

# HEALTH CONSULTATION

Technical Support Document for Assessment and Selection of a new Perfluorooctane Sulfonate (PFOS) Reference Dose (RfD) and Relative Source Contribution (RSC) as the basis for Michigan Fish Consumption Screening Values (FCSVs)

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## Background

The Michigan Department of Health and Human Services's (MDHHS) Michigan Fish Consumption Advisory Program (MFCAP) issues fish consumption guidelines, which are public health advisories. This is done under the authority of the Michigan Public Health Code (Act 368 of 1978). Fish consumption guidelines rely upon fish consumption screening values (FCSVs), which are calculated using several variables, including the reference dose (RfD) and relative source contribution (RSC). These variables are combined with others such as exposure duration and frequency. The FCSVs are concentrations of a contaminant in fish tissue below which there should be negligible risk of toxicity at a consumption rate intended to be protective of most recreational anglers. The process by which Michigan FCSVs are developed is described in the *Michigan Fish Consumption Advisory Program Guidance Document* (2016) and follows the U.S. Environmental Protection Agency's (EPA) *Guidance for Assessing Chemical Contaminant Data for Use in Fish Advisories* (EPA 1996; EPA 2000a; EPA 2000b). The purpose of this document is to provide the justification for an updated toxicity value and new RSC for the calculation of a new set of PFOS FCSVs for providing public health protective consumption advice about fish caught in Michigan waters.

Results from modeling in the *Drinking Water PFAS Concentrations and Exposure Factors Influencing Measured and Predicted Serum PFAS Concentrations: Report 2 of the North Kent County Exposure Assessment (NKCEA, 2024)* showed a statistically significant relationship between greater frequency of fish consumption and higher serum PFOS levels; e.g., compared to people who never eat fish, those who eat fish a few times per year or less had 18% higher serum PFOS levels on average. Positive associations between consumption of fish and serum PFOS concentrations have also been found in other US populations, including:

- a Wisconsin statewide representative population (Pomazal et al. 2024);
- licensed anglers and a Burmese population in New York (Liu et al. 2022); and,
- international populations (Yamaguchi et al 2013, Fábelová et al. 2023).

These data indicate that fish consumption contributes to serum concentrations of PFOS. Updating the MDHHS Eat Safe Fish consumption guides with the toxicity value and RSC described here may contribute to lowered blood concentrations of PFOS in real world settings.

## Toxicity Value Selection Process and Use

In 2014, MFCAP established FCSVs for PFOS using an interim RfD of 14 nanogram/kilogram-day (ng/kg-day) as the suitable toxicity value. That RfD was derived from toxicity data that showed disruptions to the thyroid and cardiovascular systems. The *Technical Support Document for Assessment of Perfluorinated Chemicals and Selection of a Perfluorooctane Sulfonate (PFOS) Reference Dose as the basis for Michigan Fish Consumption Screening Values (FCSVs)* (MDCH 2014) and the *Michigan*

*Fish Consumption Advisory Program: Guidance Document* (MFCAP, 2016) describe this approach in detail. Since 2014, federal agencies including EPA and the Agency for Toxic Substances and Disease Registry (ATSDR), as well as other groups, including the Michigan Science Advisory Workgroup, have released new or updated toxicity values for PFOS. Among other health effects, the potential for PFOS to have immunotoxicological effects has gained support in recent years and is reflected in some of the most recent toxicity values available for PFOS. The following toxicity values are among those that have been released<sup>1</sup> since MFCAP established FCSVs for PFOS in 2014:

- Michigan Science Advisory Workgroup (SOM, 2019): 2.89 ng/kg-day, based on immunological endpoints (plaque forming cell response).
- ATSDR (2021): 2 ng/kg-day, based on developmental endpoints (delayed eye opening/decreased pup body weight).
- EPA (2024a): 0.1 ng/kg-day, based on developmental and cardiovascular endpoints (decreased birthweight/increased total cholesterol).
  - The EPA (2022) released a provisional/interim toxicity value for PFOS based upon immunological endpoints which was superseded by the final (2024a) toxicity value, which did not rely upon immunological endpoints.

## Carcinogenicity

For chemicals identified by the U.S. EPA as mutagenic, MFCAP would calculate FCSVs for cancer and non-cancer endpoints and use the ones that are most protective of public health. The EPA (2024a) released a cancer slope factor (CSF) for PFOS (39.5 (milligrams/kilogram-day)<sup>-1</sup>); however, they concluded there was a lack of information to support a mutagenic mechanism of action for PFOS, and MFCAP concludes there is otherwise no clear evidence yet for the mutagenicity of PFOS (or any other PFAS).

## Justification for the Selected Toxicity Value

Since 2014, the toxicological and epidemiological literature on PFOS has expanded considerably. As a result of additional available toxicity information, the above referenced toxicity values for PFOS have been published by other public health agencies/workgroups. Based on this evolved scientific landscape, MFCAP reevaluated its current PFOS toxicity value. Upon review of the recent literature (see Appendix Tables A-1) and evaluation of the available published toxicity values, MFCAP concludes that using the Michigan Science Advisory Workgroup's toxicity value of 2.89 ng/kg-day for PFOS to update the current FCSVs would be protective of human health.

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<sup>1</sup> This is **not** a comprehensive list of all toxicity values released since 2014.

This toxicity value was selected because it:

- **Is derived from a widely evaluated study (Dong et al., 2009)**, which has the following strengths:
  - Dong et al. (2009) uses immunological endpoints. Some studies have shown that immunological effects may be the most sensitive endpoint for PFOS toxicity, although others have pointed to developmental effects. Both human epidemiological and laboratory animal studies have reported immunological effects of PFOS at concentrations lower than those associated with other health effects. Most consistent though, is the finding that several health outcomes, including immunotoxicity and developmental perturbations, may occur at similar and overlapping dose ranges. EPA (2024a) concluded that the noncancer health outcomes with the strongest evidence are hepatic, immune, cardiovascular and developmental.
  - Dong et al. (2009) reports results using an animal model. Relying upon an animal model does not negate findings associated with epidemiological studies but does reflect that the human experience is uncontrolled and imperfectly documented. Animal studies are controlled, with precisely measured exposures (SOM, 2009; ATSDR, 2021).
- **Aligns closely with all other recently published final toxicity values** available from ATSDR (2021) and EPA (2024a). The selected toxicity value is consistent (i.e., approximately within an order of magnitude) with those selected for use by all other relevant agencies and in other media (e.g., ATSDR, 2021; EPA, 2024a). In addition to alignment with actual, derived toxicity values, the health endpoints themselves, on which the toxicity values are based, also overlap.
  - Note also that all other candidate RfDs derived by the EPA from epidemiologic studies were within one order of magnitude of each other, regardless of endpoint, health outcome, or study population (EPA, 2024a).

The update of the PFOS toxicity value to 2.89 ng/kg-day reflects the evolution downward in toxicity values that has occurred since 2014, both nationally and globally. This downward trajectory has been based on replicated findings from the toxicological literature that show health effects of PFOS exposure occur at lower concentrations than those previously known.

EPA's (2024a) toxicity value is lower than ATSDR's (2021) and SOM's (2019) toxicity values for PFOS. However, it is within approximately one order of magnitude of those (i.e., EPA: 0.1 ng/kg-day vs ATSDR: 2 ng/kg-day and SOM: 2.89 ng/kg-day). Although similar, because EPA's latest (2024a) value is lower than MFCAP's selected toxicity value, MFCAP is continuing to review EPA's toxicity value and evaluating its suitability for use in developing fish consumption advisories in Michigan. MFCAP is also awaiting

EPA guidance on the use of their 2024 toxicity values for the development of fish consumption advisories.

Because the available information may continue to evolve or trend downwards, MFCAP will update the selection of a toxicity value for use in developing fish consumption advisories as needed based on available scientific information and/or federal guidance.

## Relative Source Contribution Selection Process and Use

In 2014, MFCAP applied an RSC of 100% in the calculation of the PFOS FCSVs. PFOS, however, is understood to have had many and diverse historic uses resulting in widespread environmental contamination. The National Health and Nutrition Examination Survey (NHANES) reports detectable serum concentrations of PFOS among most of the sampled population, likely driven by the continued impact of past industrial and consumer uses (EPA 2024a; ATSDR 2021).

The EPA recommends the application of an RSC between 20% and 80% when setting ambient water quality criteria protective of human health (EPA, 2000c), which prevents exposures above the toxicity value if other exposure pathways are likely. This guidance was applied here, because sources of exposure to PFOS other than fish consumption are likely relevant to large swaths of the population (EPA 2024a; ATSDR, 2021).

### RSC Calculation

The percentage of PFOS exposure that could occur from fish consumption (given the relevance of other exposure sources) was calculated using a dose converted from NHANES 2017-2018 (ages 12 and older) human serum PFOS concentration, a concentration associated with “background” exposure, and the toxicity value of 2.89 ng/kg-day (SOM, 2019).

The NHANES 2017-2018 (ages 12 and older) geometric mean of 4.25 ng/mL PFOS in human serum concentration (CDC, 2021) was used to represent “background” exposure. The geometric mean, a measure of central tendency, was selected. This is the recommended approach from the EPA when estimating an RSC (EPA, 2000c).

The NHANES serum PFOS concentration can be converted into a daily dose with the below equation and parameters. All parameters match those used by the Michigan Science Advisory Workgroup in calculation of the toxicity value (SOM, 2019).

$$Dose = serum\ concentration \times k_e \times V_d$$

Where,

- Serum concentration = 4.25 µg/L (ng/mL) (CDC, 2021)

- $V_d$  (volume of distribution) = 0.23 L/kg (SOM, 2019)
- $K_e$  (elimination rate constant) = 0.000558539 ( $5.5 \times 10^{-4}$ ) days<sup>-1</sup>, based on a human serum half-life ( $t_{1/2}$ ) of 1241 days (SOM, 2019) and the below equation  

$$k_e = \ln(2)/t_{1/2}$$
- Dose, in micrograms per kilogram-day ( $\mu\text{g/kg-day}$ ) = 0.00055  $\mu\text{g/kg-day}$  = 0.55 ng/kg/day

The percentage of the toxicity value represented by background exposure was then calculated.

$$\frac{\text{"Background" Dose}}{\text{Toxicity value}} \times 100 = \frac{0.55}{2.89} \times 100 = 19\%$$

With 19% attributable to background, 81% may be attributable to fish consumption. This was rounded down to 80% to align with EPA's guidance to use an RSC between 20% and 80%.

The application of an 80% RSC to the PFOS FCSVs has the following uncertainties:

- Exposure scenarios that include localized elevated exposures to PFOS from one or more environmental media are not represented by the current approach, which allocates only 20% of the RfD to sources of PFOS other than fish.
  - Individuals with a PFOS serum concentration at the 95% Percentile (NHANES 2017-2018) have approximately 66%<sup>2</sup> attributable to background and would only have approximately 34% to allocate to PFOS from fish consumption. However, extensive statewide investigative work conducted by State of Michigan agencies has likely identified most or all high-strength sources of PFOS in drinking water, a primary source for elevated exposure.
- Assumptions about bioavailability/bioaccessibility of PFOS:
  - Evidence related to the bioavailability of PFOS from fish tissue continues to accumulate and could inform future evaluations by MFCAP. For instance, laboratory studies (Zhao et al., 2023; Alves et al., 2017) describe less than 100% bioaccessibility of PFOS when exposure occurs through diet, with reports ranging from 40% bioaccessibility of PFOS in steamed salmon to 60-65% in steamed carp and snakehead (Zhao et al., 2023) and 62% bioaccessibility for PFOS in flounder (Alves et al., 2017).
- Use of NHANES Data:
  - The NHANES data describe a downward trend over time in PFOS blood levels nationwide.

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<sup>2</sup> NHANES (2017-2018) 95% Percentile = 14.6  $\mu\text{g/L}$ ; Using the equations described, that equals a dose of 0.0019  $\mu\text{g/kg-day}$  (1.9 ng/kg-day) and  $(1.9/2.89 \times 100 = 66\%)$

- These data suggest exposures to PFOS from all routes are likely changing over time, which could have implications for MFCAP's selection of an RSC for fish consumption in the future.
- The NHANES data used to estimate background exposure across the United States may not reflect current background PFOS levels in Michigan residents.
  - MDHHS is currently performing the Michigan Chemical Exposure and Monitoring Study (MiChEM), which will provide Michigan-specific chemical background exposures for future evaluation of RSCs.
- Available data (Terry et al., 2018) suggest approximately 20% of adults (ages 20+) reported consuming seafood (fish + shellfish) at least two times per week during NHANES 2013-2016. Therefore, the use of NHANES to calculate “background” exposures may already include some portion of PFOS from fish consumption.

## Per-and Polyfluoroalkyl Substances (PFAS) other than PFOS

The EPA now recommends monitoring four PFAS in addition to PFOS in fish and shellfish advisory programs and suggests a further seven to watch (EPA, 2024b). For more than a decade, the MFCAP program has reviewed data for 11 PFAS found in the edible portions of fish, including PFOS and the four others recommended by EPA. In the past several years, the MFCAP has evaluated data from an expanded list of 39 PFAS that are now analyzed in the edible portions of fish in Michigan (inclusive of the five PFAS recommended by EPA to monitor *and* inclusive of the seven PFAS on EPA's expanded watch list).

MFCAP has observed that among all measured PFAS, PFOS is found:

(1) most often (i.e., found in 94% of fish filets sampled from Michigan waters by the Michigan Department of Environment, Great Lakes, and Energy (EGLE)<sup>3</sup>, and found in 100% of fish randomly sampled in the U.S. portion of the Great Lakes by the EPA<sup>4</sup>); and,

(2) at higher concentrations relative to other PFAS (i.e., average concentration of PFOS in filets of fish from Michigan waters is 69 ng/g, compared to PFOA, for example, at 1 ng/g).

Further, PFAS other than PFOS that are detected in fish tissue have roughly similar, or higher, toxicity values than PFOS (see EPA's Integrated Risk Information System (IRIS)

<sup>3</sup> EGLE Fish Contaminant Monitoring Program, data as of November 2022

<sup>4</sup> 2020 Great Lakes Human Health Fish Fillet Tissue Study (data tables, US EPA, 2024)



for details on relative toxicity values). Therefore, consumption guides that are based on PFOS are currently understood to be protective of the other PFAS that may be present at lower concentrations in fewer fish.

Although no action or programmatic updates are needed at this time to follow EPA's new recommendations for fish monitoring, the MFCAP will continue to evaluate data from all available PFAS and may update recommendations if additional relevant information becomes available.

## Statewide Exposure Prevention Guidance for PFAS

Given myriad exposure routes, accumulation of toxicological data, a rapidly evolving regulatory landscape and recent federal and international determinations related to carcinogenicity, among other recent findings, MDHHS encourages all people to reduce their exposures to all sources of PFAS as much as possible to reduce the likelihood of adverse health outcomes. Personal decisions about fish consumption including following MFCAP's fish consumption guides are one, among many, important ways to reduce or avoid exposure to PFAS from the environment. Everyone is encouraged to learn more about ways to reduce exposure to PFAS by visiting [Michigan.gov/pfasresponse/health](https://Michigan.gov/pfasresponse/health).

## Recommendation

The updated toxicity value (2.89 ng/kg-day) and the new RSC (80%) described here should be used to calculate updated FCSVs for PFOS. Embedded considerations that add to the protectiveness of these values include:

- The toxicity value (2.89 ng/kg-day) is based on a no observable adverse effect level, which is 10 times below the identified dose in mice that lead to observed effects (SOM, 2019).
- The toxicity value (2.89 ng/kg-day) includes a total uncertainty factor of 30, to account for laboratory animal to human toxicodynamic differences and human variability (SOM, 2019).
- The toxicity value is based on an immune health endpoint and immune endpoints have been identified as one of several considered most sensitive, indicating that this value would be protective for other health endpoints (SOM, 2019; ATSDR, 2021; EPA, 2024a).
- The toxicity value is consistent (i.e., approximately within an order of magnitude) with those selected for use by all other relevant agencies and in other media (e.g., ATSDR, 2021; EPA, 2024a).
- An assumption that 100% of the ingested PFOS in fish will be absorbed by a person's body, which may overestimate the percentage of PFOS that is actually absorbed (Zhao et al., 2023; Alves et al., 2017).
- An assumption that NHANES 2017-2018 serum PFOS currently represents the Michigan's general population serum PFOS levels. Serum concentrations from 2017-2018 may overestimate serum PFOS as levels nationally have been

declining over time. And, for Michigan's general population, extensive statewide investigative work over the past nearly a decade has likely identified most or all high-strength sources of PFOS in drinking water.

Updating the FCSV with these inputs and updating relevant fish consumption guidelines will further protect public health in Michigan and will provide noncommercial anglers and fish consumers with updated information they can use to make decisions about their health and exposure to PFOS.

## Supporting Documentation

- [ATSDR] Agency for Toxic Substances and Disease Registry. 2021. Toxicological profile for Perfluoroalkyls. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service.
- [CDC] U.S. Center for Disease Control and Prevention. 2021. National Report on Human Exposure to Environmental Chemicals. 2021. Early Release: Per- and Polyfluorinated Substances (PFAS) Tables, National Health and Nutrition Examination Study (NHANES) 2011-2018.
- [EPA] U.S. Environmental Protection Agency. 1996. Guidance for Assessing Chemical Contamination Data for Use in Fish Advisories: Volume 3 Overview of Risk management. Washington, DC: Office of Water. EPA 823-B-96-006.
- [EPA] U.S. Environmental Protection Agency. 2000a. Guidance for Assessing Chemical Contaminant Data for Use in Fish Advisories: Volume 1 Fish Sampling and Analysis: Second Edition. Washington, DC: Office of Water. EPA 823-B-00-007.
- [EPA] U.S. Environmental Protection Agency. 2000b. Guidance for Assessing Chemical Contaminant Data for Use in Fish Advisories: Volume 2 Risk Assessment and Fish Consumption Limits: Second Edition. Washington, DC: Office of Water. EPA 823-B-97-008.
- [EPA] U.S. Environmental Protection Agency. 2000c. Methodology for deriving ambient water quality criteria for the protection of human health. Washington, DC: Office of Water. EPA 822-B-00-004.
- [EPA] U.S. Environmental Protection Agency. 2022. INTERIM Drinking Water Health Advisory: Perfluorooctane Sulfonic Acid (PFOS) CASRN 1763-23-1. Washington, DC: Office of Water. EPA 822/R-22/004.
- [EPA] U.S. Environmental Protection Agency. 2024a. Final human health toxicity assessment for perfluorooctane sulfonic acid (PFOS) and related salts.
- [EPA] U.S. Environmental Protection Agency. 2024b. Contaminants to monitor in fish and shellfish advisory programs: Compilation of peer review-related information.
- [MDCH] Michigan Department of Community Health. 2014. Health consultation: Technical support document for assessment of perfluorinated chemicals and selection of a perfluorooctane sulfonate (PFOS) reference dose as the basis for Michigan Fish Consumption Screening Values (FCSVs). Lansing, MI.
- [MFCAP] State of Michigan. 2016. Michigan Fish Consumption Advisory Program Guidance document. Lansing, MI. <https://www.michigan.gov/>

- [/media/Project/Websites/mdhhs/Folder1/Folder19/MFCAP\\_Guidance\\_Document.pdf?rev=12920be7b3564359a7ff683a0064df05](#)
- [NKCEA, 2024] Michigan Department of Health and Human Services. Drinking Water PFAS Concentrations and Exposure Factors Influencing Measured and Predicted Serum PFAS Concentrations: Report 2 of the North Kent County Exposure Assessment. Lansing, MI. [North Kent County Exposure Assessment - Report 2](#)
- [SOM] State of Michigan. Michigan Science Advisory Workgroup. 2019. Health-based drinking water value recommendations for PFAS in Michigan. Lansing, MI. <https://www.michigan.gov/-/media/Project/Websites/PFAS-Response/Reports/2019-Health-Based-Drinking-Water-Value-Recommendations-PFAS-MI.pdf?rev=1779be946a5c41439f1db4f3eeaec4ec>
- Alves RN, Maulvault AL, Barbosa VL, Cunha S, Kwadijk CJAF, Álvarez-Muñoz D, Rodríguez-Mozaz S, Aznar-Alemán O, Eljarrat E, Barceló D, Fernandez-Tejedor M, Tediosi A, Marques A. 2017. Preliminary assessment on the bioaccessibility of contaminants of emerging concern in raw and cooked seafood. *Food and Chemical Toxicology* 104:69-78. doi: 10.1016/j.fct.2017.01.029. Epub 2017 Feb 13. PMID: 28202359.
- 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. *Archives of Toxicology* 83(9):805-815.
- Fábelová L, Beneito A, Casas M, Colles A, Dalsager L, Den Hond E, Dereumeaux C, Ferguson K, Gilles L, Govarts E, Irizar A, Lopez Espinosa M J, Montazeri P, Morrens B, Patayová H, Rausová K, Richterová D, Rodriguez Martin L, Santa-Marina L, Schettgen T, Schoeters G, Haug LS, Uhl M, Villanger GD, Vrijheid M, Zaros C, Palkovičová Murínová L. 2023. PFAS levels and exposure determinants in sensitive population groups. *Chemosphere*, 313, 137530. <https://doi.org/10.1016/j.chemosphere.2022.137530>
- Liu M, Nordstrom M, Forand S, Lewis-Michl E, Wattigney W A, Kannan K, Wang W, Irvin-Barnwell E, Hwang S A. 2022. Assessing exposures to per- and polyfluoroalkyl substances in two populations of Great Lakes Basin fish consumers in Western New York State. *International Journal of Hygiene and Environmental Health*, 240, 113902. <https://doi.org/10.1016/j.ijheh.2021.113902>
- Pomazal R, Malecki K, Stanton N, Shelton B, Lange M, Irving R, Meiman J, Remucal CK, Cochran A, Schultz AA. 2024. Determinants of per- and polyfluoroalkyl substances (PFAS) exposure among Wisconsin residents. *Environmental Research*, 254, 119131. <https://doi.org/10.1016/j.envres.2024.119131>
- Terry AL, Herrick KA, Afful J, Ahluwalia N. 2018. Seafood consumption in the United States, 2013–2016. NCHS Data Brief, no 321. Hyattsville, MD: National Center for Health Statistics. 2018. [NCHS Data Brief, Number 321, September 2018](#)
- Yamaguchi M, Arisawa K, Uemura H, Katsuura-Kamano S, Takami H, Sawachika F, Nakamoto M, Juta T, Toda E, Mori K, Hasegawa M, Tanto M, Shima M, Sumiyoshi Y, Morinaga K, Kodama K, Suzuki T, Nagai M, Satoh H. 2013. Consumption of seafood, serum liver enzymes, and blood levels of PFOS and PFOA in the Japanese population. *Journal of Occupational Health*, 55(3), 184–194. <https://doi.org/10.1539/joh.12-0264-oa>

Zhao A, Wang W, Zhang R, He A, Li J, Wang Y. 2023. Tracing the Bioaccessibility of Per- and Polyfluoroalkyl Substances in Fish during Cooking Treatment. *Journal of Agricultural and Food Chemistry* 71(48):19066-19077. doi: 10.1021/acs.jafc.3c06038. Epub 2023 Nov 20. PMID: 37984055.

Table A-1. Selected studies from independent literature review.

Citation	Study population	Health Effect Endpoint(s)
Alam MN, Han X, Nan B, Liu L, Tian M, Shen H, Huang Q. 2021. Chronic low-level perfluorooctane sulfonate (PFOS) exposure promotes testicular steroidogenesis through enhanced histone acetylation. <i>Environmental Pollution</i> 284:117518.	Male rats	Reproductive  Histone modification, Steroid hormone synthesis in rat testis
Birukov A, Andersen LB, Andersen MS, Nielsen JH, Nielsen F, Jyhl HB, Jorgensen JS, Grandjean P, Dechend R, Jensen TK. 2021. Exposure to perfluoroalkyl substances and blood pressure in pregnancy among 1436 women from the Odense Child Cohort. <i>Environment International</i> 151:106442.	Pregnant women from the Odense region of Denmark	Cardiovascular
Budtz-Jorgensen E and Grandjean P. 2018. Application of benchmark analysis for mixed contaminant exposures: Mutual adjustment of perfluoroalkylate substances associated with immunotoxicity. <i>PLOS One</i> 13(10):e0205388.	Two birth cohorts from the Faroe Islands	Immunological
Chen L, Liu Y, Mu H, Li H, Liu S, Zhu M, Bu Y, Wu B. 2022. Effects of perfluorobutane sulfonate and perfluorooctane sulfonate on lipid homeostasis in mouse liver. <i>Environmental Pollution</i> 315:120403.	Adult C57BL/6 male mice	Hepatic, Metabolic (lipid homeostasis)
Cheng X, Wei Y, Zhang Z, Wang F, He J, Wang R, Xu Y, Keerman M, Zhang S, Zhang Y, Bi J, Yao J, He M. 2022. Plasma PFOA and PFOS levels, DNA methylation, and blood lipid levels: A pilot study. <i>Environmental Science &amp; Technology</i> 56:17039-17051.	Patients enrolled in a hospital in Hubei Province, China	Metabolic
Conley JM, Lambright CS, Evans N, Farraj AK, Smoot J, Grindstaff RD, Hill D, McCord J, Medlock-Kakaley E, Dixon A, Hines E, Gray Jr. LE. 2023. Dose additive maternal and offspring effects of oral maternal exposure to a mixture of three PFAS (HFPO-DA, NBP2, PFOS) during pregnancy in the Sprague-Dawley rat. <i>Science of the Total Environment</i> 892:164609.	Pregnant Sprague-Dawley rats and offspring	Hepatic, developmental

Citation	Study population	Health Effect Endpoint(s)
Conley JM, Lambright CS, Evans N, Medlock-Kakaley E, Dixon A, Hill D, McCord J, Strynar MJ, Ford J, Gray Jr. LE. 2022a. Cumulative maternal and neonatal effects of combined exposure to a mixture of perfluorooctanoic acid (PFOA) and perfluorooctane sulfonic acid (PFOS) during pregnancy in the Sprague-Dawley rat. <i>Environment International</i> 170:107631.	Pregnant Sprague-Dawley rats and offspring	Developmental, reproductive, metabolic, hepatic, nephrological
Conley JM, Lambright CS, Evans N, Medlock-Kakaley E, Hill D, McCord J, Strynar MJ, Wehmas LC, Hester S, MacMillan DK, Gray Jr. LE. 2022b. Developmental toxicity of Nafion byproduct 2 (NBP2) in the Sprague-Dawley rat with comparisons to hexafluoropropylene oxide-dimer acid (HFPO-DA or GenX) and perfluorooctane sulfonate (PFOS). <i>Environment International</i> 160:107056.	Pregnant Sprague-Dawley rats and offspring	Thyroid, Developmental, reproductive, hepatic
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. <i>Arch Toxicol</i> 83:805-815.	Adult male C57BL/6 mice	Immunological, hepatic
Grandjean P, Andersen EW, Budtz-Jorgensen E, Nielsen F, Molbak K, Weihe P, Heilmann C. 2012. Serum vaccine antibody concentrations in children exposed to perfluorinated compounds. <i>JAMA</i> 307(4):391-397.	A birth cohort from the Faroe Islands	Immunological
Horikoshi T, Nishimura T, Nomura Y, Iwabuchi T, Itoh H, Takizawa T, Tsuchiya KJ. 2021. Umbilical cord serum concentrations of perfluorooctane sulfonate, perfluorooctanoic acid, and the body mass index changes from birth to 5 ½ years of age. <i>Nature Scientific Reports</i> 11:19789.	Randomly selected children from Japan	Body mass index/Metabolic
Li J, Quan X, Lei S, Huang Z, Wang Q, Xu P. 2021. PFOS inhibited normal functional development of placenta cells via PPAR $\gamma$ signaling. <i>Biomedicines</i> 9:677.	Human choriocarcinoma cell line HTR-8/SVneo and JEG-3 cells  Pregnant mice	Reproductive
Liu Y, Yu G, Zhang R, Feng L, Zhang J. 2023. Early life exposure to low-dose perfluorooctane sulfonate disturbs gut barrier homeostasis and increases the risk of intestinal inflammation in offspring. <i>Environmental Pollution</i> 329:121708.	Pregnant rats and offspring	Developmental, Immunological

Citation	Study population	Health Effect Endpoint(s)
Luebker DJ, Case MT, York RG, Moore JA, Hansen KJ, Butenhoff JL. 2005. Two-generation reproduction and cross-foster studies of perfluorooctanesulfonate (PFOS) in rats. <i>Toxicology</i> 215(1-2):126-148.	Two generations of Sprague-Dawley rats (females through gestation and lactation)	Developmental
Mandour DA, Morsy MM, Fawzy A, Mohamed NM, Ahmad MM. 2023. Structural and molecular changes in the rat myocardium following perfluorooctane sulfonate (PFOS) exposure are mitigated by quercetin via modulating HSP 70 and SERCA 2. <i>Journal of Molecular Histology</i> 54:283-296.	Male Sprague-Dawley rats	Cardiac toxicity, inflammatory and thyroid effect on heart tissue
Narizzano AM, Lent EM, Hanson JM, East AG, Bohannon ME, Quinn Jr. MJ. 2022. Reproductive and developmental toxicity of perfluorooctane sulfonate (PFOS) in the white-footed mouse ( <i>Peromyscus leucopus</i> ). <i>Reproductive Toxicology</i> 113:120-127.  Narizzano, A. M., Lent, E. M., Hanson, J. M., East, A. G., Bohannon, M. E., & Quinn, M. J., Jr (2022). Corrigendum to "Reproductive and developmental toxicity of perfluorooctane sulfonate (PFOS) in the white-footed mouse ( <i>Peromyscus leucopus</i> )" [Reprod. Toxicol. 113 (2020) 120-127]. <i>Reproductive toxicology (Elmsford, N.Y.)</i> , 114, 32. <a href="https://doi.org/10.1016/j.reprotox.2022.10.004">https://doi.org/10.1016/j.reprotox.2022.10.004</a>	Male and female white-footed mice and offspring	Reproductive, developmental
Ninomiya A, Mshaty A, Hajima A, Yajima H, Kokubo M, Khairinisa MA, Ariyani W, Fujiwara Y, Ishii S, Hosoi N, Hirai H, Amano I, Koibuchi N. 2022. The neurotoxic effect of lactational PFOS exposure on cerebellar functional development in male mice. <i>Food and Chemical Toxicology</i> 159:112751.	Female mice and male offspring	Neurodevelopmental
Osorio-Yanez C, Sanchez-Guerra M, Cardenas A, Lin PID, Hauser R, Gold DR, Kleinman KP, Hivert MF, Fleisch AF, Calafat AM, Webster TF, Horton ES, Oken E. 2021. Per- and polyfluoroalkyl substances and calcifications of the coronary and aortic arteries in adults with prediabetes: Results from the diabetes prevention program outcomes study. <i>Environment International</i> 151:106446.	Prediabetic adults enrolled in the Diabetes Prevention Program trial	Cardiovascular

Citation	Study population	Health Effect Endpoint(s)
Peden-Adams MM, Keller JM, EuDaly JG, Berger J, Gilkeson GS, Keil DE. 2008. Suppression of humoral immunity in mice following exposure to perfluorooctane sulfonate. <i>Toxicological Sciences</i> 104(1):144-154.	Adult male and females B6C3F1 mice	Immunological
Qiu L, Wang H, Dong T, Huang J, Li T, Ren H, Wang X, Qu J, Wang S. 2021. Perfluorooctane sulfonate (PFOS) disrupts testosterone biosynthesis via CREB/CRTC2/StAR signaling pathway in Leydig cells. <i>Toxicology</i> 449:152663.	Male ICR mice	Reproductive
Rudzanova B, Vlaaderen J, Kalina J, Piler P, Zvonar M, Klanova J, Blaha L, Adamovsky O. 2023. Impact of PFAS exposure on prevalence of immune-mediated diseases in adults in the Czech Republic. <i>Environmental Research</i> 229:115969.	Young adults from the Central European Longitudinal Study of Parents and Children (CELSPAC)	Immunological
Sevelsted A, Gurdeniz G, Rago D, Pedersen CET, Lasky-Su JA, Checa A, Zhang P, Wheelock CE, Normann SS, Kristensen DM, Rasmussen MA, Schukkehner J, Sdougkou K, Martin JW, Stokholm J, Bonnelykke K, Bisgaard H, Chawes B. 2022. Effect of perfluoroalkyl exposure in pregnancy and infancy on intrauterine and childhood growth and anthropometry. Sub study from COPSAC2010 birth cohort. <i>eBioMedicine</i> 83:104236.	A Danish mother-child cohort	Developmental
Timmermann CAG, Pedersen HS, Weihe P, Bjerregaard P, Nielsen F, Heilmann C, Grandjean P. 2022. Concentrations of tetanus and diphtheria antibodies in vaccinated Greenlandic children aged 7-12 years exposed to marine pollutants, a cross sectional study. <i>Environmental Research</i> 203:111712.	Greenlandic children ages 7-12 years old	Immunological
Torres L, Redko A, Limper C, Imbiakha B, Chang S, August A. 2021. Effect of perfluorooctanesulfonic acid (PFOS) on immune cell development and function in mice. <i>Immunology Letters</i> 233:31-41.	Adult male and female C57BL/6 mice	Immunological



Citation	Study population	Health Effect Endpoint(s)
Van Larabeke N, Koppen G, Decraemer S, Colles A, Bruckers L, Den Hond E, Govarts E, Morrens B, Schettgen T, Remy S, Coertjens D, Nawrot T, Nelen V, Baeyens W, Schoeters G. 2022. Per- and polyfluoroalkyl substances (PFAS) and neurobehavioral function and cognition in adolescents (2010-2011) and elderly people (2014): Results from the Flanders Environment and Health Studies (FLEHS). <i>Environmental Sciences Europe</i> 34:98.	Adolescents and adults (50-65 years) old from an industrialized area of Flanders	Neurobehavioral/neurological
Wen Y, Rashid F, Fazal Z, Singh R, Spinella MJ, Irudayaraj J. 2022. Nephrotoxicity of perfluorooctane sulfonate (PFOS)-Effect on transcription and epigenetic factors. <i>Environmental Epigenetics</i> 8(1):1-11.	Adult CD-1 male mice	Nephrological
Zhang H, Zhang C, Xu D, Wang Q, Xu D. 2023. Effects of subchronic exposure of perfluorooctane sulfonate on cognitive function of mice and its mechanism. <i>Environmental Pollution</i> 329:121650.	Male C57BL/6J mice	Neurological
Zhao Y, Liu W, Qu J, Hu S, Zhang L, Zhao M, Wu P, Xue J, Hangbiao J. 2022. Per-/polyfluoroalkyl substance concentrations in human serum and their associations with immune markers of rheumatoid arthritis. <i>Chemosphere</i> 298:134338.	Patients that had rheumatoid arthritis (RA) and patients without RA in Hangzhou, China	Immunological