L/kg/day)		Varied (sum of life stages based on MDH breast milk model)
Water guidance value (ng/L)		51

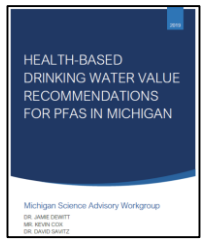
- Unpublished study
- Rat is not an ideal model to study human thyroid
- Fundamental differences exist between rats and humans
- Negative bias present with high serum [PFHxS] for free T4 measurements with analog methods
- Well-documented for PFOS and other PPARα activators
- Equilibrium dialysis-based assays should be used (NTP most likely did not use this method)
- MI SAW failed to recognize that thyroid histopathology and serum TSH in NTP study were **normal** (key indicators for thyroid status, not FT4)

- Use of $BMDL_{20}$ is not justified

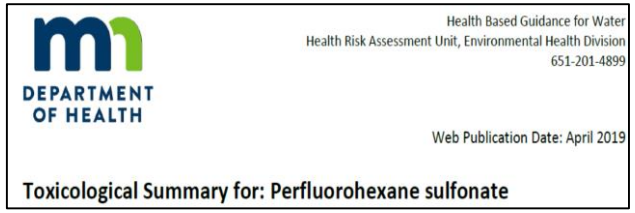
- What does "Reasonable Maximum Exposure (RME) Mean?

Inconsistencies in the Breast Milk Model Parameters

(Sources: MI SAW, 06/2019; MDH / MDHHS, 04/2019)



MI SAW (06/2019)



Minnesota
Department of Health (04/2019)

Page 17: PFOS Exposure parameters for drinking water HBV	Pages 2 - 3: Toxicokinetic Model Description
Breast-fed infant, which is also protective of a formula-fed infant Placental transfer of 80% (MDHHS 2019) Breastmilk transfer of 1.2% (MDHHS 2019) Human serum half-life of 1935 days (Li et al. 2018)	In both scenarios the simulated individuals began life with a pre-existing body burden through placental transfer of PFHxS (maternal serum concentration x 70%) based on median cord to maternal serum concentration ratios reported in the literature. The serum concentration of the mother at delivery was assumed to be at steady-state and was calculated by using the equation above with a time-weighted 95th percentile intake from birth to 30 years of age (0.047 L/kg-d). During lactation a 95th percentile water intake rate of 55 mL/kg-d and a body weight of 65.2 kg ((USEPA 2011), Table 3-3) was used to calculate daily maternal serum concentrations. Consistent with MDH methodology, 95th percentile water intake and upper percentile breastmilk intake rates were used to simulate a reasonable maximum exposed individual. A PFHxS breastmilk transfer factor of 1.4%, based on average breastmilk to maternal serum concentration ratios reported in the literature, was used to calculate breastmilk concentration.

PFBS

2019 MI SAW Recommended Health-Based Drinking Water Value for PFBS

Reference Study		Mouse developmental (Feng et al., 2017)
Effects		↓ Total T4
Basis		$BMDL_{20}$
POD (serum PFBS level)		28.19 mg/L
Human Equivalent Dose (HED)		0.0892 mg/kg-d [= (POD) / ($T_{1/2}$ human / $T_{1/2}$ mouse) = 28.19 / 316]
Uncertainty Factor (UF)	Interspecies	3
	Intraspecies	10
	Database	10
Toxicity Value		300 ng/kg-d (=HED / UF = 0.0892 x 10^6 / 300)
RSC (%)		20%
Water consumption (L/kg/day)		1.106 L/day for 7.8-kg child (TWA from birth to 1 year old)
Water guidance value (ng/L)		420

- Mouse is not an ideal model to study human thyroid
- Fundamental differences exist between mice and humans
- Hypothyroxinemia ≠ hypothyroidism
- Well-documented for PPARα activators
- Feng et al. did not offer thyroid histopathology or serum TSH data (key indicators for thyroid status, not TT4)

- Use of $BMDL_{20}$ is not biologically justified
- $BMDL_{1SD}$ should be used (approximately 2X ↑)

- Inconsistent dose adjustment used by MI SAW

Compound	Dose adjustment formula
PFOS, PFOA, & PFHxS	POD x V_d x 0.693 / $T_{1/2\ human}$
PFBS	POD / ($T_{1/2\ human}$/$T_{1/2\ mouse}$)

2019 MI SAW Recommended Health-Based Drinking Water Value for PFBS

Reference Study		Mouse developmental (Feng et al., 2017)
Effects		↓ Total T4
Basis		$BMDL_{20}$
POD (serum PFBS level)		~~28.19~~ 60 mg/L
Human Equivalent Dose (HED)		~~0.0892~~ 0.190 mg/kg-d [= (POD) / ($T_{1/2}$ human / $T_{1/2}$ mouse) = ~~28.19~~ 60 / 316]
Uncertainty Factor (UF)	Interspecies	3
	Intraspecies	10
	Database	10
Toxicity Value		~~300~~ 633 ng/kg-d (=HED / UF = ~~0.0892~~ 0.190 x 10^6 / 300)
RSC (%)		20%
Water consumption (L/kg/day)		1.106 L/day for 7.8-kg child (TWA from birth to 1 year old)
Water guidance value (ng/L)		~~420~~ 892

PFHxA

2019 MI SAW Recommended Health-Based Drinking Water Value for PFHxA

Reference Study		Rat 2-year study (Klaunig et al. 2015)
Effects		↑ Renal tubular degeneration ↑ Renal papillary necrosis
Basis		$BMDL_{10}$
POD (serum PFHxA level)		90.4 mg/L
Human Equivalent Dose (HED) (mg/kg-d)		24.8 mg/kg-d (= POD / $BW_{human}/BW_{rat})^{1/4}$ = 90.4 / 3.65)
Uncertainty Factor (UF)	Interspecies	3
	Intraspecies	10
	Database	10
Toxicity Value		83,000 ng/kg-d (=HED / UF = 24.8 x 10^6 / 300)
RSC (%)		20%
Water consumption (L/kg/day)		3.353 L/day for 80-kg adult
Water guidance value (ng/L)		400,000

- MI SAW did not adjust for human TK

Page 14 of MI SAW Report:

"The Workgroup took into consideration the available serum half-life data presented in Russell et al. (2013) and concluded that, unlike most PFAS, allometric scaling could be supported."

Inconsistent Human TK Adjustment for PFHxA and PFBS

	Human $T_{1/2}$	Rodent $T_{1/2}$	Did MI SAW use TK adjustment based on human $T_{1/2}$?
PFHxA	32 days	2 - 9 hours (rats)	NO
PFBS	27.7 days	4 hours (mouse)	YES

Health-Based Drinking Water Values To Be Considered (Based on this Presentation)

		PFOS	PFOA	PFHxS	PFBS	PFHxA
Reference Study		Dong et al. 2009	Onishchenko et al. 2011; Koskela et al. 2016	NTP, 2018 (unpublished data)	Feng et al. 2017	Klaunig et al. 2015
Critical effect(s)		↓ Plaque forming cells ↑ liver weight	Neurobehavioral effects Skeletal alteration	↓ Free T4	↓ Total T4	↑ Renal tubular hyperplasia ↑ Renal papillary necrosis
Species		Rats	Mice	Rats	Mice	Rats
Serum Elimination Toxicokinetics (TK)	Rodent $T_{1/2}$	40 - 60 days	~ 7 days	~ 30 days	~0.08 day	~ 0.08 day
	Human $T_{1/2}$	1241 days	840 days	1935 days	27.7 days	32 days
TK adjustment sought by MI SAW?		Yes	Yes	Yes	Yes	No
Relative Source of Contribution		50%	50%	50%	20%	20%
Exposure Scenario for drinking water		MDH breast milk model	MDH breast milk model	MDH breast milk model	7.8-kg child; 1.106 L/day	80-kg adult; 3.353 L/day
Current Drinking Water Value (ng/L)		16	8	51	420	400,000
Possible Drinking Water Value		↑	↑	↑	↑	↓

September 17, 2019

Mr. Steve Sliver, Executive Director, Michigan PFAS Action Response Team (MPART)
Constitution Hall
525 West Allegan St.
Lansing, MI 48909-7973

Dear Mr. Sliver,

Thank you again for meeting with us on August 23rd to discuss our concerns about MPART's Science Advisory Workgroup (Workgroup) health-based values (HBVs). We are confident the Department of Environment, Great Lakes, and Energy staff want to begin the rulemaking process with HBVs that better ensure the safety of Michigan's drinking water. Consequently, we trust that MPART's steering committee will review the scientific evidence provided during our meeting and in this document to adopt more health protective values.

I. Total PFAS MCL.

Although MPART was directed to investigate the ability of different water treatment technologies to reduce concentrations of a range of PFAS chemicals in water, the Workgroup focused on quantitative limits for individual chemicals. We urge MPART to reconsider its decision to forego a treatment-based water standard for drinking water systems with detectable PFAS. A focus on treatments that are effective for broad numbers of PFAS chemicals will have significant co-benefits of reducing the bulk of unclassified PFAS chemicals, which include precursors to PFOS, PFOA and other chemicals with individual health-based values.

Of note is a recent Harvard Nurses Study publication that used a novel method, EOF, to measure total organic fluorines in drinking water in five Northeast cities. The authors report that the total "unknown" fluorochemicals dwarfed the amount of identifiable per- and poly-fluorinated carboxylates and sulfonates in treated drinking water. The amount of total organic fluorines also increased dramatically in each of the water systems between 1990 and 2016.[1]

II. Class-based regulation.

The Workgroup recommended HBVs for seven individual PFAS chemicals, and screening level for all other long-chain PFAS detected with Method 537.1, based on their strictest HBV of 6 ppt for PFNA. As the Workgroup noted, "these compounds are expected to produce similar health effects." We agree with this approach for screening levels for poorly studied chemicals.

However, MPART's proposed health-based values for individual PFAS chemicals are not protective against the likelihood of additive effects from multiple PFAS. Michigan water testing confirms that when water is contaminated with PFAS, people are nearly always ingesting multiple chemicals.

Vermont and Massachusetts have taken a different approach in setting a group standard for the better-studied PFAS chemicals. EPA review suggest that PFAS chemicals, including newer generation PFBS and GenX share many of the same toxicity endpoints, including harm to the liver, thyroid, and kidney. MPART should set group values, at minimum for all the carboxylic acids (PFOA, PFNA, PFHxA, Genx) and a separate combined HBV for all the sulfonic acids (PFOS, PFHxS, PFBS) on their list.

III. Strengthening MCLs for individual PFAS.

Since HBVs are goals and not themselves enforceable drinking water standards, the numbers should be low enough to account for scientific uncertainties as well as the additive effects of exposure to multiple PFAS chemicals over a lifetime of exposure. Our comments underscore multiple opportunities for MPART to tighten its level of protection of human health and better reflect the possibility that PFAS concentrations in public drinking water systems could pose a risk to the developing fetus, infant, and child, as well as increasing risks of diseases that manifest in adulthood.

1. Protecting fetuses, infants and children.

We support the Workgroup's use of the Minnesota transgenerational toxicokinetic model[2] to estimate drinking water exposures over a person's lifetime (and the use of infant exposure assumptions when there was not enough data to use the model) for PFOA, PFOS, PFNA, PFHxS, and PFBS. We take exception to the Workgroup's decisions for GenX and PFHxA, where adult exposure assumptions were used (discussed in Section III.2.d and III.5.b below).

Fetuses and infants have greater exposure to PFAS than adults, and are also more sensitive to the effects of these contaminants.[3] Almost all fetuses and infants will have some degree of exposure, including exposure as fetuses during pregnancy through placental transfer.[4] For infants, exposure may be further elevated due to ingestion of contaminated breastmilk (a result of the mothers' ingestion of contaminated water and other sources) or infant formula prepared with contaminated drinking water.[5]

Levels of PFOA and PFOS in breastmilk are much higher than what is typically found in drinking water, as PFOA and PFOS bioaccumulate in the body and are then transferred into the breastmilk.[6] Moreover, since infants consume approximately five times more water per body weight than adults,[7] their exposure is likely higher than adults regardless of whether they are breastfeed or are fed infant formula prepared with PFOA- and PFOS-contaminated drinking water. Infant blood serum levels of PFOA and PFOS are often the highest of any age group in studies that compare people in multiple stages of life.[8]

Compounding the issue of increased exposure, fetuses, infants, and children are also more vulnerable to exposure-related health effects than adults. The young may be more sensitive to the effects of PFOA and PFOS due to their immature, developing biological systems (such as the immune system), and rapid body growth during development.[9] For example, exposure to PFAS before birth and/or in early childhood may result in decreased birthweight, decreased immune responses, and hormonal effects later in life.[10]

Decisions made when developing a health benchmark, such as evaluation of data gaps, the selection of uncertainty factors, and choice of exposure parameters to use, should be made to be protective of the most vulnerable populations, particularly developing fetuses, infants, and children. In fact, **the National Academy of Sciences (NAS) has recommended the use of an additional uncertainty factor of 10 to ensure protection of fetuses, infants and children who often are not sufficiently protected from toxic chemicals such as pesticides by the traditional intraspecies (human variability) uncertainty factor**.[11] Congress adopted this requirement in the Food Quality Protection Act for pesticides in foods.[12] Considering the many health effects linked to PFAS that affect this vulnerable population and the substantial data gaps on exposure and toxicity of these compounds in complex mixtures, **we recommend the use of this uncertainty factor when deriving health-protective benchmarks for PFAS.**

2. The HBV for GenX does not fully acknowledge the uncertainty in the risk assessment process and is not protective of fetuses, infants and children, the most vulnerable populations to PFAS exposure.

a. Derivation of human equivalent oral exposures.

Like the EPA, the Workgroup used the Body Weight$^{3/4}$ allometric scaling approach to calculate a human equivalent dose from an animal-based point of departure. The Body Weight$^{3/4}$ allometric scaling approach is based on body surface area and basal metabolic rate in adults.[13] While the liver effects in the critical study for GenX occurred in adult mice, developmental effects also occur at low doses, and infants and children may be a more vulnerable population. The EPA states that this approach is not suitable for estimating an equivalent dose in infants and children. Therefore, it is unclear how the human equivalent dose based on liver effects in adults would compare to the human equivalent dose based on developmental effects in infants and children. **This uncertainty should be acknowledged in an additional uncertainty factor to protect fetuses, infants and children.**[14]

Furthermore, this approach does not account for differences in toxicokinetics between animals and humans, which for PFAS are often vastly different.[15] Even within animal models, data suggest a potentially complex toxicokinetic profile for GenX when dosing occurs over multiple days.[16] When male mice received doses of 1, 10 and 100 mg/kg/day for 28 days, their serum levels did not reach a steady state. This indicates possible changes in toxicokinetics after repeated dosing, which is relevant when considering safety levels in a public drinking water supply.

Depending on the specific PFAS, human clearance time can be an order of magnitude, or more, higher than in animal models. Therefore, the Netherland's National Institute for Public Health and the Environment (RIVM) determined that although the elimination rates for GenX are faster than PFOA in animal models, without data in humans, it is not possible to make assumptions on the human toxicokinetics of GenX chemicals.[17] Due to the uncertainty from lack of human toxicokinetic data on GenX chemicals, RIVM calculated and applied an additional uncertainty factor to account for the potential kinetic difference between animals and humans. RIVM postulated that the vast differences in clearance rates between animals and humans may be due to species differences between organic anion transporters (OATs). Differences in OATs could result in stronger reabsorption of anions, like the anion forms of PFOA and HFPO dimer acid, from the lumen of the kidney back into the blood in humans.[18]

It is possible that the shorter half-live of GenX in animal models is due to little to no reabsorption by OATs in these species. However, RIVM reasoned that it could not be assumed this would be the same for humans, due to the genetic differences of the OATs between animal models and humans.[19] RIVM states, "contrary to other perfluorinated compounds, no data are available for FRD-902 [GenX chemical] to confirm whether the fast elimination and absence of accumulation as seen in several animal species also applies to humans. In view of the above, an additional toxicokinetic assessment factor is applied to take into account the uncertainty in the human elimination rate of FRD-902." This additional toxicokinetic factor used by RIVM is based on the difference in half-lives between cynomolgus monkeys and humans for PFOA. A half-life ratio was calculated using a half-life of 1378 days in humans[20] and of 20.9 days in male cynomolgus monkeys[21] resulting in an additional toxicokinetic factor of 66 (1378 / 20.9). **This additional uncertainty factor to account for the potential kinetic difference between animals and humans is an example of an alternative approach to extrapolating animal doses to human doses for PFAS that do not yet have human toxicokinetic data. At the very least an uncertainty factor of 10, not 3, should be used for animal to human differences.**

b. Database uncertainty.

There are significant database limitations for GenX. **A factor of 3 is insufficient to cover this level of uncertainty in the database.** In contrast, the Agency for Toxic Substance and Disease Registry (ATSDR) used a database uncertainty factor of 10 for PFNA and PFHxS (two PFAS with far more data than GenX) due to lack of, or limited

testing of developmental and immunological effects, which ATSDR identified as two of the most sensitive PFAS endpoints.[22] Uncertainties in the database on GenX include:

- No human data.

Human data has significantly improved our understanding of the toxicological profile of many PFAS.[23] Human data is especially important considering the difference in elimination rates for PFAS between animal models and humans. A lack of human data to complement and compare to animal toxicological data is a critical data gap.

- No chronic studies in mice.

The single chronic study was performed in rats, which are less sensitive than mice to GenX chemicals. An additional limitation of this study is that there were higher than normal early deaths across all study groups.[24]

- Limited data on developmental toxicity and immunotoxicity.

Developmental toxicity and immunotoxicity are common health effects associated with PFAS exposure, both of which can occur at extremely low levels of exposure.[25] Two developmental toxicity studies, only one of which was in mice, and a single study that specifically assesses immune effects is a serious database limitation. One critical data gap is the lack of a full 2-generation toxicity study evaluating exposures during early organogenesis. Additionally, there are many developmental and immune effects that have yet to be assessed, including reproductive system development (i.e. mammary gland development and function), neurodevelopment, autoimmunity, infectious disease resistance, and immune hypersensitivity (i.e. asthma and allergies).

- Limited peer-reviewed, independently funded studies for GenX.

Of the studies that assess health effects of GenX, only three were peer-reviewed. Of these three, one was independently funded,[26] one was funded by DuPont,[27] and one was independently funded but excluded from the EPA assessment,[28] on which the Workgroup's assessment is based.

- Lack of toxicity data from inhalation and dermal exposure routes.

GenX can be transported through air.[29] Inhalation could be a significant exposure route, especially in areas where GenX processing or use occurs. In 2017 the North Carolina Division of Air Quality estimated that despite some cutback in emissions, the Chemours Fayetteville Works plant emitted approximately 2,700 pounds of GenX chemicals per year[30] and GenX chemicals have been found in rainwater up to 7 miles from the Chemours Fayetteville Works plant.[31] Minimal dermal absorption of GenX has also been demonstrated,[32] however, there is a lack of information on the dermal absorption potential or toxicity of GenX.

- New toxicity data on GenX chemicals

New toxicity data on GenX chemicals is expected to be available soon, as there were several studies abstracts presented at the 2019 Society of Toxicology meeting.[33] Additionally, preliminary data on GenX was presented at the 2nd National Conference on PFAS in June.[34]

c. Overall uncertainty not addressed.

The total uncertainty factor used by North Carolina's Department of Environmental Quality was 1000.[35] The total uncertainty factor used by the RIVM was 1088. Both North Carolina and RIVM concluded that the current overall uncertainty in assessing the toxicity of GenX is at least three times greater than what the Workgroup is acknowledging through its application of a total uncertainty factor of 300.

d. Use of adult drinking water exposure assumptions

The Workgroup applied drinking water exposure parameters for adults, which does not account for the most vulnerable populations to PFAS exposure in drinking water. Sensitive members of the population, such as fetuses, infants, children, pregnant women, nursing mothers, and those with certain pre-existing conditions, face particular risk from chemicals of such persistence, and which demonstrate clear adverse effects at very low levels of exposure. Michigan should develop a health benchmark protective of the of the most vulnerable populations, particularly developing fetuses, infants, and children, by accounting for these sensitive subgroups in the choice of exposure parameters to use.[36]

The Workgroup states that it used adult drinking water exposure assumptions because the critical effect (liver damage) they selected occurred in adults and at a lower dose than the developmental effects seen. However, as discussed in Section III.2.b, there is limited data on developmental toxicity for GenX. There is not enough data to confidently determine how fetuses, infants and children are affected by GenX, in their livers and in general. Until there is more confidence that development is not being affected at lower levels than liver effects in adults, infant exposure assumptions should be applied. As explained above in Section III.1, infants are more likely to have higher exposure than adults to these contaminants because they ingest more water per kilogram of body weight than adults. **Accounting for the unique exposure situation of infants would significantly reduce the health-based value for GenX to approximately 109 ppt. The health-based value would be lowered to approximately 11 ppt if full uncertainty factors for database limitations and animal to human differences, discussed above, were applied, and to 1 ppt with an additional uncertainty factor to ensure adequate protection of fetuses, infants and children,** as recommended by the National Academy of Sciences and as required in the Food Quality Protection Act.[37]

3. The HBV for PFOA is not protective of altered mammary gland development, the most sensitive health endpoint associated with PFOA exposure.

The Workgroup did not select the most sensitive health effect associated with PFOA exposure, altered mammary gland development. It states, "mammary gland effects may represent a delay that may not be considered adverse."

However, in a 2009 a workshop of experts in mammary gland biology and risk assessment came to the consensus that changes in mammary gland growth and differentiation, including changes in developmental timing, are a health concern.[38] Altered mammary gland development may lead to difficulty in breastfeeding and/or an increase in susceptibility to breast cancer later in life.[39]

Only one animal study has assessed the effects of PFOA exposure on mammary gland growth and differentiation for multiple generations.[40] The authors saw striking morphological abnormalities in the lactating glands of dams (mothers) chronically exposed to environmentally relevant levels of PFOA; however, no effects on body weight of their pups were seen. It is possible that compensatory behavior, such as increased number of nursing events per day or longer nursing duration per event masked a decreased potential in milk production by the dams, however the authors did not evaluate these endpoints in the study. It is also possible that PFOA exposure could increase time to peak milk output through the reduction in number and density of alveoli available to produce milk.

For human mothers, low-level functional effects on lactation that cause even a short delay in substantial milk output might result in cessation in breastfeeding before the recommended time-frame. This is supported by three human studies which have reported that maternal PFOA exposure is associated with decreased duration of breastfeeding.[41]

Early life exposures to factors that disrupt development may influence susceptibility to carcinogens later in life. For example, hormone disruption is an important determinant of breast cancer susceptibility in humans and rodents.[42] Proliferating and undifferentiated structures, such as terminal end buds, display elevated DNA synthesis compared to other mammary gland structures; which is why terminal end buds are considered the most vulnerable mammary gland target structure of carcinogen exposure.[43] Delays in mammary gland development would result in a prolonged window of increased vulnerability to carcinogens. In humans, perturbations to the timing of menarche is linked to breast cancer.[44] This further raises the concern that changes in patterns of breast development in U.S. girls could be contributing to an increased risk of breast cancer or other adult diseases later in life.[45] However, an increase in susceptibility to breast cancer later in life was not explored in the multigeneration mammary gland development study.

In general, as the 2018 Michigan Science Advisory Panel states, "developmental delay can reflect an overall detrimental effect of chemical exposure that lead to growth and developmental deficit in the offspring."[46]

While the Workgroup applied an extra uncertainty factor of 3 to protect against the possibility of endocrine effects (related to mammary gland development) occurring at lower levels than the health effect they chose, this is not sufficient to protect against mammary gland effects. **Indeed, New Jersey has calculated a reference dose for mammary gland development, and if this had been used, the HBV for PFOA would be less than 1 ppt.**[47]

4. **The HBV for PFHxS does not incorporate the most recent science on PFHxS associated health effects.**

As noted by the Workgroup's use of an uncertainty factor of 10 for database deficiencies (lack of a two-generational study and limited understanding of immunotoxicity and early life sensitivity), the science on possible health effects associated with exposure to PFHxS is still developing. In fact, a new derivation of a chronic reference dose for PFHxS based on a different study (Chang et al., 2018[48]) and health endpoint (impaired reproduction – reduced litter size) was just published.[49] This approach was originally used by New Hampshire to set a MCL of 18 ppt for PFHxS in July 2019, and then published in September 2019. Considering the significantly stricter level that results from use of this new information it is imperative that Michigan consider this recent publication to ensure it sets a health-protective MCL for PFHxS.

In short, the new study reviewed available toxicity studies using a weight-of-evidence approach, which led them to choose a 42-day reproductive study in mice (Chang, 2018). They performed benchmark dose modeling to derive a point of departure (13,000 ng/ml PFHxS in serum) for reduced litter size. The authors then used a similar dosimetric adjustment factor and the same total uncertainty factor as the Workgroup to arrive at a chronic reference dose of 4 ng/kg/day, approximately 2.5 times lower than the Workgroup's reference dose. Like the Workgroup, New Hampshire used the Minnesota transgenerational toxicokinetic model to generate a drinking water limit from its reference dose.

The Workgroup does state that its point of departure was comparable to the NOAEL of the Chang, 2018 study, however it also states that in general a benchmark dose modeling-based point of departure is preferred to a NOAEL. A benchmark dose level (BMDL) for the Chang, 2018 study was not available to the Workgroup at the time to compare its point of departure to (based on thyroid effects). However, now that New Hampshire has derived a BMDL-based point of departure for the Chang, 2018 study, we can see that the two points of departure are not comparable and that the point of departure for the Chang, 2018 study is significantly lower.

The Workgroup stated that the health outcome (reduced litter size) in Chang, 2018 was a marginal effect. However, it was statistically significant and more than a 10% decrease in litter size in the study. Given the enormous personal and societal impact of infertility and pregnancy complications in a human population, the Workgroup should not dismiss these crude but important indicators of harm in animal models.

5. **The HBV for PFHxA does not fully acknowledge the uncertainty in the risk assessment process and is not protective of fetuses, infants and children, the most vulnerable populations to PFAS exposure.**

    a. Derivation of human equivalent oral exposures.

Due to limited data on PFHxA, the Workgroup used the Body Weight$^{3/4}$ allometric scaling approach to calculate a human equivalent dose from an animal-based point of departure. The Body Weight$^{3/4}$ allometric scaling approach is based on body surface area and basal metabolic rate in adults.[50] This approach resulted in a dose adjustment factor of approximately 3. The EPA states that this approach is not suitable for estimating an equivalent dose in infants and children. Therefore, it is unclear how the human equivalent dose based on kidney effects in adults would compare to the human equivalent dose based on developmental effects in infants and children. **This uncertainty should be acknowledged in an additional uncertainty factor to protect fetuses, infants and children.**[51] **And, due to the limited data on how humans process PFHxA, an uncertainty factor of 10, not 3, should be used to account for animal to human differences.**

Furthermore, this approach does not account for differences in toxicokinetics between animals and humans, which for PFAS are often vastly different.[52] Depending on the specific PFAS, human clearance time can be an order of magnitude, or more, higher than in animal models. PFBS is also a short-chain PFAS, with shorter half-life than long-chain PFAS, such as PFOA and PFAS. However, the dose adjustment factor the Workgroup used for PFBS was based on the ratio of human to animal half-lives for PFBS, not the Body Weight$^{3/4}$ allometric scaling approach. The Workgroup states,

> "As that [half-life-based dose adjustment factor] allowed conversion of the point of departure to a human equivalent dose using chemical-specific information, the Workgroup selected this approach over the allometric scaling used in the draft USEPA (2018) PFBS toxicity assessment."

Although the half-life of PFBS and PFHxA is significantly shorter than long-chain PFAS (665 hours vs. 1241 days for PFOS), the half-life in humans is still much longer than in animals (665 hours in humans vs 2.1 hours mice) for PFBS. The dose adjustment factor for PFBS was 316.

This is similar to PFHxA, the human half-life for PFHxA is estimated to be 32 days, or 768 hours (geomean), 1 hour for mice, between 0.4 and 9.8 hours for rats, and from 2 to 5 hours for monkeys, resulting in dose adjustment factors ranging from 78 to 1920, depending on the mammalian species used.[53] As the critical study occurred in rats, the dose adjustment factor for calculating a human equivalent dose from the rat dose would be based on the human to rat half-life ratio. The most health-protective choice would be to use the half-life estimate of 0.4 hours for rats, resulting in a dose adjustment factor of 1920. In comparison, the dose adjustment factor based on Body Weight$^{3/4}$ allometric scaling is 3.65 for PFHxA, suggesting that the Body Weight$^{3/4}$ allometric scaling

approach for PFAS, even short-chain PFAS, is not an appropriate approach to convert animal dose to human equivalent doses and that the human equivalent dose (and thus the health-based value) for PFHxA could be off by at least a couple orders of magnitude. Although the same level of information is available for PFBS and PFHxA, the Workgroup does not clearly explain why it chooses a different approach for the two chemicals. The PFBS approach to extrapolating from animal to human doses is more relevant to the unique properties of PFAS and would result in a point of departure for PFHxA ranging from 0.0471 to 1.15 mg/kg/day, depending on the dose adjustment factor used. **Application of full uncertainty factors for human variation, animal to human differences, database deficiencies, and to protect fetuses, infants and children would then result in a toxicity value ranging between 4.7 to 115 ng/kg/day.**

b. Use of adult drinking water exposure assumptions

The Workgroup states that it used adult drinking water exposure assumptions because the critical effect (kidney effects) they selected occurred in adults. However, there is limited data on developmental toxicity for PFHxA. There is not enough data to confidently determine how fetuses, infants and children are affected by PFHxA, in their kidneys and in general. Until there is more confidence that development is not being affected at lower levels than kidney effects in adults, infant exposure assumptions should be applied. As explained above in Section III.1, infants are more likely to have higher exposure than adults to these contaminants because they ingest more water per kilogram of body weight than adults. **The health-based value would be between 7 to 162 ppt if the Workgroup's infant exposure assumptions (0.142 L/kg/day, 20% relative source contribution) were applied to the toxicity values listed above.**

6. PFBS, PFOS and PFNA

We support the Workgroup's use of a half-life-based dose adjustment factor over the BodyWeight ¾ allometric scaling method for generating a human equivalent dose from an animal point of departure (as discussed in Section III.5.a). We also support the use of drinking water exposure assumptions based on infants, in order to better protect this vulnerable population. However, we suggest Michigan consider applying a full uncertainty factor for animal to human variability, as there is a lack of toxicological information on PFBS, and the Workgroup's preferred models were not able to be used for deriving the HBV.

We also generally support the Workgroup's choices in developing HBVs for PFOS and PFNA, however, would urge Michigan to consider (for all the PFAS analyzed) NAS' recommendation to apply an additional uncertainty factor of 10 to ensure protection of fetuses, infants and children who often are not sufficiently protected from toxic chemicals by the traditional human variability uncertainty factor.

Conclusion

The Whitmer Administration has moved quickly to address the dangers posed by PFAS in Michigan's drinking water. The Workgroup was charged with reviewing PFAS scientific data on a compressed timeline, and it presented its findings to MPART at your June 27, 2019 meeting. These recommendations became the basis for the Department of the Environment, Great Lakes, and Energy's (EGLE) proposed enforceable drinking water protections. However, with additional time, our scientific review identified significant shortcomings in the recommendations adopted by MPART in June. EGLE staff have indicated the only way they can alter the HBVs and incorporate other necessary health protections is by securing support for our recommendations from MPART.

Therefore, we urge MPART to adopt the recommendations included herein to strengthen the health protections embedded within EGLE's enforceable drinking water standards.

Respectfully,

Anna Reade, Ph.D.
Staff Scientist
Healthy People & Thriving Communities Program
Natural Resources Defense Council

Sonya Lunder, MPH
Senior Toxics Advisor
Gender, Equity & Environment Program
Sierra Club

Christy McGillivray
Great Lakes State Organizer
Sierra Club

Cyndi Roper
Michigan Senior Policy Advocate
Healthy People & Thriving Communities Program
Natural Resources Defense Council

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MPART Draft Motion for Health Based Values
September 27, 2019

Motion #1

Motion to accept the summary and conclusions presented in the Executive Director's September 23, 2019, memorandum to the Michigan PFAS Action Response Team (MPART) Members regarding "Public Input on Health Based Values for PFAS in Drinking Water," and further to notify the Michigan Department of Environment, Great Lakes, and Energy that MPART supports moving forward with draft rules to establish drinking water standards founded on the health-based values MPART accepted from the Science Advisory Workgroup on June 27, 2019.

Motion #2

Motion to form the Citizens Advisory Workgroup consistent with the September 20, 2019, draft charter and to authorize the Executive Director to appoint its members accordingly.