Endocrine disruptors and policy approaches for reducing risks

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Hazard issues

- Carcinogenicity
- Neurotoxicity
  - (mostly with in utero exposure)
- Ecotoxicity (best established)
- There are disagreements, largely because of the uncertainties in extrapolating from animals to humans and how difficult it is to do the epidemiology

Toxicity tests (EPA guidelines) required for approval of food use pesticides

- Acute Illness
- Cancer
- Neurotoxicity
- Developmental effects
- Immunologic effects
- Endocrinologic effects
- Reproductive toxicity

Pollutants: Endocrine disruption

- **Endocrine disruption** is defined by the EPA as “an exogenous agent which interferes with the synthesis, secretion, transport, binding action, or elimination of natural hormones in the body which are responsible for homeostasis, reproduction, development, or behavior.”

Potential risks from ED's (1)

- Estrogens / Anti-androgens
  - Feminization of male: evidence for increases in hypospadias, undecended testicles and lowered sperm counts
  - Overstimulation of female at times when estrogen is low (in utero, prepubertal, postmenopause): ?polycystic ovary, precocious puberty, premature thelarchy
  - Cancers?: ?prostate, testicle, breast, ovary

Potential risks from ED's (2)

- Thyroid
  - Growth
  - Central nervous system development
  - Thyroid related carcinogenesis

Persistent Organic Pollutants

- Toxic
- Transported, through air, water and migratory species, across international boundaries and deposited far from their place of release
- Resist degradation
- Bioaccumulate in terrestrial and aquatic ecosystems

DDT/DDE Endocrine Effects

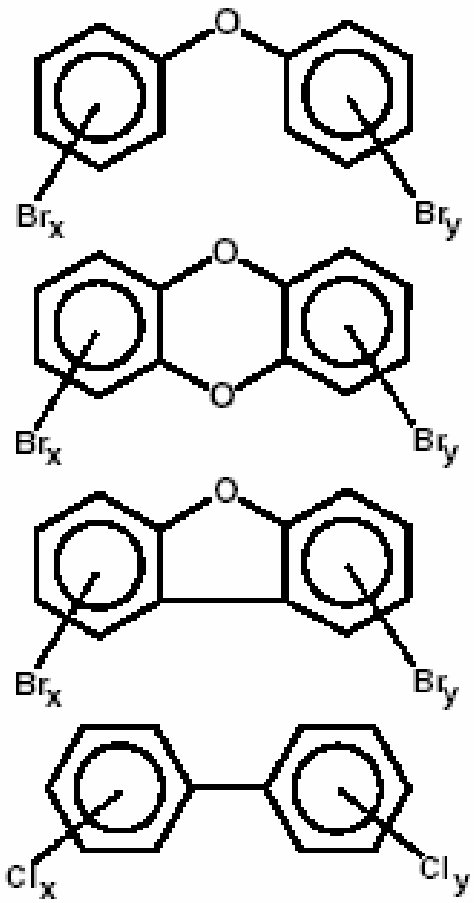
- DDE and Duration of Lactation
  - Rogan et al 1987, North Carolina
  - Gladen et al 1995, Mexico
    - 7.5 vs. 3 months
  - *It appears that DDE shortens duration of lactation; mechanism unknown*
- DDE and preterm birth
  - Longnecker et al 2001
  - Pre 1966 blood samples from the Collaborative Perinatal Health Study
  - *Mothers of preterm births had higher levels of DDE in blood than mothers of term births*
  - *(average levels were 5X levels found in blood today)*

PCBs, Dioxins, Furans

- PCB = polybrominated diphenyl ethers
- Dioxins
- Furans
- Health concerns include:
  - **Carcinogenicity of dioxins and certain PCBs**
  - **Adverse reproductive outcomes dioxins and certain PCBs (including developmental neurotoxicity)**

A family of persistent chemicals

- PCBs long banned
- Dioxins inadvertent product o combustion and other processes
- Europe has banned or restricted these chemicals.
- PBDE levels have increased: states have begun to take action, beginning with legislation in California.



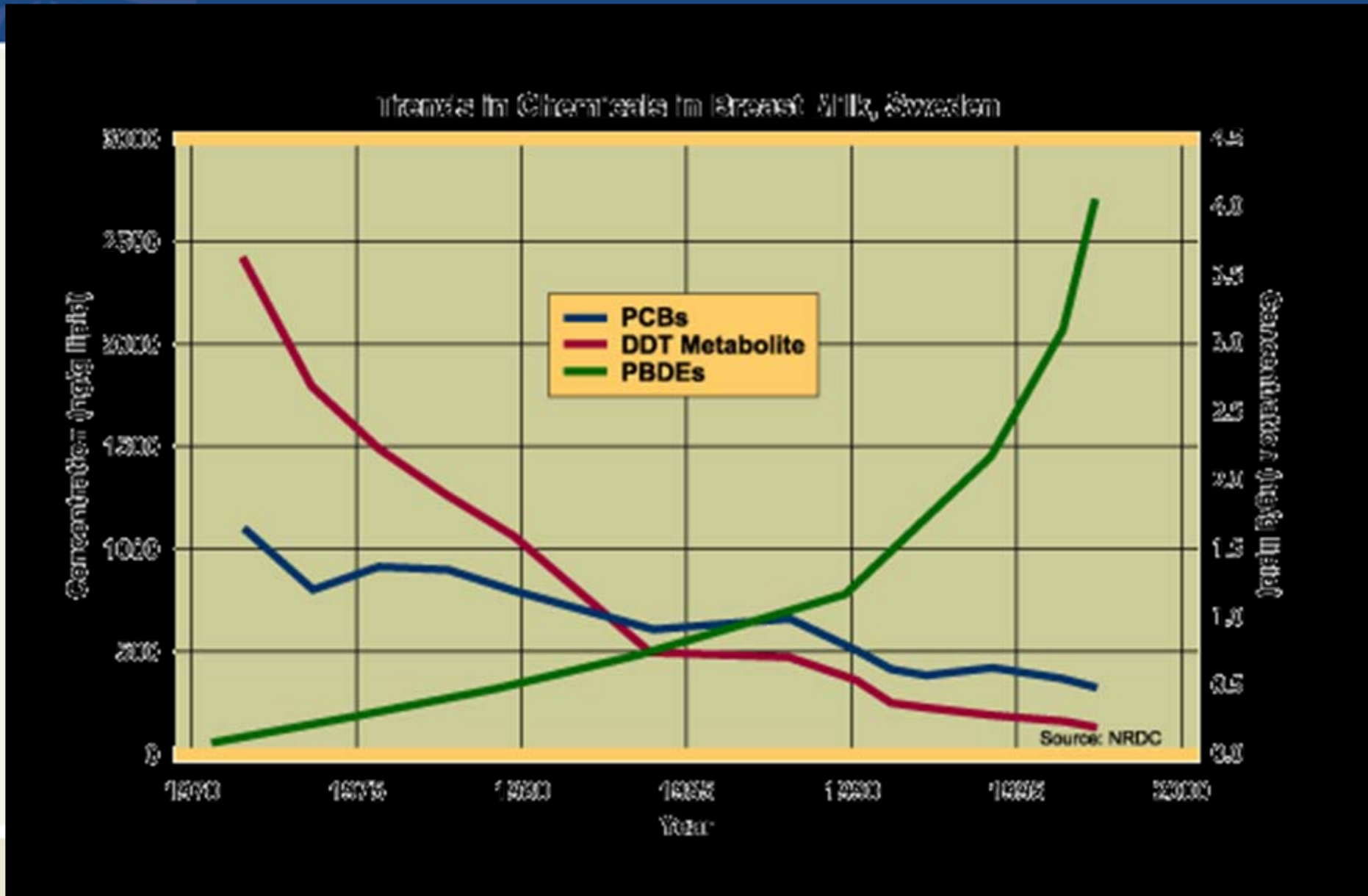
Polybrominated Diphenyl Ether (PBDEs)

Polybrominated Dibenzo-p-dioxin (Dioxin)

Polybrominated Dibenzo-furan (Furan)

Polychlorinated Biphenyl (PCBs)

PBDE Trends in Exposure



PFOS/PFOA Perfluorinated Compounds (PFCs)

- Fully fluorinated, man-made compounds used in a wide variety of commercial and industrial products and processes

  - protective coatings; non-stick cooking material; commercial and industrial surfactants; insecticides

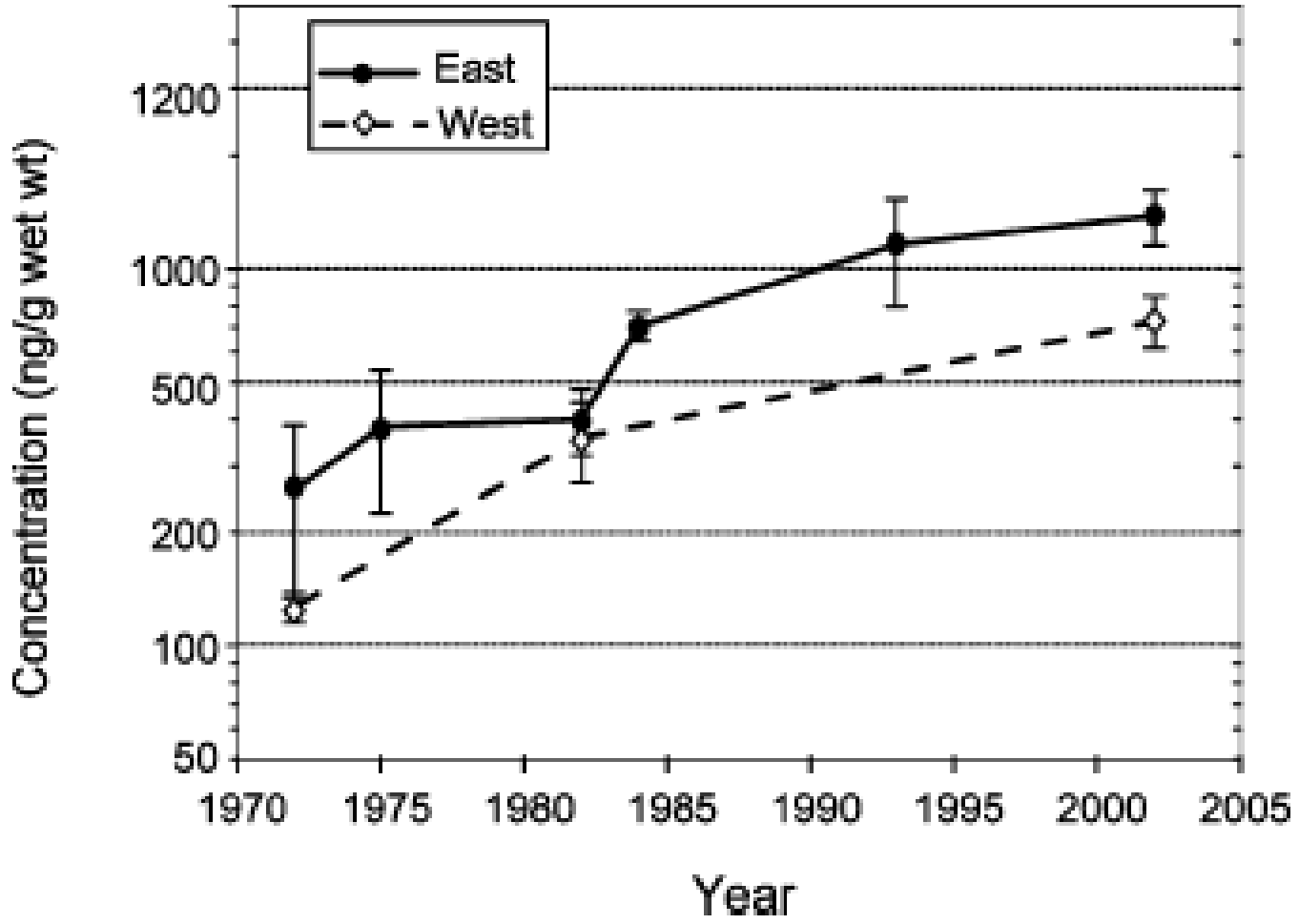
- Physicochemical properties
  - C-F bond is resistant to degradation
  - Hydrophobic and oleophobic (repel water and oil)

Perfluorinated Compounds (PFCs)

- Toxicity in humans largely unknown
  - PFOS: reduced thyroid hormone production; reduced birth weight
  - PFOA: developmental effects observed in animals
  - Occupational epidemiology studies show slight positive association between PFOS/PFOA and serum lipids

- Exposure
  - Increasing trend over last several decades *(Olsen et al, 2003)*
  - Long half-lives (4-9 years) *(Olsen et al, 2005)*
  - Accumulates in liver/serum, not fat
  - Importance of food chain is highly uncertain

Increasing PFOS/PFOA levels in polar bears illustrates global importance

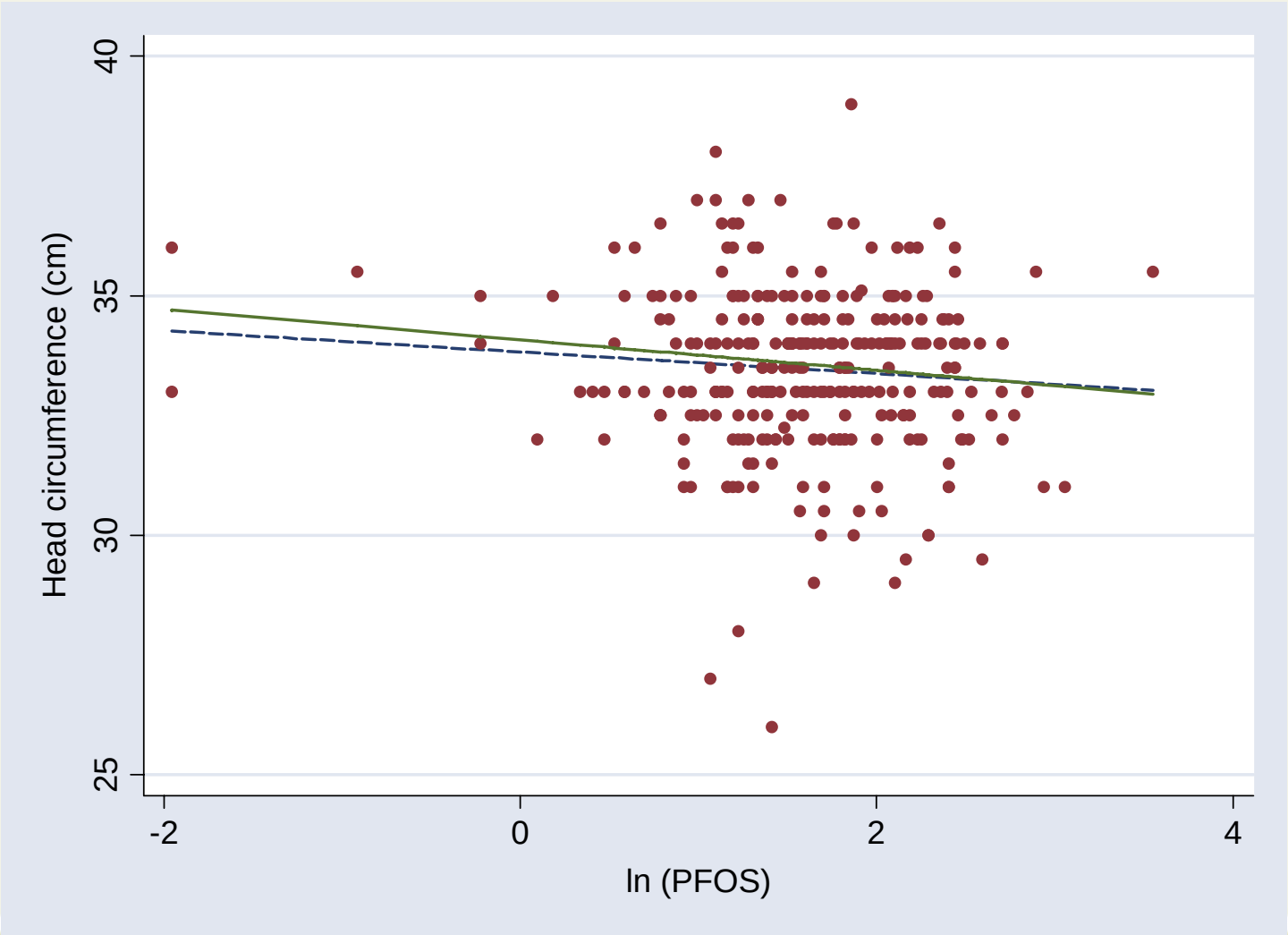


Mabury et al ES&T 2006

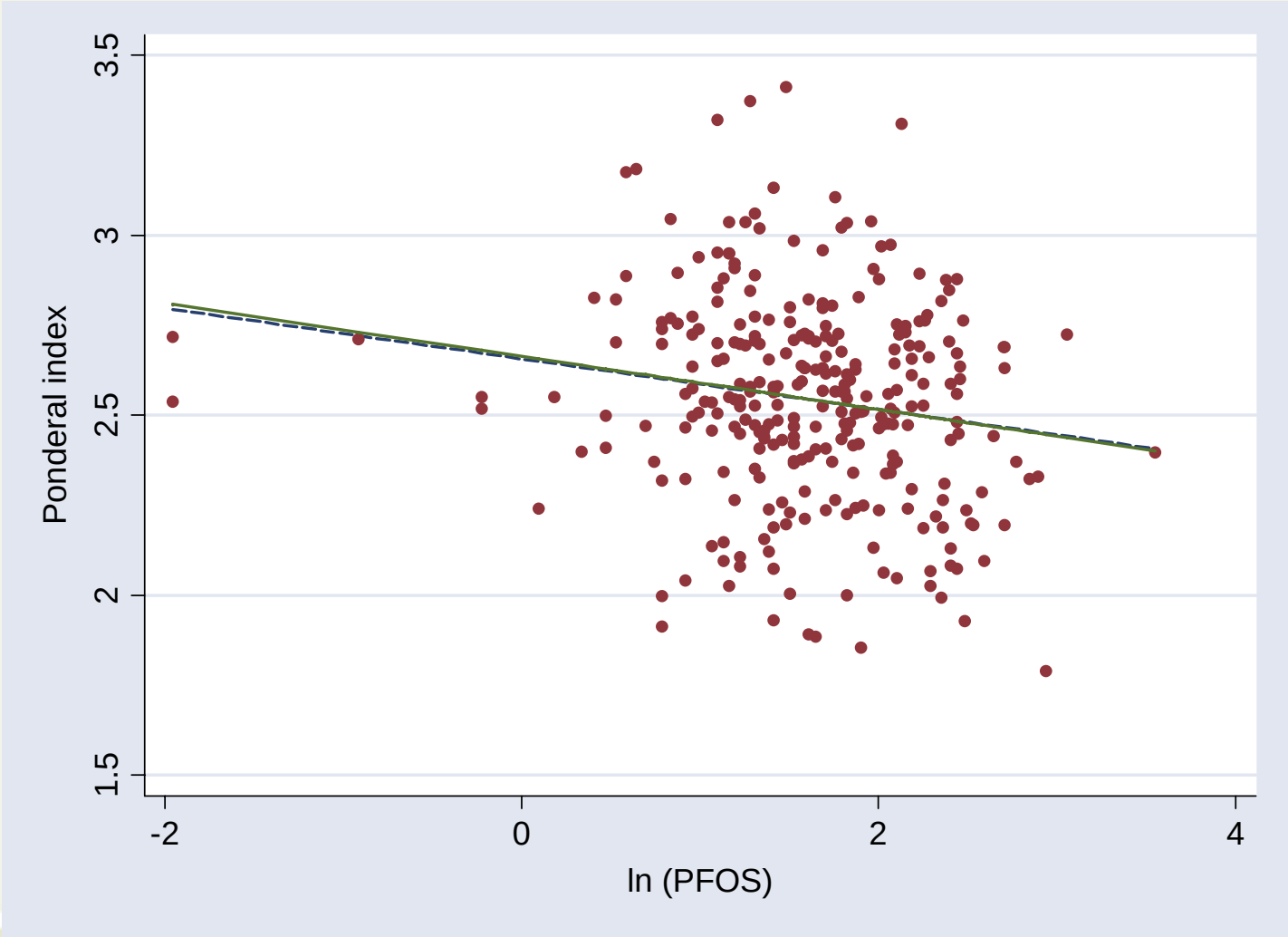
Cord blood study

- Findings to date:
  - PFOS and PFOA in virtually everyone (accepted)
  - PBDEs and PCBs ditto (preparation)
  - PFOS and PFOA associated with smaller weight for length and head circumference (submitted)
  - PBDEs and PCBs associated with altered TH status (preparation)
  - PFOS and PFOA associated with altered TH status (under analysis)
- Unanswered questions: precisely how exposures are occurring to these compounds

PFOS and Head Circumference



PFOS and Ponderal Index



Mixtures of chemicals in cord blood

	PCBs	PBDEs	DDT/DDE	PFCs	PBDE	Chordane	HCBs	Hg	PCBs
lip_pp_ddt	0.017	-0.078	0.509	0.263	0.017	0.065	-0.0897	0.0051	-0.0789
lip_pp_dde	0.036	-0.107	0.515	0.301	0.059	0.031	0.0264	-0.0336	-0.0390
lip_hcb	0.141	-0.167	0.029	0.070	0.211	-0.031	0.2855	-0.1033	0.0921
lip_b_hcch	0.015	-0.103	0.331	0.275	0.073	-0.069	0.2917	-0.1367	0.0601
lip_oxychlor	0.190	-0.082	0.152	0.094	-0.128	0.253	-0.4537	0.0577	-0.0533
lip_t_nona	0.173	-0.049	-0.010	0.016	-0.164	0.229	-0.4831	0.1007	-0.0617
lip_pbde28	0.067	0.336	0.022	0.022	0.345	0.033	-0.0440	0.0677	-0.0259
lip_pbde47	0.083	0.381	0.036	0.030	0.317	0.076	-0.0408	0.0710	-0.0704
lip_pbde99	0.057	0.269	0.001	0.027	0.410	0.136	-0.0666	0.1220	0.0431
lip_pbde100	0.106	0.404	0.038	0.044	0.173	-0.009	-0.0029	0.0225	-0.0418
lip_pbde153	0.038	0.172	-0.025	0.059	0.111	0.043	-0.1621	-0.2706	0.1050
lip_pcb28	0.033	-0.003	0.054	-0.022	-0.009	0.041	0.0214	0.2962	0.8843
lip_pcb74	0.268	0.095	0.039	0.014	-0.184	0.015	0.0006	0.0106	0.1996
lip_pcb105	0.165	0.302	0.064	0.032	-0.291	-0.138	0.1628	-0.0557	-0.0017
lip_pcb118	0.200	0.277	0.056	0.040	-0.299	-0.101	0.1366	-0.0560	-0.0056
lip_pcb156	0.275	-0.015	0.001	-0.119	-0.123	0.045	-0.0629	-0.0120	-0.0037
lip_pcb99	0.223	0.265	0.040	0.024	-0.260	-0.091	0.1193	-0.0389	-0.0242
lip_pcb138+158	0.301	0.056	0.010	-0.036	-0.140	-0.018	0.0428	-0.0297	-0.0312
lip_pcb146	0.300	-0.059	-0.037	-0.031	-0.020	-0.007	-0.0186	0.0020	-0.0659
lip_pcb153	0.307	-0.078	-0.025	-0.046	0.027	-0.007	0.0795	-0.0389	-0.0188
lip_pcb170	0.275	-0.174	-0.028	-0.066	0.140	-0.006	0.1170	-0.0446	0.0074
lip_pcb180	0.265	-0.188	-0.046	-0.053	0.177	-0.019	0.1447	-0.0394	0.0035
lip_pcb187	0.273	-0.155	-0.074	0.002	0.189	-0.014	0.0311	0.0183	-0.0629
lip_pcb196+203	0.252	-0.157	-0.071	-0.064	0.118	0.024	-0.0451	0.0242	0.0262
lip_pcb199	0.235	-0.181	-0.108	-0.024	0.187	0.004	-0.0286	0.0448	-0.0544
lead (blood)	0.008	-0.019	0.151	0.083	0.016	0.107	-0.1002	0.0374	0.0820
mercury (blood)	0.052	-0.016	-0.131	0.288	0.001	-0.288	0.0566	0.3403	-0.2263
me_pfosa_a~h	-0.024	0.033	-0.073	0.051	-0.069	0.591	0.2950	0.1578	-0.0771
pfdea	0.026	-0.027	-0.251	0.472	-0.048	-0.100	-0.0450	0.1609	0.1099
pfoa	0.009	0.032	-0.260	0.306	0.009	0.175	-0.0813	-0.4183	0.1303
pfos	-0.008	0.004	-0.221	0.281	-0.010	0.178	0.0271	-0.5156	0.0782
pfosa	-0.017	0.004	-0.080	0.070	-0.135	0.511	0.3544	0.2605	-0.1320
pfua	0.022	-0.036	-0.260	0.465	-0.019	-0.160	-0.0725	0.2767	-0.0323

Children's health protection: Toxic Substances Control Act (TSCA)

- No provisions specifically directed at children but rather:
  - The "unreasonable risk" standard includes economic benefits to those who manufacture, process and otherwise use chemicals
  - No requirement to protect children and other sensitive populations
  - No deadlines or specific expectations for action
  - "Least burdensome" requirement has "killed" management of even the riskiest chemicals (e.g. asbestos) under TSCA
- Significant barriers for bringing newer safer chemicals to market

New chemicals approvals-TSCA

- Only chemical structure and physical characteristics are supplied
- Agency uses SARs (Structure Activity Relationships) and physicochemical properties for most decisions
- Agency can require additional information or issue “Significant New Use Rules” for new chemical uses
- But the burden for industry for a new chemical is more stringent than an existing chemical

Assessment of existing chemicals - TSCA

- In 1976 70,000 existing chemicals grandfathered into use and placed on the “inventory”; between 1,500-3,000 have been reviewed by EPA as “new chemicals” every year since
- The “inventory” is only partially updated
- To required testing EPA must write a test rule that contains a finding of “unreasonable risk” (can be based on exposure); EPA must meet a heavy burden to justify testing
- Generally EPA assumes that production volumes is a good proxy for exposure and misses low production/high exposure situations, because it has little information on exposures
- 2,500 chemicals/groups involved in the industry/EPA voluntary “HPV” program
- Generally, ignorance about hazard (and risk) is rewarded since the law presumes that chemicals are safe unless proven otherwise by the EPA
- EPA rarely inspects/enforces GLP test provisions in labs

Right to know; access to information

- In 1998, more than 65 % of the information filings directed to the Agency through TSCA were claimed as confidential.
- Submissions under the former Inventory Update Rule show that about 20 % of facility identities were claimed as confidential.
- In 1998, 40 % of Section 8(e) substantial risk notices had chemical identity claimed as confidential.
- States cannot receive CBI filings under the statute, yet many chemical risk management decisions in this country are done at the state and local level
- No information about chemicals hazards (or even contents) is on products in the US save those covered by California's Proposition 65
- Therefore communities and individual citizens do not have right to know under TSCA

Children's health protection: FQPA as a standard

- Clear deadlines were set for action for ALL food use chemicals
- All existing pesticide food standards were assessed by a stringent standard:
  - Children are safe from hazards of individual pesticides across all (*aggregate*) exposures. Health-only standard of "reasonable certainty of no harm"
  - Children are safe from hazards of multiple pesticides with *cumulative* risks
  - An additional 10X factor applied unless children's hazards AND exposures have been taken into account
- Labeling of pesticide active ingredients

Pollution Prevention is Not Rewarded

- Lack of control of existing chemicals means that older riskier chemicals stay on the market forever; it is harder to get a new chemical on the market
- Lack of information about chemical USE and TOXICITY means that most people cannot get good information about processes that can enable pollution prevention substitutes
- EPA has engaged voluntarily in the past:
  - 33/50 program
  - Green chemistry challenge competition
  - Design for environment (dry cleaners, screen printers, etc.)
  - Reduced risk pesticide registrations
  - Green cleaners project

Making chemicals “child safe”

- Clear specific expectations of EPA and industry
- Shift the “burden of proof” to industry
- Require information/right to know
- Reward innovation/safer substitutes
- Adopt child specific safety standards
- Prioritize to protect kids
- Strengthen enforcement
- Promote right to know
- Support international efforts

Clear expectations for protecting children

- No exposure to chemicals that do not meet core information requirements to assure that they are safe for children.
- Shift the burden of proof to industry to demonstrate safety of a chemical for kids.
- Establish clear deadlines and mechanisms for ensuring that measures to protect children are adopted by default if timely action is not taken.

Child specific safety standards

- An additional safety margin for children, to assure a “parent’s right to a healthy child.”
- Utilize protocols for hazard and exposure assessments that explicitly consider children and their most sensitive and vulnerable health effects.
- Consider aggregate and cumulative risks of chemicals..
- Require periodic reassessments to take into account new science.

Prioritization

- A transition process that prioritizes review and approval of existing chemicals.
- Priority is to be given to “the worst first” -- after consideration of
  - Children’s exposure pathways
  - Biomonitoring data
  - Cancer, developmental and reproductive effects
  - Production volumes
  - Bioaccumulative or environmental persistence properties
  - Use patterns

Information

- Reward industry for creating information
- Increase the transparency and access to information about chemicals

Enforcement

- Strong enforcement provisions including routine inspections and random audits of facilities and laboratories.
- Strong citizen suit and petition provisions, and clear deadlines for action written into the law.

Biomonitoring

- Require generation of biomonitoring data and methods for interpreting and understanding biomonitoring data; biomonitoring must be scientifically standardized and collected under guidelines established by EPA.

International commerce

- Management of chemicals in commerce internationally In this regards, the U.S. should be a leader and a good partner in international efforts for sound management of chemicals, including:
  - Ratify Stockholm Convention on Persistent Organic Pollutants (POPs)
  - Ratify Rotterdam Convention on Prior Informed Consent (PIC)

Making chemicals child safe (conclusion)

- EPA needs clear requirements and regulatory authority that requires placing a high priority on protecting children's health (as defined above) and on protecting other vulnerable subpopulations.

- A strong safety standard: health protection of children should be the basis for chemical regulatory decisions.