2022 BLACK HILLS DEFENSE & INDUSTRY SYMPOSIUM:

LEADING THE NATIONAL DEFENSE DISCUSSION

MARCH 14-16, 2022

RAPID CITY, SD

CO-HOSTED BY:

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SOUTH DAKOTA MINES
An engineering, science and technology university

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Dr. Doug Cox is a senior environmental toxicologist and risk assessor at Sundance Consulting Inc. He has a Ph.D. and M.S. in Pharmacology and Toxicology and a B.A. in Anthropology. Dr. Cox has over 30 years of experience in human health and ecological risk assessment and risk management support for both private and public sector clients. He currently provides toxicology and risk assessment expert witness advice regarding risks from poly- and per-fluoroalkyl substances (PFAS) contamination and has given numerous presentations on PFAS toxicology. He was previously the risk assessment subject matter expert for the Bureau of Land Management Abandoned Mines Land/Hazardous Materials program and has worked as a toxicologist for the Air Force Civil Engineer Center and the Air Force Institute for Operational Health. He has managed risk assessment groups at several national and international environmental consulting firms and is a full member of the Society of Toxicology. Recently Dr. Cox was the co-chair of the toxicology and risk assessment team for the PFAS Experts Symposium #2, the proceedings of which will soon be published in the journal Remediation.

TOXICOLOGY AND RISK ASSESSMENT OF PFAS

DOUG COX, Ph.D.

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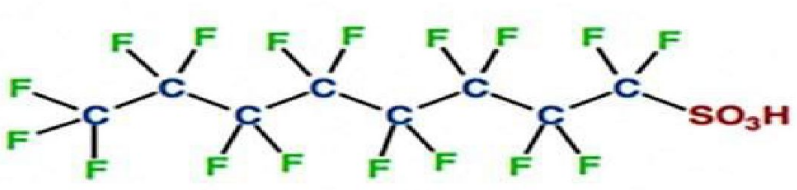
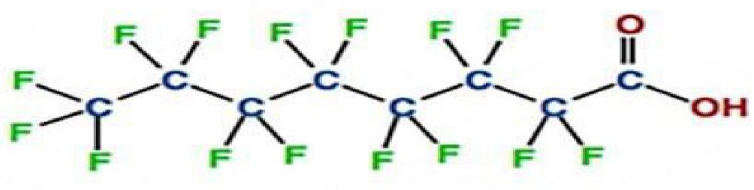
MARCH 16, 2022

PFOA and PFOS – Most Thoroughly Studied

- Historically included in many commercial products
  - Widespread human exposure
- Both are components of “legacy” AFFF
- 3M stopped manufacturing PFOS in 2002; EPA enacted the PFOA Stewardship Program in 2005 to reduce its use
- EPA developed first toxicity criteria in 2009
- Part of EPA’s 3rd unregulated contaminant monitoring rule (UCMR)
  - Found to be widely distributed in drinking water supplies across country



PFOS - perfluorooctanesulfonic acid



PFOA - perfluorooctanoic acid

Attributes Influencing PFAS Toxicity

- **Classified as "persistent, bioaccumulative, and toxic" – PBT**
- Persistent
  - resistant to metabolism or breakdown; strong carbon-fluorine bond
- Bioaccumulative
  - Long half lives (PFOA, PFOS have half lives of 3-6 years in humans)
  - Recycled by the kidneys
  - Binds to albumin and other proteins
- Toxic
  - Adverse effects on multiple organ systems
  - Some PFAS are considered carcinogenic

Applications and Uses of Toxicity Criteria

- A reference dose (RfD) is the amount of a non-carcinogenic chemical likely to be without an appreciable risk of deleterious effects during a lifetime.
- Toxicity criteria are used in a variety of ways:
  - Drinking water standards – maximum contaminant levels, health advisories
  - Remediation cleanup standards
  - Groundwater and soil risk-based screening levels
  - Human health risk assessment
  - Food product safety
  - Litigation support

What PFAS Have EPA Toxicity Criteria?

- PFOA, PFOS – 8 carbon molecules
  - 2016 Health Effects Summary Documents
  - 2021 – Draft toxicity criteria updates; undergoing review
- PFBS – 4 carbons
- Gen X – 6 carbons
  - (Hexafluoropropylene Oxide (HFPO) Dimer Acid and its Ammonium Salt)
- PFHxA – 6 carbons; undergoing review

- In development: PFHxS, PFDA, PFNA, PFBA

Potential Exposures to PFAS

- Human Health
  - Groundwater contamination – DoD facilities, landfills, industrial sites
  - Consumer products – waterproofing, non-stick applications
  - Food packaging
  - Plastics, cosmetics, and other products
  - Household dust - inhalation
- Environmental and Ecological
  - Releases to surface water – fish and other aquatic organisms
  - Soil and sediment– uptake into plants, crops, meat, milk, eggs
  - Waste-water treatment plant sludge - fertilizer
  - Food chain bioaccumulation

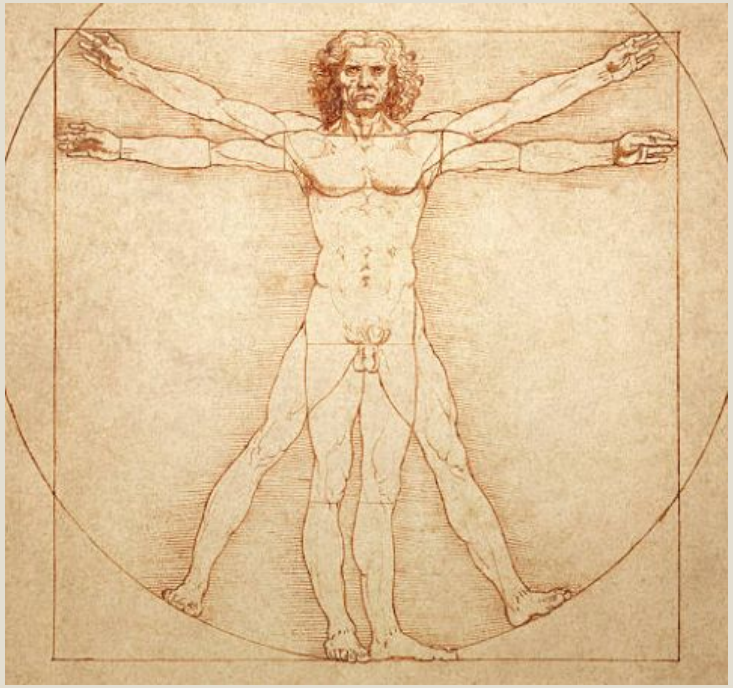
PFAS Toxicology – Significant Issues

- Toxicologists do not agree on target organ or critical adverse effect
- Epidemiology has “linked” PFOA exposure with multiple human diseases
- Animal tests provide input into human toxicity criteria
  - PFOA half life in rats – 10 to 20 days; in humans – 3 to 6 years
  - Significant renal reuptake of PFAS in humans - recirculation
  - Pharmacokinetic models created to account for these differences
- Result: different assumptions = different toxicity criteria
  - Up to two order of magnitude range between agencies
- Recent advances are suggesting PFAS are more toxic than previously understood

Organs Affected by PFOA and PFOS

- Liver – increased weight, cellular impacts
- Reproductive/developmental – reduced birth weight, bone growth delays in offspring; mammary gland
- Immune system – reduced response to vaccines
- Endocrine – thyroid
- Increased blood cholesterol levels
- Kidney and testicular cancer

- Most effects observed in both animals and humans



Human Toxicity Endpoints For PFOA

Human health conditions linked to high level environmental exposure to PFOA (C8) include:

- high cholesterol
- kidney cancer
- testicular cancer
- thyroid disease
- pregnancy-induced hypertension/preeclampsia, and
- ulcerative colitis

- Findings of the C8 Science Panel, convened for exposed populations near the DuPont Washington Works facility in W.Va. and the mid-Ohio Valley
- A "probable link" means that given the available scientific evidence, it is more likely than not that among class members a connection exists between PFOA exposure and a particular human disease.

Toxicokinetics of PFOA and PFOS

- Stable and resistant to metabolic and environmental degradation
- Not readily eliminated from humans and other primates
  - Major differences in half-lives between rodents (days) and humans (multiple years)
- Soluble in water and well absorbed following oral exposure
- Binds to proteins in the blood
- Distributes to a wide range of tissues, organs, and matrices
  - Blood and liver are major sites of PFOA accumulation
- Passes from mother to fetus *in utero* and in milk
- Urine is the primary route of excretion

EPA Draft 2021 Toxicity Criteria Updates

- **Noncancer Reference Doses (RfDs):** Proposed PFOA and PFOS draft RfDs are four orders of magnitude lower than 2016 values
  - PFOA: 1.5 X 10-9 mg/kg/day (draft) compared to 2 X 10-5 mg/kg/day (2016)
  - PFOS: 7.9 X 10-9 mg/kg/day (draft) compared to 2 X 10-5 mg/kg/day (2016)
- Critical effects are developmental immune health outcomes from epidemiological studies; ***decreased serum anti-tetanus (PFOA) or anti-diphtheria (PFOS) antibody concentration in children***
- **Cancer:**
  - **PFOA:** cancer classification changed to ***'likely'*** compared with 2016 Health Advisory, based on renal cell carcinomas
  - **PFOS:** cancer classification of ***'suggestive' ,*** unchanged from the 2016 Health Advisory

Immunotoxicity Measurement Endpoint

- For tetanus and diphtheria, a clinically significant adverse effect from PFOA/PFOS would reduce a person's antibody concentration below the level thought to provide protection (0.1 International Unit (IU)/mL)
  - If a person had an antibody concentration above 0.1 IU/mL but a 5% decrease brought their concentration below 0.1 IU/mL, that would be clinically significant
- EPA used studies in children from the Faroe Islands, a self-governing nation under the sovereignty of the Kingdom of Denmark
  - The Faroe peoples are primarily exposed to PFAS through consumer products as well as from consumption of pilot whale meat and blubber
- It is unknown if PFOA exposure could impact antibody response to vaccinations other than tetanus and diphtheria

Risk Assessment Approaches for PFAS

- Currently relies primarily on comparison of PFAS water concentrations with drinking water health advisory levels (70 ppt for PFOA and PFOS)
- EPA has proposed groundwater screening values of 40 ppt for PFOA and PFOS for comparison purposes but not as cleanup values
- No widely adopted screening values for soil, surface water, meat, milk or other foods or crops
- CERCLA style multi-pathway risk assessments are lagging behind
- Ecological screening levels in development but not widely used
  - Bioaccumulation in food chain is a major concern

PFAS Risk Assessment Activities Underway

- EPA MCL Development – PFOA, PFOS, others?
- State MCLs – for up to six PFAS
- Future findings from Unregulated Contaminant Monitoring Rule #5
- Increased number of PFAS with toxicity criteria
- Advances in our understanding of toxicity and metabolism
- Screening values for multiple media – soil, food, surface water
- Ecological risk assessment criteria
- Development of landfill acceptance criteria – leachability

EPA December 2021 MCLG Announcement

- EPA has begun the process of developing Maximum Contaminant Level Goals (MCLGs) for PFOA and PFOS under the Safe Drinking Water Act
- "Proposed Approaches to the Derivation of a Draft Maximum Contaminant Level Goal for Perfluorooctanoic Acid (PFOA) in Drinking Water" and PFOS
  - *DRAFT DELIBERATIVE: DO NOT CITE, QUOTE, OR DISTRIBUTE. DOES NOT CONSTITUTE AGENCY POLICY.* Currently under review by Scientific Advisory Board
- These documents do not actually calculate an MCLG for either compound, only toxicity values and the relative source contribution (RSC)
- Likely to result in significantly lower MCL values for PFOA and PFOS

Basis of Drinking Water Criteria

- DW criteria combine toxicology values, exposure assumptions, professional judgement, regulatory requirements, engineering and cost assumptions, and policy decisions
- MCLs are the most common promulgated standards
  - Various non-promulgated criteria include screening levels, public health goals, action levels, health advisories …
- Designed to be protective for a lifetime of water consumption
  - Often include assumption that people may be exposed by other pathways
- EPA MCLs are mandatory nationwide for applicable water systems unless states set lower standards

MCLGs versus MCLs

- The MCLG is the maximum level of a contaminant in drinking water at which no known or anticipated adverse effect on the health of persons would occur, allowing an adequate margin of safety
  - For carcinogens, MCLGs are typically set at zero exposure
  - For noncarcinogens, the MCLG is the minimal risk level
- By comparison, the MCL is the highest level of a contaminant that is allowed in drinking water
  - Based on risk, feasibility, and cost
  - May be higher than the MCLG
  - Promulgated legal standard under the Safe Drinking Water Act

Example EPA and State Drinking Water Values

Agency	PFOA (ng/L, ppt)	PFOS (ng/L, ppt)
U.S. EPA Lifetime Health Advisory	70 (sum of 2 PFAS)	70 (sum of 2 PFAS)
U.S. EPA Regional Screening Levels Groundwater screening levels	400 40	400 40
Massachusetts	20 (sum of 6 PFAS)	20 (sum of 6 PFAS)
Michigan	8	16
Minnesota	35	30
New Jersey	14	13
New Mexico	70 (sum of 3 PFAS)	70 (sum of 3 PFAS)
Vermont	20 (sum of 5 PFAS)	20 (sum of 5 PFAS)
California draft Public Health Goals	0.007	1

Toxicology Challenges for PFAS

- Difficult to evaluate risk for complex mixtures of numerous PFAS
  - Current approach is chemical by chemical
  - Toxicity values only available for ~ 6 PFAS
- EPA considering “relative potency factor” approach
  - Comparing toxicity to an index chemical, such as PFOA
  - Classifying chemicals by carbon chain length
  - Bioaccumulation
  - Mechanism(s) of action of toxic effects
- Ultimately it is difficult to determine overall mixture toxicity and risk
  - ∑ PFAS Risk = PFAS(1) + PFAS(2) + PFAS(3) …

Questions and Discussion

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