Proposed Public Health Goals for Perfluorooctanoic Acid (PFOA) and Perfluorooctane Sulfonic Acid (PFOS) in Drinking Water

Public Workshop

September 28, 2021

Office of Environmental Health Hazard Assessment

California Environmental Protection Agency

Public Workshop Agenda

Proposed Public Health Goals (PHGs) for Perfluorooctanoic Acid (PFOA) and Perfluorooctane Sulfonic Acid (PFOS) in Drinking Water

Tuesday, September 28, 2021
Workshop | 1:00 p.m. to 4:00 p.m. Pacific Time or until business is concluded

Instructions for Submitting Questions/Comments

Welcome and Introductions
- Vincent Cogliano, Ph.D., Deputy Director of Scientific Programs, Office of Environmental Health Hazard Assessment (OEHHA)

Process for Developing PHGs
- Elaine Khan, Ph.D., Chief, Water Toxicology Section, OEHHA
- Clarifying questions and comments from the public

Draft Technical Support Document
- Overview of Technical Support Document
  - Chris Banks, Ph.D., Staff Toxicologist
  - Anatoly Soshilov, Ph.D., Staff Toxicologist
  - Craig Steinmaus, M.D., Public Health Medical Officer III
- Clarifying questions and comments from the public

Public Comments

Next Steps & Closing Comments
- Vincent Cogliano

Adjourn

Outline of Presentation

- Program background and overview of proposed PHGs

- Evidence of toxicity in laboratory animals

- Derivation of cancer-based health-protective concentration for PFOS using animal data

- Toxicokinetic considerations and derivation of human clearance factors

- Derivation of health-protective concentrations for cancer and noncancer effects based on human data

Program Background

- A Public Health Goal (PHG) is the level of a chemical contaminant in drinking water that does not pose a significant risk to health over a lifetime

- PHGs are analogous to US EPA's Maximum Contaminant Level Goals (MCLGs)

- PHGs for carcinogens are set at a risk level of one in one million

- CA law requires the State Water Resources Control Board (SWRCB) to set Maximum Contaminant Levels (MCLs) as close to the corresponding PHG as is economically and technologically feasible

- OEHHA derives health-protective concentrations based on both cancer and noncancer effects; the most health-protective level is chosen as the PHG

PFOA and PFOS

PFOA
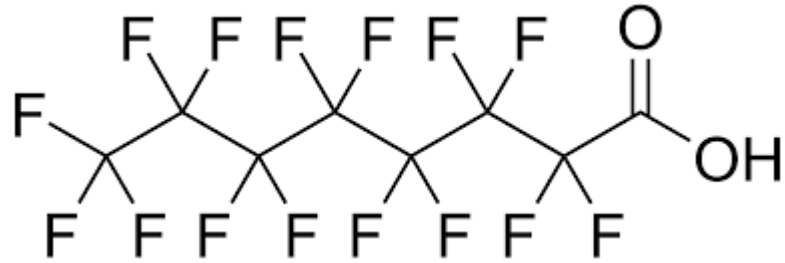
PFOS

- Many industrial uses due to resistance to water, oil, and grease
- Very persistent in the environment and bioaccumulative
- The State's Biomonitoring California Program – detected in >98% of Californians tested

Proposed Public Health Goals (PHGs) and Health Protective Concentrations

Chemical	PHG (ppt)	PHG Effect	HPC (ppt)	HPC Effect
Perfluorooctanoic acid	0.007	Kidney cancer (human data)	3	Increased risk of liver damage (human data)
Perfluorooctane sulfonic acid	1	Liver and pancreatic tumors (animal data)	2	Increased total cholesterol (human data)

Literature Search Strategy – Animal Toxicity

- Multiple databases searched – 2016 to September 2019
    - PubMed, Embase, Scopus, Toxline, Toxnet DART, SciFinder-n
    - 2,766 unique references identified

- Title/Abstract and full-text screening
    - Distiller – two reviewers
    - Inclusion based on PECO (population, exposure, comparator, outcome) criteria
    - Identified 90 references for inclusion

PFOA – Noncancer Toxicity in Animals

Toxicity Category	Associated Effects
Immunotoxicity	Immunosupression Spleen/Thymus effects Changes in natural killer cell activity
Liver toxicity	Increased liver weight Histopathology Biomarkers of liver damage
Perturbation of lipid homeostasis	Decreased serum triglycerides and cholesterol
Thyroid toxicity	Perturbation of hormone levels
Developmental/Reproductive toxicity	Testicular/epididymal effects Decreased litter size/pup survival Offspring effects (birth weight, liver)
Additional toxicity	Reduced body weight Adipose tissue/bone effects Perturbation of glucose homeostasis

PFOA – Cancer in Male Rats

- NTP (2020) – 107 week dietary study
- Significant increase and positive trend in hepatocellular adenomas and pancreatic acinar cell adenomas/carcinomas

Concen-tration in feed (ppm)	Dose (mg/kg-day)	Plasma concentration (mg/L)	Hepatocellular adenoma	Pancreatic acinar cell adenocarcinoma	Pancreatic acinar cell adenoma or adenocarcinoma
0	0	BD	0/36***	0/36	3/43***
20	1.0	81.4	0/42	3/42	29/49***
40	2.3	130.8	7/35**	1/36	26/41***
80	4.8	159.6	11/37***	3/38	32/40***

Treatment group tumor incidences with asterisks indicate significant results from Fisher pairwise comparison with controls (conducted by OEHHA): **, $p < 0.01$; ***, $p < 0.001$.

Control group tumor incidences with asterisks indicate significant results from exact trend test (conducted by OEHHA): ***, $p < 0.001$.

PFOA – Cancer in Female Rats

- NTP (2020) – 107 week dietary study

- Significant increase and positive trend in uterine adenocarcinomas

- Occurrence of rare tumors: pancreatic acinar cell adenoma and carcinoma, and hepatocellular carcinoma (only in animals with additional perinatal exposure to PFOA)

Concen-tration in feed (ppm)	Dose (mg/kg-day)	Plasma concentration (mg/L)	Pancreatic acinar cell adenoma or adenocarcinoma	Uterine adenocarcinoma	Uterine adenoma or adenocarcinoma
0	0	BD	0/24	1/32*	2/32
300	18	20.4	0/30	5/39	5/39
1,000	63	72.3	2/27	8/35*	8/35

Treatment group tumor incidences with asterisks indicate significant results from Fisher pairwise comparison with controls (conducted by OEHHA): *, p <0.05.
Control group tumor incidences with asterisks indicate significant results from exact trend test (conducted by OEHHA): *, p <0.05.

PFOS – Noncancer Toxicity in Animals

Toxicity Category	Associated Effects
Immunotoxicity	Immunosupression Spleen/Thymus effects Changes in natural killer cell activity
Liver toxicity	Increased liver weight Histopathology Biomarkers of liver damage
Thyroid toxicity	Perturbation of hormone levels
Developmental/Reproductive toxicity	Testicular/epididymal effects Increased neonatal mortality Offspring effects (body weight, hormones)
Neurotoxicity	Behavioral alterations Learning/memory impairment Changes in chemical signaling
Additional toxicity	Reduced body weight

PFOS – Cancer in Male Rats

- Butenhoff et al. (2012) and Thomford (2002) – 2 year dietary study
- Significant increase and positive trend in hepatocellular adenomas
- Positive trend for pancreatic islet cell carcinomas

Concen-tration in feed (ppm)	Dose (mg/kg-day)	Serum conc. (mg/L)	Hepatocellular adenoma	Pancreatic islet cell adenoma	Pancreatic islet cell carcinoma	Pancreatic islet cell adenoma or carcinoma
0	0	0.014	0/41**	4/44	1/38*	5/44
0.5	0.024	2.64	3/42	3/44	2/41	5/44
2	0.098	12.1	3/47	4/48	2/44	6/48
5	0.242	32.3	1/44	4/46	5/44	8/46
20	0.984	121	7/43**	4/44	5/40	9/44

Treatment group tumor incidences with asterisks indicate significant results from Fisher pairwise comparison with controls (calculated by OEHHA): **, $p < 0.01$.

Control group tumor incidences with asterisks indicate significant results from exact trend test (conducted by OEHHA): *, $p < 0.05$; **, $p < 0.01$.

PFOS – Cancer in Female Rats

- Butenhoff et al. (2012) and Thomford (2002) – 2 year dietary study

- Significant increase and positive trend in hepatocellular adenomas, and hepatocellular adenomas and carcinomas combined

- Occurrence of rare tumors: thyroid follicular cell adenoma and carcinoma

Concen-tration in feed (ppm)	Dose (mg/kg-day)	Serum conc. (mg/L)	Hepatocellular adenoma	Hepatocellular carcinoma	Hepatocellular adenoma or carcinoma
0	0	0.841	0/28**	0/28	0/28**
0.5	0.029	5.49	1/26	0/29	1/29
2	0.120	23.0	1/15	0/16	1/16
5	0.299	66.4	1/28	0/31	1/31
20	1.251	215	5/31*	1/32	6/32*

Treatment group tumor incidences with asterisks indicate significant results from Fisher pairwise comparison with controls (reported by study authors): *, p <0.05.
Control group tumor incidences with asterisks indicate significant results from exact trend test (conducted by OEHHA): **, p <0.01.

PFOS – Cancer Slope Factor

- Benchmark dose multisite tumor analysis using US EPA's Benchmark Dose Software – Benchmark response (BMR) of 5%
  - Based on combined incidence of liver and pancreatic tumors in male rats
  - Lower 95% confidence limit of the benchmark dose ($BMDL_{05}$) of 14.7 mg/L
  - Converted to 0.0057 mg/kg-day using clearance factor of 3.9×10^{-4} L/kg-day

- Body weight (BW) scaling to determine human equivalent cancer potency
  - $BMDL_{05(human)} = BMDL_{05(animal)} \times (BW_{animal}/BW_{human})^{1/8}$
  - $BMDL_{05(human)}$ = 0.0057 mg/kg-day x 0.56 = 0.0032 mg/kg-day

- Human cancer slope factor = BMR ÷ $BMDL_{05(human)}$
  - 0.05 ÷ 0.0032 mg/kg-day = 15.6 $(mg/kg\text{-}day)^{-1}$

PFOS Public Health Goal

- PHG = R ÷ (CSF × DWI)
  - R = risk level of one in one million (10^{-6})
  - CSF = cancer slope factor of 15.6 (mg/kg-day)$^{-1}$
  - DWI = drinking water intake of 0.053 L/kg-day (OEHHA, 2012)

- PHG = 10^{-6} ÷ (15.6 (mg/kg-day)$^{-1}$ × 0.053 L/kg-day) = **1 ng/L or 1 ppt**

- Age sensitivity factors were not applied

Toxicokinetic Considerations and Derivation of Human Clearance Factors

PFOA and PFOS: dramatic differences in toxicokinetic (TK) properties among species

Table 1. PFOA and PFOS serum half-lives in species (Pizzurro et al., 2019)

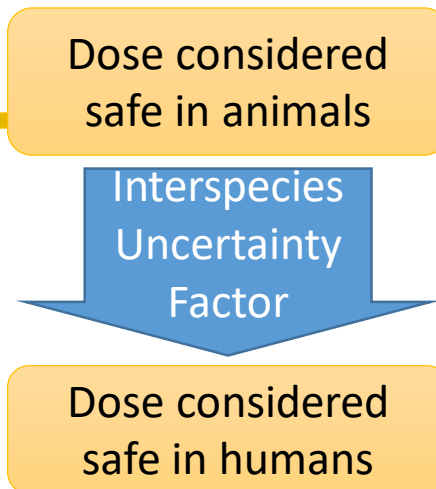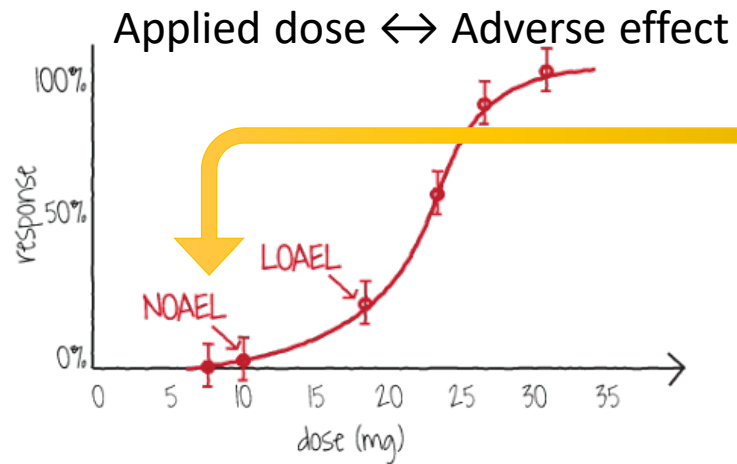|	PFOA		PFOS	
	female	male	female	male
Rat	1.9-4.6 h (<25mg/kg) 16.2 h (25 mg/kg) 24 h (50 mg/kg)	1.5-15 d (<25 mg/kg) 6.5 d (25 mg/kg) 4.4 d (50 mg/kg)	24-83 d	26-82 d
Mouse	1.2 d (20 mg/kg-d[a]) 15.6 d (1 or 10 mg/kg)	21.7 d (1 or 10 mg/kg)	38 d (1 mg/kg-d) 30 d (20 mg/kg-d)	43 d (1 mg/kg-d) 36 d (20 mg/kg-d)
Cynomolgus monkey	32.6 d	20 d	110-200 d	132-200 d
Human	2.3 years (US EPA, 2016b)		5.4 years (US EPA, 2016d)	

Serum half-life is the time required for the serum concentration to decrease in half when exposure is discontinued. Differences in half-lives indicate different ability to eliminate the compound. Organisms with greater half-lives would bioaccumulate the compound to a greater extent.

Typical interspecies extrapolation (without TK adjustment)

Uncertainty factors include a specific adjustment for possible (unknown) kinetic differences between species. However, when kinetic differences are known, interspecies extrapolation can be adjusted to reflect it.

Applied dose ⟷ Adverse effect

Dose considered safe in animals

Interspecies Uncertainty Factor

Dose considered safe in humans

PHG

Toxicokinetic (TK) adjustment

- Kinetics = concentration inside the body.
- Organisms with slower elimination (longer half-life) would have a higher internal concentration from a given dose.
- Organisms with faster elimination (shorter half-life) would have a lower internal concentration from a given dose.
- Thus, extrapolating from internal concentrations (such as serum concentration) would account for differences in half-lives.
- With this method, the interspecies uncertainty factor needs to be adjusted since the toxicokinetic component of UFs is no longer needed.

Interspecies extrapolation with TK adjustment

Applied dose ↔ Adverse effect

Animal serum concentration

Interspecies Uncertainty Factor corrected for TK

Human serum concentration

?
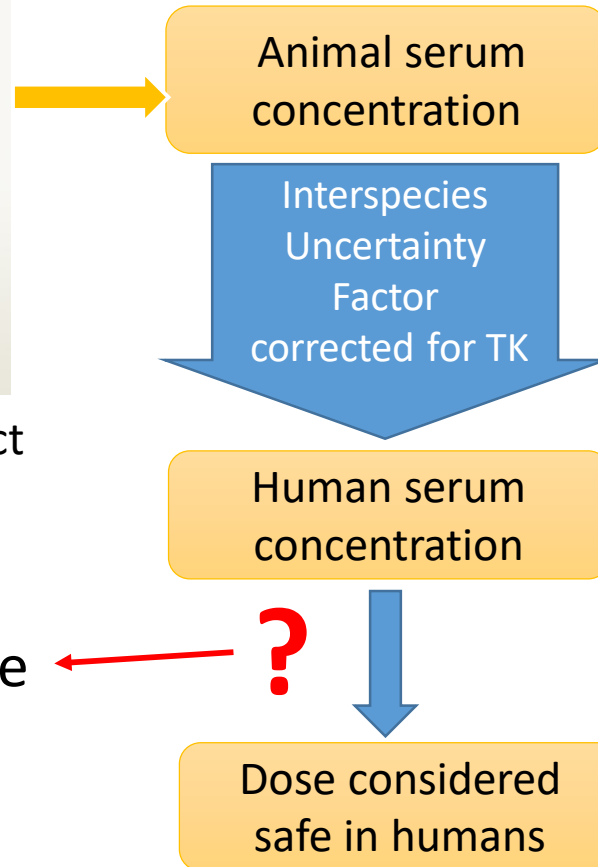
Still need to extrapolate from human serum concentration to human dose

Dose considered safe in humans

PHG

TK adjustment for human serum concentrations of PFOA/S

- Due to long half-life (slow elimination), humans can be considered a one-compartment model with first-order elimination.

- In a steady state (input = elimination), the input DOSE would equal elimination, which in this model is expressed as CLEARANCE*C_{serum}

- Thus, DOSE = CLEARANCE*C_{serum}

- OEHHA considered several methods to estimate the TK parameter of CLEARANCE and decided that the best method is to estimate it from published studies of exposure to PFOA or PFOS, in which both DOSE and C_{serum} were reported.

Human clearance for PFOA

Figure 4.9.1. Regression of PFOA exposure studies

$y = 0.2777x - 0.3505$

$R^2 = 0.9167$
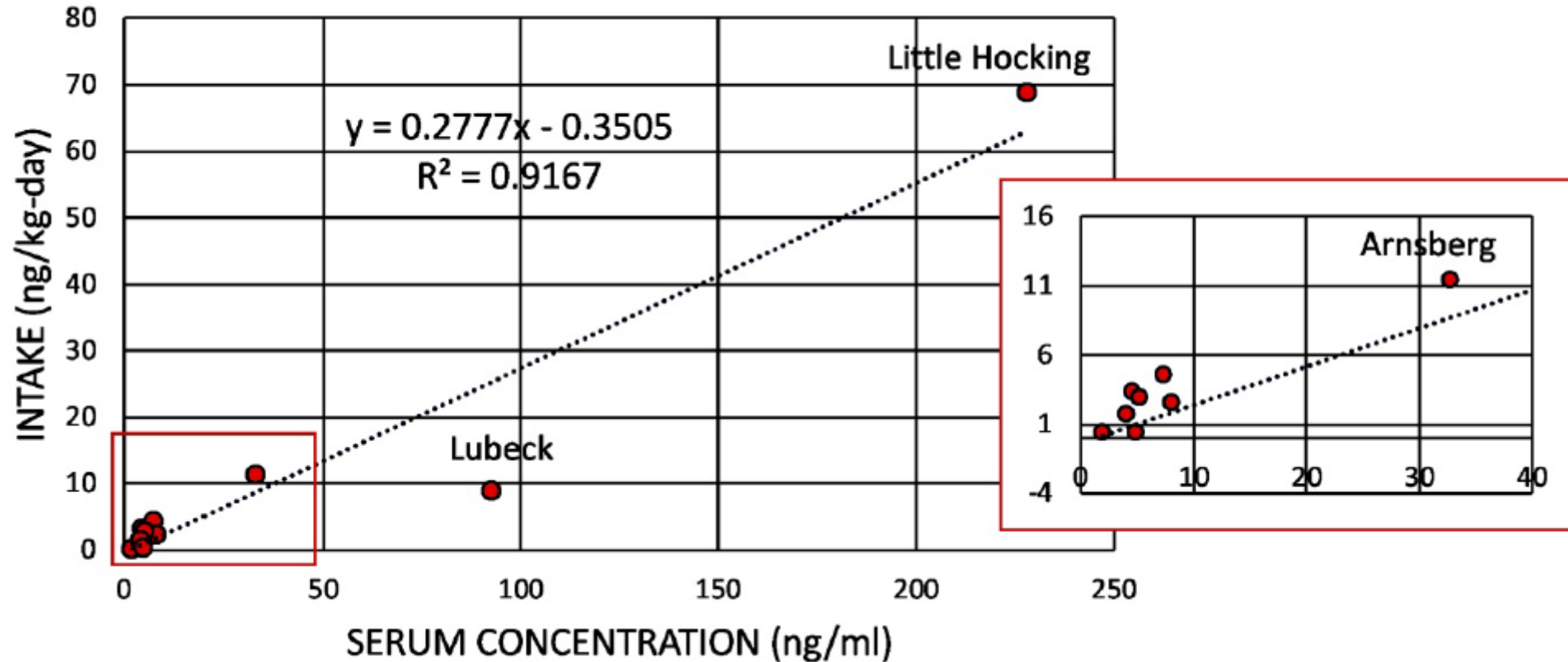
Each datapoint is a study with known DOSE (intake) and C_{serum}
CLEARANCE is the slope of the regression line, 2.8×10^{-4} L/kg-day

Human clearance for PFOS

- For PFOS, only one exposure scenario (Ronneby, Sweden) provided estimates of high oral intake through drinking water and matching serum concentrations.

- The population (N=1,176) was exposed for at least 10 years, with C_{serum} of 372 ng/mL at the end of exposure period (Silva et al., 2020).

- Intake can be calculated based on PFOS concentration in water, which was 8,000 ng/L (Li et al., 2018).

- Using these values, CLEARANCE was calculated as 3.9×10^{-4} L/kg-day.

Derivation of Health Protective Concentrations for Cancer and Noncancer Effects Based on Human Data

Epidemiology: PFOA and PFOS

	Public Health Goal		Noncancer Health Protective Concentration	
	ppt	Outcome	ppt	Outcome
PFOA	0.007	Kidney cancer (human data)	3	Increased risk of liver damage (human data)
PFOS	1	Cancer (animal data)	2	Increased total cholesterol (human data)

ppt, parts per trillion

PFOA PHG: Epidemiologic studies of PFOA and kidney cancer

Author, Year	Design Location	Exposure method	Outcome method	Results: summary
Shearer et al., 2021	Nested case-control US (10 sites)	Serum	Surveys, physicians, relatives, NDI, cancer registries	Association
Vieira et al., 2013	Case-control C8 area	Modeled*	Cancer registries	Association
Barry et al., 2013	Retrospective cohort C8 area	Modeled*	Self-reports and adjudication	Association
Steenland & Woskie, 2012	Occupational C8 (DuPont)	Modeled*	NDI, death certificates	Association
Raleigh et al., 2014	Occupational Minnesota (3M)	Modeled	Cancer registries, NDI	No association
Mastrantonio et al., 2017	Ecologic Veneto, Italy	Residence	Death records	Less informative (ecologic)
Girardi & Merler, 2019	Occupational Veneto, Italy	Job exposure matrix	Local and national death records	Less informative (only two cases)

* Validated exposure model; NDI, National Death Index

Possible reasons why the Raleigh et al. (2014) findings are inconsistent with other studies?

- Evidence of a fairly strong healthy worker effect

- The comparison group appears less healthy than the PFOA exposed group (i.e. higher all-cause and all-cancer SMRs)

- Modeled exposures; based only on a small number of actual measurements; inhalation exposures only; no validation data

- Small sample size: only 4 cases in the highest exposure category

- No information on other risk factors for kidney cancer (smoking, BMI, other chemicals...)

Causal inference: key criteria

Bradford Hill criteria

National Toxicology Program: Risk of Bias

Expertise and experience
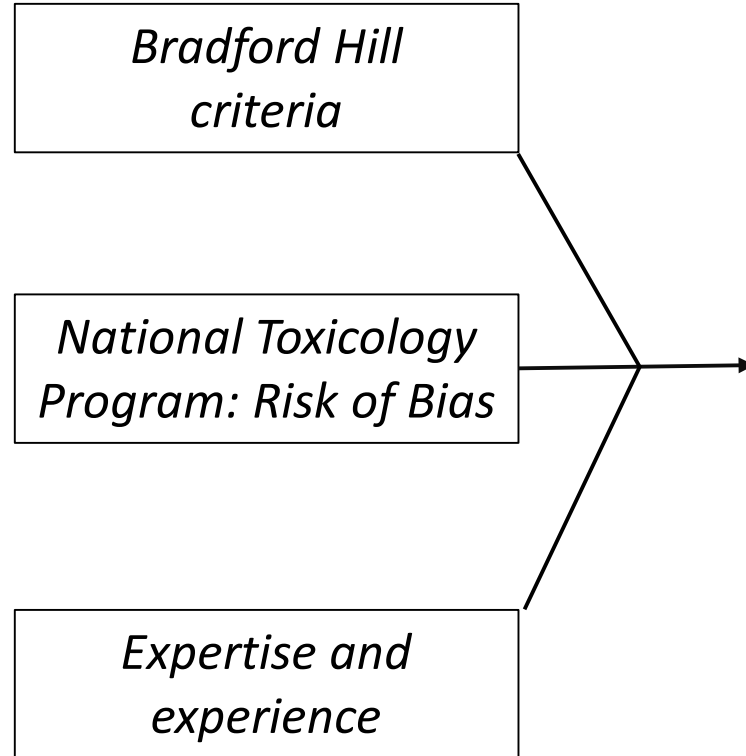
- External consistency
- Internal consistency
- Confounding (e.g., other PFAS)*
- Selection bias
- Exposure misclassification*
- Outcome misclassification
- Dose-response
- Temporality
- Chance
- Magnitude of the effect
- Biologic plausibility

Shearer et al., 2021

Key attributes

- Case-control study nested in a large National Cancer Institute prospective study (n=150k)
- Ten locations through the US
- Serum PFOA: collected in 1993-2000 (peak US exposures)
- 8.8 years of follow-up
- Cases: renal cell carcinoma from cancer registries, questionnaires, death records
- Medical records review and histology reports
- Controls: cohort members matched to cases by age, sex, race/ethnicity, study center, and year of blood draw

Shearer JJ, Callahan CL, Calafat AM, Huang WY, Jones RR, Sabbisetti VS, Freedman ND, Sampson JN, Silverman DT, Purdue MP, Hofmann JN (2021). Serum concentrations of per- and polyfluoroalkyl substances and risk of renal cell carcinoma. J Natl Cancer Inst 113(5):580-587

Vieira et al., 2013

Key attributes

- Cancer registry based case-control study
- C8 study area in Ohio: local water contamination from a nearby PFOA manufacturing plant
- Cases: all kidney cancers from the Ohio Cancer Incidence Surveillance System (OCISS)
- Controls: cancers thought not to be related to PFOA (e.g., lung, colon, prostate, breast…)
- Modeled serum PFOA: facility emissions data, fate and transport characteristics of PFOA, and hydrogeological properties of the study area; participants' residences

Vieira VM, Hoffman K, Shin HM, Weinberg JM, Webster TF and Fletcher T (2013). Perfluorooctanoic acid exposure and cancer outcomes in a contaminated community: a geographic analysis. Environ Health Perspect 121(3): 318-323.
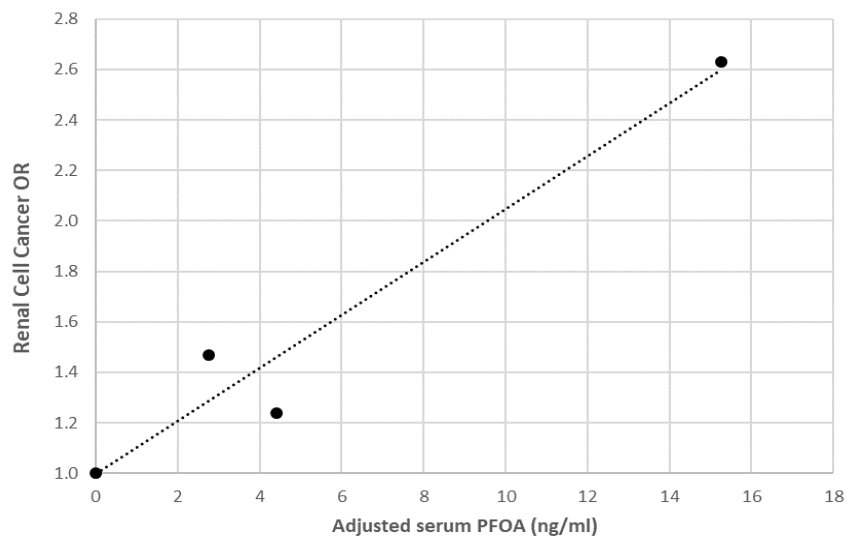
Shearer et al., 2021

Serum PFOA*	Cases	Controls	OR (95% CI)
2.0	47	81	1.00 (ref)
4.7	83	79	1.47 (0.77-2.80)
6.4	69	83	1.24 (0.64-2.41)
17.3	125	81	2.63 (1.33-5.20)

*Category midpoint (ng/ml)
p-trend = 0.007
CI, confidence interval; OR, odds ratio

Vieira et al., 2013

Serum PFOA*	Cases	Controls	OR (95% CI)
5.2	187	5957	1.0 (ref)
8.2	11	446	0.8 (0.4-1.5)
21.8	17	455	1.2 (0.7-2.0)
69.9	22	339	2.0 (1.3-3.2)
507#	9	142	2.0 (1.0-3.9)

*Category midpoint (ng/ml)
Dose level excluded due to model fitting and generalizability issues
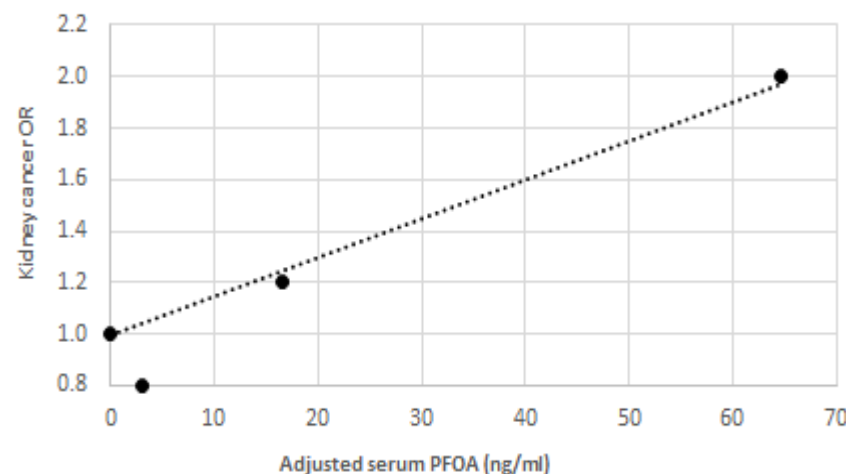
Confounding: considering other kidney cancer risk factors

Shearer et al., 2021

Study design

Controls were from the same study centers as the cases

Matching

Controls matched to cases by age, sex, race/ethnicity, study center, and year of blood draw

Statistical adjustments

Body mass index (BMI), smoking, hypertension, estimated glomerular filtration rate (eGFR), freeze-thaw cycles, and year of blood draw

Stratification

Results were similar in strata of age, gender, BMI, hypertension, smoking, eGFR, race, histologic subtype

Vieira et al., 2013

Study design

Controls were selected from the same cancer registry as the kidney cancer cases

Cancers thought to be linked to PFOA were excluded as controls (kidney, pancreatic, testicular, and liver)

Statistical adjustments

Age, sex, diagnosis year, smoking, insurance provider (indicator of socioeconomic status), race

Stratification

OR higher in women than men but small numbers and difference is not statistically significant (p=0.10)

Odds ratios (OR) for renal cell carcinoma before and after adjustment for other PFAS

PFOA: | OR = 1.71 (1.23-2.37) | → *Adjustment for PFOS & PFHxS* → | OR = 1.68 (1.07-2.63) |

PFOS: | OR = 1.39 (1.04-1.86) | → *Adjustment for PFOA & PFHxS* → | OR = 0.92 (0.60-1.42) |
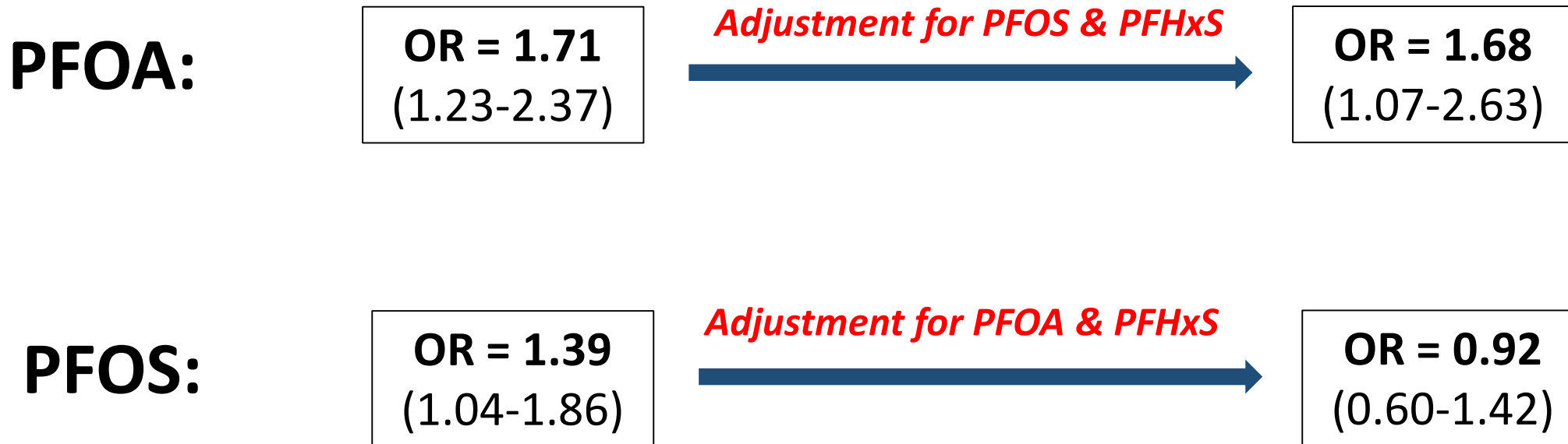
ORs are for each doubling of PFOA or PFOS serum concentration
Findings are from Shearer et al., 2021

Evaluating other potential confounders

Example: asbestos*

Assessing the magnitude of potential confounding (Axelson 1978, Scand J Work Environ Health, 4:85-

Confounder exposure				
None	Heavy		← Confounder RR	
1.00	2.00			
%	%	I_0	PFOA RR	PFOA category
96%	4%	1.04	1.00	Reference (low PFOA)
92%	8%	1.08	1.04	High PFOA
90%	10%	1.10	1.06	High PFOA
80%	20%	1.20	1.15	High PFOA
70%	30%	1.30	1.25	High PFOA
60%	40%	1.40	1.35	High PFOA
50%	50%	1.50	1.44	High PFOA
40%	60%	1.60	1.54	High PFOA
30%	70%	1.70	1.63	High PFOA
20%	80%	1.80	1.73	High PFOA
10%	90%	1.90	1.83	High PFOA
0%	100%	2.00	1.92	High PFOA

RR, relative risk; I_0 relative risk from the confounder in the category
The reference group is the unexposed comparison population (i.e. those without the exposure of interest). The percentages are the percentage of people in each PFOA group that have the confounder of interest

This slide is for demonstration purposes only and may not represent the final analyses

Overall conclusions

- TCE, asbestos, arsenic
- Medications: acetaminophen
- Family history
- Genetics
- Rare kidney diseases
- Other

Low prevalence

Relatively weak associations with PFOA or kidney cancer

No evidence for major confounding

Was PFOA exposure measured accurately?

Shearer 2021: measured serum PFOA

- Well accepted metric for assessing PFOA exposure

- Samples collected during a time of peak PFOA exposure in the US

- Long half-life: several years

- Serum PFOA concentrations well correlated over time

- Average time from blood draw to cancer diagnosis is 8.8 years – appropriate cancer latency

- Collected and measured similarly in cases and controls so errors would most likely not cause a false positive effect

Vieira: modeled serum PFOA

- Large validation study (n=45,276) shows good accuracy compared to serum PFOA (R = 0.67)

- Some errors greater in certain parts of the C8 area

- But analyses show these errors would most likely either not cause false positive effects or their impacts would be minor (Rothman and Greenland. Modern Epidemiology 1998 pg 347-52)

- Similar results in a retrospective cohort study in the same area (Barry et al., 2013)

- Similar results for cumulative exposure (Barry et al., 2013)

Cancer slope factor (CSF) and PHG calculations

PFOA PHG

Plot odds ratios vs. PFOA serum levels

⬇ Rothman KJ (1986) Modern Epidemiology: US EPA IRIS TCE

Dose-response slope (b)
Separately for Shearer & Vieira studies

⬇ Multiply by US lifetime kidney cancer risk to convert OR to risk
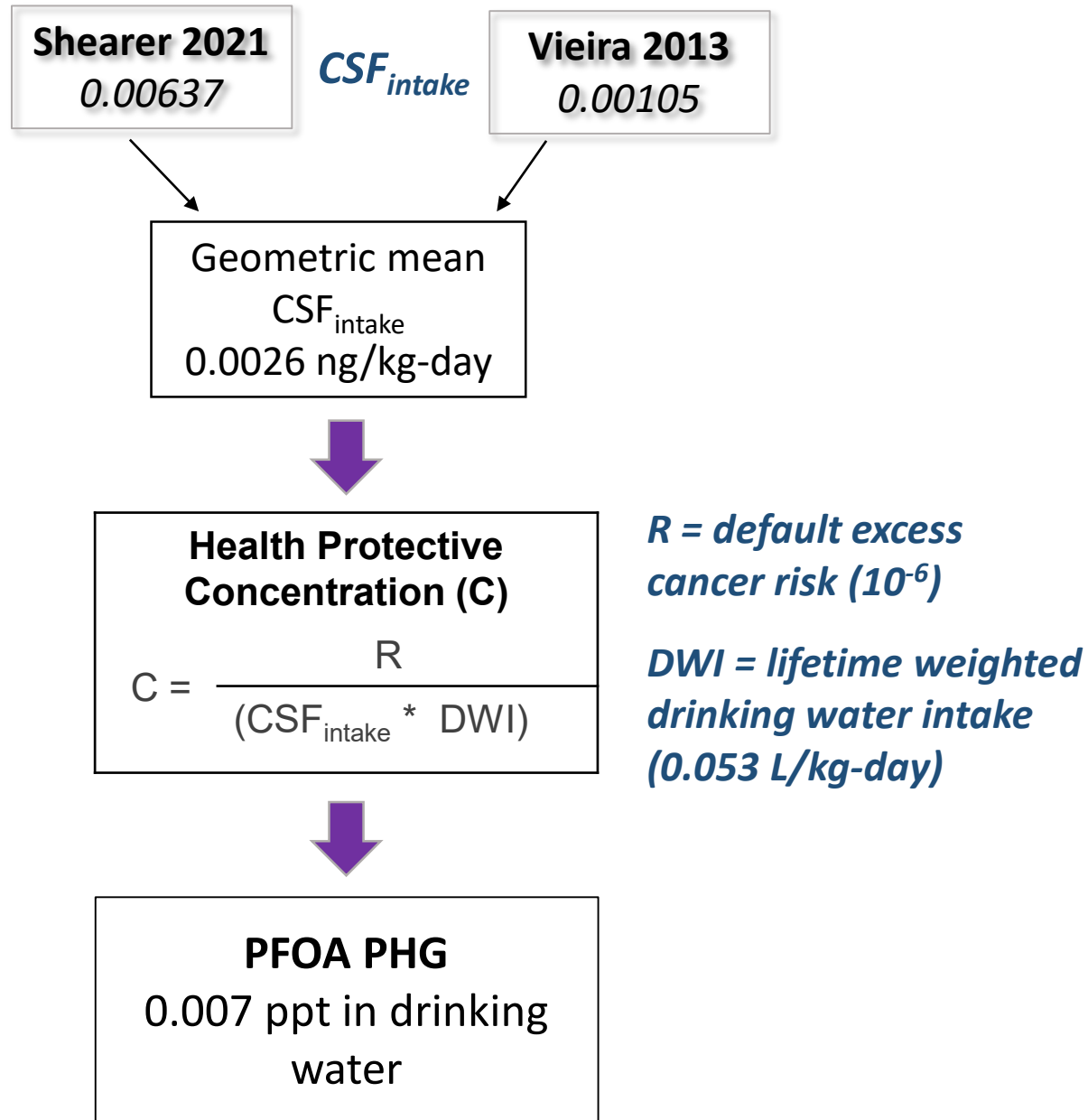
CSF_{serum}
Cancer risk per ng/ml serum PFOA

⬇ Use PFOA clearance to convert PFOA serum to PFOA intake levels

CSF_{intake}
Cancer risk per ng/kg-day PFOA intake

PFOA PHG

Shearer 2021
0.00637

CSF_{intake}

Vieira 2013
0.00105

Geometric mean
CSF$_{intake}$
0.0026 ng/kg-day

Health Protective Concentration (C)

$$C = \frac{R}{(CSF_{intake} * DWI)}$$

R = default excess cancer risk (10^{-6})

DWI = lifetime weighted drinking water intake (0.053 L/kg-day)

PFOA PHG
0.007 ppt in drinking water

Epidemiology: PFOA and PFOS

	Public Health Goal		Noncancer Health Protective Concentration	
	ppt	Outcome	ppt	Outcome
PFOA	0.007	Kidney cancer (human data)	3	Increased risk of liver damage (human data)
PFOS	1	Cancer (animal data)	2	Increased total cholesterol (human data)

ppt, parts per trillion

Noncancer Health Protective Concentration: PFOA

Gallo et al., 2012:

- Cross-sectional

- Serum PFOA

- Serum alanine aminotransferase (ALT)

- C8 study area (OH and WV)

- n=46,452

- Odds ratios (ORs) for an elevated ALT (about the upper 10%)

- Adjusted for age, sex, alcohol intake, SES, fasting, race, smoking, BMI, exercise, insulin resistance

ORs for an elevated ALT by deciles of serum PFOA (ng/ml). The NOAEC is in green.

Decile	PFOA	N	OR	95% CI
1	5.8	4,645	1.00	Ref
2	9.8	4,645	1.09	0.94-1.26
3	13.5	4,645	1.19	1.03-1.37
4	18.0	4,645	1.26	1.09-1.45
5	24.2	4,645	1.40	1.22-1.62
6	32.7	4,645	1.39	1.21-1.60
7	47.1	4,645	1.31	1.14-1.52
8	70.9	4,645	1.42	1.23-1.64
9	117.9	4,645	1.40	1.21-1.62
10	353.1	4,645	1.54	1.33-1.78

Abbreviations: CI, confidence interval; OR, odds ratio; N, number of participants; NOAEC, no observable adverse effect concentration; Ref, reference category

Noncancer Health Protective Concentration: PFOS

Steenland et al., 2009:

- Cross-sectional
- Serum PFOS
- Serum total cholesterol (TC)
- C8 study area (OH and WV)
- n=46,294
- Adjusted for age, gender, BMI, SES, exercise, smoking, alcohol
- Association remained after PFOA adjustment
- Association also seen prospectively (Fitz-Simon et al., 2013)
- Reverse causation unlikely (draft PHG pages 194-6)

Odds ratios for an elevated serum TC level by quartiles of serum PFOS (ng/ml). The LOAEC is in blue.

Quartile	PFOS	N	OR	95% CI
1	6.6	11,574	1.00	Ref
2	16.4	11,574	1.14	1.05-1.23
3	23.8	11,574	1.28	1.19-1.39
4	34.0	11,574	1.51	1.40-1.64

Abbreviations: CI, 95% confidence interval; LOAEC, lowest observable adverse effect concentration; N, number of participants; OR, odds ratio; Ref, reference category

NONCANCER

Point of Departure (POD)

PFOA: NOAEC 9.8 ng/ml for high ALT (Gallo '12)

PFOS: LOAEC 16.4 ng/ml high TC (Steenland '09)

↓ *PFOA and PFOS clearance: convert serum levels to intake*

Add uncertainty factors ($\sqrt{10}$ for PFOA; 10 for PFOS)

Acceptable Daily Dose (ADD)

Intake (ng/kg-day)

↓

Health Protective Concentration (C)

$$C = \frac{ADD * RSC}{DWI}$$

RSC = estimated percent of PFOA intake from drinking water

DWI = time weighted drinking water intake (0.053 L/kg-day)

PFOA: 3 ppt

PFOS: 2 ppt

Conclusions

- Draft PHGs and HPCs are based on a rigorous review of the science
- There is mounting human evidence that environmental levels of PFOA and PFOS can adversely affect human health, and this is corroborated by experimental evidence
- New human studies were used in deriving toxicity estimates and clearance rates
- The PHGs use drinking water intake rates that are representative of California
- Draft PHGs are developed to be protective of the health effects associated with PFOA and PFOS, including cancer and developmental, immune, lipid, liver, and thyroid effects

Chemical	PHG (ppt)	PHG Effect	HPC (ppt)	HPC Effect
PFOA	0.007	Kidney cancer in humans	3	Liver damage in humans
PFOS	1	Liver and pancreatic tumors in rats	2	Increased total cholesterol in humans

Next Steps

- The public comment period is open till October 28

    https://oehha.ca.gov/comments

- The first draft will receive independent, external peer review

- A second draft will address peer-review and public comments, followed by further opportunity for public comment

- Final Public Health Goals are based solely on science and public-health

    The State Water Board will consider these final PHGs, along with economic factors and technical feasibility, when they set standards for drinking water