Chemical Safety in a Vulnerable World

Chemicals and Children’s Health:
Submitted by: International Council of Chemical Associations

ROOM DOCUMENT

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The International Council of Chemical Associations recognizes the importance of healthy children in assuring a sustainable and productive future for the world. The IFCS plays an important role in addressing the contribution of chemical safety in securing and maintaining the health of children. Industry is a critical partner in this effort, and we are pleased to participate in the Forum IV discussions on this issue. The products of chemistry are essential to solving some of the most serious threats that children face globally and the industry has an interest in, and the expertise to implement, the sound management of chemicals so that they do not cause harm to children. Working together, industry and the global community can make considerable progress in addressing common concerns.

The products of chemistry are essential components for nearly all of the products and services that improve our lives -- making life easier, safer, healthier, more secure, more comfortable and more fun. Chemistry assures a safe food supply by enabling crop protection, food preservation, refrigeration, transport and sanitary food handling. Chemistry is necessary to assure safe sources of drinking water. It helps create our homes with building supplies, safe water transport, furnishings and bedding. It is essential to the paints, papers and fabrics that color our lives. Of course, chemistry is essential to medicine and health care. The list is nearly limitless. Yet, with the benefits of chemistry come potential risks. The chemical industry appreciates the need to understand what those risks might be and to manage them. This is particularly true with respect to the potential for adverse effects on children’s health.

The scientific issues presented by the effects of chemicals on children’s health are complex. How and when might children be differently affected by exposures, or exposed differently, to chemicals? Are the existing testing and assessment methodologies scientifically sound and adequate to yield a satisfactory picture of the potential effects on children? How do we make sure children are adequately protected? The attached paper prepared by Dr. Laura Plunkett, contains a discussion of some of those issues. The current practices of toxicological evaluation and scientific risk assessment provide many answers to these questions. Yet as knowledge about children’s health, biological systems and environmental factors associated with maintenance of health and the onset of disease processes continues to expand in both the scientific and medical communities, there are many avenues for further research. Clearly, we need to undertake more research and explore new testing and evaluation paradigms, such as the tiered approach that also incorporates lifestage exposure information now being piloted by US EPA.

Actions identified in the Forum IV Decision Document: Protecting Children From Harmful Chemical Exposures can help lead to constructive actions to address these issues and to more effective protection of children’s health. ICCA supports those action items, and in particular it endorses as critical actions the following:

- Identifying the most serious problems facing children on a national basis and targeting actions to address those problems.
- Developing mechanisms to facilitate international collaboration on research into the potential effects of chemicals and the environment on children.
- Sharing information about effective strategies for protecting children, including building the capacity to assess risks to children effectively and efficiently.

The chemical industry represented by ICCA is committed to working towards a safer world for all children. The official views of ICCA on this issue, which follow, reflect a
commitment to develop an understanding of the potential effects of chemicals on children and to work collaboratively to address all threats to children’s health.

**Perspective of the International Council of Chemical Associations on Children’s Health**

Protecting children is a shared societal value. The United Nations states that “Today people live longer and healthier lives than any generation in history.”

“Modern medicine and better living conditions have dramatically lowered the global death rate, especially for infants and children. Since 1950, average life expectancy has risen from 46 to 66 years.”

To ensure this positive trend is sustained, especially for those potentially sensitive subpopulations such as children, will require a continued commitment by all of society. The International Council of Chemical Associations (ICCA) and its industry members are committed to this effort.

While great progress in enhancing the well being of children has been made, many real risks remain. Society recognizes the substantial risks to children from well-known sources such as poverty, inadequate nutrition, infectious diseases, accidents, violence, and tobacco use. More recently, concern has been expressed about the possibility of risks to children’s health arising from chemicals in products and in the environment. ICCA understands that more work is needed to understand risks from such exposures. ICCA believes history clearly demonstrates that advances in chemistry and allied technologies have played a critical role in improving the lives of children around the world. At the same time, we recognize that more work is needed to understand the potential risks to children’s health arising from exposures to chemicals in products and the environment. We believe that progress in the scientific and medical understanding of these potential risks will continue at an even faster pace and that industry has a responsibility to be involved -- playing an active role in responding to these concerns and to improving children’s lives.

As with other health and environmental issues, the industry approaches its role in the children’s health issue within the framework of the Responsible Care® initiative, which is a condition of membership in the ICCA associations. Responsible Care® represents a commitment to make continuous progress toward a shared vision of no accidents, injuries or harm to the environment, and in doing so, to operate ethically to the benefit of society, the economy and the environment. Responsible Care® has an internationally recognized track record of sustained health, safety and environmental performance improvement and can provide a basis for further contributing to our industry’s role in protecting children’s health.

Industry believes that improvements in children’s health can be best accomplished through concerted public and private strategies that:

- Focus research and chemical evaluation programs on answering questions about any unique susceptibilities and potential disproportionate exposures of children to natural and synthetic substances.

- Begin with an appreciation of the most serious risks to children while focusing on an understanding of any linkages between environmental contaminants and other environmental factors. Society must prioritize resources on those issues of greatest concern to children’s health.

- Rely upon scientific knowledge as the foundation for risk-based decision-making by government, industry and other stakeholders, taking into account the precautionary approach as set out in Principle 15 of the Rio Declaration.

- Encourage cooperative efforts among those who play critical roles in child health and safety protection by providing relevant and understandable information to policy makers, parents and concerned citizens, health care providers and businesses.

- Build on existing research and testing programs to ensure global harmonization and mutual acceptance and availability of data to improve and hasten decision-making.

Consistent with its Responsible Care® initiative, the global chemical industry, working with governments and other stakeholders, has major initiatives underway that put these principles into practice. For example:
• The ICCA recognizes that in addition to factors such as nutrition, hygiene, and infectious diseases, chemicals in the environment may affect children in a different way than adults. Those differences may occur because of differences in the physiology of children as well as differences in diet and activity patterns. Understanding those differences and how chemicals might uniquely affect children is important to society. To that end, the chemical industry has committed to support a global Long-Range Research Initiative\textsuperscript{v}, a key focus of which is an understanding of factors that may make certain groups, including children, more vulnerable than others.

• The chemical industry is committed to producing safe and beneficial products. Building a scientifically credible database for governmental decision-making about our products related to children’s health is critical. As part of their ongoing commitment to product stewardship under Responsible Care®, industry members have volunteered to participate in a U.S. Environmental Protection Agency “pilot” initiative designed to assess the feasibility and usefulness of a tiered approach for evaluating exposure and testing chemicals for potential effects on children. The overall goal of this “pilot” initiative is to determine whether the existing databases for a selected set of chemicals are sufficient or whether there is a need for further testing.

• The chemical industry is committed to learn more about the role of chemical environmental exposures and their potential link to adverse health trends. With this in mind, a European led initiative is underway to produce a global ‘state of the science’ report that will assess current scientific knowledge on the potential impact of environmental chemicals on children’s health and health trends. The goal is to identify the knowledge gaps and construct a targeted research program to help provide industry and regulators with the information they need to make sound policy decisions, in light of European regulatory change.

Together, policy makers, industry, children’s advocates, the medical and scientific communities and the public need to work in partnership to ensure that the greatest threats to children’s health and safety are identified and addressed in a timely fashion. The ICCA and industry members are committed to making positive contributions to this effort.

\textsuperscript{i} The International Council of Chemical Associations (ICCA) is an organization of leading trade associations representing almost 80% of chemical manufacturers worldwide. ICCA members include: Conselho das Associacões da Indústria Química do Mercosul (CIQUIM) [representing Argentina and Brazil], the European Chemical Industry Council (CEFIC), the Japan Chemical Industry Association (JCIA), Asociación Nacional de la Industria Química (ANIQ) [representing Mexico], the American Chemistry Council [representing the USA], the New Zealand Chemical Industry Council (NZCIC), the Plastics and Chemical Industry Association (PACIA) [representing Australia] and the World Chlorine Council [representing the global business of chlorine chemistry]. The ICCA provides forum to discuss policy issues of international interest to the chemical industry, including health, safety, and the environment, and trade policy, among others.

\textsuperscript{ii} Remark attributed to Dr. Nafis Sadik, Executive Director of the United Nations Population Fund cited in the Canadian International Development Agency web site discussing population. See www.acdi-cida.gc.ca/cida_ind.nsf


\textsuperscript{iv} The 1992 Rio Declaration on Environment and Development contains the statement of Precautionary Approach, “where there are threats of serious or irreversible damage, lack of full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent environmental degradation.

\textsuperscript{v} The ICCA Long-Range Research Initiative (LRI) is a globally coordinated investment by the chemical industry to sponsor research to expand scientific knowledge of the potential impacts that chemicals may have on the health of human and wild life populations and the environment. The LRI sponsors projects at leading research institutes, government agencies, academic institutes, and independent research organizations and makes award decisions based on highest scientific merit and relevance to the program’s mission and objectives through a competitive Request for Proposal’s (RFP) process. The LRI embodies the industry’s commitment to Responsible Care® - the chemical industry’s global initiative to improve environment, health, and safety.
CHILDREN AND CHEMICAL SAFETY AND RISK ASSESSMENT

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I. Introduction

Protecting the health of our children is an important and necessary goal for countries worldwide. From the outset and contrary to the claims of some, it should be recognized that scientists (i.e., toxicologists, biologists, physicians, risk assessors) have focused on the issue of children’s health for decades and have recognized children as a potentially vulnerable subgroup in their assessments of the toxicity of natural and synthetic chemicals, where children have represented just one of the sensitive groups considered. In discussing the risks to children posed by exposure to chemicals in the environment, however, it is critical to put the discussion in context with the current state of knowledge surrounding children’s health, including all of the potential risks (e.g., malnutrition, poverty, disease, exploitation through child labor, etc.) before generalizing about the risks posed by one potential source, chemical exposure. It is also important to remember that age is only one of the biologic variables that can affect the response of an individual to a chemical, with the others being sex, race, genetics, diet, concurrent disease states, and concurrent exposures, each of which can alone modify the likelihood of toxicity, regardless of the age of the individual.

II. Biological Considerations Unique to Children in Chemical Risk Assessment

It is well documented and generally understood that there are differences in the basic biology, physiology and behavior of children as compared to adults. Because of these well known scientific facts, there has been a great deal of interest in defining how these differences in biology and behavior might affect the risks posed to children by unintended chemical exposures in their environments. It is important to specify “unintended” exposure since there are intended and necessary uses of chemicals that are protective of child health (e.g., water purification, pharmaceuticals used to treat disease, etc.). The key issue for risk assessors in the context of children is determining whether children may be disproportionately impacted and thus at greater risk compared to other age groups or populations of concern. In other words, how important is age as a determinant in predicting risks posed by chemicals?

Although it is often true that developing organisms can be more sensitive to chemical exposures than an adult, this is not a universal axiom. It is also true that children are not “little adults” in terms of their responses to chemicals and their exposure

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to chemicals (Guzelian et al. 1992. *Similarities and Differences Between Children and Adults: Implications for Risk Assessment*. ILSI Press, Washington, DC.). Fetuses, infants and children are growing and developing and thus their metabolic rates are more rapid than that of adults. The ability of a child to activate, detoxify and excrete chemicals is different as compared to adults (National Research Council. 1993. *Pesticides in the Diets of Infants and Children*. National Academy Press: Washington, DC). The scientific literature shows that children may be more sensitive, equally sensitive or less sensitive to effects from chemical exposures than adults (Guzelian *et al.* 1992. *Similarities and Differences Between Children and Adults: Implications for Risk Assessment*. ILSI Press, Washington, DC.; Schuplein *et al.* 2002. *Reg Toxicol Pharm* 35: 429-447). However, there is no simple way to predict whether children are at increased risk for chemical toxicity.

Additionally, age is only one of the factors that can lead to susceptibility of an individual to chemical exposure and in some cases may not be the most important factor. Therefore, it is generally accepted that each chemical must be considered on a case-by-case basis in order to determine if fetuses, infants and children would be considered at less risk, at the same risk, or at greater risk when exposed to a particular chemical as compared to an adult. For example, if a chemical being considered in a risk assessment requires activation by metabolic enzymes in order to produce the active chemical toxicant, and those enzymes are not present in the developing or young individual, as is true of many enzyme systems (Calabrese E.J. 1986. *Age and Susceptibility to Toxic Substances*. John Wiley & Sons: New York), then that chemical will likely produce less toxicity in the individual when exposed as an infant or young child. An example of this is the decreased toxicity of ethylene dibromide in children due to decreased ability of infants and young children to activate the chemical to produce the ultimate toxic molecule. In another case, however, if a chemical is rapidly detoxified by enzymes in the human body and those enzymes are not present or are less active in an infant or child, then the chemical might produce greater levels of toxicity in the infant or child. An example of this is acetaminophen, where conjugation with glutathione, an event that deactivates the chemical, is reduced in infants and young children (Spielberg, S.P. 1992. In: *Similarities and Differences Between Children and Adults: Implications for Risk Assessment*, Guzelian *et al.* (eds.) ILSI Press: Washington, D.C., pp. 16-23).

Of even greater impact than age when considering any particular chemical, however, may be the role of genetics. It is well-established that genetics influence the basic biological responses of any given individual (Spielberg, S.P. 1992. In: *Similarities and Differences Between Children and Adults: Implications for Risk Assessment*, Guzelian *et al.* (eds.) ILSI Press: Washington, D.C., pp. 16-23). An example would be the evidence that has been accumulated on the etiology of asthma. There is clear evidence that both genetics and the environment can be important factors in development of asthma from studies in twins where identical twins were more affected than fraternal twins (Sarafino, E.P. and J. Goldberg. 1995. *Arch. Dis. Child.* 73:112-116). Considerations of genetic differences among individuals in a population, however, are almost impossible to incorporate into risk assessment strategies and are instead accounted for by employing safety factors, as discussed in the next section.

Ethnic or cultural differences among populations can also be an important factor that influences day-to-day behaviors in children as well as adults. Such behavioral differences among populations may be the most important consideration for a particular chemical, an example being exposure to air pollutants due to cooking on wood-burning stoves or propane fueled stoves without proper ventilation. Thus, genetics and cultural
factors must be considered simultaneously in order to properly understand the risks posed to children’s health by any environmental condition or chemical.

As a result, chemical risk assessment for industrial chemicals has developed toxicity testing strategies designed to consider the unique properties of that particular chemical. The approach of toxicologists and scientists involved in chemical risk assessment around the world has been to consider the unique properties of a chemical when designing toxicity testing and when assessing potential human health risks. Research efforts on children’s health and chemical exposure should be focused on understanding the unique properties of a particular chemical that might affect the response of humans, properties that would include the extent of human exposure in the environment, the degradation of that chemical both in the environment before it enters the human body and once inside the human body, consideration of humans of all ages and backgrounds (e.g., age, ethnicity, sex), and the expected toxicity of the chemical.

There are situations where the behavior patterns of children alone would lead to a prediction that exposure to a particular chemical might be of greater concern for children as opposed to adults. This is because a child’s exposure may be disproportionate compared to an adult. For example, intake of food, water, or air, the most likely routes of chemical exposure for a child, is higher on a unit of body weight basis in children than in adults (USEPA. 1997. Exposure Factors Handbook. EPA/600/P-95/002F). This intake is higher because children engage in activities such as crawling, frequent mouthing of objects, and in general have an increased level of hand-to-mouth activity. Because of these behaviors, as well as their smaller body size, children are often exposed to more of any given chemical on a day-to-day basis. It must be remembered, however, that exposure to a chemical must be considered in terms of its level before any conclusions regarding health risks can be made. This is because it is generally accepted by the scientific community that there are thresholds for effects of chemicals (Eaton, D.L. and C.D. Klaassen. 2001. Principles of toxicology. In: Casarett & Doull’s Toxicology: The Basic Science of Poisons, C.D. Klaassen (ed.), pages 13-15). A “threshold” is a level that must be reached before biological effects will be seen. In other words, in order for a chemical to produce any effect it must be present in the body at a level sufficient enough and for a long enough period of time to elicit that effect. If exposure to any chemical is too low or for too short a period of time, it will not produce biological activity. Yet, as discussed above, intake level of a chemical alone is not the only consideration when predicting whether children are at greater risk when exposed to chemicals. Biological differences in metabolism alone between children and adults could, in some cases, result in no difference in toxicity. Clearly, when defining risks posed by chemicals in the environment, it is not acceptable to always generalize that children are at greater risk than adults. Research needs to consider all aspects of human biology that can affect the response of humans to chemical exposures.

III. Do Current Chemical Risk Assessment Methods Adequately Consider Children as a Potentially Vulnerable Population?

Contrary to suggestions that have appeared in the popular and scientific press, current toxicity testing paradigms for drugs, food, pesticides, industrial chemicals and even medical devices provide important and useful information relevant to assessing risks to infants and children, as well as the developing fetus. The battery of tests performed for these types of products include evaluations of acute, subchronic and chronic toxicity, as well as genotoxicity, reproductive toxicity, and developmental toxicity (for example, the OECD SIDS program guidelines:
It is a general principle of toxicology and risk assessment that results of toxicity test batteries in animals are predictive of effects expected in humans of all ages (Faustman, EM and Omenn, GS. 2001. Risk Assessment. In: C.D. Klaassen (ed.), Casarett & Doull’s Toxicology: The Basic Science of Poisons, 6th edition, pp. 83-101, McGraw-Hill, New York, NY. Faustman and Omenn 2001). In fact, currently employed risk assessment methods for chemicals assume that vulnerable subgroups, such as children, are protected when risk assessments are performed based on standard toxicity tests (Renwick, AG and Lazarus, NR. 1998. Regul Toxicol Pharm 27: 3-20). Factors such as genetics, gender, ethnicity, nutritional status and behavior or lifestyle all contribute to the differences seen in responses to chemicals among individuals (Pastino et al. 2000. Environ Health Perspect 108:201-214.). Thus, the standard of practice in science is to employ toxicity tests in laboratory animals to identify target sites of toxicity and dose-response information for hazard assessment. These tests will provide vital information to risk assessors on the potential risks to humans of all ages and backgrounds. It should also be remembered that as scientific developments lead to identification of new test designs that might be useful in identifying critical effects of chemical exposure, these designs are incorporated into test batteries and become part of the standard of practice for toxicologists.

Once toxicity testing has identified effect levels or hazard levels for particular chemicals in animals, uncertainty factors (sometimes referred to as safety factors), modifying factors, or modeling are used to extrapolate from responses in laboratory animals to responses expected in humans (Faustman, E.M. and G.S. Omen, 2001. Risk Assessment. In: C.D. Klaassen (ed.), Casarett & Doull’s Toxicology: The Basic Science of Poisons, 6th edition, pp. 83-101, McGraw-Hill, New York, NY). These factors are designed to span the breadth of vulnerability in the human population. The most common application of such safety factors is a factor of 10 to account for intra-species variability (variability between and among humans, e.g., influenced by genetics) followed by another factor of 10 to account for inter-species extrapolation (animal to human). The logic behind use of such safety factors, and the use of more than one safety factor in almost every case has been to assure that all vulnerable subgroups, including children, will be protected. Application of safety factors, therefore, has been used for decades by toxicologists and risk assessors as the method to address the issue of protection of children when interpreting animal toxicity data and applying their results to human populations. Furthermore, Dourson et al. (2002. Reg Toxicol Pharm 35: 448-467) conclude that, taking into account relative sensitivities of adults and children and the types and the scope of toxicity test protocols that substances are subjected to, that additional uncertainty factors, over and above those traditionally used (i.e., a factor of 100), are generally not supported. Thus, with the requirement to apply uncertainty or safety factors when extrapolating data from animals to humans, children as a population are considered and likely protected, as are other vulnerable subgroups (Schneider K, Gerdes H, Hassauer M, Oltmanns J, Schulze J (2002) Consideration of children as a risk group in the derivation of health-based environmental standards. Report no. UBA-FB. Forschungs-und Beratungsinstitut Gefahrstoffe. Freiburg; EC/European Commission (2000) First Report on the Harmonisation of Risk Assessment Procedures; Part 1, Health & Consumer Protection Directorate -General).

It must also be remembered that the endpoints examined in standard toxicity tests are numerous and involve all of the major organ systems, both acute and repeated exposures, and animals of different ages. The battery of standard toxicity testing of the
type that is routinely performed for safety testing of chemicals in commerce around the world specifically includes evaluation of exposures of the fetus during gestation and, in the reproduction toxicity tests, evaluation of the postnatal developing organism. These endpoints are particularly relevant for assessing potential hazards to children because the exposure periods evaluated are those associated with critical windows of developmental sensitivity. (See OECD SIDS guideline testing at 
http://www.oecd.org/document/7/0,2340,en_2649_34379_1947463_1_1_1_1,00.html
and http://www.oecd.org/dataoecd/39/59/1840221.pdf.) While this battery defines the core screening tests, in many cases the toxicity information data base for industrial chemicals that would have potential impacts on children’s health (e.g., pesticides) is much more extensive, and includes studies in multiple species and more complex toxicity studies, such as chronic toxicity/carcinogenicity testing in rodents (for example, see any of the toxicity profiles prepared by the Agency for Toxic Substances and Diseases Registry, ATSDR; http://www.atsdr.cdc.gov/toxpro2.html). Controlled toxicology studies in laboratory animals provide a sound scientific basis for establishing causal relationships between exposure to an agent and various forms of toxicity. It is important for non-toxicologists to realize that results from toxicity testing in animals of all ages (i.e., animals exposed in utero, postnatally and as adults) is integrated into the risk assessment for any particular chemical, and is validly used by toxicologists to assess potential risks to vulnerable subgroups, including children.

While many seem to think that we are just discovering the issue, for some time now an important concern for scientists involved in assessing risks associated with exposure to chemicals in the environment has been chemical mixtures and the potential for the effects of mixtures of chemicals to produce either additive effects, antagonistic effects or synergistic effects. For more than a decade, the issue of chemical additivity has been employed in risk assessments in the United States (see for example the Risk Assessment Guidance Manual for Superfund, Volume 1, Human Health Evaluation Manual, Part A, 1989; http://www.epa.gov/superfund/programs/risk/ragsa/). It has been recognized that humans encounter an ever-changing combination of natural and synthetic chemicals in their environment. Although it is generally not anticipated that low-level environmental chemical exposure presents a particular health risk to humans of any age, scientists have increased their level of effort at understanding the toxicological properties of chemical mixtures.

Therefore, it is incorrect and without scientific basis to assert that the current knowledge concerning the toxicity of industrial chemicals that would be encountered in environments around the world is incapable of defining the potential risks to children. Further, current risk assessment strategies that are used by regulatory bodies around the world have always considered children as one of the many potentially vulnerable subgroups. As a result, risk-based decision making worldwide should continue to rely on the scientific knowledge currently available when making decisions about children’s health. At the same time, research programs should attempt to move towards global harmonization and mutual acceptance and availability of data collected under regulatory initiatives in order to ensure that all parties involved in promoting children’s health initiatives will understand the actual risks that might be posed by exposure to chemicals, as opposed to only the perceived risks. Examples of such science-based initiatives would be the current programs such as the U.S. EPA Voluntary Children’s Chemical Evaluation Program (VCCEP) pilot (http://www.epa.gov/chemrtk/vceep/) and the High Production Volume (HPV) Challenge program
IV. What Do We Know About the Major Risks to Children’s Health?

Although the preceding discussion has pointed out that predicting whether children will be more susceptible than adults to any given chemical exposure should be considered on a case-by-case basis, a situation that might suggest little is known about the risks posed to children by chemicals in the environment, there is actually a good deal of information available that allows one to quantify, at least in some degree of magnitude, the degree of risk posed to children by chemical exposures in general. Further, chemical contaminants in the environment should not be treated in isolation from other factors (e.g., malnutrition, poverty) if an effective strategy for protecting and improving public health, particularly children’s health, is desired. In other words, children’s health policies must take into account far more than exposures to chemical contaminants in the environment.

For example, consider what is known about childhood mortality. The U.S. Public Health Policy Advisory Board has attributed about 1% of childhood mortality to occupational and environmental toxins, while noting that their contribution to morbidity and mortality later in life is less clear (U.S. Public Health Policy Advisory Board. 1999. *Health and the American Child.* Washington, D.C. http://www.phpab.org/HealthandtheAmericanChild/phpab1.pdf). With respect to cancer deaths, the World Health Organization has indicated that air and water pollution and food contamination by chemicals can be linked to 2% of deaths worldwide, while infection has been linked to 10%, diet to 35% (malnutrition), and tobacco to 30% (WHO. 2002. *Main risks to children from exposure to environmental hazards.* Fact sheet at: http://org.eea.eu.int/documents/newsreleases/health). Thus, more than 50% of deaths in children worldwide can be attributed to malnutrition, infectious disease (e.g., malaria, vaccine-preventable diseases, diarrheal disease due to ingestion of unclean water, respiratory infection). Additionally, low birth weight continues to be an important determinant of infant mortality and morbidity. However, infant mortality rates, which may vary by country and region of the world, have consistently declined in virtually every region around the world, a finding that is consistent with the conclusion that children’s health is improving worldwide. Meanwhile, in nation after nation, the current generation outscores the last generation on average by some 9 to 20 IQ points, another observation that points to a generally positive influence of the current environment on intelligence (Dickens, W.T. and J.R. Flynn. 2001. *Psycholog. Rev.* 108:346-369). These types of statistics are evidence that factors other than chemicals in the environment are greater concerns for children’s health.

Therefore, when determining where effort is to be spent in order to improve and protect children’s health worldwide, it is not as simple as examining exposure to environmental chemicals alone. There can be valuable information collected by assessing patterns of disease (e.g., cancer rates and trends) and using such information for hypothesis based epidemiological studies. However, focusing on chemicals alone can lead to missed opportunities for improving children’s health. As illustrated by the scope of the prospective US National Children’s Study (NCS) (http://nationalchildrensstudy.gov/), it is necessary to consider a child’s environment in total. To address the totality of a child’s environment, the NCS has adopted a broad definition of environment, which includes natural and man-made environmental factors, biological and chemical factors, physical surroundings, social factors, behavioral
influences and outcomes, genetics, cultural and family influences and geographic locations. It is within such a context of understanding the whole of a child’s environment that ongoing and new research efforts to evaluate and improve children’s health has the highest likelihood of identifying real opportunities for public health authorities to initiate actions that yield demonstrable improvements in the quality of the lives of children across the globe.