

Dioxins vs. PFOA/PFOS: Similarities and Differences

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Overview (Dioxins vs. PFAS)

- Is there something to learn from the Dioxin experience?
- Chemical properties
- Biologic half-life in humans
- Environmental half-life
- Acute toxicology
- Chronic Toxicology (Cancer)
- Epidemiology
- Precautionary Principle vs Risk Assessment

My Past:

- In 1984, I was assigned to a team to deal with Times Beach, Missouri, a town contaminated with 2,3,7,8-TCDD
- From 1985-2005, I published 20+ papers on dioxins
- Served on several science advisory panels from 1985-2005
- *The similarities between dioxins/furans and PFAS/PFOS are striking*

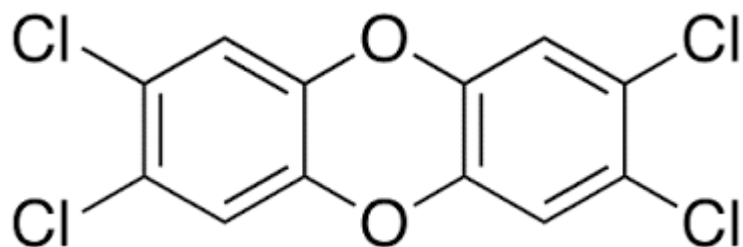
Revisiting the History of 2,3,7,8-TCDD

- 1899: Chloroacne recognized
- 1949: Nitro incident in West Virginia
- 1962-1970: Agent Orange in Vietnam
- 1976: ICMESA explosion (Seveso, Italy)
- 1978: Kociba rat study identified cancer at a very low dose
- 1990: Claims of altered blood lipid levels in humans
- 1985 – 2005: A myriad of possible effects (irrespective of dose and species)
- 2004: Poisoning Yushchenko
- 1980-2015: Debate about human toxicity

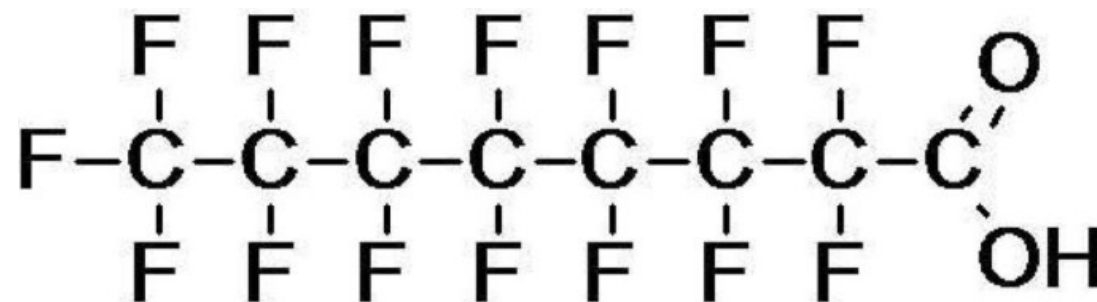
Visiting the History of PFOA

- 1947: PFAS production at 3M
- 1960-1980: Mixed results in toxicology studies
- 1981: Concern about developmental effects
- 1987: Rat study shows cancer risk at high doses
- 2012 A study in the Faroe islands suggests decreased effectiveness of vaccinations (but within normal limits)
- 2020: Some claim of blood lipid and kidney effects
- 2010-2023: A myriad of possible effects are claimed (irrespective of dose and species)

2,3,7,8 TCDD



PFOA

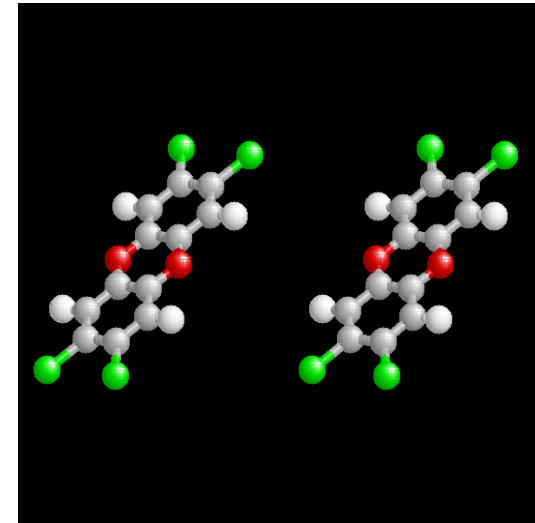


You would not expect them to be similar, based on structure, but in some ways, they are...

Both are environmentally and biologically persistent, as well as lacking human toxicity at typical doses

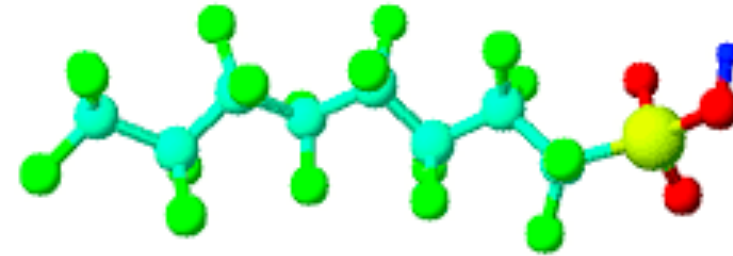
What Are “Dioxins”?

- **2,3,7,8-Tetrachlorodibenzo-p-dioxin**
 - Was known as “The Most Toxic Man-Made Compound”
- Dioxins and Furans are a family of structurally related chemicals which have a common mechanism of action
- Environmentally and biologically persistent

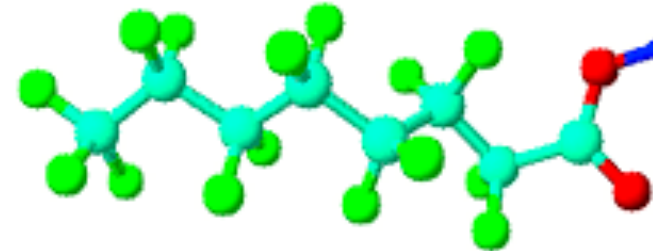


What are PFAS?

- A family of over 8000 chemicals (reportedly)
- Used for decades in hundreds of applications
- Now known as the “forever chemicals”
- Environmentally and biologically persistent



Perfluorooctanesulfonic Acid



Perfluorooctanoic Acid

Chemical Properties

	2,3,7,8 TCDD	PFOA
Water solubility (mg/L)	0.0001295 (very low)	9500 (very high)
Lipid solubility [Kow]	6.80 (very high)	0.002 (very low)
Vapor pressure (mm Hg)	0.0000000015 (very low)	0.0316 (low)
Bioconcentration factor (BCF)	155 (humans)	

Biological Half-Life ($t_{1/2}$) In humans

- 2,3,7,8-TCDD = 8.5 yrs
- PFOA = 0.5 to 15 years (best est. = 3 yrs)
- PFOS = 3-4 years

Biological Half-Life In Rat, Mouse, and Monkey (Quite Similar)

	Dioxin	PFOS	PFOA
Rat	10-20 d	53 d	4 d
Mouse	15-25 d	18.5 d	19 d
Cynomolgus Monkey	60-90 d	121 d	25.5 d

Acute Toxicology (LD₅₀)

2,3,7,8-TCDD (µg/kg)

Mouse: 35 µg/kg

C57B16 mice: 110 µg/kg

Rat: 30 µg/kg

Long-Evans rats: 13 µg/kg

Guinea Pig: 2 µg/kg

Hamster: 5051 µg/kg (oral)

Rabbit: 115 µg/kg (oral)

PFOA (µg/kg)

Mouse: 250- 500,000 µg/kg (Glaza, 1997)

Rat: 500,000 µg/kg (Dean and Jessup 1978)

LD₅₀ for Human (2,3,7,8 TCDD)

- Interestingly, many persons have tried to poison folks with dioxin, but they failed to consult a good toxicology textbook!
- The most toxic chemical known to man has never killed anyone; even when they tried.
- LD₅₀ is at least 100-1000 times higher than in animals. Some believe there is no lethal dose for humans.

Other Persistent Chemicals and Cancer – Is There Something to be Learned?

DDT: No known lethal dose (No clear increased cancer risk in humans)

PCB: No known lethal dose (No clear increased cancer risk in humans)

Deca BDE: No known lethal dose (No clear increased cancer risk in humans)

HCBD: No known lethal dose (No clear increased cancer in humans)

Note: the similarity is that they are all fundamentally non-genotoxic

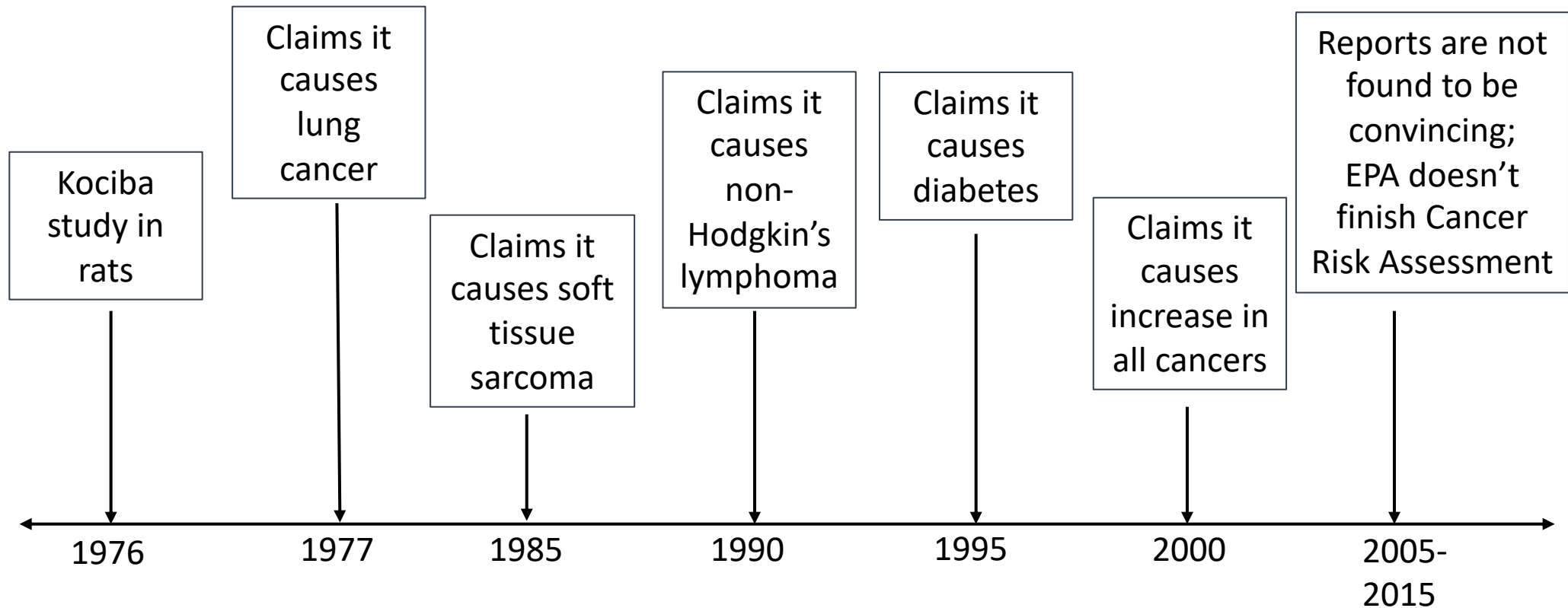
Cancer in animals (Dioxin)

- The Kociba study shocked toxicologists (1976)... it was highly potent
- Later animal studies showed it to be carcinogenic via ingestion in many species
- No human study clearly showed it to be carcinogenic at any dose (this belief is fraught with controversy)

Cancer in animals (PFOA/PFOS)

- Liver cancer was observed in rats at highest dose; but was not statistically significant from controls.
- Increase in liver carcinomas at doses around 15 mg/kg day; not statistically significant and there was no dose-response relationship.
- No human studies, of the 24 epidemiology studies conducted, has indicated that it causes an increased risk of any cancer (some believe Kidney is the best candidate)

Dioxins: An Epidemiology Journey



In the 1990s through the 2000s, some toxicologists and epidemiologists said that dioxin was “A chemical in search of a disease”

PFAS: An epidemiology journey which is just beginning

Steenland and Winquist 2022: Performed a review of 16 cohort (or case-cohort) studies, 10 case-control studies (4 nested within cohorts and 6 non-nested), 1 cross sectional study and 1 ecologic study

They concluded that “overall, the evidence for an association between cancer and PFAS remains **sparse**”.

A couple studies suggest possible effects on kidney

Dioxins and PFAS Seem to Inflamm Emotions



Alleged Adverse Effects of Dioxins

(Irrespective of dose or species tested)

- Lethality/Wasting
- Gonadal/Lymphoid Atrophy
- Hyperplasia/Metaplasia
- Endocrine Disruption
- Carcinogenicity
- Repro/Developmental toxicity
- Functional Developmental Toxicity
- Dermal Toxicity
- Immunotoxicity
- Neurotoxicity
- Hepatic Toxicity
- Cardiovascular Toxicity
- Bone/Teeth Toxicity
- Type 2 Diabetes

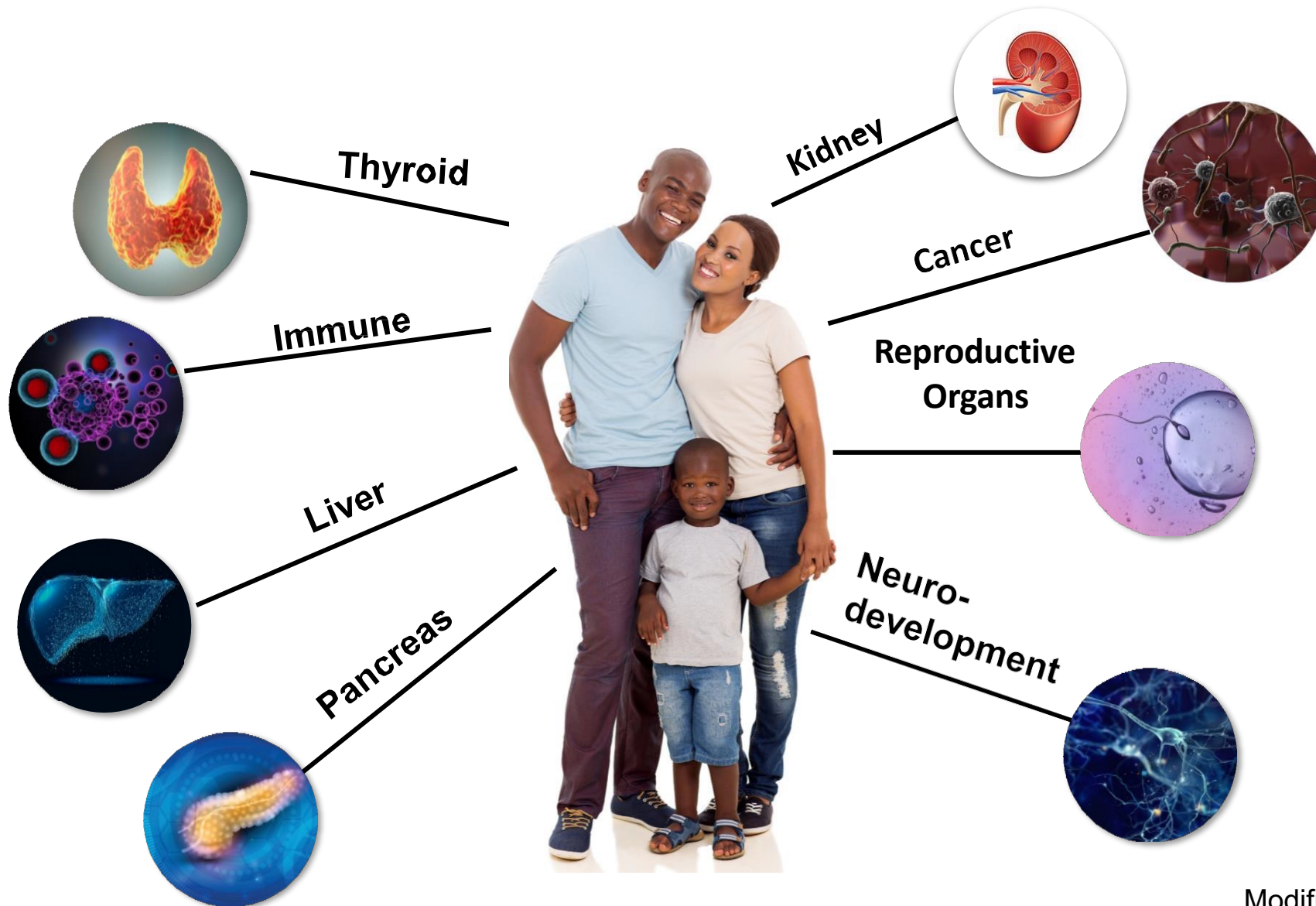
Alleged Adverse Effects of PFAS

(Irrespective of dose or species used)

- Testicular cancer
- Kidney cancer
- Ulcerative colitis
- High cholesterol
- Pregnancy-induced hypertension
- Thyroid disruption
- Hormonal changes
- Liver malfunction
- Obesity
- Immunotoxicity
- Lower birth weight and size
- Reduced testosterone
- Prostate cancer
- Ovarian cancer
- Bone density decrease

An Inflammatory Way to Discuss PFAs Toxicology

(Multi-System Toxicant; but no discussion of dose)



Most classic epidemiologists or toxicologists are bothered by such claims since dose, species, and epidemiology are rarely discussed.

Historically, few chemicals (at commonly encountered human doses) have effects on numerous target organs.

Most often, chemicals effect one or two target organs (always based on dose and duration)

- Inhaled Benzene ➡ acute myelogenous leukemia
- Inhaled Chromium 6 ➡ lung cancer
- Inhaled Vinyl Chloride ➡ angiosarcoma of the liver
- Inhaled BCME ➡ bladder cancer

One Can't Help but Think... There is Something Similar to These Two Classes of Chemicals

- Uneven acute tox across species
- Long biological half-life
- Wasting syndrome seen at high doses in some animals
- Very weak or no signal for carcinogenicity in humans
- Lack of clear genotoxicity

Who isn't bothered by these labels?

- “Forever” Chemicals
- “Most Toxic Chemical Known to Man”



The question in the EU and Australia (not so much in the US) is whether the costs and allocation of resources make sense to achieve incredibly low regulatory water goals.

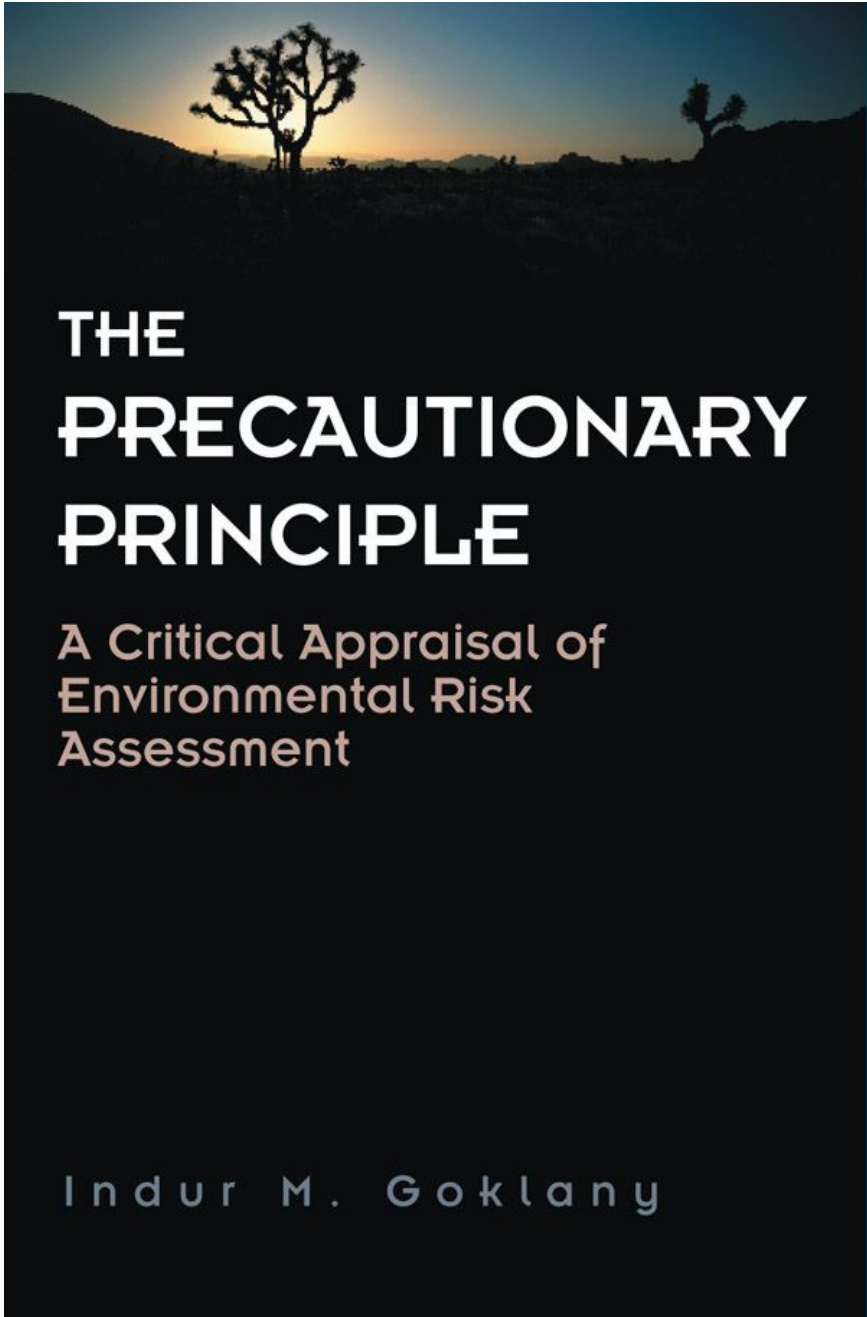
Is spending tens or hundreds of billions of dollars to achieve a particular water guideline a reasonable use of money compared to other needs in society?

Benzene Decision (1980)

- The Supreme Court ruled over 30 years ago that if a lower regulation did not lower the health risk... it should not be promulgated
- Is there a lesson to be learned with respect to PFOA/PFOS in water?

The Historical Dynamic Tension within the Environmental Movement

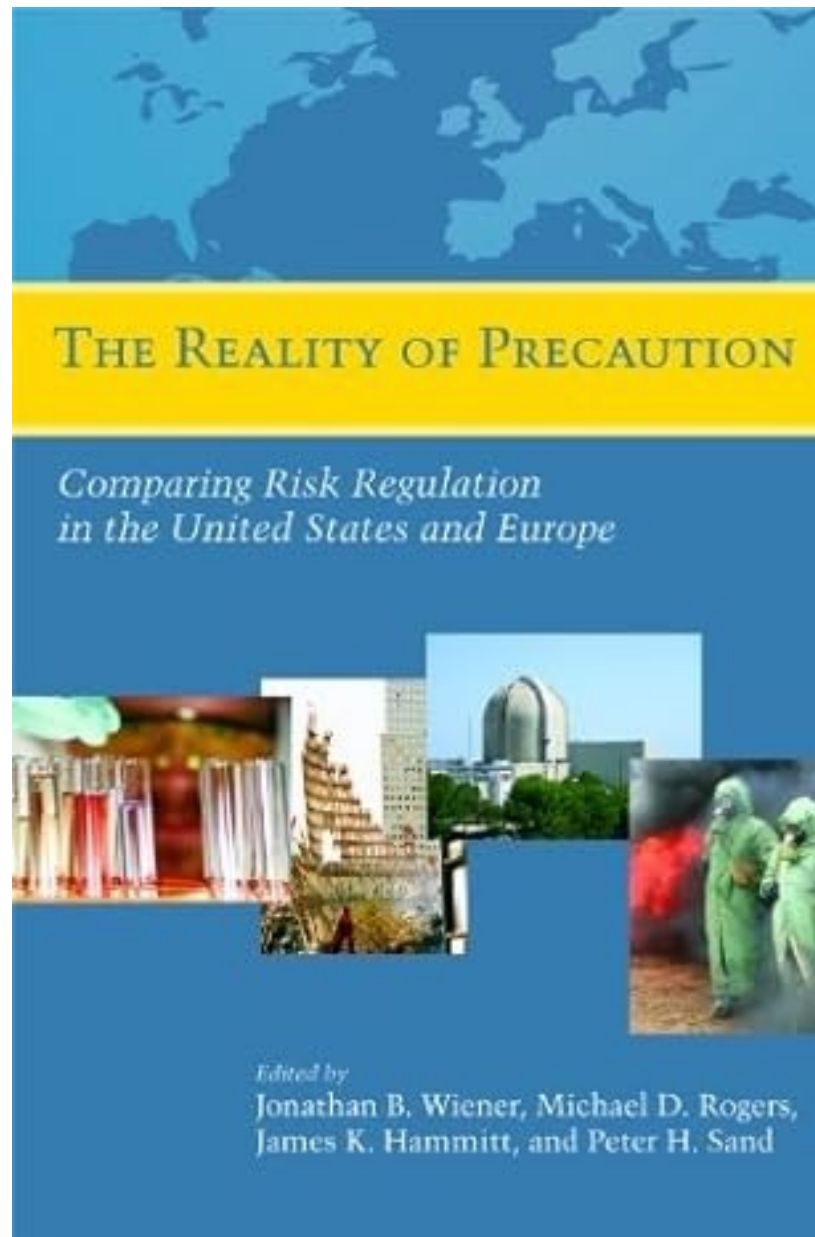
(Risk Assessment vs. Precautionary Principle)



THE PRECAUTIONARY PRINCIPLE

A Critical Appraisal of
Environmental Risk
Assessment

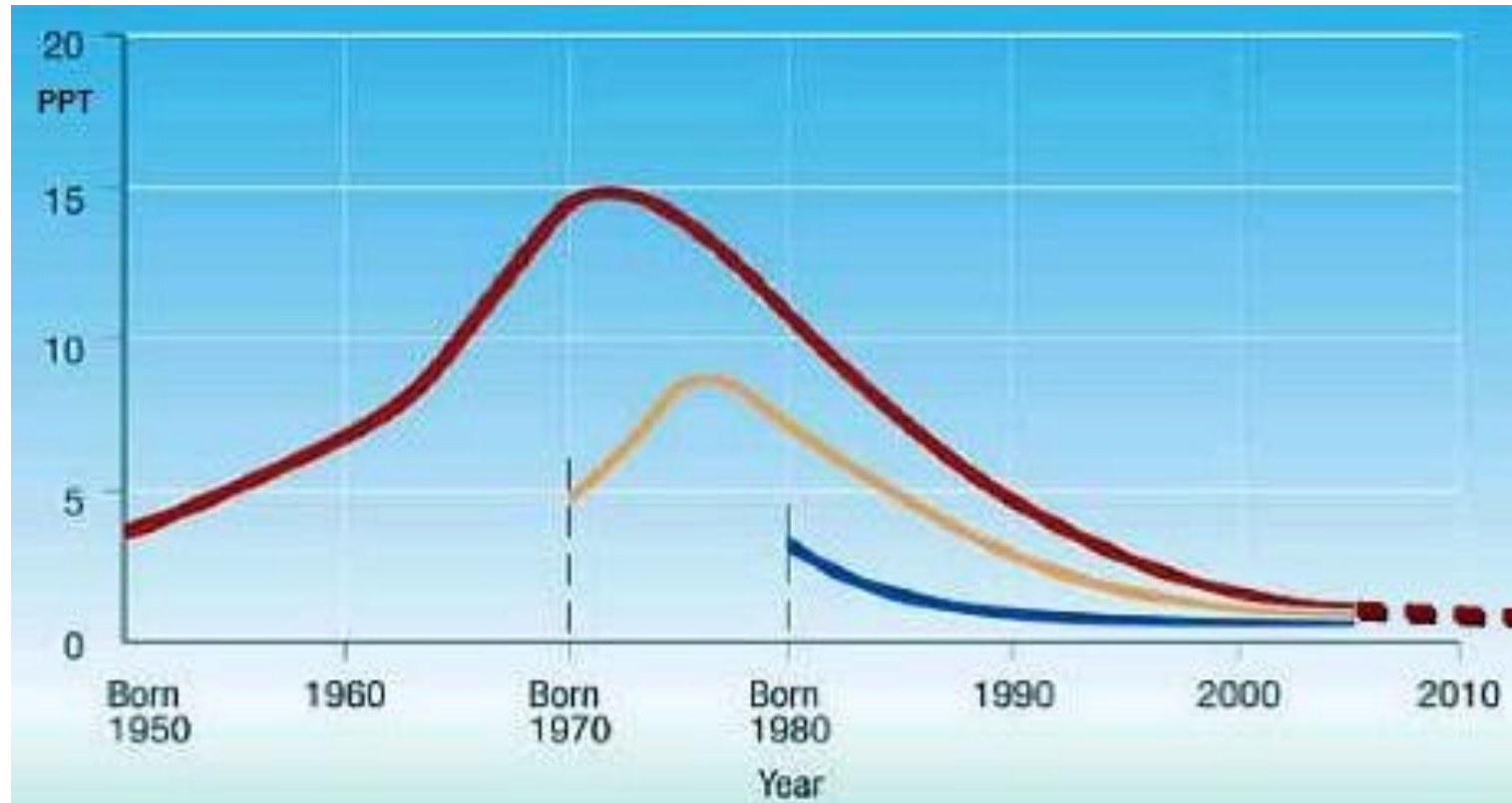
Indur M. Goklany



Just like the dioxins, the threat of additional regulation and personal injury claims regarding PFAS have encouraged firms and public agencies to go into action with less than definitive data and no regulations.



Blood Levels of TCDD Have Been Decreasing Dramatically (US)

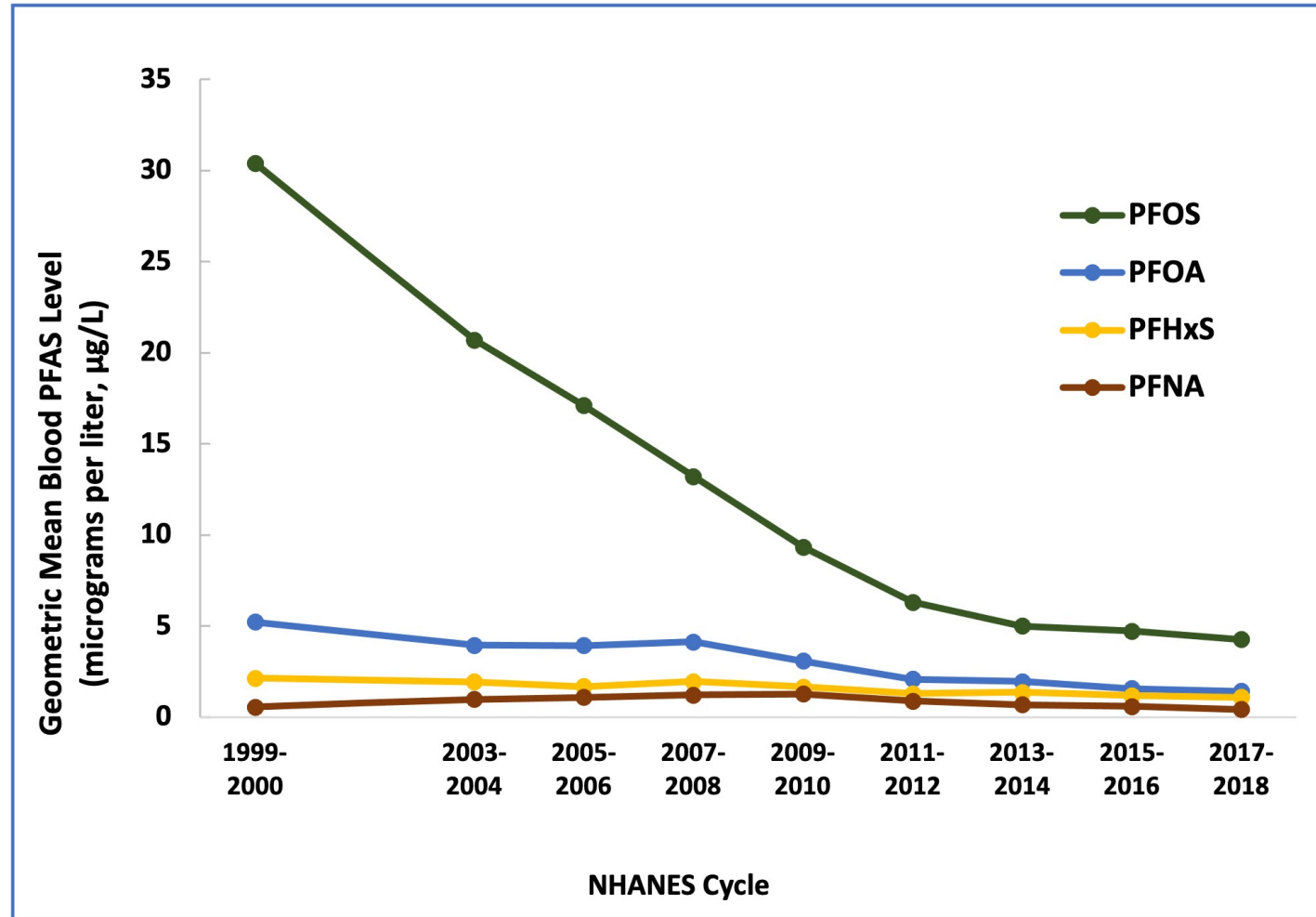


[TCAS, LLC 2017](#)

<http://experttoxicologist.com/toxicology-toxic-exposures-tcdd-dioxin.aspx>

Adapted from Aylward, Hays et al. 2002

Blood Levels of the Most Common PFAS in People in the United States Over Time



The Press and Legal System

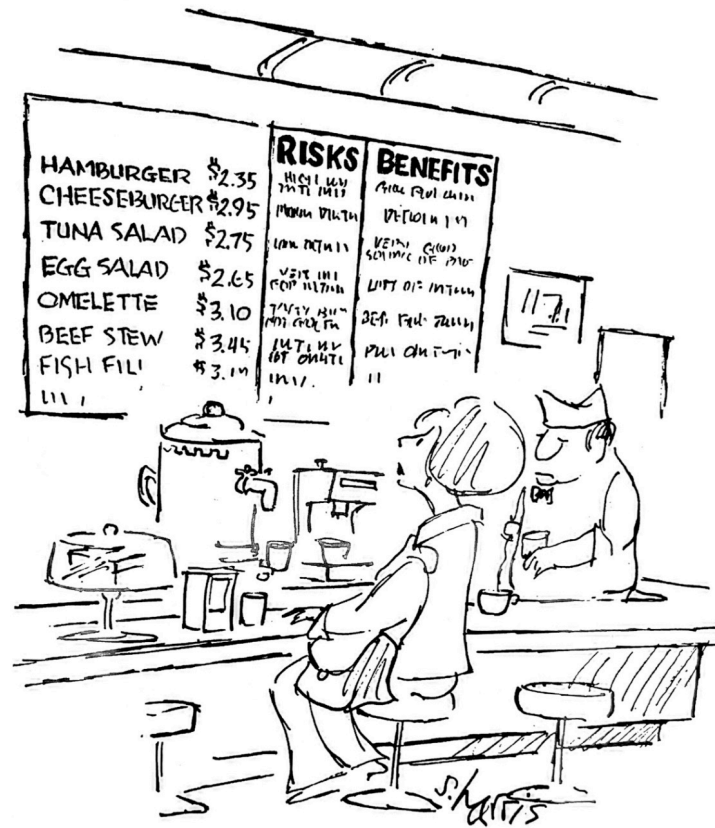
Dioxins

- In the news nearly every week from 1978-2010
- All bad news, even though Operation Ranch Hand cohort showed minimal, if any, adverse effects
- Billions in personal injury claims were filed (many dollars were distributed in the U.S.)

PFAS

- In the news nearly every week from 2010-2023
- All bad news even though epidemiology studies have been equivocal. More work is needed to really understand the hazard.
- Billions in personal injury claims have been filed

Is there no longer a place for Risk/Benefit Analyses



Closing

- Can we learn anything from the dioxin journey?
- Will public outcry, TV ads to sue, and the precautionary principle over-ride risk assessment and scientific methods?
- Will the court system in the U.S. be overrun with claims that may later be found invalid (Silicon breast implant, Bendectin, talc, etc.)
- The risk assessment methodology was adopted globally in the 1980s to avoid less-than-optimal decisions based on emotion. Hopefully, this conference will bring more clarity to what the current scientific information tells us.
- It was intended to help risk managers spend money where it would yield the most reduction in harm or risk.

The end

