# ORD Human Health Toxicity Value for Perfluoropropanoic Acid (PFPrA)

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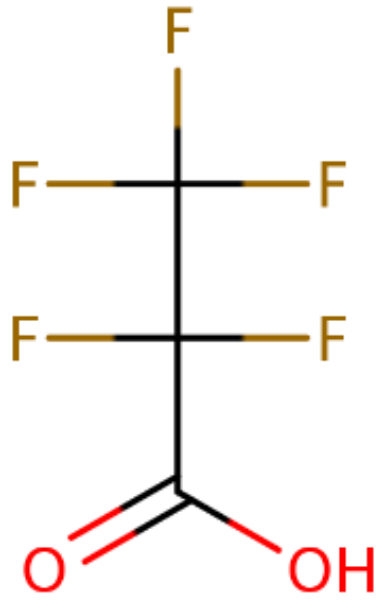
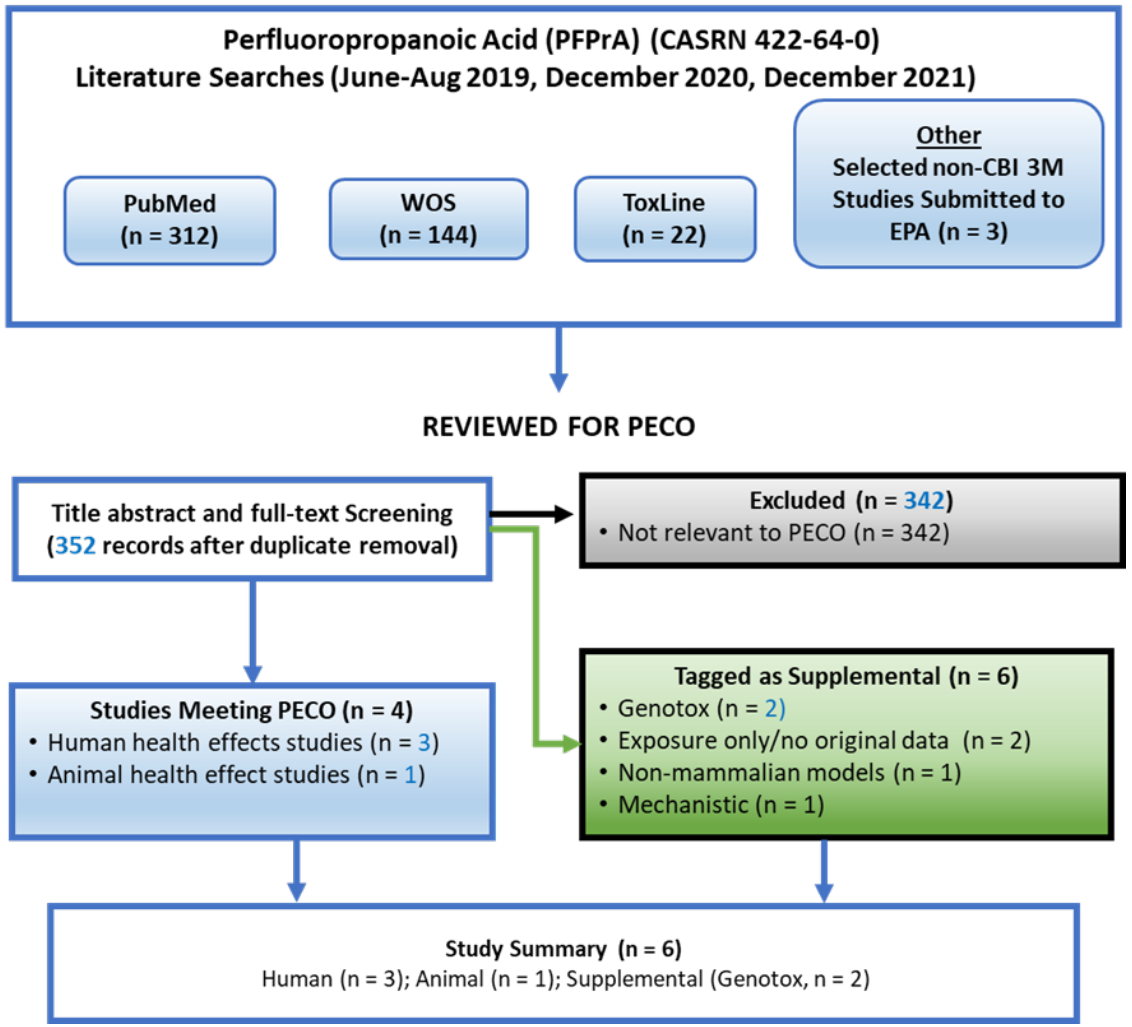
# Background on PFPrA Request and Need

- **Wastewater sampling data around an active manufacturing plant from 2020 to 2021** revealed PFPrA was among the highest PFAS concentrations with unknown toxicological impacts
- **EPA's Office of Enforcement and Compliance Assurance (OECA) requested technical support and nominated PFPrA** for evaluation
- **ORD reviewed publicly available and industry toxicological information on PFPrA** to inform development of a toxicity assessment for site-specific evaluation of chemicals under the Safe Drinking Water Act (SDWA) in support of preliminary water screening of PFAS contamination
- ORD modeled the PFPrA assessment after the Provisional Peer Reviewed Toxicity Value (PPRTV) assessment format and process and leveraged existing literature databases to develop this **fit-for-purpose assessment product**



# Literature Search and Screen for PFPrA

- Leveraged **PFAS Systematic Evidence Map**[1] for search and screen
- In addition, non-CBI industry studies were identified
- Documentation in **Health Assessment Workspace Collaborative** [HAWC]: https://hawcprd.epa.gov/assessment/100500281/).
- **Human:** one *medium* confidence (Duan et al., 2020) and two *low* confidence (Song et al., 2018; Li et al., 2017) epidemiological studies
- **Animal:** one *high* confidence repeat-dose (28-day) oral gavage study in rats [conducted by the Chemicals Evaluation and Research Institute, Japan; (CERI, 2002c)].




[1]See Carlson et al. (2022) and Radke et al. (2022)

# Candidate PFPrA $POD_{HEDs}$ for Chronic RfD derivation

| Endpoint | BMDL mg/kg-d | POD type | $POD_{HED}$[a] mg/kg-d | Reference |
|---|---|---|---|---|
| **Increased relative liver weight in adult male rats** | **6.3** | **$BMDL_{10}$** | **1.6** | **CERI (2002c)** |
| Increased hepatocyte hypertrophy in adult male rats | 7.9 | $BMDL_{10}$ | 2.0 | CERI (2002c) |
| Increased serum ALP in adult male rats | 20 | $BMDL_{1SD}$ | 5.0 | CERI (2002c) |
| Increased serum ALT in adult male rats | 28 | $BMDL_{1SD}$ | 7.0 | CERI (2002c) |

# PFPrA Chronic RfD – Uncertainty and Confidence

Chronic RfD = $POD_{HED} \div UF_C$

= 1.6 mg/kg-day ÷ 3,000

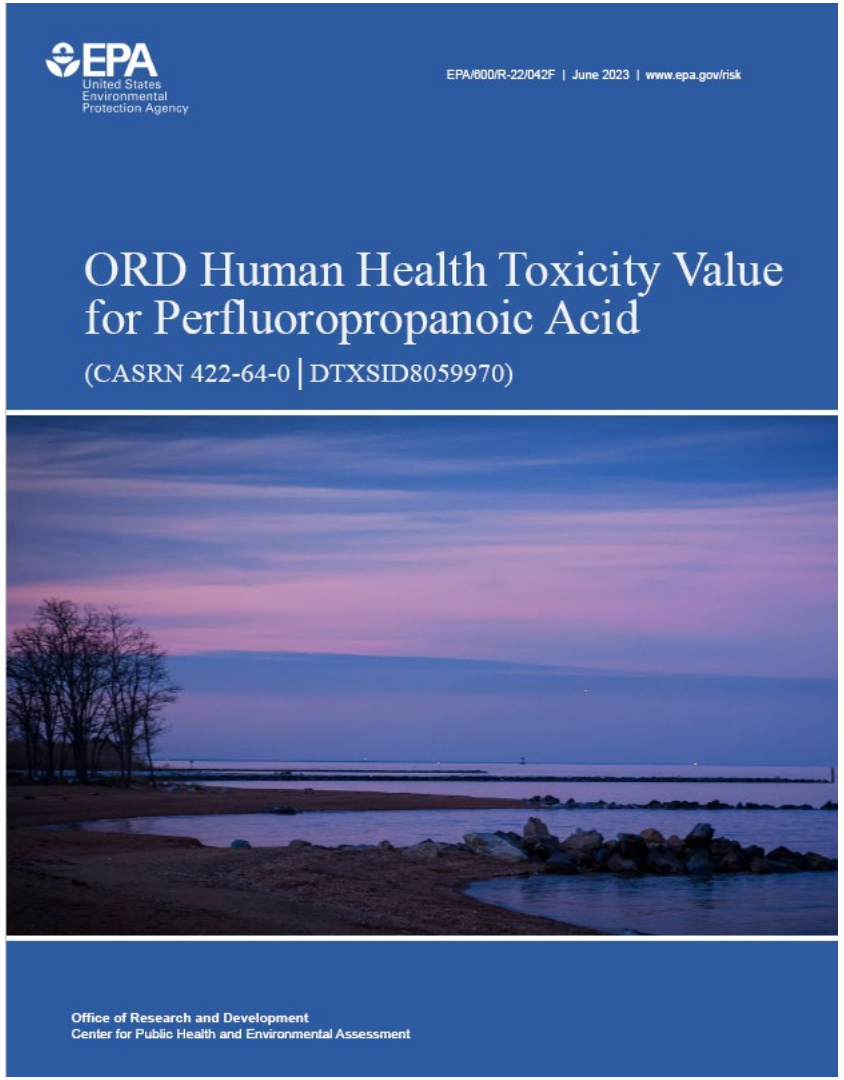
= 0.0005 or $5 \times 10^{-4}$ mg/kg-day

| UF | Value |
|---|---|
| $UF_A$ | 3 |
| $UF_D$ | 10 |
| $UF_H$ | 10 |
| $UF_L$ | 1 |
| $UF_S$ | 10 |
| **$UF_C$** | **3,000** |

| Confidence Categories | Designation | Discussion |
|---|---|---|
| Confidence in study | H | Confidence in the principal study CERI (2002c) is *high*. The study was performed by an industry/contract lab using an established OECD protocol for 28-day oral exposures in rodents and under GLP conditions. All but one of the toxicity study rating criteria were of "Good" or "High" confidence (see Figure 3 and information available on HAWC). |
| Confidence in database | L | Confidence in the database for PFPrA is *low*. The relevant human health assessment database consists of one *medium* and two *low* confidence human epidemiological studies, and a single 28-day repeat-dose oral rat study. No longer-duration repeat-dose studies, examining potential systemic, reproductive, developmental or immunotoxicity effects are available following exposure via any route. |
| Confidence in quantification of the $POD_{HED}$ | M | Confidence in the quantification of the POD and RfD is *medium*. The POD was based on BMD modeling within the range of the observed data. Dosimetric adjustment of the POD was based on default $BW^{3/4}$ scaling due to the lack of chemical specific toxicokinetic data (e.g., clearance, half-life). |
| **Confidence in the chronic RfD** | **L** | **The overall confidence in the chronic RfD is *low* and is primarily driven by *low* confidence in the available database for PFPrA.** |

# Summary

- **ORD developed a human health toxicity assessment for PFPrA**
- **Modeled after PPRTV format and process includes:**
  - Internal peer review by EPA/ORD scientists
  - Contract-led, independent external letter peer review
  - No public comment period
- **Leveraged ORD investments in Systematic Evidence Mapping (SEM).** Literature search, screening, and study quality conducted under PFAS 150/430/Universe SEM effort
- **Example for deriving human health reference values for site-specific evaluation of chemicals under SDWA** and do not require the full Integrated Risk Information System (IRIS) review process



# Thank you!


## EPA Authors, Contributors, Support, Review

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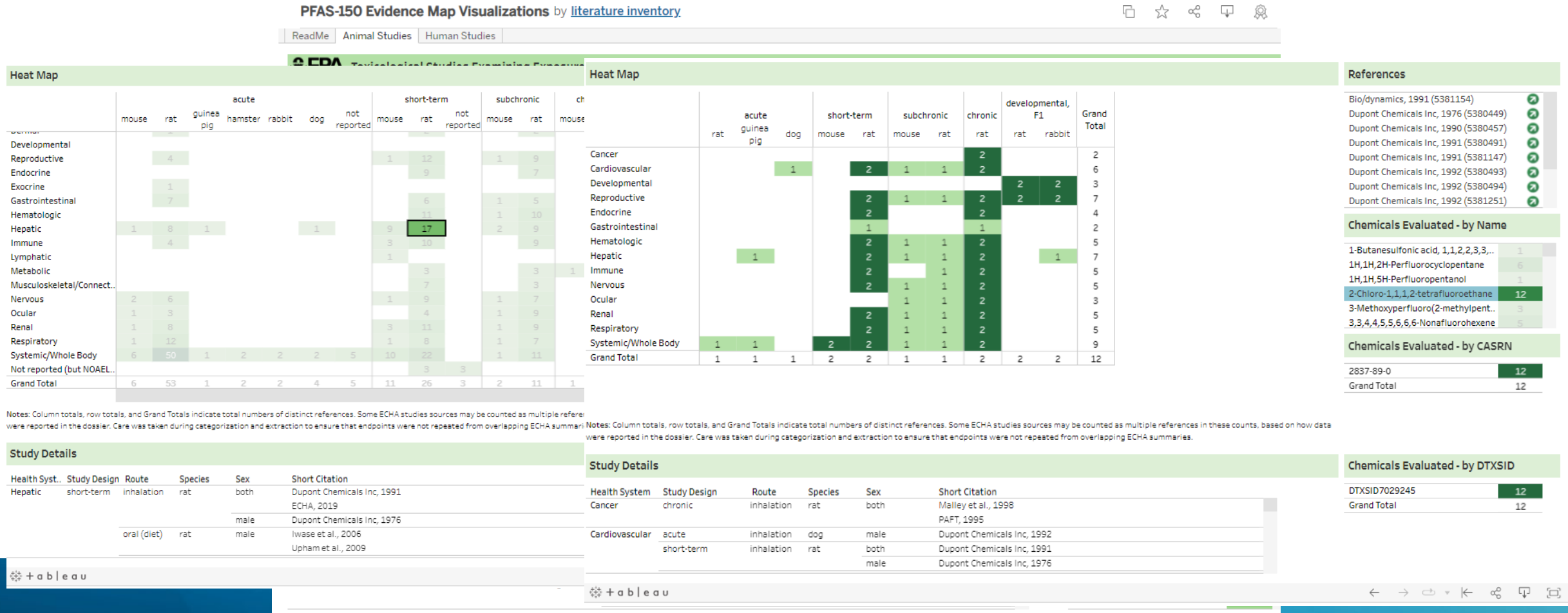
# PFAS SEM Activities

- **PFAS 150 SEM:** Initial effort from EPA ORD's Center for Computational Toxicology and Exposure (CCTE) identified ~150 PFAS chemicals testing a range of PFAS structures, chemistries, and with environmental relevance (Patlewicz et al. 2019, Patlewicz et al. 2022)
- **Expanded PFAS SEM:** Expanded effort that includes additional ~345 PFAS (manuscript submitted)
- **PFAS Universe:** ~15,000 PFAS substances and structures includes most of the chemicals in the EPA CompTox Chemicals Dashboard (https://comptox.epa.gov/dashboard/chemical-lists/PFASSTRUCTV5)

- Specific goals and uses:
  - Create a repository that is easily updated, web-based, and shareable
  - Identify *in vivo* evidence to inform CCTE efforts to characterize PFAS library
  - Characterize data gaps and key research needs, including tiered toxicity testing
  - Be positioned to quickly address new PFAS assessment needs

# Interactive Heat Map: Animal Studies

From: Systematic Evidence Map for Over One Hundred and Fifty Per- and Polyfluoroalkyl Substances (PFAS) Environmental Health Perspectives (Carlson et al., 2022)



# Interactive Heat Map: Epi Studies

From: Epidemiology evidence for health effects of 150 per- and polyfluoroalkyl substances: A systematic evidence map Environmental Health Perspectives (Radke et al., 2022)