PFAS Health & Toxicology Subgroup

Draft Meeting Minutes

WebEx, Office of Drinking Water, 109 Governor Street 6th Floor, Richmond, VA 23219

February 12, 2021 from 1:30 – 3:30 p.m.
2 hours (appx)

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1. Opening Remarks

VDH State Toxicologist, Dwight Flammia, Ph.D. called the meeting to order 1:33 p.m. The meeting was conducted in a public format and recorded minutes will be posted on Town Hall. He discussed the tasks and presented a power point presentation.

2. Member Introduction

Jillian Terhune (City of Norfolk)
Kelly Ryan (Va American Water)
David Jurgens (City of Chesapeake)
Erin Reilly (James River Association)
Steve Risotto (ACC)
Benjamin Hollard (DEQ)
Dwight Flammia (VDA, State Toxicologist)
Steve Herzog (Hanover County)
Paul Nyffeler

Guest

Ellen Egen
Dr. Mann

ODW Participants

Kris Latino, ODW

3. Review of previous meeting

The group determined that there were no changes to the previous meetings notes.

4 Presentation

The goal of this meeting was to discuss PFOS (perfluorooctane sulfonate) by looking at the states that have adopted PFOS MCLs and the different ways each state developed their plans.

Currently only a few states have developed PFOS MCLs. They include:

Massachusetts	20 ppt (sum of the PFAS not to exceed)
Michigan	16 ppt
New Hampshire	15 ppt
New Jersey	13 ppt (sum PFOS & PFOA)
New York	10 ppt
Vermont	20 ppt (sum of PFAS not to exceed)

Dwight presented a PowerPoint presentation (attached) that went into detail explaining each state and the methods they used to explain with their conclusions. (The papers can be found in SharePoint)

5 Discussion

Paul questioned the Toxicology subgroups contribution to the PFAS workgroup and stated he would come up with a list of group recommendations. He will email them to Dwight before the next meeting.

Paul was also was tasked with looking into the NJ documents and finding where they state the MCL is 13 or 14.

Steve also has some information to share with the subgroup.

For the next meeting, the group should confirm the states that currently have PFOA (perfluorooctanoic acid) MCLs and provide documentation for the group.

Dwight will share a video link to the members on New York. It will also be posted on SharePoint.

6 Closing items:

The next Toxicology subgroup will be March 12, 2021. The login information can be found on the SharePoint calendar and will also be emailed prior to the meeting.

PFAS Health, Toxicology Regulatory Subgroup Meeting

Virginia Department of Health Office of Drinking Water
(Discuss States with PFOS MCLs)
February 12, 2021
1:30pm – 3:30pm

Opening Remarks

Member Roll Call

Review of Previous Meeting

Presentation

Discussion

Public Comment

Closing items

Establishing Regulatory Limits for PFAS in Virginia Drinking Water

PFAS Toxicology Regulatory Workgroup

Dwight Flammia, Ph.D.
State Public Health Toxicologist
Virginia Department of Health

February 12, 2021

PFAS Workgroup Meeting Overview

Meeting Overview

- Opening Remarks
- Review of previous meeting
- Workgroup Members Introductions
- Presentation
- Discussion
- Assignments
- Public Comment
- Next Meeting

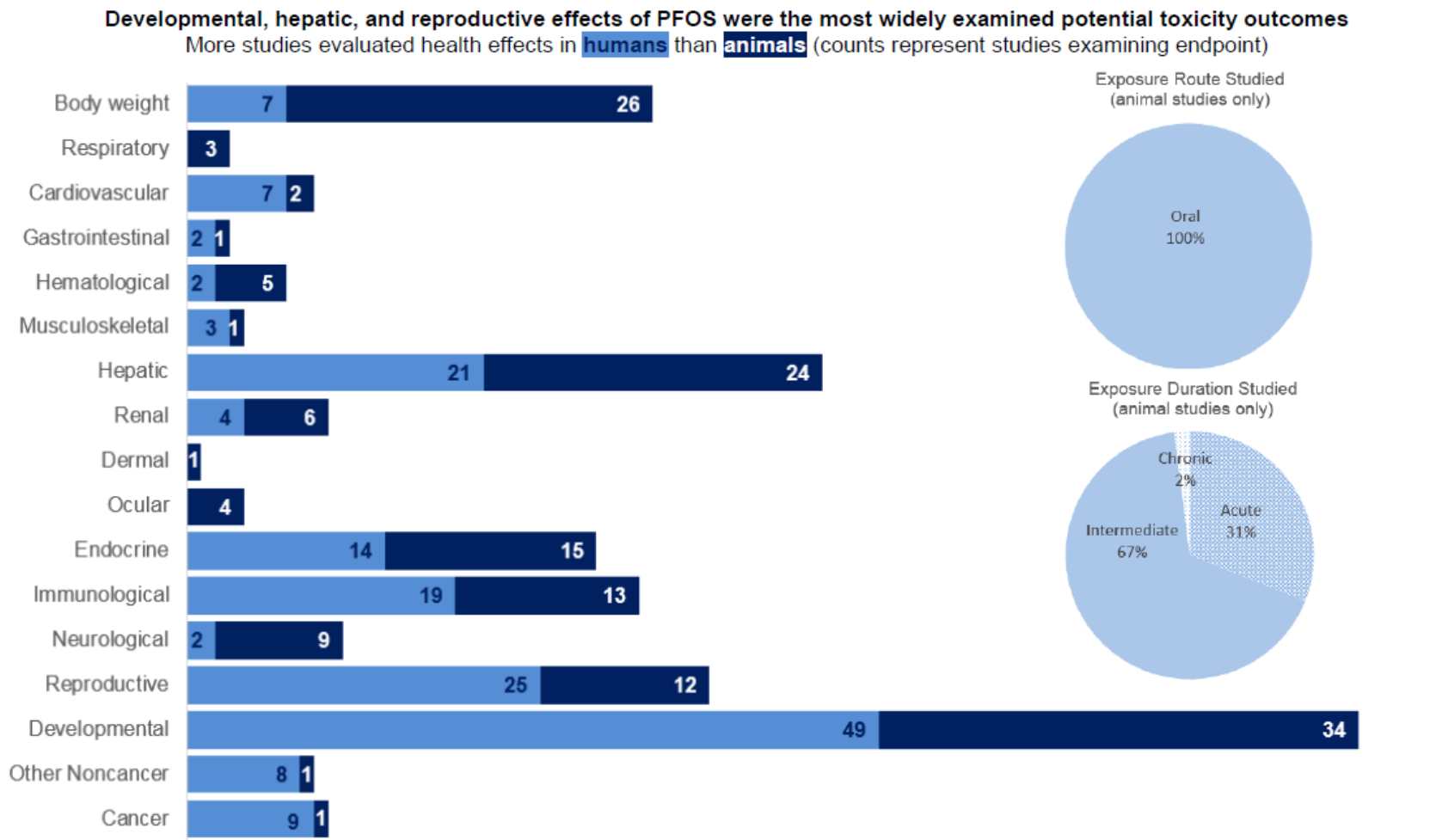
States with PFOS MCLs

• Massachusetts	• 20 ppt (sum of five PFAS not to exceed)
• Michigan	• 16 ppt
• New Hampshire	• 15 ppt
• New Jersey	• 13 ppt (sum PFOS & PFOA)*
• New York	• 10 ppt
• Vermont	• 20 ppt (sum of five PFAS not to exceed)

EPA steps in developing an MCL

- For **chemical contaminants that are non-carcinogens** the MCLG is based on the reference dose. A **reference dose** (RfD) is an estimate of the amount of a chemical that a person can be exposed to on a daily basis that is not anticipated to cause adverse health effects over a lifetime.
- **To determine** the RfD, the concentration for the non-carcinogenic effects from an epidemiology or toxicology study is divided by uncertainty factors This provides a margin of safety for consumers of drinking water.
- The RfD is multiplied by body weight and divided by daily water consumption to provide a Drinking Water Equivalent Level (DWEL).
- The DWEL is multiplied by the relative source contribution. The relative source contribution is the percentage of total drinking water exposure for the general population, after considering other exposure routes (for example, food, inhalation).

Figure 2-2. Overview of the Number of Studies Examining PFOS Health Effects*



*Includes studies discussed in Chapter 2. A total of 218 studies (including those finding no effect) have examined toxicity; most animal studies examined multiple endpoints. In this figure, the number of human studies is referring to the number of publications.

Figure 2-7. Levels of Significant Exposure to PFOS – Oral
Acute (≤14 days)

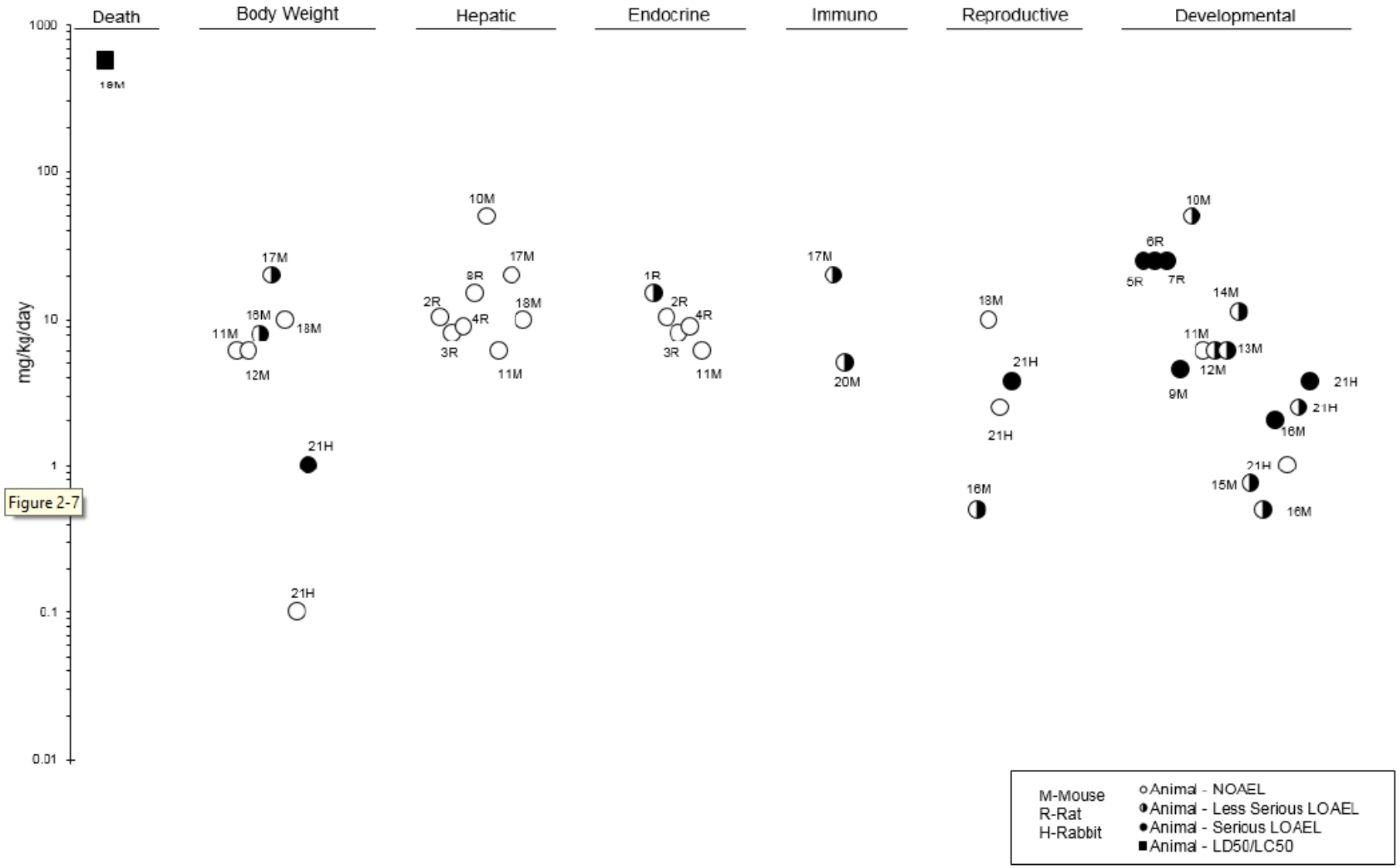


Figure 2-7. Levels of Significant Exposure to PFOS – Oral

Intermediate (15–364 days)

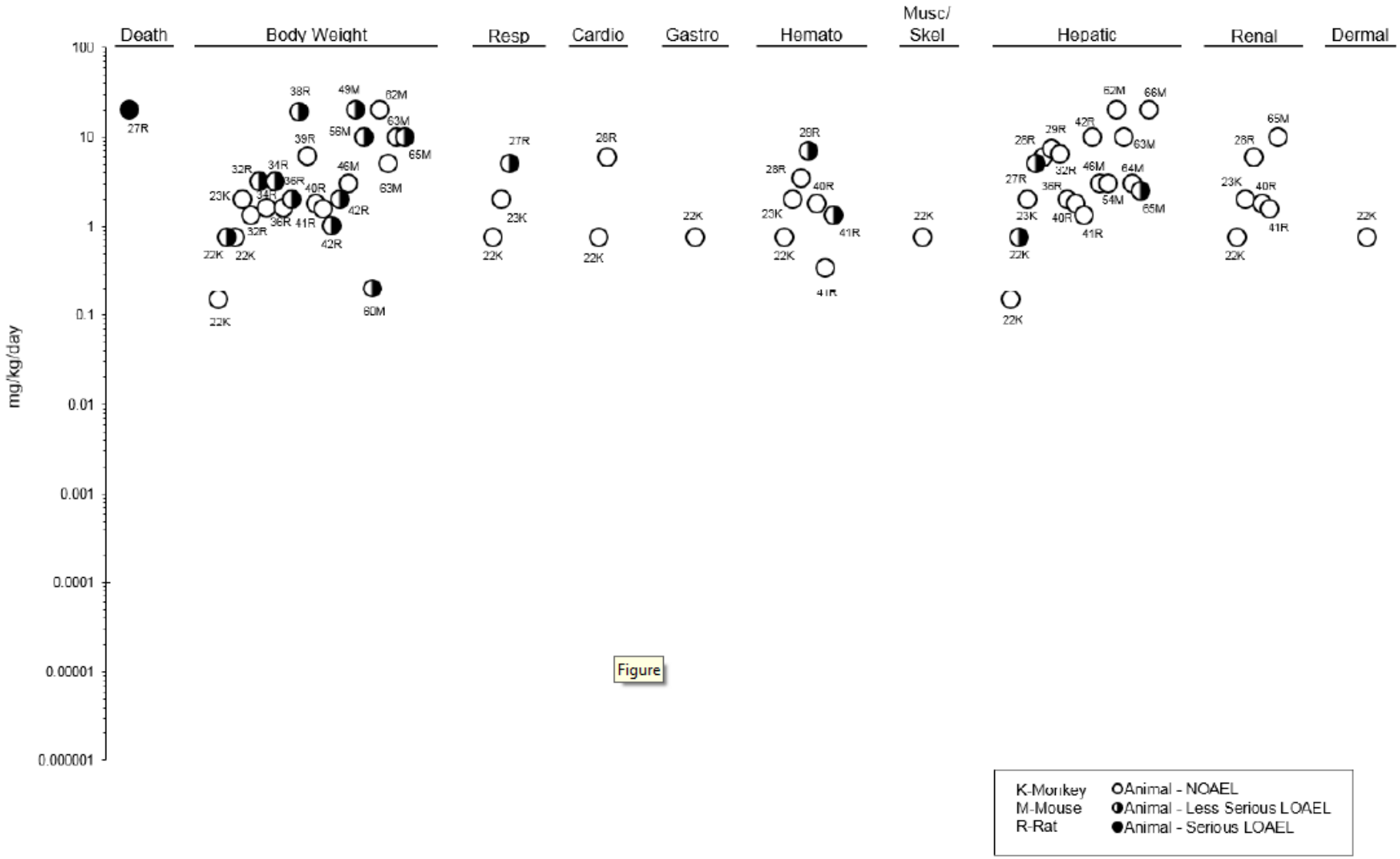


Figure 2-7. Levels of Significant Exposure to PFOS – Oral

Intermediate (15–364 days)

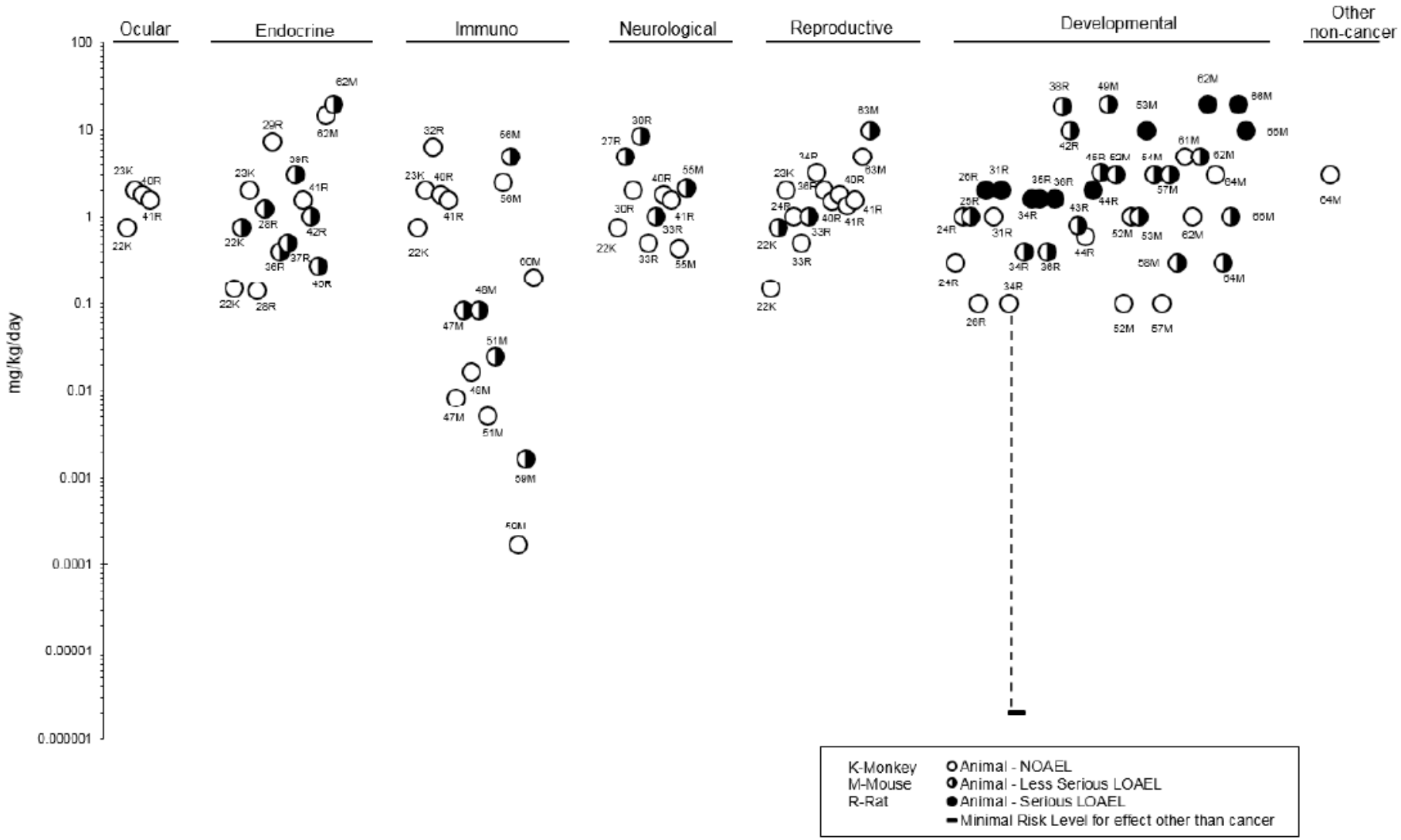
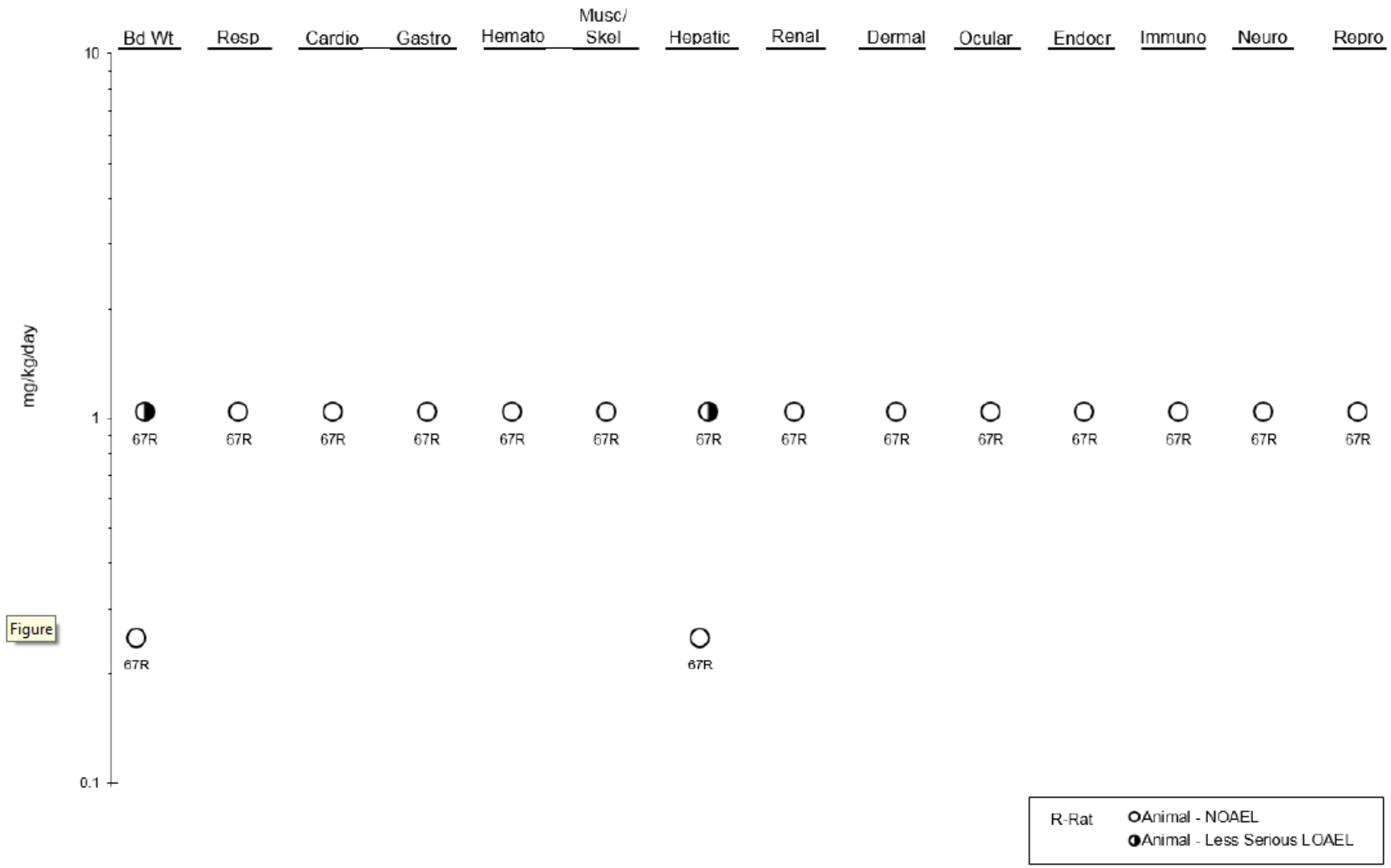


Figure 2-7. Levels of Significant Exposure to PFOS – Oral

Chronic (≥365 days)



Figure

Luebker 2005 Two-generation reproduction and cross-foster studies of perfluorooctanesulfonate (PFOS) in rats

Two-generation reproduction study was conducted in rats.

Male and female rats were dosed via oral gavage at dose levels of 0, 0.1, 0.4, 1.6, and 3.2 mg/(kg day) for 6 weeks prior to mating, during mating, and, for females, through gestation and lactation, across two generations.

second generation was limited to F1 pups from the 0, 0.1, and 0.4 mg/(kg day) groups.

Statistically significant reductions in body-weight gain and feed consumption were observed in F0 generation males and females at dose levels of 0.4 mg/(kg day) and higher, but not in F1 adults.

PFOS did not affect reproductive performance (mating, estrous cycling, and fertility); however, reproductive outcome, as demonstrated by decreased length of gestation, number of implantation sites, and increased numbers of dams with stillborn pups or with all pups dying on lactation days 1–4, was affected at 3.2 mg/(kg day) in F0 dams.

These effects were not observed in F1 dams at the highest dose tested, 0.4 mg/(kg day). Neonatal toxicity in F1 pups, as demonstrated by reduced survival and body-weight gain through the end of lactation, occurred at a maternal dose of 1.6 mg/(kg day) and higher while not at dose levels of 0.1 or 0.4 mg/(kg day) or in F2 pups at the 0.1 or 0.4 mg/(kg day) dose levels tested.

slight yet statistically significant developmental delays occurred at 0.4 (eye opening) and 1.6 mg/(kg day) (eye opening, air righting, surface righting, and pinna unfolding) in F1 pups.

Based on these data, the NOAELs were as follows: reproductive function: F0 ≥3.2 and F1 ≥0.4 mg/(kg day); reproductive outcome: F0 = 1.6 and F1 ≥0.4 mg/(kg day); overall parental effects: F0 = 0.1 and F1 ≥0.4 mg/(kg day); offspring effects: F0 = 0.4 and F1 ≥0.4 mg/(kg day).

Dong 2009, Chronic effects of perfuorooctanesulfonate exposure on immunotoxicity in adult male C57BL/6 mice

In this study, adult male C57BL/6 mice were exposed to PFOS daily via gavage for 60 days [0, 0.5, 5, 25, 50, or 125 mg/kg total administered dose (TAD)]. (0, 8.33, 83.33, 416.67, 833.33, or 2083.33 µg PFOS/kg body weight/day)

- Liver mass was significantly increased at ≥5 mg PFOS/kg TAD and in a dose-dependent manner.
- Lymphocyte proliferation and natural killer cell activity were altered in male mice.
- Plaque forming cell (PFC) response was suppressed beginning at 5 mg/kg TAD.

Based on the liver mass and PFC response, the no observed adverse effect level and lowest observed adverse effect level for male mice exposed PFOS for 60 days was 0.5 and 5 mg/kg TAD, respectively.

Measured PFOS serum concentrations at these dose levels were 0.674 ± 0.166, and 7.132 ± 1.039 mg/l, respectively.

These results indicate that PFOS exposure can affect the immunity function in mice at levels approximately 50-fold for highly exposed human populations.

Dong 2011 Sub-chronic effect of perfluorooctanesulfonate (PFOS) on the balance of type 1 and type 2 cytokine in adult C57BL6 mice

ability of PFOS to potentially perturb T-helper (TH)-1 and TH-2 cell cytokine secreting activities, as well as to cause shifts in antibody isotype levels, and possible mechanisms involved in PFOS-induced immunotoxicity.

Adult male C57BL/6 mice were exposed to PFOS daily via gavage for 60 days [0, 0.5, 1, 5, 25, or 50 mg/kg total administered dose (TAD)]. One day after the final exposure, the ex vivo production of the TH1-type cytokines (IL-2 and IFN-c), TH2-type (IL-4), and IL-10 cytokines by isolated splenocytes, serum levels of immunoglobulin (Ig) were assessed

results showed that IL-4 secretion was increased at exposure C5 mg PFOS/kg TAD in a dose-dependent manner. PFOS exposure increased IL-10 but decreased IL-2 and IFN-c formation markedly at 50 mg PFOS/kg TAD

Serum levels of sheep red blood cells (SRBC)-specific IgM synthesis decreased significantly with PFOS exposure in a dose-related manner; serum SRBC-specific IgG, IgG1, and IgE levels increasedwith 50 mg PFOS/kg TAD regimens

Michigan PFOS Summary

Chemical Summary for PFOS

	Decision point	Rationale/justification
Critical study	Dong GH, Zhang YH, Zheng L, Liu W, Jin YH, He QC. (2009). Chronic effects of perfluorooctanesulfonate exposure on immunotoxicity in adult male C57BL/6 mice. Arch Toxicol. 83(9):805-815.	The Workgroup discussed the available evaluations, particularly MDH (2019) and New Jersey Department of Environmental Protection (NJDEP) (2018), and selected a critical study with an immune system functional assay rather than observational data.
Description of the critical study	Adult male C57BL/6 mice were exposed to PFOS daily via oral gavage for 60 days with 0, 0.5, 5, 25, 50 or 125 mg/kg total administered dose, equivalent to 0 or approximately 0.008, 0.08, 0.4, 0.8 or 2.1 mg/kg/day. The NOAEL for suppression of plaque forming cell response and increase in liver mass was 0.5 mg/kg total administered dose which corresponded to a serum concentration of 0.674 mg/L.	The Workgroup acknowledged that immune effects in mice were seen at lower doses in Peden-Adams et al. (2008). Serum concentrations from Peden-Adams et al. (2008) were well below both the NOAEL and LOAEL serum concentrations measured from several other studies as described by Pachkowski et al. (2019) and may be an outlier in the database.
Point of Departure	The NOAEL for suppression of plaque forming cell response and increase in liver mass was 0.5 mg/kg total administered dose which corresponded to a serum concentration of 0.674 mg/L.	The Workgroup decided that serum-based points of departure were appropriate for PFAS.
Human equivalent dose	The serum concentration of 0.674 mg/L was converted to the HED using the below equation (based on ATSDR 2018). $NOAEL_{HED}$ = (TWA serum x k x V_d) = 0.0000866 mg/kg/day Ke = 0.000558539 (5.5×10^{-4}) based on a human serum half-life of 1241 days (Li et al. 2018) Vd = 0.23 L/kg (Thompson et al. 2010)	The Workgroup selected the serum half-life from a non-occupationally exposed population as it is closer to the general population's exposure. The Workgroup selected volume of distributions based on human data, when available.
Uncertainty factors	A total uncertainty factor of 30: • 1 for LOAEL to NOAEL • 10 for human variability • 3 ($10^{0.5}$) for animal to human difference (toxicodynamics) • 1 for subchronic to chronic • 1 for database deficiencies	The Workgroup reviewed the uncertainty factors selected by MDH (2019) and adjusted the database uncertainty factor to 1 based on the critical study selection. With consideration of the selected immunotoxicity endpoint, the database uncertainty factor of 1 was supported by the assessments by USEPA (2016), NJDEP (2018), ATSDR (2018) and New Hampshire (2019).

Michigan PFOS Summary

Toxicity value	2.89 ng/kg/day (2.89 x 10^{-6} mg/kg/day) which corresponds to a serum concentration of 0.022 µg/ml Serum levels used in development of these toxicity levels 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.	Human equivalent dose or serum level divided by the total uncertainty and modifying factors = toxicity value
Exposure parameters for drinking water HBV	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) 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]) Relative Source Contribution of 50% Based on NHANES 95th percentiles for 3-11 (2013-2014) and over 12 years old (2015-2016) participants (CDC 2019)	The Workgroup discussed the Goeden et al. (2019) model which considered full life stage exposure, from fetal exposure, to infant exposure through breastfeeding, and into adulthood. While the model was also developed for a formula-fed infant, the breastfed infant scenario is protective of a formula-fed infant. The Workgroup selected this model for developing drinking water HBVs when the needed inputs were available.
Drinking water HBV	16 ng/L (ppt)	Numeric HBV derived and justified using the above information

Massachusetts Study Selection

Based on its review of the data, MassDEP ORS has concluded that the overall evidence regarding immunotoxicity is convincing and sufficient to support a lower RfD for PFOS than previously derived by USEPA (2016b). However, the utility of the available studies for providing an alternative POD is limited by several issues including variable results; uncertainties relating to the execution of some studies, which raise some concerns about potential study bias (as noted in the NTP 2016 review); and small sample sizes (Table 5). Consequently, MassDEP ORS elected not to rely on the immunotoxicity study data to identify an alternative POD. Instead, as discussed below, MassDEP ORS concluded that it is more appropriate to account for this data by including an additional UF for database uncertainty in the PFOS RfD derivation.

Massachusetts Reference Dose Discussion

The MassDEP RfD for the subclass is based on that for PFOA and PFOS. The bases of MassDEP's updated RfDs for these compounds was previously described. In summary, MassDEP relied on the same POD and HED calculations used by USEPA with inclusion of an additional UF to account for data indicating effects at lower dose levels, resulting in a RfD of 5.3 x 10^{-6} (rounded to 5 x 10^{-6} mg/kg/day) for PFOA[23] and of 5.1 x 10^{-6} mg/kg/day (rounded to 5 x 10^{-6} mg/kg/day) for PFOS.[24] The RfDs rounded to one significant figure are the same (5 x 10^{-6} mg/kg/day) and this value was adopted for the PFAS subgroup addressed by MassDEP.

Massachusetts Uncertainty Factors

Agency	Study/Endpoint	Dosing duration (days)	NOAEL (Av serum mg/L)	HED (ug/kg-day)	UFs (total and components)	RfD (mg/kg-day)
MassDEP ORS	Luebker et al. (2005a) Sprague-Dawley rat Decreased F2 pup body weight	84	6.26 [a]	0.51	100 $UF_H = 10$ $UF_A = 3$ **$UF_D = 3$ immune effects**	5×10^{-6} (5.1×10^{-6})

[a] Average serum concentration modeled by USEPA (2016a) using Wambaugh et al. (2013) to estimate an AUC.

Massachusetts UF Comparison

Table 8. Human Equivalent Doses and RfDs Derived from the Modeled Animal Average Serum Values of PFOS by Various Agencies

Agency	Study/Endpoint	Dosing duration (days)	NOAEL (Av serum mg/L)	HED (ug/kg-day)	UFs (total and components)	RfD (mg/kg-day)
USEPA (2016b)	Luebker et al. (2005a) Sprague-Dawley rat Decreased F2 pup body weight	84	6.26 [a]	0.51	30 $UF_H = 10$ $UF_A = 3$	2×10^{-5} (1.7×10^{-5})
ATSDR (2018a)	Luebker et al. (2005a) Sprague-Dawley rat Delayed eye opening and decreased F2 pup body weight	84	7.43 [b]	0.51	300 $UF_H = 10$ $UF_A = 3$ **$UF_D = 10$ immune effects**	2×10^{-6}
MDH (2019a)	Dong et al. (2011) C57BL/6N mice Suppressed immune response	60	2.36 [c]	0.31	100 $UF_H = 10$ $UF_A = 3$ **$UF_D = 3$ thyroid effects**	3×10^{-6} (3.1×10^{-6})
NJDWQI (2018)	Dong et al. (2009) C57BL/6N mice Suppressed immune response	60	0.674 [c]	0.054	30 $UF_H = 10$ $UF_A = 3$	2×10^{-6} (1.8×10^{-6})
NHDES (2019b)	Dong et al. (2011) C57BL/6N mice Suppressed immune response	60	2.36 [c]	0.31	100 $UF_H = 10$ $UF_A = 3$ **$UF_D = 3$ thyroid effects**	3×10^{-6}
MISAW (2019)	Dong et al. (2009) C57BL/6N mice Suppressed immune response	60	0.674 [c]	0.0866	30 $UF_H = 10$ $UF_A = 3$	3×10^{-6} (2.9×10^{-6})
NYDOH (2019)	Same as NJ					

Massachusetts Drinking Water Standard

The derivation of the MassDEP drinking water value based on this RfD is described below:

$$\text{Drinking water value} = \frac{\text{RfD} \times \text{RSC}}{\text{Water consumption rate per kg body weight}}$$

Where:

RfD	$= 5 \times 10^{-6}$ mg/kg-day
Water consumption rate for lactating woman	= 0.054 L/kg-day
Relative Source Contribution Factor (RSC)	= 0.2

$$\text{Drinking Water Value} = \frac{5 \times 10^{-6} \text{ mg/kg-day} \times 0.2}{0.054 \text{ L/kg-day}}$$

$$= 0.0000185 \text{ mg/L}$$

= 0.00002 mg/L or 20 ng/L (20 ppt), rounded to one significant figure

When these six compounds occur alone, together, or in any combination, the sum of their concentrations should be compared to 0.00002 mg/L.

New Hampshire Principal Study and Point of Depature

For the derivation of a RfD for PFOS, NHDES recommends the critical health effect of suppressed immunoglobulin M (IgM) production in male mice (Dong et al., 2011). While NHDES previously proposed a RfD based on developmental toxicity, the review of existing and emerging evidence and technical comments suggest that the use of this immunotoxic endpoint represents a more appropriately cautious approach for the risk assessment of PFOS.

This POD is based on serum concentrations of PFOS at the no observable adverse effect level (NOAEL) for suppressed IgM production in male mice following 60-d oral exposure (Dong et al. 2011).

New Hampshire

As summarized by MDH (2019), the critical effect reported in Dong et al. (2011) was suppressed IgM production with a NOAEL of 2,620 ng/mL (oral dose, 0.0167 mg/kg-d) and a LOAEL of 10,750 ng/mL (oral dose, 0.083 mg/kg-d). A prior study by Dong et al. (2009) reported a NOAEL of 674 ng/mL (oral dose, 0.008 mg/kg-d) for reduced plaque forming cell response to sheep red blood cells, and a similar oral LOAEL as Dong et al. (2011). However, the early work by Dong et al. (2009) did not include the intermediate dose of 0.0167 mg/kg-d that was identified as a NOAEL in their later work (Dong et al. 2011). This is further complicated as the specific effect was not replicated in both studies where plaque forming cell response was only measured in Dong et al. (2009) and IgM concentrations in the later Dong et al. (2011).

New Hampshire Uncertainty Factors

Intraspecies variability (10) × Interspecies variability (3) × Database limitations (3) = 100

The full factor of 10 for intraspecies variability was deemed appropriate to protect for the poorly characterized differences in toxico-dynamics (× 3) and -kinetics (× 3) within the human population. As NHDES applied a DAF to convert the rodent serum concentration to an oral human dose, only a partial uncertainty factor (× 3) was applied for interspecies variability. The POD was based on the NOAEL described in Dong et al. (2011); thus, there was no need for additional uncertainty factors to account for LOAEL to NOAEL conversion. Dong et al. (2011) conducted a 60-day exposure so no additional uncertainty factor was applied for acute-to-chronic duration of exposure.

New Hampshire

Estimation of a human equivalent oral dose

The POD represents an internal animal serum level associated with the adverse health outcome of concern. Dividing the POD by the total uncertainty factor yields a protective target serum level equivalent for the human population. *This is not a clinical or diagnostic value, nor should it be interpreted as such*.

$$\text{Target serum level for PFOS} = \frac{2{,}360\ \text{ng/mL}}{100} = 23.6\ \text{ng/mL}$$

To estimate how this internal blood level corresponds to an external oral dose of the specified compound, a dosimetric adjustment factor is applied by multiplication to identify a dose in ng of specific PFAS per kg of individual body weight per day (ng/kg-d). This step accounts for the highly-bioaccumulative nature and unique half-life estimates of each compound, and is consistent with prior risk assessment methods for derivation of RfDs for PFAS (EPA, 2016ab; NJDWQI, 2017, 2018a; ATSDR, 2018b; MDH, 2018, 2019ab). The human equivalent oral dose is estimated by the following equations:

$$\text{Reference dose (RfD)} = \frac{\text{Point of departure (POD)}}{\text{Total uncertainty factors (UF)}} \times \text{Dosimetric adjustment factor (DAF)}$$

New Hampshire

Where the DAF is equal to,

$$DAF = V_d \times \left(\frac{Ln(2)}{t_{1/2}}\right)$$

$$DAF = 230\ mL/kg \times \left(\frac{Ln(2)}{1{,}241\ days}\right) = 1.28\times10^{-1}\ mL/kg\text{-}d$$

Consistent with the initial PFOS MCL proposal (NHDES 2019), the V_d for PFOS was 230 mL/kg (Thompson et al., 2010). In its revised and final proposal, NHDES maintains its use of a 3.4-year half-life estimate based on the average across men and women, described in Li et al. (2018; NHDES 2019). NHDES considered the longer half-life values reported for retired fluorochemical workers (Olsen et al. 2007), and deemed these to be inappropriately conservative given the use of the Minnesota transgenerational model for exposure assessment which emphasizes early-life and breastfeeding exposures.

Thus, using this chemical-specific DAF and the aforementioned point of departure and uncertainty factors, NHDES derived an oral reference dose for PFOS of 3.0 ng/kg-d.

$$\text{Reference dose (RfD)} = \frac{2{,}360\ ng/mL}{100} \times 1.28\times10^{-1}\ mL/kg\text{-}d = 3.0\ ng/kg\text{-}d$$

New Hampshire

As rodents are not humans, the UF is applied to be protective by reducing the animal POD to a lower and acceptable human target serum level. The DAF then converts, by estimation, the blood concentration (ng/mL) to a body weight-adjusted (kg) amount of the chemical (ng) external to the body that would need to be ingested on a daily basis to reach the human target serum level.

$$\text{Reference dose (ng/kg/d)} = \frac{\text{Point of departure (ng/mL)}}{\text{Total uncertainty factors (unitless)}} \times \text{Dosimetric adjustment factor (mL/kg/d)}$$

New Hampshire Relative Source Contribution

The subtraction method (EPA 2000) estimates an apportionment of the RSC is based on assumed knowledge of the background exposure. For PFAS, the subtraction method has been mathematically applied as follows (NJDWQI 2018; MDH 2018, 2019ab):

$$\text{Relative Source Contribution} = \frac{\text{Target serum level } \left(\frac{ng}{mL}\right) - \text{Reference or background population level } \left(\frac{ng}{mL}\right)}{\text{Target serum level } \left(\frac{ng}{mL}\right)} \times 100\%$$

The difference between the target serum level and the RfD is that the former is an internal blood concentration while the latter is the external amount of the chemical that could come from multiple sources. For each of the compounds, the target serum levels were: PFOA – 43.5 ng/mL, PFOS – 23.6 ng/mL, PFNA – 49.0 ng/mL and PFHxS – 46.3 ng/mL. The reference population serum level is meant to reflect a background level of exposure from the general population, not one that is highly exposed due to a specific environmental source such as drinking water. Using the NHANES average serum values, subtracting this background level from the target serum level (the maximum allowable level) results in a proportion that is presumably permissible for drinking water alone. Other sources including food, dust, treated consumer products (e.g., carpeting, cookware, food packaging, etc.) are assumed to be included in the reference or background population blood concentrations.

Using this approach with the NHANES 2013-2014 data for children ranging in age from 3 to 19 years (as reported in Daly et al., 2018), NHDES arrived at RSCs of 50% for PFOA, PFOS, PFNA and PFHxS. Unlike its

New Hampshire MCL Calculation

Using the reference dose (RfD) derived in Section III, the MCL considers the estimated daily intake of water from a specific source and how much drinking water contributes to the total exposure from all other sources of a specified contaminant. Specific methodologies for deriving health protective water criteria are detailed by the EPA (USEPA 1989, 2004, 2017, 2018). Although NHDES chose a different approach, the conventional method for deriving drinking water values utilizes the following equation:

$$\text{Maximum contaminant level (ng/L)} = \frac{\text{Reference dose (ng/kg-d)}}{\text{Daily water ingestion rate (L/kg-d)}} \times \text{Relative source contribution (unitless)}$$

For a simple example, a drinking water value for PFOA using the currently recommended RfD, 95th percentile ingestion rate of lactating women and a relative source contribution of 0.5 (meaning 50%) is shown below. This approach was used in the initially proposed MCL, but is not being applied following consideration of breastfeeding (Goeden et al., 2019).

New Jersey

NJ examined 20 toxic endpoints in terms of the timing of biological significance and suitability for dose-response analysis, and determined 4 endpoints suitable to calculate a (POD) point of departure. The immunotoxic effect shown in the Dong et al. (2009) study was chosen as the most sensitive POD (point of departure) at 674 ng/ml.

The immunotoxic endpoint chosen to develop an MCL based on decreased plaque forming cell response, a predictor of immunosuppression, in animal studies is supported by epidemiologic studies that found associations between PFOS and PFOA blood serum levels in humans and decreases in immune function.

The National Toxicology Program concluded that “exposure to PFOS is presumed to be an immune hazard to humans based on a high level of evidence that PFOS suppressed the antibody response from animal studies and a moderate level of evidence from studies in humans”.

Of the 4 final studies chosen by NJWQI for dose-response modeling, the Dong et al 2009 study of decreased plaque forming cell response, predictive of immunotoxicity, resulted in the lowest (most sensitive) point of departure (POD).

New Jersey adult reference dose

A UF_{human} of 10 was used to account for increased sensitivity in sensitive sub-populations versus the average human population, and for general physiological and metabolic variation within the human population. A UF of 3 was used to account for interspecies (rodent to human) toxicodynamic differences. No UF is needed for toxicokinetic differences since the POD (point of departure), in this case the NOAEL, is based on blood serum PFOS levels. A UF of 3 is applied to estimate the NOAEL for chronic testing from sub-chronic testing used. Since individual UFs are as log-units the product of 3 x 3 is taken as 10. Therefore, the total UF applied is 100.

Target Human Serum Level = POD (NOAEL) $\frac{674\ ng/ml}{UF\ 100}$ = 6.74 ng/ml

The RfD (reference dose) is calculated as: target human serum level x clearance factor, where the clearance factor is the constant 1.8×10^{-5} derived by USEPA (EPA 2016b).

Reference dose (RfD) = 6.74 ng/ml x 1000ml/L x .000081 L/kg/day = ***0.55 ng/kg/day***

New Jersey MCL

Reference dose (RfD) = 6.74 ng/ml x 1000ml/L x .000081 L/kg/day = ***0.55 ng/kg/day***

Summary of variables

NOAEL (POD)	674 ng/ml
total UF	100 (10 UF_{human}, 3$UF_{subcronic\text{-}chronic}$, 3$UF_{interspecises\ toxicodynamic}$)
Target human serum level	6.74 ng/ml
RSC	0.20
clearance factor	0.000081 L/Kg/day
default adult body weight	70 kg per NJDWQI
default adult water intake	2.0 L/day per NJDWQI

To compare with NJDWQI in its derivation, the MCL is calculated using adult default exposure values of weight and intake:

$$MCL = \frac{0.55\ ng/kg/day \times 70\ kg \times 0.2}{2\ L/day} = \textbf{\textit{3.85 ng/L (rounded to 4 ng/L)}}$$

An MCL = 5 ng/L was calculated for children

NJ Reference Dose

Reference Dose: PFOS caused numerous toxicological effects in animal studies. The Reference Dose (RfD) is based on decreased plaque forming cell response in a sub-chronic mouse study, the most sensitive effect with the serum PFOS data needed for dose-response analysis (Dong et al. 2009). Decreased plaque forming cell response is a measure of immune suppression, specifically decreased antibody response to a foreign antigen challenge. In Dong et al. (2009), the serum PFOS level at the No Observed Adverse Effect Level (NOAEL) was 674 ng/ml. A total uncertainty factor of 30 was applied to the NOAEL to derive a Target Human Serum Level (i.e., a Reference Dose in terms of serum level) of 22.5 ng/ml (22.5 µg/L). This includes uncertainty factors of 10 for intraspecies variability and 3 for interspecies variability. The RfD of 1.8 ng/kg/day (1.8×10^{-5} mg/kg/day) is calculated from the Target Human Serum Level (ng/ml) using the chemical-specific clearance factor (CL) of 8.1×10^{-5} L/kg/day (8.1×10^{-2} ml/kg/day) developed by the USEPA (2016a, 2016b) as follows:

$$22.5 \text{ ng/ml} \times 0.081 \text{ ml/kg/day} = 1.8 \text{ ng/kg/day} = 1.8 \times 10^{-6} \text{ mg/kg/day}$$

Vermont Selection of End Point

The concentration of PFOA and PFOS combined is not to exceed the DWHA based on the following recommendation presented in the May 2016 U.S. Environmental Protection Agency's (EPA) Drinking Water Health Advisory for PFOA: "The effects that serve as the basis for the RfDs [oral reference dose] for both PFOA and PFOS are developmental endpoints (reduced ossification and accelerated puberty in males for PFOA and decreased pup birth weight for PFOS). Because the RfDs for both PFOA and PFOS are based on similar developmental effects and are numerically identical, where these two chemicals co-occur at the same time and location in a drinking water source, a conservative and health protective approach that EPA recommends would be to compare the sum of the concentrations ([PFOA] + [PFOS]) to the HA [health advisory]."[1]

Vermont Selection of End Point

Details of the derivation of the Drinking Water Health Advisory of 20 ppt for PFOA and PFOS combined follow.

Drinking Water Health Advisory - Noncancer

1. The general equation used to derive a noncancer-based Drinking Water Health Advisory:

   $DWHA = (HQ)(RfD_o)(1/BW_AIR)(CF)(RSC)$

   DWHA = Drinking Water Health Advisory
   HQ= Hazard Quotient
   RfD_o= chronic oral reference dose
   BW_AIR= Body Weight adjusted Water Intake Rate
   CF= Units Conversion Factor
   RSC= Relative Source Contribution

Vermont Exposure Assumptions

Exposure Assumptions, Parameter Values and Descriptions

HQ = 1

Target Hazard Quotient employed in the development of Department of Health Drinking Water Guidance Values

RfD_o = $2x10^{-5}$ mg/kgBW-d

Oral reference dose provided in EPA's 2016 Health Effects Support Document for PFOA[2] and PFOS[3]

BW_AIR = 0.175 L/kgBW-d

The 2016 EPA Drinking Water Health Advisories for PFOA[1] and PFOS[4] state that "the developing fetus and newborn are particularly sensitive to PFOA- and PFOS-induced toxicity." EPA has recommended that fine age groupings be used in the assessment of potential exposure to children[5]. A series of ten ranges between birth and 21 years of age is recommended for consideration as appropriate. The 95th percentile Body Weight Adjusted Water Intake Rate for the first year of life based on combined direct and indirect water intake from community water supplies for consumers only is 0.175 L/kgBW-d[6,7].

CF= 1000 µg/mg

Unit conversion from milligrams to micrograms

Vermont Relative Source Contribution

RSC = 0.2 (20%)

Consistent with EPA guidance[8,9], an RSC is incorporated in the development of DWHAs that are based upon a threshold type, primarily noncarcinogenic, health effect. The RSC represents the portion of an individual's total daily exposure to a specific chemical that is attributed to or allocated to drinking water. An RSC of 20% is incorporated to account for exposure to PFOA and PFOS from other sources. This follows EPA's recommendation to use an RSC of 20% when quantitative data on other sources of exposure are not available. The 2016 PFOA Health Advisory states "In cases where environmental or exposure data are lacking, the Exposure Decision Tree approach results in a recommended RSC of 20%. This 20% RSC value may be replaced where sufficient data are available to develop a scientifically defensible alternative value."[1]

New York PFOS MCL

Watch Video

Discussion

Assignments

Public Comments

Next Meeting

	puberty)					UF_L = 10			
PFOS									
USEPA (2016b)	Luebker et al. (2005a) (rats; reduced pup body weight and delayed eye opening)	6.26 NOAEL	1971	8.1×10^{-5}	0.00051	30 UF_H = 10 UF_A = 3	2.0×10^{-5} (6.26/30 = 0.209)	Water ingestion rate of a lactating woman (0.054 L/kg d)(60 kg; 3.2 L/day) RSC 20%	70
MassDEP (2019)	Luebker et al. (2005a) (rats; reduced pup body weight and delayed eye opening)	6.26 NOAEL	1971	8.1×10^{-5}	0.00051	100 UF_H = 10 UF_A = 3 **UF_D = 3 immune effects**	5.0×10^{-5} (6.26/100 = 0.0626)	Water ingestion rate of a lactating woman (0.054 L/kg d)(60 kg; 3.2 L/day) RSC 20%	20
ATSDR (2018)	Luebker et al. (2005a) (rats; reduced pup weight and delayed eye opening)	7.43 NOAEL	2000	6.93×10^{-5}	0.000515	300 UF_H = 10 UF_A = 3 **UF_D = 10 immune effects**	2.0×10^{-6} (7.43/300 = 0.025)	ND	ND
MDH (2019a)	Dong et al. (2011) (mice; immune suppression, decreased IL-4 and decreased SRBC specific IgM levels)	2.36 NOAEL	1241	1.3×10^{-4}	0.000307	100 UF_H = 10 UF_A = 3 **UF_D = 3 immune and thyroid effects**	3.1×10^{-6} (2.36/100 = 0.024)	Transgenerational toxicokinetic model developed by MDH for breast fed and bottle fed infants (Goeden et al. 2019) RSC 20%	15

Agency	Key Study (effect)	POD Animal Serum (mg/L)	Human T ½ Used (days)	Dosimetric Adjustment Factor (L/kg/d)	HED (mg/kg-day)	UF	Candidate RfD or MRL (Serum Concentration at RfD, mg/L)	DW Exposure Parameters and Relative Source Contribution Factor (RSC)	DW Value (ppt, ng/L)
NJDWQI (2018)	Dong et al. (2009) (mice; immune suppression)	0.674 $BMDL_{10}$	1971	8.2×10^{-5} [a]	0.000055	30 $UF_H = 10$ $UF_A = 3$	2×10^{-6} (0.674/30 = 0.022)	70 kg adult 2L/day RSC 20%	13
NHDES (2019b)	Dong et al. (2011) (mice; immune suppression, decreased IL-4 and decreased SRBC specific IgM levels)	2.36 NOAEL	1241	1.28×10^{-4}	0.0003	100 $UF_H = 10$ $UF_A = 3$ **$UF_D = 3$ thyroid effects in neonatal animals**	3.0×10^{-6} (2.36/100 = 0.024)	Transgenerational toxicokinetic model developed by MDH for breast fed and bottle fed infants (Goeden et al. 2019) RSC 50%	15
MISAW (2019)	Dong et al. (2009) (mice; immune suppression of plaque formation, increased liver mass)	0.674 NOAEL	1241	1.28×10^{-4}	0.0000866	30 $UF_H = 10$ $UF_A = 3$	3×10^{-6} (2.9×10^{-6}) (0.674/30 = 0.022)	Transgenerational toxicokinetic model developed by MDH for breast fed and bottle fed infants (Goeden et al. 2019) RSC 50%	16
NYDOH (2018)	Same as NJDWQI (2018)							Not specified	10
WIDHS(2019)	Same as ATSDR (2018a)							10 kg young child 1L/day RSC 100%	20
PFNA									
ATSDR (2018a)	Das et al. (2015) (mice; developmental delays; decreased body weight gain)	6.80 NOAEL	900	1.54×10^{-4}	0.001	300 $UF_A = 3$ $UF_H = 10$ $UF_D = 3$	3.0×10^{-6} (6.8/300 = 0.023)	ND	ND