Legally Poisoned:
How the Law Puts Us at Risk from Toxicants

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Bullets, knives and blunt objects are often philosophers’ examples of risk or harm bearing entities.
Molecules can also pose risks or cause harms, but diagnosing their adverse effects is much more subtle and difficult than for the grosser forms of violence. Children are especially susceptible.

How can we utilize the law and science to reduce the risks to children from toxic molecules?

**Diethylstilbestrol**

In utero exposure caused vaginal/cervical cancer at age 20, breast cancer later.
Discussion Taken from

[Image of book cover: "legally poisoned: How the Law Puts Us at Risk from Toxicants" by Carl F. Cranor]
Generic Legal Strategies to Protect the Public Health

**Postmarket laws**
Substances enter commerce with *no routine legally required testing or approval (90-80%)*

**Premarket laws**
Pre-mkt *notification laws* (1979)
No required toxicity data; only submission of what is known

Pre-mkt *testing and approval laws* legally require *routine toxicity testing & agency approval*, for drugs, pesticides, new food additives (~10-20%).

Endocrine disrupter Screening program
The U.S. and Most Countries Live in a Postmarket World

Postmarket contexts frame

- Responses to potentially toxic industrial chemicals
- Ideas about precautionary approaches, and
- Scientific research and risk assessment.
Research on the developmental origins of disease shows that *postmarket approaches* to environmental health problems are *reckless and pathetically inadequate to protect children (& population more generally)*!
The developmental origins of disease should force us to escape the paradigm of postmarket approaches.
The Developmental Basis of Disease

“*In utero* nutrition and/or *in utero* or neonatal exposures to environmental toxicants *alter susceptibility to disease later in life* [by affecting] the programming of tissue function that occurs during development.”

“[This] can . . . result in death, malformations, low birth weight or functional changes including increased susceptibility to diseases later in life.” (Heindel, 2008)
The Developmental Basis of Disease

- **Epigenetics:** “These toxicant-induced pathogenic responses are most likely the result of altered gene expression or altered protein regulation [not genomic sequencing] associated with altered cell production and cell differentiation that are involved in the interactions between cell types and the establishment of cell lineages.” (Heindel, 2008)

- In turn these “lead to altered [structural] and/or functional character of the tissues, organs and systems.” (Heindel, 2008)
Recent Science Shows the Inadequacy of Current Laws

- When we add the developmental basis of disease to the known contamination of citizens plus humans’ surprising permeability to toxicants this suggests a problem needing a legal and scientific paradigm change to address adequately.

- We cannot prevent contamination; we need to create legal institutions to prevent toxic contamination.
Contamination

- U.S. citizens are contaminated by up to 219 manmade substances, including pregnant women (PFCs, PBDEs, PCBs, organochlorine pesticides, phenols, phthalates, PAHs, and perchlorate); there will be more. Many are known toxicants. (CDC, 2009; Woodruff, et. al., 2011)

- Women’s contamination is shared with developing children *in utero*—the placenta is no significant barrier.

- Newborns can have up to 200 industrial chemicals in their bodies, some toxic. (Fimrite, 2009)
Contamination

- A significant proportion of children from poor sections of Minneapolis are concurrently contaminated with >75 substances or their metabolites: phthalates, metals [lead, mercury], organophosphate pesticides, organochlorine pesticides, PCBs, volatile organic compounds, cotinine, ETS. (Sexton... Needham, 2011)

- These include: known or suspected carcinogens, endocrine disrupters, neurotoxicants, and developmental and respiratory toxicants.
Women’s Chemical Burden is Shared with Developing Fetuses and Newborns

- 1965: The womb was seen as a time capsule, relatively impermeable to circulating drugs or toxicants. (Needleman & Bellinger, 1994)

- Contradicted by the social catastrophes of methylmercury (1950s-1960s), thalidomide (1960s), and DES (1971) showing in utero exposures can cause disease.

- Now much more evidence.
Early Catastrophes from *in utero* Contamination

**Methyl mercury** exposure *in utero* at Minimata, Japan, induced cerebral palsy as well as

- mental retardation
- limb deformities
- constricted visual field
- sensory disturbance
- ataxia (poor muscle control)
- auditory disturbance
- disturbance of gait
- death

- Cats having eaten contaminated fish “danced” strangely, jumped into the sea; birds fell from the sky. (Harada, 1995)

Sandra Bullock signs an autograph for Lisa Patrick, who suffers from Cerebral Palsy, and greets fans while at a red carpet premiere of her latest film, "The Blind Side," in New Orleans, Thursday, Nov. 19, 2009. AP Photo
Early Catastrophes from *in utero* Contamination

Thalidomide can induce
- shortened limbs,
- no ears, deafness [subsequent retardation],
- no or small eyeballs,
- spinal malformations,
- congenital heart disease,
- kidney abnormalities,
- obstetrical problems (e.g., double vaginas)
- central nervous system problems, but often normal mentality
- autism (30 x higher)
- epilepsy, learning disorders
- death
Early Catastrophes from *in utero* Contamination

Diethylstilbestrol (DES) induced vaginal/cervical cancer in daughters about 20 years after exposure; 20 years later they were at increased risk of breast cancer.

DES mothers were also at increased risk of breast cancer.

*Image description:*
- Cancerous growth
- Fallopian tube
- Ovary
- Uterus
- Cervix
- Vagina
- Cancer

Vaginal cancer is cancer that occurs in the vagina — the muscular tube that connects the uterus with the outer genitals. © Mayo Foundation for Medical Education and Research. All rights reserved.
Women’s Chemical Burden is Shared with Developing Fetuses and Newborns

- There is “no placental barrier per se: the vast majority of chemicals given the pregnant animal (or woman) reach the fetus in significant concentrations soon after administration.” (James Schardein, 2002)

- New technologies pose problems: **Plastic nanoparticles** can move from mom to baby through placenta. (29 March 2010, EHN.org)
Mother is the fetal incubator

Development is a genetic program

Development is an open system (developmental plasticity, ECO-DEVO)

1960s:
Perceived as comparatively impermeable (Needleman and Bellinger, 1995)

Toxicants

Light

Food

Hormones

Courtesy Ana Soto
Developing Children Have Greater Exposures

- They can be exposed to *larger doses of toxicants relative to the body weight* than the mother, via cord blood and breast milk. (Faroe’s Statement, 2007)
  - Mercury concentrations can be at least 5 times higher in fetal brain than in mother’s blood. (Honda, et. al., 2006)
  - Lead is mobilized as part of the “calcium stream” in pregnant women. (Bellinger & Needleman, 1994)
  - Lipophilic substances can be concentrated in cord blood and breast milk (PCBs up to 100 times greater). (Heinzow, et. al., 2007)
Once born children have

- **Higher metabolism, breathing, absorption, circulation rates.** (Miller, et. al.)

- **Higher fluid and food intake rates per body weight.** (Miller, et. al.)

- They play close to ground/floor, “mouth” everything, ingest more dust.
Developing Children Are More Susceptible

- In general, young children “tend to be more sensitive to adverse environmental influences. . . [with] tissues undergoing rapid cell division, and [having] much less capacity to metabolize [and detoxify] xenobiotics than [do adults].” (Hood, 2006)

- They have lesser defenses compared with adults (less developed immune system, blood brain barrier, liver, detoxifying enzymes). (Grandjean & Landrigan, 2006; Dietert & Piepenbrink, 2006; Dietert, et al., 2010)
Developing Children Are More Susceptible

- E.g., the **human brain** has windows of “unique susceptibility,” unlike adult brains--it must grow from a single cell into billions following “precise pathways” in the “correct sequence” to function properly. (Grandjean & Landrigan, 2006)

- The **immune system** is similarly susceptible; for both systems there seems to be “one chance to get it right.” (Dietert & Zelikoff, 2010)
Summary: Developing Children

- Have greater exposures.
- Are more susceptible to toxicants.
- Have lesser defenses.
- Have a longer lifespan for diseases to develop.
Genetic Variation Can Increase the Vulnerability

- Some developing children are more susceptible to **polycyclic aromatic hydrocarbons** (byproducts of combustion, e.g., tobacco smoke, urban smoke). (Perera, et. al.)

- Some are more susceptible to **organophosphate pesticides**. (Eskenazi, et. al., 2008)
Generalized Additive Effects Can Increase Vulnerability

- Substances can affect different “upstream” pathways producing jointly additive effects, but not affecting the same cellular receptors:

- Dioxin-like PCBs, non-dioxin-like PCBs, perchlorate, and brominated fire retardants (PBDEs), each operating by different pathways can reduce thyroid concentrations in pregnant women, potentially creating neurological risks to fetuses. (Woodruff, Zeise, et. al., 2008)
There are similar additive effects from exposures to different toxicants affecting the immune system: diazepam (Valium), diethylstilbestrol (DES) and PCBs.

(Luebke et al. (2006); Woodruff, et al., EHP, 2008)
Additive effects and Susceptibility Together Increase Vulnerability

(Woodruff, Zeise, et. al., 2008)
Effect of Sensitive Subpopulations On Shape of the Dose Response

Need for a Unified Approach for Linear and Non-linear Mechanisms of Toxicity

- “Background exposures and underlying disease processes contribute to population background risk and can lead to linearity at the population doses of concern. [Threshold models] do not quantify risk for different magnitudes of exposure but . . . provide a bright line between possible harm and safety; their use in risk-risk and risk-benefit comparisons and in risk-management decision-making is limited.

- Cancer risk assessments usually do not account for differences among humans in cancer susceptibility other than possible differences in early-life susceptibility. . . . Both threshold models and linear models of toxicity should be modified to take these points into account.” (NAS, 2008)
Particular Substances Pose Developmental Problems

- **Lead**—“Exposure to moderate levels of lead during childhood can permanently change important brain chemical levels later in life . . . [contributing to] lower IQs, violent behavior, motor skill problems and attention disorders [ADHD].” (Cecil, et. al., 4/18/11; Chen & Wessler, 2011)

- There appears to be no threshold for lead toxicity during development, early childhood, or even adulthood. (Lanphear, 2000, Canfield, 2003; Bellinger & Needleman 2003, Goyer & Clarkson, 2006; Weaver & Silberfeld, 2007)
Particular Substances Pose Developmental Problems

- Mutagenic carcinogens—appear to have no threshold for toxicity during development, early childhood, or even adulthood. (David Eastmond, UCR Environmental Toxicology)
Particular Substances Pose Developmental Problems

- Estrogen mimicking chemicals--bisphenol A and others-- may add to breast cancer rates. (Skinner, 2007, 2009; Soto, 2008)

Breast profile:
- A ducts
- B lobules
- C dilated section of duct to hold milk
- D nipple
- E fat
- F pectoralis major muscle
- G chest wall/rib cage

A normal duct cells
B ductal cancer cells
C basement membrane
D lumen (center of duct)

Particular Substances Pose Developmental Problems

- **Hormone mimicking chemicals:** possible increased prostate cancer among men, possible transgenerational effects on sperm (animal data). (Heindel, 2008; Skinner, 2007, 2009)

Particular Diseases are Exacerbated by Perinatal, and the Timing of, Exposures

- **E.g. Cancer:**
  - First trimester DES exposure caused vaginal/cervical cancer; and, later increased risk of breast cancer *(Schardein & Macina, 2007; Kortenkamp, 2008)*
  - Radiation and DDT exposure during puberty increases breast cancer vs. similar doses in older women. *(NAS 1990; Cohn, 2007).*
Particular Diseases are Exacerbated by Perinatal and the **Timing** of Exposures

- **E.g. Cancer:**
  - Most childhood cancers, e.g., acute lymphoblastic (ALL) and acute myeloid childhood leukemias (AML), **begin in the womb** (Smith, 2009; Greaves & Wiemels, 2003)
  - *In utero* exposures to pesticides are associated with ALL (11x) and with AML (14x). (Ross, *et. al.*, 1994)
  - **Paternal** exposure to solvents, plastics, petroleum products and lead, and **maternal** exposures to paints and pigments, metal dusts and sawdust also elevate risks. (Ross, *et. al.*, 1994)
Particular Diseases are Exacerbated by Perinatal and the **Timing** of Exposures

- E.g. childhood cancer:
  - The chromosomal translocations characteristic of AML or ALL are seen in a diseased child and in cord blood taken at birth.
  - This “backtracking” confirms the prenatal origins of the diseases. (Smith, 2009; Greaves & Wiemels, 2003)
  - The disease seems to require at least 2 genetic hits. (Greaves & Wiemels, 2003)
Particular Diseases are Exacerbated by Perinatal and the Timing of Exposures

- For at least one thalidomide baby a single dose from one 50 mg or 100 mg pill caused malformations.

- A single dose of valproic acid (anti-epileptic drug) in animal studies can cause autism-like behavior. (Dufour-Rainfray, et. al., 2011).

- A single dose of DES is sufficient to cause obesity in mice. (Vom Saal, 2011)
Particular Diseases are Exacerbated by Perinatal and the **Timing** of Exposures

- E.g. Cancer plus reproductive effects:
  - Prenatal exposure of rats to *some pesticides* and *bisphenol A* (individually) caused sperm damage, sterility, and a host of cancers in their offspring from wild types.
  - Other adverse effects: prostate disease, kidney disease, immune system abnormalities, testis abnormalities, and tumor development (e.g. breast).
  - These effects persisted through 4 generations (suggesting transgenerational toxic effects) (Anway, et al., 2006; Skinner, et al., 2007, 2009)
Particular Diseases are Exacerbated by Perinatal and the Timing of Exposures

- E.g. reproductive effects:
  - During gestation 3 pesticides (antiandrogens), each at concentrations below which it causes adverse effects, together produce adverse outcomes (producing “something” from “nothing”) (Kortenkamp, et. al., 2007)
  - Adverse male reproductive effects (feminization): hypospadias, anogenital distance, nipple retention.
  - Kortenkamp (2011): 30 of Europe’s highest use pesticides are anti-androgenic, potentially affecting men’s reproductive health (many previously unsuspected) (Kortenkamp, 2011)
Hypospadias
(Phthalates, various pesticides, BPA)

Urethra

Photographs courtesy Laurence Baskin, MD.
Anogenital Distance

Phthalates and some pesticides tend to feminize males leading to greater anatomical similarity, including retained nipples, reduced anogenital distance (Swan et. al., 2005, have human data on AGD).
Worse Effects in Children v. Adults at Same Dose


- Thalidomide and DES [human data].

- Pesticides, DES, BPA contribute to sperm damage and cancers in utero but not in adults to same extent [animal data].

- Infant exposure to immunotoxicants results in greater dose-sensitivity, greater severity of effects, wider and different range of effects, greater persistence of effects than adult exposure [animal data]. (Dietert, Piepenbrink, 2006)
Other Diseases Are Traceable to Early-Life Conditions/Exposures

- **Obesity:**
  - Nazi-created Dutch famine (1944-1945) increased obesity and metabolic syndrome among the affected cohort. (Hales & Barker, 2001)
  - Nutrition-deprived children *in utero* born into a nutrition-adequate world had elevated risks of metabolic syndrome.
  - Replicated in sheep experiments. (McMillan, et. al., 2008)
  - Too little nutrition *in utero*, even before pregnancy or too much can lead to metabolic syndrome. (McMillan, et. al., 2008)
Other Diseases Traceable to Early-Life Conditions/Exposures

- **Obesity and toxicants:**
  - Mice exposed *in utero* to quite low doses of DES, phytoestrogens, bisphenol A, tributyltin, benzo[a]pyrene become obese.

Obese Mouse; Normal Mouse

One gene methylated \textit{in utero} at one location (8ppb)

Same genes, same diet, same exercise, different \textit{in utero} exposures to synthetic estrogens.

Developmental exposure to BPA or DES
Results in Adult Obesity


Pictures sent by Fred VomSaal
Obese Mouse; Normal Mouse

One gene methylated in utero at one location (8ppb)

Same genome, same diet, same exercise, different in utero exposures to synthetic estrogens
Immune Dysfunctions Are Traceable to Early-Life Conditions:

- Some immunotoxicants: pesticides (chlordane and Diazepam), synthetic estrogens (DES, genistein, nonphenol, BPA, dioxin, tributyltins), lead, cigarette smoke, arsenic, and PCBs. (Dietert, Piepenbrink, 2006; Selgrade, 2007)

- Infant exposure appears to result in greater dose-sensitivity, greater severity of effects, wider and different range of effects, greater persistence of effects than adult exposure. (Dietert, Piepenbrink, 2006)
Hypothesis re: Early Immune System Dysfunctions May Signal Life-long Problems

Immune system patterns of disease:

An allergy-related disease patterns
- Atopic dermatitis
- Allergic rhinitis
- Lung cancer
- Overweight risk
- Otitis media
- Behavioral disorders
- Olfactory dysfunction
- Urinary incontinence
- Increased respiratory infections including influenza

An autoimmune-related disease patterns
- Autoimmune thyroiditis
- Celiac disease
- Atherosclerosis
- Depression
- Hearing loss
- Multiple sclerosis
- Sleep problems

Fig. 1. Two examples of patterns of immune-related diseases. Both an allergy-related example (left) and an autoimmune-related example (right) are presented. The primary pediatric-onset immune-related disease is indicated in the center of each pattern. Secondary diseases and conditions that may arise either simultaneously or later in life and are connected to the primary disease by elevated risk are shown via arrows.

(Dietert, Zellikoff, 2010)
Some Diseases Traceable to Early-Life Conditions/Exposures

- Neurological deficits and toxicants:
  - **Autism**: Valproic acid (anti-epileptic), ethanol (alcohol), thalidomide and misoprostol (for gastric ulcers) contribute to autism. (Dufour-Rainfray, et al, 2011)
  - **Autism**: also associated with freeway pollutants. (Volk, Hertz-Piciotto, 2010)

- In utero exposure to PCBs resulted in deficits in spatial reasoning, clumsy movement, lower IQ, attention deficit disorder (Birnbaum, 1998; Grandjean and Landrigan, 2007; Sagiv, et al. 2010)
“Bad Daddy” Factors
(Anthes, Miller-McCune, 2010)

- Toxic contamination of males:
  - Chemotherapeutic Agents: degrade quality of sperm, e.g., chromosome breaks, resulting in spontaneous abortion, abnormally slow growth.
  - Lead & mercury: miscarriages.
  - Pesticides: childhood leukemia.
  - Solvents, cleaning solutions, dyes, paints other chemicals: birth defects, childhood cancer. (Anthes, Miller-McCune, 2010)
“Bad Daddy” Factors
(Anthes, Miller-McCune, 2010)

- **Toxic contamination of males:**
  - **Paxil (an antidepressant):** 5-fold increase in sperm fragmentation increases chances of miscarriage.
  - **Lead:** Exposure of either parent can result in still births or other fetal problems.
  - **Anesthetic gases:** can increase miscarriages.
  - **Morphine:** can lead to profoundly abnormal, chronic late blooming, underweight offspring. (Anthes, Miller-McCune, 2010)
Experimental results:

Mice dosed *in utero* with the pesticide maneb alone (7 days) then in early adulthood dosed with paraquat (8 days) had 95% reduction in involuntary activity. Similar effects with analogous postnatal exposures.

Illustrates: silent toxicity, latency of the effects, decreased dopamine production and neurons, persistence of effects, and a two-hit model for causing PD. *Normal aging appears less of an effect.*

Maneb is an unrestricted fungicide and paraquat (restricted) is one of the most widely used herbicides in the world. (Barlow, et. al. 2007)
Parkinson’s: Human Data
(paraquat, maneb, organochlorine pesticides, TCE, lead, cocaine, bacteria)

Human data:

- **MPTP**: 5 “frozen addicts” from 26-42 years old (Langston, et. al., 1983; NOVA 1986).

- **Workers exposed to TCE** had PD or PD-like symptoms; replicated in animal studies. (Gash, et. al, 2008)

- **TCE exposure increases PD risk** nearly 6-fold (99 sets of twins--one with, one without TCE exposure). (Maugh, LA Times, February 7, 2010)

- **Excellent epi study** showing exposure to **paraquat** and **rotenone** (used because of mechanisms of action) contribute to Parkinson’s at consumer exposures (Tanner, et. al, 2011)
The evidentiary picture for the developmental basis of disease is something like a pointillist painting: parts of the picture filled with numerous data points, others partially filled, some blank, but the general background reasonably solid.

The end result is of considerable concern for children.

A Sunday Afternoon on the Island of La Grande Jatte, Georges Seurat
What Should Be Done?
Legal Failures

The U.S. legal system regulates the vast majority (80-90%) of chemical substances with postmarket laws: products are

- Permitted into commerce without any legally required premarket testing.
- And, remain in commerce until a public health agency
  - bears a legal and scientific burden of proof sufficiently strong to change the status quo to reduce exposures or remove them.
  - Typically an agency must show that they pose harm or risks of harm.
Legal Failures

Postmarket laws

- Permit, invite and encourage toxic ignorance.
- Make haphazard guinea pigs of adults and children alike.
- Create disincentives and barriers to better health protections.
- Increase our risks.
Toxic Ignorance

NRC Details:

- **12,860** substances produced in excess of one million lbs/yr (78% no toxicity data). Postmarket

- **13,911** chemicals < 1 million lbs/yr produced (76% no data). Postmarket

- **8,627** food additives (46% no data). Some postmarket

- **3,410** cosmetics (56% no data). Postmarket

- **3,350** pesticides (36% no data).

- **1,815** drugs (25% no data). (NRC, 1984)
Toxic Ignorance

- Of 62,000 industrial chemicals in commerce in 1979 the EPA has required post-market testing of 200 (.3 of 1%); it has “reviewed” 2% or 1200 of them.

- It has regulated 5 substances; the regulation of asbestos was largely vacated by a court. (GAO, 2009)
For new substances the EPA has “rarely” required any additional testing--must “issue a rule” or seek a court order for this. For about 10% EPA sought “voluntary” submission of additional toxicity data. (Guth, et. al., 2007)

About 20% of industrial chemicals in commerce are mutagens, thus about 75% are likely carcinogens, but simple Ames test was not required for them. (Zeiger & Margolin, 2000; Claxton, et. al., 2010)
Barriers to Protecting Citizens’ Health

Postmarket laws create barriers to remove toxicants and improve health protections:

- **Theory:** most postmarket laws permit the use of surrogates, e.g., animal studies, other non-human evidence to identify the risks before they cause actual human harm.

- However, agencies are pressured to show human harm and to substantiate claims with multiple sources of data and multiple studies.

- Health protections become slothfully mired in procrastination, obfuscation, and endless disputes--TCE (20+ years), dioxin (20+), perc (13+), formaldehyde (11+), naphthalene (9+) (GAO, 2005).
Legal Failures

Premarket testing and approval laws (e.g., for drugs and pesticides) are not free from critique:

- Some developmental effects of pharmaceuticals and pesticides have been missed, as history and Kortenkamp’s work shows.
- These will need improvement.
Generic Legal Strategies for Public Health Protections

**Postmarket laws**

Substances enter commerce with *no* required testing or approval (90-80%)

**Premarket laws**

Premkt *notification laws* (1979)

*No required testing; only submission of what is known*

Premkt *testing and approval laws* require testing & agency approval, for drugs, pesticides, new food additives (~10-20%).

**Endocrine disrupter Screening program**
Learning from Medical Testing

Ethical constraints on medical testing require *inter alia*:

- Prior preparations and reasonable assurances of safety.
- Careful assessment of safe exposures.
- Special concern for children; testing of children only if no other way to obtain data to benefit children.
- Independent scientific or ethical oversight.
- Concern for contaminated person is central.
Learning from Medical Testing

Ethical constraints on medical testing reveal shortcomings of postmarket laws that permit contamination of citizens without toxicity data:

- No prior preparations and reasonable assurances of safety.
- No careful assessment of safe exposures.
- No special concern for children.
- No independent scientific or ethical oversight.
- Concern for contaminated person is not central.
Failure to Observe Ethical Constraints on Toxic Exposures Resembles:

- **Battery**: If a person knowingly causes foreign substances to come in contact with a person without her consent in a manner she would reasonably regard as offensive, he has committed a battery against her. (*Mink v. U. of Chicago* (1978), a DES case), or

- **Trespass**: It is also “directed at the vindication of a right,” e.g., foreign substances entering property or one’s body without authorization or without permission.
Ethical constraints on medical experiments, premarket testing and review laws, plus data about contamination and susceptibility together provide good reasons for laws to permit industrial chemicals into market and citizen contamination *only if* there is

- *Prior testing* and reasonable *assurances of safety*

- *For all of us* but especially for *children* and others in sensitive life-stages.
What Should Be Done?

- Both pesticides and industrial chemicals can be ingested, inhaled, or absorbed through the skin.

- The pesticide laws seek to protect us from these sources of contamination; we need the same protections from industrial chemicals.
What Should Be Done?

"[I]t is neither practical nor desirable to attempt to test every chemical (or mixture) against every end point during a wide range of life stages.

The committee recommends toxicity screening of every agent for which there is a strong potential for human exposure.

A well-designed tiered strategy could help to set priorities among environmental agents for screening and could identify end points of mechanisms of action that would trigger more in-depth testing for various end points or in various life stages." (NAS, Toxicity Testing for Environmental Agents, 2007)
What Should Be Done?

- Diseases are expensive: $76.6 billion in 2008 for the portion of diseases attributable to lead poisoning, childhood cancer, asthma, intellectual disability, autism, attention deficit disorder (3.5% of all healthcare costs). (Trasande and Liu, *Health Affairs*, May 4, 2011).

- Toxicity testing seems reasonable: The 11-year cost to test and review 30,000 chemicals under REACH is about $5 billion, or less than 1 euro per European citizen per year for 11 years. (Ackerman, 2006)

- Premarket testing to reduce adverse health effects would be a bargain at twice that amount.
What Should Be Done?

- Look for clues of **additive effects** then test for them:
  - When they likely act via **similar receptors**, e.g., estrogenic compounds and dioxin-like compounds.
  - When they act via **similar mechanisms** (organophosphate pesticides inhibit cholinesterase)
  - When they affect different upstream pathways producing the **same adverse outcomes**, like planar and non-coplanar PCBs, PBDEs and perchlorate that affect the thyroid cycle.
Some Conclusions

- Molecular contamination is inevitable, unavoidable; no place to hide.
- Contamination by toxic molecules is the problem.
- The law permits toxic contamination; it can prevent it.
Some Conclusions

- We must determine the toxicity of molecules before the public and workforce are exposed; otherwise children and the rest of us become haphazard guinea pigs.

- We must implement defensible premarket toxicity testing and licensing laws for industrial chemicals.
Some Conclusions

- The best way to implement precautionary approaches—because of children’s susceptibility and our exquisite permeability to industrial chemicals and pesticides—is to prevent *in utero* and childhood contamination by toxicants.

- Postmarket efforts at precaution are pathetic by contrast (yet we may be forced to use them).
Some Conclusions

- Risk assessments and scientific research should occur during premarket assessment and evaluation of chemicals as with pharmaceuticals and pesticides. This will reduce time-consuming, science-intensive postmarket risk assessments (some will remain because toxicants will be missed).

- Scientists must reconceptualize how they approach the assessment of potential adverse health effects from industrial chemicals. They must imaginatively conduct research prior to exposure to prevent health problems from arising in the first place. Focus less on after the fact problem-solving.
HOW THE LAW PUTS US AT RISK FROM TOXICANTS

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4 Caveat Parens: A Nation at Risk from Contaminants
5 Reckless Nation: How Existing Laws Fail to Protect Children
6 A More Prudent Approach to Reduce Toxic Invasions
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Thank you