Testimony of

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Thank you for the opportunity to submit testimony to this Committee. My name is Ted Schettler and I am Science Director of the Science and Environmental Health Network (SEHN). SEHN is a not-for-profit organization working in collaboration with environmental and public health groups, health professionals, legal scholars, ethicists, government officials, legislators, and others seeking to protect public health and the environment for this and future generations.

I am a physician and also have training in public health, toxicology, epidemiology, and environmental medicine. I practiced medicine for more than 30 years. I served on the U. S. Environmental Protection Agency's (EPA) Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC) from 1996-1998 and the Endocrine Disruptor Methods Validation Subcommittee from 2001-2003. I also served on the National Academy of Sciences' committee on defining concerns associated with products of animal biotechnology.

The Vulnerability of Developing Children

From an extremely large body of scientific work we know that, compared to adults, developing children are uniquely susceptible to hazardous environmental exposures. Windows of vulnerability during *in utero* development, infancy, and childhood increase risks of some adverse health outcomes resulting from exposures, often with lifelong consequences. Among the better known examples, lead exposures that have minimal or no discernable impacts in adults can permanently alter brain development and function in a child. Similarly, fetal alcohol exposures can have lifelong impacts in children, while the same exposure in adults has only mild, transient effects.

Many of the reasons for this vulnerability are well understood and others are being worked out at the molecular, cellular, and tissue levels. During fetal, infant, and child development, cells rapidly divide, tissues and organs are formed, and signaling mechanisms, hormone levels, feedback loops, and their set points are established. Exposures to hazardous chemicals as well as other environmental influences may perturb these events through various mechanisms with long-term consequences.

It is also important to recognize the substantial and growing evidence showing that environmental exposures during development can increase the risk of chronic, degenerative diseases much later in life.[1] For example, life-long cumulative exposures to lead, including developmental exposures, increase the risk of cognitive decline and Parkinson's disease in people decades later. Animal studies show that early life exposure to certain pesticides seem to prime the brain, making it more susceptible to further exposures in adulthood, resulting in neurodegeneration in areas responsible for Parkinson's disease. Indeed, epidemiologic studies show an increased risk of Parkinson's disease in agricultural communities where pesticides are heavily used.[2,3] Thus, while protecting children, we are also lowering the risk of various diseases and disabilities much later in life.

Endocrine disruptors

One area of concern that I would like to highlight is the potential for some pesticides, metals, and various other industrial chemicals to disrupt the function of hormones and other chemical messengers that are vital to normal human development and function. These chemicals are known as endocrine disruptors.

An endocrine disruptor is "an exogenous agent or mixture of agents that interferes with or alters the synthesis, secretion, transport, metabolism, binding action, or elimination of hormones that are present in the body and are responsible for homeostasis, growth, neurological signaling, reproduction and developmental processes."[4] Endocrine disruptors interfere with the body's key signaling pathways and can cause harm, especially during fetal and early life development.

Endocrine disruptors gained increased public and scientific attention during the 1990s, although the capacity for certain industrial chemicals to mimic or otherwise interfere with hormone function was known at least as long ago as the 1930s. For example, in 1938, scientists showed that bisphenol A, a chemical used to make many consumer products today, has estrogen-like properties, although its molecular structure is quite different from naturally-occurring estrogen.[5] The use of this chemical is now so widespread that, according to the Centers for Disease Control and Prevention, 93% of all Americans have residues of bisphenol A in their urine.[6] Recent studies link bisphenol A levels to altered brain development, heart disease, and diabetes.[7] [8]

In the 1950s, 1960s, and early 1970s the potent synthetic estrogen, diethylstilbestrol was purposely given to many pregnant women with the unfounded promise that it would help to prevent miscarriages and promote healthier pregnancies. Tragically, fetal exposure to DES resulted in abnormalities of reproductive tract development in females and males and a sharply increased risk of reproductive tract cancers in women decades later.[9] [10] Thus, we learned through uncontrolled human experimentation that certain chemicals could profoundly alter development with consequences that were often not apparent at birth and might only become manifest decades later.

During the 1980s and 1990s exposures of wildlife to industrial chemicals and their health effects were increasingly reported in the scientific literature.[11] [12] Reproduction and development of birds, amphibians, reptiles, and mammals have been affected by exposure to endocrine disrupting chemicals.[13] Fish in numerous rivers, including the Potomac, have disrupted sexual development —specifically feminized male fish. When this finding was first noted in England in the 1990's,[14] it was considered unusual. It is now recognized as a widespread, pervasive phenomenon.

Based on findings in wildlife and laboratory animal studies, many scientists are concerned that in humans, the increasing incidence of cancer of the testis, prostate, and breast, birth defects of the male reproductive tract, lower sperm counts, behavioral disorders, diabetes, and a wide range of other abnormalities may result, at least in part, from exposures to endocrine disrupting chemicals.[15]

A recent report shedding new light on a puzzling observation that has baffled scientists for years is illustrative.[16] Many studies find a higher incidence of testicular cancer and male reproductive tract abnormalities in Danish men than in nearby Finland. Finnish boys have larger testes and higher sperm counts than Danish boys. Reasons for these differences have been unclear.

Recently, scientists analyzed the breast milk of 68 women from the two countries for 121 different chemicals and found significantly higher levels in the milk of the Danish women. The chemicals tested for included flame retardants, pesticides, phthalates, polychlorinated biphenyls, dioxins, and furans. These chemicals are commonly identified in biomonitoring studies around the world, including in the US. Their concentration in breast milk is a good indicator of fetal exposures during pregnancy. Clearly, this kind of study cannot definitively establish a causal relationship between the different levels of these industrial chemicals in mothers in Denmark and Finland and the patterns of male reproductive tract abnormalities in the two countries. But a causal relationship is entirely plausible, based on what we know about the effects of many of these chemicals in laboratory animal studies. Current environmental exposures also include hundreds if not thousands of chemicals that were not tested for in this study that may also be part of the problem.

Because of growing concern about endocrine disrupting chemicals, in 1996 the EPA created the Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC) in response to a Congressional mandate in the Food Quality Protection Act and authorization in the Safe Drinking Water Act Amendments of 1996.

These laws specified that EPA:

> "…develop a screening program, using appropriate validated test systems and other scientifically relevant information, to determine whether certain substances may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or other such endocrine effect as the Administrator may designate."

The laws required EPA to develop a screening program by August 1998, to implement the program by August 1999, and to report on the program's progress by August 2000. Unfortunately, EPA is now about a decade behind.

I served on the EDSTAC. The committee included representatives from industry, government, environmental and public health groups, and academia. We were charged with developing consensus-based recommendations for a screening program that would provide EPA the necessary information to make regulatory decisions about endocrine effects of chemicals.

The committee delivered a final report by the statutory deadline of August 1998.[17] It included a groundbreaking priority setting, screening and testing approach that encompasses the universe of chemicals in use today, evaluates a range of human health and ecological effects, and recommends a feasible, health-protective, approach. The committee:

- recognized that problems with endocrine disruption go beyond estrogen, and also called for screening of chemicals for interference with male androgens and thyroid hormone.
- recommended the use of new technologies to rapidly pre-screen numerous chemicals to see if they interact with hormone receptors *in vitro* (in the "test-tube"). The committee recommended that this technology be used to rapidly evaluate the ten thousand most widely-used chemicals within one year.

- recommended a computer-based tracking system allowing information about health effects and exposure to be collected in one place to facilitate prioritization. That database didn't exist then, and it doesn't exist today.
- urged EPA to accept nominations from the public of chemicals or *chemical mixtures* for expedited testing. This would allow workers, or impacted communities to press for more information about chemicals to which they are exposed.

Unfortunately, EPA missed deadline after deadline and became bogged down in an endless set of validation exercises that remain unfinished. Many of the recommendations were discarded. Finally, a decade late, EPA implemented an extremely scaled down version of the program when it issued the first test orders in October, 2009. Only 67 chemicals are on the list for this first round of screening – mostly pesticides, including a number of chemicals that are already well-known endocrine disruptors.[18] Meanwhile tens of thousands of chemicals in consumer products, food, water, and air have not been tested for endocrine disrupting properties.

In 2009 the Endocrine Society evaluated the science on endocrine disruptors and concluded:

> "The evidence for adverse reproductive outcomes (infertility, cancers, malformations) from exposure to endocrine disrupting chemicals is strong, and there is mounting evidence for effects on other endocrine systems, including thyroid, neuroendocrine, obesity and metabolism, and insulin and glucose homeostasis."[19]

The Endocrine Society is the premier professional organization devoted to research on hormones and the clinical practice of endocrinology. It is comprised of over 14,000 research scientists and physicians from over 100 countries. This statement has since been endorsed by the American Medical Association, which is joining the Endocrine Society in calling for decreased public exposure to endocrine disrupting chemicals. The American Chemical Society just issued a similar statement with additional recommendations for: "More rapid advancement of the congressionally-mandated effort by the EPA, called the Endocrine Disruptor Screening Program (EDSP)."[20]

As a result of EPA's failure to implement a strong endocrine disruptor screening program, the *Endocrine Disruption Prevention Act* was introduced in Congress in 2009. This act would authorize a new research program at the National Institute of Environmental Health Sciences (NIEHS) to identify endocrine disrupting chemicals, using the most current science. It would establish an independent panel of scientists to oversee research and develop a prioritized list of chemicals for investigation. If the panel determined that a chemical presented endocrine-disrupting concerns, it would compel the federal agencies with established regulatory authority to report to Congress and propose next steps within six months. NIEHS has the capacity to carry out such a research program if provided with appropriate resources. But EPA remains the regulatory authority responsible for protecting children from environmental threats.

I have focused here on endocrine disrupting chemicals, but my concerns about human exposures to industrial chemicals are not limited to those with endocrine disrupting properties. Well-known flaws in the Toxic Substances Control Act (TSCA) have allowed tens of thousands of untested industrial chemicals to stay on the market and new ones brought to market with limited or no

toxicity information. These include chemicals to which workers and people in the general population, including pregnant women and children, are regularly exposed.

The EPA Office of the Inspector General's (OIG) report, released in February, 2010, and previous GAO reports clearly describe these problems.[21] [22] Not only are basic safety data lacking, but whatever limited information is submitted to the agency is frequently accompanied by requests to protect it from public disclosure. The OIG report concludes that the agency's process is "predisposed to protect industry information rather than to provide public access to health and safety studies." Physicians and other health care professionals do not have access to the data they need in order to appropriately advise patients, and workers and communities remain ignorant of the potential hazards of the chemicals to which they may be exposed.

Meaningful TSCA reform is essential in order to protect developing children and people of all ages from the impacts of exposure to hazardous chemicals in consumer products, food, water, and air.

The impacts of industrial chemicals, including pesticides, on brain development and function

Another area of concern to bring to your attention is the failure of EPA to require adequate evaluation of the impacts of industrial chemicals, including pesticides, on brain development and function in children. Ample scientific evidence confirms the unique susceptibility of the developing brain to chemical exposures that can disrupt one or more of a number of biologic processes that must proceed in an orderly fashion as brain architecture and chemistry are established throughout pregnancy, infancy, and childhood.

Lead, mercury, polychlorinated biphenyls (PCBs), arsenic, ethyl alcohol, and toluene are recognized causes of neurodevelopmental disorders.[23] A large body of experimental and human epidemiologic evidence shows diverse, long-lasting impacts of these substances on the ability of children to learn, remember, pay attention, and behave appropriately. The effects can occur after relatively low-level exposures that have no discernable effects in adults.

Policies that reduce exposures to these substances have been successful. For example, the removal of lead from gasoline resulted in a sharp decline in average blood levels in children throughout the US. Even so, the economic consequences of lower IQ resulting from lead levels in children in the US today are conservatively estimated to be in excess of $40 billion annually.[24] That figure does not take into account costs to society incurred by responding to special educational needs and disruptive or criminal behavior.

Unfortunately, these well-studied substances are the exception. The large majority of industrial chemicals have never been evaluated for their potential impact on the developing brain of children. This is true even for those chemicals known to be toxic to the nervous system more generally.

Pesticides and organophosphates

Under the Federal Insecticide, Fungicide, and Rodenticide Act, the EPA has the authority to require pesticide registrants to provide data about the impacts of their chemicals on the developing brain. But these data are not part of the core requirement, and the agency may decide on a case-by-case basis whether to require their submission. Historically, the EPA has always been reluctant to exercise this authority, even when a food-use pesticide was known to have nervous system toxicity as the mechanism whereby it killed pests.

Organophosphates are a group of pesticides that are notorious nervous system toxicants. They disrupt nerve impulse transmission and can cause a plethora of symptoms. In the 1990s and early 2000s a delayed, slow trickle of developmental neurotoxicity data on various organophosphates was delivered to EPA by registrants after a data call-in. These data finally led to some restrictions, including a phase out of chlorpyrifos-containing products for home and garden use. Chlorpyrifos is among the organophosphate pesticides known to adversely impact the developing brain of children as well as laboratory animals.[25] But chlorpyrifos remains in widespread agricultural use in the US today.[26] About 8 million pounds are applied to US crops annually. Children in farming communities are regularly exposed to this and other organophosphate neurotoxins.[27] It is difficult to imagine the justification for continued use of chlorpyrifos in agriculture.

Methyl iodide

Recently, the EPA considered a registrant's application for the agricultural use of the fumigant methyl iodide (MeI). This chemical should have waved red flags within EPA, demanding neurodevelopmental toxicity testing before registration. Yet, EPA failed to require it and registered the chemical for use without knowing what it might do to the developing brain of a fetus, infant, or child.

MeI was developed as a substitute for methyl bromide, a fumigant that is supposed to be phased out under the Montreal Protocol because it depletes stratospheric ozone. MeI is an extremely toxic chemical that must be handled with extraordinary care in the laboratory setting. It is damaging to DNA, causing mutations, and is listed on the California Proposition 65 list as "known to the State of California to cause cancer." But, here I want to focus on impacts of MeI on the developing brain.

Methyl iodide is highly likely to be a developmental neurotoxicant, with long-lasting impacts on the brain of fetuses, infants, and young children at levels of exposure lower than those that cause damage to the adult brain. This concern is based on several lines of evidence:

Methyl iodide is a documented neurotoxicant. The Material Safety Data Sheet from Mallinkrodt-Baker Inc. (italics added) states[28] "DANGER! MAY BE FATAL IF SWALLOWED, INHALED OR ABSORBED THROUGH SKIN. *AFFECTS CENTRAL NERVOUS SYSTEM.* CAUSES IRRITATION TO SKIN, EYES AND RESPIRATORY TRACT.

U.S. EPA's own risk assessment begins the discussion of MeI (here called iodomethane) toxicity with the following statement (italics added):

> "The pattern of toxicity attributed to iodomethane exposure *via* the inhalation route includes developmental toxicity (manifested as fetal losses and decreased live births), histopathology findings (respiratory tract lesions and salivary gland squamous cell metaplasia), thyroid toxicity, *neurotoxicity* and generalized systemic toxic effects (body weight and body weight gain decreases). The critical effects of iodomethane exposure via the inhalation route are the fetal losses observed in two developmental toxicity studies in rabbits, the histopathological lesions reported in three studies, and *the neurotoxic effects (clonic convulsions, decreased body temperature and motor activity)* seen in the acute neurotoxicity study in rats." (U.S. EPA, Human Health Risk Assessment: Iodomethane, page 4)
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> and
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> "**Acute inhalation:** Three critical endpoints have been identified for this risk assessment: nasal histopathology in the subchronic inhalation toxicity study in rats, the fetal losses in the developmental toxicity study in rabbits, and *neurotoxicity in rats*." (U.S. EPA, Human Health Risk Assessment: Iodomethane, page 4)
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> and
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> "*In regards to the potential role of iodomethane as a neurotoxicant, the inhalation acute neurotoxicity study in rats revealed that iodomethane exposure elicited clonic convulsions (repetitive mouth and jaw movement), a 2-3^{o}C decrease in body temperature, and an 80% decrease in motor activity in the absence of neuropathology.*" (U.S. EPA, Human Health Risk Assessment: Iodomethane, page 13)

Reports of human exposure to MeI are published in the medical literature. Individuals who have been acutely exposed to sufficient levels of MeI, usually accidentally in an occupational setting, may develop "symptoms of irritability, headache diplopia, nystagmus, lethargy, somnolence, slurred speech, ataxia, dysmetria, and visual disturbances. Parkinsonism and cerebellar neurologic dysfunction are manifest. These symptoms may progress to paralysis, convulsions, coma, and death. If recovery occurs, the acute neurologic symptoms may recede over several weeks, giving way to late neuropsychiatric sequelae such as behavioral disturbances, and cognitive deficits, psychoses, and emotional lability." [29] [30]

The mechanism(s) by which MeI exerts its neurotoxic effects are not completely understood. However, it is clear that glutathione (GSH) depletion is an important contributor in the causal pathway leading to neurotoxicity. [31] Glutathione is a naturally-occurring antioxidant that enables the body to cope with toxic substances that cause oxidative stress. Several studies conclude that glutathione depletion alone leads to neurotoxicity. [32] [33] In these studies, depletion of glutathione prior to methyl iodide exposure enhanced neural cell damage and supplementation of glutathione prior to exposure was protective. The authors conclude that oxidative stress and associated mitochondrial damage are critical components of the neurotoxicity of MeI.

With the above in mind, it is worth noting that fetuses and infants normally have lower levels of glutathione in their tissues than young adults. [34] [35] [36] [37] (Glutathione levels also decline in older people. That is, general anti-oxidant capacity is diminished in the very young and the aged.) Children's exposures can also be predicted to be higher than adult's per pound of body weight because of higher respiration rates of the child relative to an adult. Lower baseline levels of

glutathione would be anticipated to increase susceptibility to a neurotoxicant like iodomethane whose mechanism of action depends, at least in part, on glutathione depletion. For that reason alone, it can be predicted that the developing brain is more vulnerable to MeI neurotoxicity than the fully developed adult brain. Beyond that, however, impacts of oxidative stress differ in the developing brain because of unique developmental events without counterparts in the adult.[38] Moreover, the results of impairment of developmental processes in the brain are typically long-lasting and often irreversible.

Despite all this, the EPA did not request a developmental neurotoxicity test for MeI, indicating in its response to 54 scientists who expressed their concerns that:

> "In the case of iodomethane, the thyroid-related effects are more sensitive (i.e., occur at lower exposure levels) than the neurotoxic effects seen in the data. Moreover, given the pivotal role that thyroid hormones play in the development of the nervous system, the Agency concluded that by regulating at an exposure level that would prevent perturbations in the thyroid hormone balance it would in turn be protective of potential effects on the developing nervous system. As a result, the Agency did not require the DNT since the point of departure use in the risk assessment is based on a more sensitive endpoint." (October 5, 2007 letter from Jim Gulliford to Professor Robert Bergman; UC Berkeley)

This rationale suggests that the agency believes either that: 1) thyroid toxicity is the only pathway available for developmental neurotoxicity for this chemical and if fetal thyroid toxicity is prevented, any and all developmental neurotoxicity will be prevented, or 2) neurodevelopmental impairment due to oxidative stress is a less sensitive endpoint than impairment due to thyroid hormone changes. Unfortunately, there is no basis for either of these conclusions.

The toxicological literature documents a variety of mechanisms by which neurodevelopmental toxicants may impart damage to the developing brain, most of them unrelated to the thyroid gland. (they include, but are not limited to, oxidative stress, nitrative stress, alteration in neurotransmitter levels, alterations of cell adhesion molecules, alterations in DNA synthesis) Some developmental neurotoxicants have multiple mechanisms of action. In a meeting report on alternatives to animal developmental neurotoxicity testing, the authors concluded:[39]

> ". . . because of the complexity of the developing brain, it is likely that there are many molecular mechanisms of developmental neurotoxicity, a conclusion borne out by mechanistic studies of neurodevelopmental diseases. However, significant advances in our understanding of the cellular and molecular mechanisms of neurodevelopment over the past 10 years have identified and characterized key cellular events that are critical to the formation of a functional nervous system. These include neural induction, precursor cell proliferation, pattern formation, cell migration, neuronal and glial differentiation, formation of axons and dendrites, axonal guidance and target recognition, cell survival and apoptosis, synapse formation and pruning, and neurotransmitter specification."

Recent work on the developmental neurotoxicity of organophosphate pesticides demonstrates that chlorpyrifos interferes with DNA synthesis in neuronal cells in the developing brain, leading to a number of adverse impacts.[40]

> "In animal studies or *in vitro* models of neurodevelopment, chlorpyrifos has direct and indirect effects on neural cell replication and differentiation, resulting in immediate and delayed-onset changes in synaptogenesis, neurotransmitter release, expression of neurotransmitter receptors, and intracellular signaling over and above the consequence of cholinesterase inhibition."

Moreover, Slotkin et al. have shown that impacts on DNA synthesis occur at levels of exposure that are insufficient to significantly alter neurotransmitter levels. Oxidative stress plays a role in these outcomes.[41] The point here is not to suggest that MeI should be compared to organophosphates. Rather, the point is that multiple mechanisms of developmental neurotoxicity have been documented, and protecting against one does not necessarily protect against others.

Nevertheless, in October, 2007 the EPA approved a time-limited conditional registration of MeI and extended that registration in 2008, without requiring neurodevelopmental toxicity testing. Subsequently, while considering registering MeI for use in California, the Department of Pesticide Regulation carried out its own risk assessment and sent it out for external review by a Scientific Review Committee (SRC). In its final report, when describing their process and conclusions, the SRC said:[42]

> "The comments provided by the farm workers made a particular impression on the SRC by providing a real world perspective specifically based on their experience with the analogous toxin, methyl bromide. From this testimony (predominantly from a group organized by growers), it was abundantly clear that respiratory protection, despite strict regulations on paper, is commonly inappropriate, inadequate, or inaccessible.
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> An equally important element in our review was the data that we would have wished to assess but that was insufficient or non-existent altogether. This palpable lack of sufficient data raises serious doubts about the adequacy of any risk assessment to fully estimate the risks that would be associated with the introduction of methyl iodide into the general environment.
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> The lacunae in our knowledge about methyl iodide are particularly wide and deep in relation to key aspects of its potential toxicity such as neuro- and other developmental effects, neuro-toxicity beyond the development stage (in particular, following chronic exposure), and mechanisms of carcinogenicity."

This is a description of the existing data gaps pertaining to this dangerous, highly toxic chemical. EPA had the authority to require neurodevelopmental testing before registration but didn't, despite concerns voiced by numerous scientists. EPA's rationale simply does not stand up to scrutiny.

Recommendations:

EPA should:

1. Move more quickly to implement the Endocrine Disruptor Screening Program for chemicals in consumer products, air, food, and water, using current, up-to-date scientific methods. Evaluation should include commonly encountered mixtures as identified in environmental media (air, water, food) and biomonitoring studies. If NIEHS becomes the institution in which the endocrine disrupting properties of chemicals are evaluated, EPA must then promptly respond to the findings with health protective interventions.
2. Require developmental neurotoxicity testing of MeI and suspend its registration until data gaps are filled and risks have been re-evaluated.
3. Routinely require neurodevelopmental toxicity testing of pesticides proposed for registration or continued use when they are known or suspected to be toxic to the nervous system.

Congress should pass comprehensive chemical regulatory policy reform. Effective reform should:

- **Immediately Initiate Action on the Worst Chemicals**: Persistent, bioaccumulative toxicants (PBTs) are uniquely hazardous. Any such chemical to which people could be exposed should be phased out of commerce.
- **Require Basic Information for All Chemicals**: Manufacturers should be required to provide basic information on the health hazards associated with their chemicals, how they are used, and the ways that the public or workers could be exposed.
- **Protect the Most Vulnerable:** Chemicals should be assessed against a health standard that explicitly requires protection of the most vulnerable subpopulations. That population is likely to include children, but it could also be workers, pregnant women, or another vulnerable group.
- **Use the Best Science and Methods**: The National Academy of Sciences' recommendations for reframing risk assessment at the EPA should be adopted. Regulators should expand development and use of information gleaned from "biomonitoring" for setting priorities.
- **Hold Industry Responsible for Demonstrating Chemical Safety**: Chemical manufacturers should be responsible for evaluating and demonstrating the safety of their products.
- **Ensure Environmental Justice**: Effective reform should contribute substantially to reducing the disproportionate burden of toxic chemical exposure placed on people of color, low-income people, and indigenous communities.
- **Enhance Government Coordination**: The EPA should work effectively with other agencies such as the Food and Drug Administration that have jurisdiction over some chemical exposures. The ability of the states to enact stricter chemical policies should be maintained and state/federal cooperation on chemical safety encouraged.
- **Promote Safer Alternatives**: There should be national support for basic and applied research into green chemistry and engineering, and policies should favor chemicals and products that are benign over those that are hazardous.
- **Ensure the Right to Know**: The public, workers, and the marketplace should have full access to chemical safety data and information about the way in which government safety decisions are made.

Congress should also adopt legislation establishing the Endocrine Disruption Prevention Program so that 1) environmental chemicals can be screened for endocrine disrupting properties using the most current science in a timely manner and 2) regulatory agencies are obligated to take action to protect public health based on the best available science.

References

[1] Stein J, Schettler T, Rohrer B, Valenti M. Environmental Threats to Healthy Aging: with a closer look at Alzheimer's and Parkinson's diseases. Greater Boston Physicians for Social Responsibility and Science and Environmental Health Network. Available at www.agehealthy.org. Accessed March 13, 2010.
[2] Manthripragada A, Costello S, Cockburn M, et al. Paraoxonase 1, agricultural organophosphate exposure, and Parkinson disease. Epidemiology 2010. 21(1):87-94.
[3]Brown T, Rumsby P, Capleton A, et al. Pesticides and Parkinson's disease—is there a link? Environ Health Perspect. 2006. 114(2):156-164.
[4] Based on Kavlock RJ, Daston GP, et al. Research needs for the risk assessment of health and environmental effects of endocrine disruptors: A report of the U.S. EPA-sponsored workshop. Environ. Health Perspect. 1996. 104 Suppl 4:715-740.
[5] Vogel S. The Politics of Plastics: The making and unmaking of bisphenol A "safety". Amer J Public Health. 2009. 99(S3), S559-S566.
[6] Centers for Disease Control. National Report on Human Exposure to Environmental Chemicals. Available at http://www.cdc.gov/exposurereport/ Accessed March 13, 2010.
[7] National Toxicology Program. Centers for Evaluation of Risks to Human Reproduction. Bisphenol A. Available at http://cerhr.niehs.nih.gov/chemicals/bisphenol/bisphenol.html Accessed March 13, 2010.
[8]Lang I. Association of urinary bisphenol A concentration with medical disorders and laboratory abnormalities in adults. JAMA. 2008. 300(11):1303-10. Epub 2008 Sep 16.

[9] Palmer J, Herbst A, Noller K. Urogenital abnormalities in men exposed to diethylstilbestrol in utero: a cohort study. Environ Health. 2009. 18;8:37.
[10] Herbst A. The current status of the DES-exposed population. Obstet Gynecol Annu 1981: 10:267-278.
[11] Colborn T, vom Saal F, Soto A. Developmental effects of endocrine-disrupting chemicals in wildlife and humans. Environ Health Perspect. 1993. 101(5):378-384.
[12] National Research Council. Hormonally Active Agents in the Environment. Washington DC. National Academy Press. 1999.
[13] National Research Council. Hormonally Active Agents in the Environment. Washington DC. National Academy Press. 1999.
[14] Jobling S, Nolan M, Tyler CR, Brighty GC, Sumpter JP. Widespread sexual disruption in wild fish. Environ Sci Tech. 1998;32(17):2498–2506.
[15] Diamanti-Kandarakis E et al. 2009 Endocrine-Disrupting Chemicals: An Endocrine Society Scientific Statement. Endocrine Reviews 30(4):293-342. http://www.endo-society.org/journals/scientificstatements/upload/edc_scientific_statement.pdf (Accessed March 13, 2010).
[16]Krysiak-Baltyn K, Toppari J, Skakkebaek N, et al. Country-specific chemical signatures of persistent environmental compounds in breast milk. Intl J Androl. 2009. Sept 24. [Epub ahead of print]
[17] http://www.epa.gov/endo/pubs/edspoverview/finalrpt.htm (Accessed February 21, 2010).
[18] http://www.epa.gov/endo/pubs/edsp_orders_status_021610.pdf (Accessed February 21, 2010).
[19] Diamanti-Kandarakis E et al. 2009 Endocrine-Disrupting Chemicals: An Endocrine Society Scientific Statement. Endocrine Reviews 30(4):293-342. http://www.endo-society.org/journals/scientificstatements/upload/edc_scientific_statement.pdf (Accessed March 13, 2010).
[20]http://portal.acs.org/portal/PublicWebSite/policy/publicpolicies/promote/endocrinedisruptors/CNBP_023441 (Accessed February 22, 2010).
[21] EPA Office of the Inspector General. EPA Needs a Coordinated Plan to Oversee Its Toxic Substances Control Act Responsibilities. Report No. 10-P-0066 February 17, 2010. http://www.epa.gov/oig/reports/2010/20100217-10-P-0066.pdf (Accessed February 21, 2010).
[22] GAO report. Chemical Regulation. Options exist to improve EPA's ability to assess health risks and manage its chemical review. June, 2005. Available at http://www.gao.gov/new.items/d05458.pdf Accessed March 13, 2010.
[23] Grandjean P, Landrigan P, Developmental neurotoxicity of industrial chemicals. Lancet. 2006. 368(9553):2167-78
[24] Landrigan P, Schechter C, Lipton J, et al. Environmental pollutants and disease in American children: estimates of morbidity, mortality, and costs for lead poisoning, asthma, cancer, and developmental disabilities. Environ Health Perspect 2002. 110(7):721-728.
[25]Rauh V, Garfinkel R, Perera F, et al. Impact of prenatal chlorpyrifos exposure on neurodevelopment in the first 3 years of life among inner-city children. Pediatrics. 2006. 118(6):e1845-59.
[26] EPA. Chlorpyrifos summary document. Available at http://www.epa.gov/oppsrrd1/registration_review/chlorpyrifos/index.htm Accessed March 13, 2010.
[27] Pesticide Action Network. Airborne Pesticide Drift. Available at http://www.panna.org/drift/ Accessed March 13, 2010.
[28] http://www.jtbaker.com/msds/englishhtml/m5369.htm
[29] Schwartz M, Obamwonyi A, Thomas J, et al. Acute methyl iodide exposure with delayed neuropsychiatric sequelae: report of a case. Am J Ind Med. 2005. 47(6):550-446. .

[30] Hermouet C, Garnier R, Efthymiou M, Fournier P. Methyl iodide poisoning: report of two cases. Am J Ind Med. 1996. 30(6):759-764.
[31] Chamberlain M, Sturgess N, Lock E, Reed C. Methyl iodide toxicity in rat cerebellar granule cells in vitro: the role of glutathione. Toxicology. 1999. 139(1-2)27-37.
[32] Bonnefoi M. Mitochondrial glutathione and methyl iodide-induced neurotoxicity in primary neural cell cultures. Neurotoxicology. 1992. 13(2):401-412.
[33] Bonnefoi M, Davenport C, Morgan K. Metabolism and toxicity of methyl iodide in primary dissociated neural cell cultures. Neurotoxicology. 1991. 12(1):33-46.
[34] Lavoie J, Chessex P. Development of glutathione synthesis and gamma-glutamyltranspeptidase activities in tissues from newborn infants. Free Radic Biol Med. 1998. 24(6):994-1001.
[35] Lavoie J, Chessex P. Gender and maturation affect glutathione status in human neonatal tissues. Free Radic Biol Med. 1997. 23(4):648-57.
[36]Ergen-Inal M, Sunal E, Kanbak G. Age-related changes in the glutathione redox system. Cell Biochem Funct. 2002. 20(1):61-6.
[37] Hussain S, Ali S. Antioxidant enzymes. Developmental Profiles and their role in metal-induced oxidative stress. In: Handbook of developmental neurotoxicology. Eds: Slikker, Chang. Academic Press 1998.
[38]Haynes R, Baud O, Li J, Kinney H, Volpe J, Folkerth D. Oxidative and nitrative injury in periventricular leukomalacia: A review. Brain Pathol. 2005. 15(3):225-33.
[39] Lein P, Locke P, Goldberg A. Meeting Report: Alternatives for Developmental Neurotoxicity Testing, Environmental Health Perspectives, 2007: 115, 764–768.
[40] (a) Jameson R, Seidler F, Qiao D, Slotkin T. Chlorpyrifos Affects Phenotypic Outcomes in a Model of Mammalian Neurodevelopment: Critical Stages Targeting Differentiation in PC12 Cells. Environ Health Perspect. 2006: 114, 667–672. (b) Slotkin T, Seidler F, Fumagalli F. Exposure to Organophosphates Reduces the Expression of Neurotrophic Factors in Neonatal Rat Brain Regions: Similarities and Differences in the Effects of Chlorpyrifos and Diazinon on the Fibroblast Growth Factor Superfamily. Environ Health Perspect., 2007: 115, 909–916.
[41] Slotkin T, Oliver C, Seidler F. Critical periods for the role of oxidative stress in the developmental neurotoxicity of chlorpyrifos and terbutaline, alone or in combination. Brain Res Dev Brain Res. 2005. 157(2):172-180.
[42] Report of the Scientific Review Committee on Methyl Iodide to the Department of Pesticide Regulation. Available at http://www.cdpr.ca.gov/docs/risk/mei/peer_review_report.pdf Accessed March 13, 2010.