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# Provisional Health Advisories for PFOA and PFOS

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Fish Forum

Portland, Oregon

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# Topics Covered

- Health Advisory Background
  - Perfluorooctanoic acid (PFOA) Background
    - Derivation of the PFOA Provisional Health Advisory
  - Perfluorooctanesulfonate (PFOS) Background
    - Derivation of the PFOS Provisional Health Advisory
  - Other State Standards
    - Differences among advisory values
  - Next Steps for EPA
  - Fish Tissue Considerations
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# Health Advisories

- Guidance for State and Local Health Departments and Utilities
  - Provides less than lifetime values for regulated and unregulated contaminants
    - Spills and short term exposures
  - Provides lifetime values for noncancer effects from long-term exposures to unregulated contaminants
    - No lifetime Health Advisory for carcinogens that have a linear response to dose and where the mode of action for the cancer response cannot be determined.
  - Subject to change as new data become available
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# Health Advisory Derivation

- Determine the Point Of Departure (POD)
  - BMDL, NOAEL, or LOAEL ÷ Uncertainty Factors (UF)
- Determine the Drinking Water Equivalent Level (DWEL)
  - $DWEL = POD/UF \times \text{body weight} \div \text{drinking water intake/day}$
  - Consider sensitive life-stage when choosing the body weight and drinking water intakes for the DWEL calculation
- Health Advisory = DWEL X Relative Source Contribution (RSC)
  - RSC = contribution to total exposure from water
    - Allows for the presence of chemical in food, air, soils, etc.
    - RSC Data derived where possible
    - Options for 20%, 50% or 80% defaults depending on data

BMDL = Lower confidence bound on the benchmark dose; NOAEL = No Observed Adverse Effect Level; LOAEL = Lowest Observed Adverse Effect Level

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# Uncertainty Factors (UFs)

- Factors Considered:
    - Intra-human variability
    - Interspecies variability
    - Use of a exposure duration less than the duration of concern
    - Use of a LOAEL rather than a BMDL or NOAEL
    - Deficiencies in the database
  - Individual factors are data derived or assigned values of 1, 3, or 10 depending on the supporting data and combined to a composite UF
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# Duration Considerations

- Short Term

- ☐ 1-day
- ☐ 10-day
- ☐ Mostly for spills

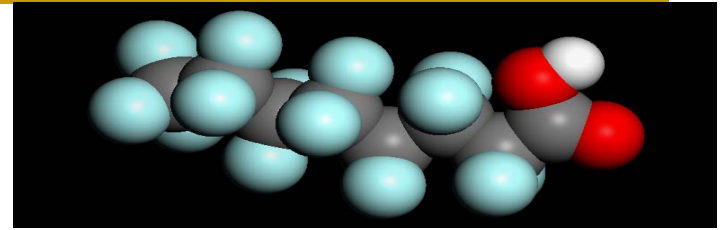
- Longer-term

- ☐ About seven years
- ☐ Values usually provided for an child and an adult

- Lifetime

- ☐ 70 years
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# PFOA Characteristics



- Distinctly different species half lives and times to steady state
    - Years for humans, hours/days for rats and mice, intermediate for monkeys
    - Requires toxicokinetic interspecies adjustments for risk assessment
  - Noncancer effects
    - Humans
      - Serum levels lower than those causing effects in animals
      - Significant associations observed in occupation cohorts for some animal health effects (serum lipids, hormones, some tumors); not consistent across studies
    - Laboratory animals (rats, mice and monkeys)
      - Liver (↑ liver weight a hallmark of exposure)
      - Hormone changes (estrogenic)
      - Altered serum lipids; hematological changes
      - Reproductive and developmental effects
        - Neonatal death; alteration of mammary gland development
  - Tumorigenic effects
    - Carcinogenic in rats
      - Liver, Leydig cell, and pancreatic tumors
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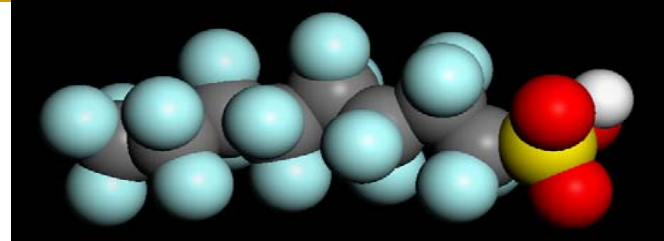
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# PFOA Provisional Health Advisory

- Determine the Point Of Departure (POD)
    - $0.46 \text{ mg/kg/day (BMDL)} \div 2430 \text{ (UF)} = 0.000189 \text{ mg/kg/day}$
    - Critical Effect – increased maternal liver weight in a mouse developmental study (17 day exposure)
    - Uncertainty factors
      - Intraspecies = 10
      - Interspecies = 243
        - 81 for toxicokinetic differences between human and animals
          - It takes 81 times longer for PFOA to reach steady state conditions in serum in humans than it does in mice
        - 3 for toxicodynamic differences between humans and animals
  - Determine the Drinking Water Equivalent Level (DWEL)
    - $\text{DWEL} = 0.000189 \text{ mg/kg/day} \times 10 \text{ kg (one-year old child)} \div 1 \text{ L/day} = 0.00189 \text{ mg/L}$
  - Health Advisory =  $\text{DWEL} \times 0.2 = 0.00038 \text{ mg/l}$  rounded to 0.4 ug/L
    - 20% default RSC
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# PFOS Characteristics



- Distinctly different species half lives and times to steady state
    - Years for humans and hours/days for rats and mice; monkeys intermediate
  - Noncancer effects
    - Humans
      - Serum levels lower than those causing effects in animals
      - Significant associations observed in occupation cohorts for some animal health effects (decreased cholesterol, thyroid); not consistent across studies
    - Laboratory animals (rats, mice and monkeys)
      - Liver (↑ liver weight a hallmark of exposure)
      - Hormone changes (thyroid)
      - Altered serum lipids
      - Reproductive and developmental effects
        - Neonatal deaths; decreases in sperm counts
  - Tumorigenic effects
    - Carcinogenic in rats
      - Liver adenomas
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# PFOS Provisional Health Advisory

- Determine the Point Of Departure (POD)
    - $0.03 \text{ mg/kg/day (NOAEL)} \div (\text{UF}) = 0.0000769 \text{ mg/kg/day}$
    - Critical Effect: for  $\uparrow$  thyroid stimulating hormone levels in male monkeys,  $\downarrow$  triiodothyronine (T3) and  $\downarrow$  levels of high-density lipoproteins in females (182 day exposure)
    - Uncertainty factors
      - Intraspecies = 10
      - Interspecies = 39
      - 13 for toxicokinetic differences between human and animals
        - It takes 13 times longer for PFOS to reach steady state conditions in serum in humans than it does in monkeys
      - 3 for toxicodynamic differences between humans and animals
  - Determine the Drinking Water Equivalent Level (DWEL)
    - $\text{DWEL} = 0.0000769 \text{ mg/kg/day} \times 10 \text{ kg (one-year old child)} \div 1 \text{ L/day} = 0.000769 \text{ mg/L}$
  - Health Advisory =  $0.000769 \times 0.2 = 0.000154 \text{ mg/L}$  rounded to  $0.2 \text{ ug/L}$ 
    - 20% default RSC
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# State Guidelines

Three States have established drinking water guidelines for PFOA and one for PFOS. The State Standards are listed below.

- PFOA

- Minnesota (MN)

- 0.3 µg/L

- New Jersey (NJ)

- 0.04 µg/L

- North Carolina (NC)

- 2 µg/L

- PFOS

- Minnesota (MN)

- 0.2 µg/L

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# Differences among PFOA Assessments

Critical Studies					
EPA	BMDL <sub>10</sub> : 0.46 mg/kg/day	↑ liver weight	17 days	female rat	Lau et al., 2007
MN	LOAEL 3 mg/kg/day; BMDL <sub>10</sub> : 23 mg/L serum	↑ liver weight	26 weeks	monkey	Butenhoff et al., 2002
NJ	NOAEL 1.6 mg/kg/day; 18000 µg/L serum	↓ body wt., ↓ red blood cell effects	2 year	female rat	Sibinski 1987
NC	LOAEL: 1 mg/kg/day	↑ liver weight, ↓ body wt.	~13 weeks	male rat	Buttenhoff et al 2002; York et al., 2002

# Differences among PFOA Assessments

Assessment	UF	Body Weight	Water intake	Relative Source	Value
OW	2430	10Kg	1 L/day	20%	0.4 mg/L
MN	38,960 equivalent	0.053 L/kg/day (95 <sup>th</sup> percentile water intake to body weight ratio for time to steady state- 19 years)		20%	0.3 mg/L
NJ	~280,700 equivalent	70 kg assumed	2L/day assumed	20%	0.04 mg/L
NC	30,000	70 kg	2 L/day	20%	2 mg/L
<p>The toxicokinetic adjustments to the BMDL, NOAEL or LOAEL by MN and NJ have been converted to an UF equivalent and combined with UFs given in the state assessment. The NJ value applies to a lifetime exposure. Thus, adult body weight and drinking water intakes were assumed when making the comparison across assessments</p>					

# Differences between PFOS Assessments

Critical Studies					
OW	NOAEL : 0.03 mg/kg/day	↑ TSH, ↓T3 and HDL	182 days	monkey	Seacat et al., 2002
MN	NOAEL 0.03 mg/kg/day (35 mg/L serum )	↑ TSH, ↓T3 and HDL	182 days	monkey	Seacat et al., 2002;

## Differences between PFOS Assessments

Assessment	UF	Body Weight	Water intake	Relative Source	Value
OW	390	10 Kg	1 L/day	20%	0.2 µg/L
MN	375 equivalent	0.049L/kg/day (95 <sup>th</sup> percentile water intake to body weight ratio for time to steady state - 27 years)		20%	0.3 µg/L
The toxicokinetic adjustments to the NOAEL by MN has been converted to an UF equivalent and combined with UFs given in the MN assessment.					

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## Next Steps for EPA

- Draft the toxicology chapters for the document that will support a CCL3 Regulatory Determination in the future
    - ❑ Cancer and noncancer effects
    - ❑ Short-term and chronic
    - ❑ National finished water monitoring data needed for regulatory determination
  - Peer review the assessment
  - Prepare and issue a Health Advisory based on the peer reviewed assessment
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# Fish Tissue Considerations

- PFOA and PFOS are oleophobic and do not accumulate in fatty tissues
  - PFOA and PFOS bind to serum proteins.
    - Can lead to presence in fish tissues.
  - Muscle tissues have lower concentrations per gram tissue than liver, kidney, and other organs
    - Portion size and tissue concentration are both important variables for fish as a food source
  - Monitoring studies indicate that PFOS is usually found at higher concentrations than PFOA
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