Chemicals of Emerging Concern

Linda Schweitzer
Associate Professor
Oakland University

“Definition”

- Chemicals not widely monitored or detected in environmental media
- Chemicals in which the ecosystem or human health impacts are not well known
- New chemicals being used on the market that are just starting to show up in sewage effluent, etc.

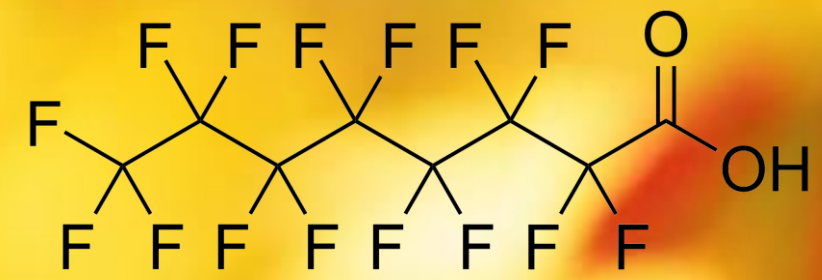
As opposed to legacy contaminants…ones which have been a known problem for a long time

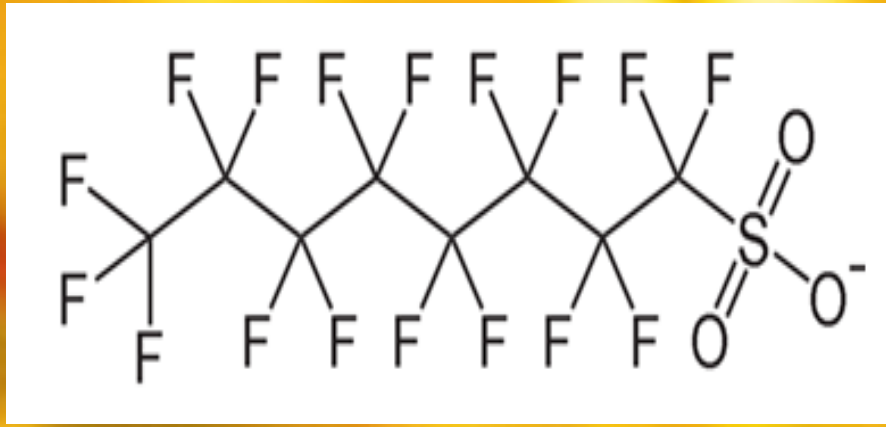
Now Trending in the category of emergent:

- Pharmaceuticals and Personal Care Products
- Triclosan and Triclocarban: Antimicrobial soaps, etc.
- Pesticides
- Flame retardants (brominated types; organophosphate types, etc.)
- Perfluorinated compounds
- X-ray contrast media (e.g., Iopromide, iopamidol, diatrizoate)
- Disinfection byproducts (from chlorination, ozone, UV)

Example of how chemical or class of chemical becomes a CoEC

perfluorinated compounds used in Flame retardants, Scotchguard, etc.





Building blocks (monomers) of polymers

- Perflourinated compounds PFOS and PFOA first detected in human blood 1968.
- However, no known human or ecological effects after first 30 years of use.
- Chemicals have low fat solubility and were not predicted to bioaccumulate…but do so by different mechanism (protein binding).
- MSU finds PFOS in wildlife in 1997 (Giesy et al.) and tells 3M manufacturer; 3M funds studies on occurrence and toxicity. Later, EPA (NTP) funds more studies.
- High occurrence in wildlife and humans found by year 2000.
- Unexpected toxicity (e.g., reproductive effects, thyroid, lipid peroxidation, etc.). ATSDR profile (2008)
- Chemicals voluntarily phased out by manufacturer
- 2010: PFOS restricted Stockholm POPs treaty. Canada restricts some PFCs

TSCA = Toxic Substance Control Act (1976)

The long and winding road?

- Allowed many chemicals being manufactured to continue to be manufactured unless EPA deemed chemicals to pose undue risk
- Requires application for new chemicals to be manufactured, but little testing for chemicals that are not intended to be ingested by humans. Uses SARs to determine whether to permit manufacturing initially.
- Allows mechanism for banning, regulating, or restricting use of chemicals once they are shown to pose undue risk
- Different classes of chemicals may be further regulated by other statutes

European REACH

Registration, Evaluation, Authorisation and Restriction of Chemicals

- Burden of proof put on chemical manufacturers
- Have to register chemicals with ECHA – European Chemicals Agency
- Will require a phase-out of chemicals that have been posing health threats such as phthalates, brominated flame retardants, certain herbicides/pesticides that are endocrine-disruptors;
- Recognizes that although many chemicals are not intended to get into the human body, they end up there because the chemicals enter the environment and partition between air, soil, water, sediments, biota

USA Safe Chemicals Act of 2013

- https://www.govtrack.us/congress/bills/113/s696

- Legislation proposed. Gov tracking website gives it an 11% chance of passing.
- However, EU is spending the money to evaluate chemicals – they can continue to take the lead in phasing out chemicals.
- Question of why USA lagging in phasing out chemicals such as atrazine and glyphosate when toxicity data are piling up against these chemicals. These are the “DDT’s” of the future

13 chemical additives that have been

⊘ BANNED ⊘

for use in food in other countries

but are still approved for use in the US

coloring agents

1 blue 1

2 blue 2

3 yellow 5

4 yellow 6

olestra/olean

5

BHA and BHT

6 & 7

azodicarbonamide

8

arsenic

9

synthetic hormones

10 rBGH

11 rBST

potassium bromate

a.k.a. brominated flour

12

brominated vegetable oil

a.k.a. BVO

13

www.bodyunburdened.com

source: Rich Food, Poor Food

Pharmaceuticals and Personal Care Products

- Oakland University studies with University of Windsor and MOE, and IJC found several PPCPs in sewage effluent and drinking water.
- Levels not thought to pose much of a risk. Compared concentrations with known levels of effects in aquatic organisms (sensitive species) and concentrations were almost always below any known levels of effects.
- Continued monitoring should be done to make sure water and wastewater utilities performing well. What about sewage overspills? People on septic systems and wells may not be safe…high rate of septic system failures.

Chemical	Description
Acetaminophen	Anti-inflammatory drug
Androstenedione	Male hormone
Atenolol	Beta Blocker drug
Atorvastatin	Cholesterol (statin) drug
Caffeine	Stimulant drug
Carbamazepine	Anticonvulsant and mood stabilizing drug
Cimetidine	Stomach acid drug
DEET	Insect repellant
Diphenhydramine	First-generation antihistamine drug
Equilin	Hormone Replacement Therapeutic (HRT)
Erythromycin	Antibiotic
Estriol	Endogenous hormone or HRT
Estrone	Endogenous hormone or HRT
Ethinylestradiol, 17-a	Contraceptive hormone drug
Fluoxetine	Endogenous hormone or HRT
Gemfibrozil	Cholesterol drug
Hydrocodone	Semi-synthetic opiod
Ibuprofen	Nonsteroidal anti-inflammatory drug
Isobutylparaben	Cosmetics
Metoprolol	Cardiovascular system drug
Naproxen	Nonsteroidal anti-inflammatory drug
Sulfamethoxazole	Sulfonamide bacteriostatic antibiotic

Compound	**Mean % Actual Removal**		
	Conventional	**UV**	**O_3**
Acetaminophen	75	47	100
Androstenedione	7	50	
Atenolol	8	95	83
Atorvastatin	100	100	
Caffeine	50	42	100
Carbamazepine	50	96	
Cimetidine	28	97	
DEET	62	85	72
Diphenhydramine	40	0	
Equilin	50	0	
Estriol	39	7	
Estrone	60	60	
Ethinylestradiol	41	50	
Fluoxetine	38	100	
Gemfibrozil	29	52	
Hydrocodone	18	94	100
Ibuprofen	50	100	
Isobutylparaben	70	0	
Metoprolol	0	100	100
Naproxen	23	89	100
Sulfamethoxazole	50	57	

Emerging Problems to Investigate

- Instead of targeting chemicals to see if they are present in the environment, investigate human health problems that may be caused by chemicals in the environment
- Emerging contaminants have been identified in the past by first noticing sex-alterations in wildlife, then figuring out culprit chemicals
- Chemical spills (over 900 in past 30 years) in St Clair River provided opportunity for acute exposure of uncommon chemicals, effects of which would be completely unknown

Wilm's Tumor (WT) or Nephroblastoma

- The St. Clair County Health Department (SCCHD) reported occurrences of cancer cases in the St. Clair County area through the Michigan Cancer Registry (MCR).

The period between 1990 and 2009

- 11 children were diagnosed having Wilmes tumor (WT) or Nephroblastoma
- 63% of which occurred in children of age < 5 years.
- 72% of the WT cases were in Marine City with a prevalence rate of approximately 1:500 based on the 2010 population census in the area (SCCHD, 2013)
- **Greatest risk factor is proximity to St Clair River.**

Cause-and-Effect Difficult to Determine

- Kristensen et al. (1996) report Odds Ratio of 9:1 probable WT development in children with parents exposed to pesticides through farm use than parents without….is it really the pesticides, though? Or could it be something else on the farm, such as fertilizer?
- Wilm's cancer cases tend to cluster, indicating likely environmental or occupational exposure as main cause. However, indications of genetic susceptibility, also.
- The chemical has to make sense mechanistically. What kinds of chemicals can cause a Wilm's Tumor?

MNU or NMU
N-Nitroso-N'-Methyl Urea (methylnitrosourea)

- Animal models show that mutations from alkylating agents such as NMU create kidney tumors and other effects that have the same morphology, mutations, and epigenetic events as Wilm's in humans. (Sharma et al. 1994 – *PNAS* 9931-9935).
- A single oral dose of NMU (<< sub-lethal) results in tumors in 50% rodents injected; very potent carcinogen. (Leaver et al. 1968. *British J Cancer)*

NDMA

- Not reported to be linked to Wilms, but no one knows.
- Chemical can be metabolized by liver in humans to a potent alkylating agent, methydiazonium ion.

NDMA and other nitrosamines - Sources

- NDMA is a byproduct in manufacturing of fertilizers, rubber tires, dyes and other products, or it can form in sewage treatment or water treatment during disinfection (chloramines or free chlorine).
- Nitrosamines are also found in meats preserved with sodium nitrite.
- NDMA can form from nitrite and dimethylamine
- Herbicides as dimethylamine salts such as:
  - 2, 4-D
  - Mecoprop
  - Dicambra

Preliminary Study – water samples St Clair

Date	Description	Conc. NDMA	Total Ammonia
5.6.13	Raw SCR Marine City	ND	0.25
5.8.13	Raw SCR Marine City	17 ng/L	0.25
5.13.13	Raw SCR Marine City	ND	0
5.10.13	Raw SCR Marine City	ND	0.25
5.23.13	Raw SCR Marine City	ND	0.25
5.29.13	Raw SCR Marine City	ND	0.25
5.30.12	Raw SCR Marine City	53 ng/L	0.25
5.1.13	Tap water Marine CIty	<MDL (6 ng/L est.)	0.5
5.6.13	Tap water Marine CIty	ND	0.25
5.8.13	Tap water Marine CIty	ND	0.25
5.13.13	Tap water Marine CIty	ND	0.25
5.23.13	Tap water Marine CIty	ND	0.25
5.23.13	Tap water Marine CIty	ND	0.25
5.29.13	Tap water Marine CIty	ND	0.25
5.30.12	Tap water Marine CIty	ND	0.25

Future Research

- Dr. Richard Olawoyin at Oakland University School Health Sciences

Conducting air sampling for nitrite, nitrate, ammonia and other contaminants along the St Clair River near Marine City. Samples being analyzed.

Water samples and soil pore water will be analyzed for NMU and NDMA and possibly other contaminants.

Conclusions

- Chemicals should be tested before mass production
- However, some chemicals may be byproducts of formation or degradation products and would not necessarily be detected even in preliminary toxicity testing. Also, some endpoints of toxicity may yet to be discovered. Example of PFOS and PFOA seemingly non-toxic and end up being a problem years later.
- Could the Wilm's tumor be caused by current or past exposure to some chemical(s) completely off the radar screen?
  If so, it would be a chemical of Emerging Concern.