Children's Health Protection Advisory Committee

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March 31, 2011

Lisa P. Jackson, Administrator
United States Environmental Protection Agency
1200 Pennsylvania Ave, NW
Washington, DC 20460

RE: Criteria for Identifying Chemicals of Concern for Children (including prenatal and preconception exposures)

Dear Administrator Jackson:

We appreciate your leadership in emphasizing children's health through actions taken by the U.S. Environmental Protection Agency (EPA), including those related to implementation of the Toxic Substances Control Act (TSCA).

The idea that children are not little adults and often have greater exposure and greater susceptibility to environmental hazards has been supported by considerable research. We now know much more about the significance of preconception and prenatal exposures for children. We also know more about the importance of early life exposure for the development of diseases in later life, with increasing evidence that exposure to chemicals during critical periods of growth and development can speed the onset and increase the risk of many diseases and disorders. Risks are also higher for children from communities that bear a disproportionate burden of ongoing and cumulative exposure to chemical contaminants as a result of proximity to hazardous sites and emissions. Actions to improve chemical safety for all children will move us closer to the goal of practices that are sustainable over the long term.

As requested by the EPA Office of Children's Health Protection, the Children's Health Protection Advisory Committee (CHPAC) has considered how EPA could identify chemicals that would be a high priority for actions available under TSCA, as well as other federal authorities, to protect children's health. We understand that such steps would build on EPA's actions to date, which include plans for specific chemicals, measures to improve public availability of TSCA inventory information, and restriction of unwarranted claims for confidential business information.

To respond to EPA's charge, we provide recommendations on:

- Actions that EPA can take to protect children's health, and
- Criteria for identifying chemicals of concern for children.

These criteria and recommendations are relevant to preconception, prenatal, perinatal, childhood and adolescent exposures, which may also be described as early life exposures. We note that EPA views childhood as a sequence of life stages from conception through fetal development, infancy, and adolescence, rather than considering children as a subpopulation.

Actions that EPA Can Take to Protect Children's Health

1. Partnerships

We are very encouraged by EPA's partnerships to address children's environments, particularly the work that EPA is doing with schools and communities on school siting criteria and with the Department of Housing and Urban Development and the Centers for Disease Control and Prevention on implementing policies for healthy housing.

Building on these successes, CHPAC recommends that EPA also engage with other federal agencies such as the Occupational Safety and Health Administration and National Institute of Occupational Safety and Health to prevent chemical exposures to parents that may have an impact on their children. Occupational conditions can contribute to preconception, prenatal, and lactational exposures of concern, as well as to "take home" exposures to children and adolescents, and to direct exposures of children working in agricultural, industrial, or other occupational settings.

Furthermore, consumer products designed for infants, children, adolescents, or pregnant women can be important sources of exposure to chemicals that pose hazards. CHPAC recommends that EPA engage with agencies responsible for such products, particularly the Food and Drug Administration and the Consumer Product Safety Commission, to develop and share information to reduce hazards.

Finally, CHPAC recommends that EPA explore how inter-agency partnerships could provide opportunities for sharing data relevant to the identification of harmful exposures and health effects to children. For example, the National Institute of Occupational Safety and Health has collected data pertinent to workplace exposures that may impact children's health. Ultimately these data can provide a foundation for a national data warehouse.

2. Community Exposures and Health Disparities

There are disparities in exposure and health for children from communities of color or lower socioeconomic status, and from tribal communities. There are multiple sources of exposure in these communities including industrial and agricultural sources, highly contaminated sites, and transportation. Moreover, while most children do not spend time at workplaces or industrial sites, millions of children do work in agricultural, industrial, and other occupational settings and so are not shielded from workplace exposures to chemicals. In addition, many adults who are or may become parents or caregivers have occupational exposures that may affect their children.

To reduce the burden on children in highly impacted communities, CHPAC recommends that EPA consider cumulative exposures and stressors such as socioeconomic and nutritional status, in addition to routine exposures to multiple chemicals in homes, child care centers,

schools, and playgrounds. CHPAC recommends that EPA consider whether TSCA action plans might focus on chemicals that contribute to disparities in a focused effort to prevent exposures, by removing toxic substances from highly impacted communities or other actions.

3. Safe Materials and Products

As a related measure, CHPAC recommends that EPA develop and implement methods to allow for the identification of products known to be safe for children. Such information would help builders, building managers, school districts, child care centers, educators, parents, and others to determine whether products and materials would pose hazards for children. This would be a logical extension of EPA's work to implement principles of green chemistry and to work toward materials that are benign by design.

4. Chemical Testing and Assessment

CHPAC recommends that EPA conduct a full review of the testing and assessment methods now in use and under development to ensure their capacity to detect effects of concern for children, including those that occur as a result of preconception and prenatal exposure. The timing of exposures is a key issue. As we have noted, there is substantial evidence that chemical exposure to parents before conception and exposure to children *in utero* can have detrimental health effects and lead to the development of disease later, likely due in part to epigenetic mechanisms. Children may also remain more susceptible to effects of chemicals until they reach adulthood. This means that regimens for testing and assessment of chemicals for hazards need to incorporate consideration of these time periods and to assess doses that may be relevant at highly sensitive time periods. This is a departure from the common practice of focusing on average lifetime doses.

We recognize that some testing and assessment protocols, particularly those specifically directed at reproductive and developmental effects, consider critical time periods and cross generational effects. However, exposure during critical time periods can also contribute to the likelihood of other outcomes such as cancer and neurodevelopmental or neurological effects. Moreover, how such concerns will be addressed through new initiatives such as Tox21 and ToxCast with high throughput methods or the NextGen initiative for risk assessment is also important.

5. Chemical Safety for the Future

While we offer these recommendations for the near term, we also recognize that the data and information currently available to EPA under current authorities are not sufficient. We are encouraged by EPA's progress in removing barriers to disclosure of health and safety information based on claims of confidential business information. We urge EPA to take every possible step to obtain the information that is needed to ensure that children are protected over the long term and that chemicals can be assessed before they are used rather than after. CHPAC recommends that EPA continue to work toward a more effective chemicals safety program that is fully capable of protecting children across all life stages.

Criteria for Identifying Chemicals of Concern for Children (including prenatal and preconception exposures)

We have developed recommendations and suggestions regarding data that EPA could use to identify chemicals of potential concern for children. These are presented in this section and include discussion of data sources as well as ways that data could be evaluated.

As we have noted above, prevention of harmful exposures early in life will have an impact throughout a person's lifetime. A focus on prevention throughout development (from prior to conception, during early development, and through adolescence) is an important and effective public health protection. EPA has an important role in assessing and managing potentially harmful exposures to chemicals in order to maximize protection to children.

In the long term, in order to determine the safety of chemicals for children, EPA will need to develop improved testing methods capable of detecting effects of concern for children, and require that adequate health and safety information, including toxicity testing data on effects of concern for children, be submitted for evaluation.

In the short term, EPA can make use of currently available information to identify chemicals of concern for children. The CHPAC suggests using the criteria presented below (beginning on page 5). The criteria are organized in five categories: (1) potential for persistence or bioaccumulation; (2) occurrence of chemicals in environments relevant to children; (3) occurrence in humans; (4) ubiquitous chemicals; (5) toxicities of particular concern for children. These criteria categories are inter-related and reflect our awareness that health and safety data are not available for many or most chemicals.

CHPAC recommends that EPA consider diverse sources of information to systematically identify and address chemicals likely to be used or present in environments relevant for children. CHPAC recommends that EPA then determine whether sufficient health and safety data are available for these chemicals. If not, this would indicate that such chemicals are candidates for actions under TSCA to obtain health and safety data. Those that are found to pose potential hazards would be candidates for control actions or adoption of alternatives.

When applying the criteria, in the absence of complete and adequate health and safety information, EPA should use information that is available to make the best possible prediction about whether the chemical is of concern for children. Such information could be about the chemical's physical and chemical properties, biological monitoring data (including biomarker data), environmental monitoring data, chemical use information, toxicity information, and data on structurally similar chemicals. A chemical with information that suggests a possible concern could be a priority for obtaining health and safety data or for actions to reduce hazards, including warnings or use restrictions.

The types of data that should be utilized are varied and include data about physical and chemical properties, biological and environmental monitoring data, chemical use information, toxicity data, and predictions based on characteristics of similar chemicals. For example,

- A chemical's *physical and chemical properties* can be used to estimate several attributes. These include persistence and likelihood of bioaccumulation, as well as the

likelihood that it will: be absorbed into the body, be present in blood or tissues, cross the placenta or the blood-brain barrier, or occur in breast milk, foods, water, house dust, etc.

- *Biological and environmental monitoring data*, including biomarker data, can inform determinations regarding persistence; bioaccumulation; absorption and distribution; and presence in blood, tissues, amniotic fluid, cord blood, breast milk, foods, water, air, or house dust, etc. In the absence of adequate biological and environmental monitoring data, there will be cases where analogies with similar chemicals, processes or uses can be used to predict the presence in specific biological or environmental media (*e.g.*, use of a chemical as an additive flame retardant suggests its presence in indoor air and/or house dust).

- Chemical *use information* can be used to assess several criteria. EPA should take into consideration how individuals might be exposed to a chemical through its production, manufacture, use, and disposal, and which specific groups within the population are likely to be exposed (*e.g.*, men and women of child-bearing age, pregnant women, nursing women, babies, children).

- *Toxicity information* for a chemical is used to assess the toxicity-based criteria listed below. Toxicity information may come from a variety of sources, including epidemiology studies, animal toxicity studies, and *in vitro* studies. It is anticipated that newer types of toxicity information, such as data from high throughput assays, toxicogenomic studies, and biologic/toxicity pathway analysis will be increasingly available in the coming years.

- It is an important principle that in the absence of chemical-specific data on specific health effects EPA should make predictions based on what is known about the toxicity of *structurally similar chemicals* rather than to assume that a chemical is without hazard. The absence of evidence should not be taken as evidence that there is no hazard.

Criteria

1. Potential for Persistence or Bioaccumulation

Is the chemical likely to or known to

- Be persistent in the environment?
  This is important because persistent chemicals pose an increased concern for children based on an increased likelihood of exposure (preconception, prenatal, and direct to the child) via multiple possible exposure pathways.
- Bioaccumulate?
  This is important because bioaccumulative chemicals pose an increased concern for children based on an increased likelihood of exposure (preconception, prenatal, and direct to the child) via placental transfer, lactational transfer, or consumption of contaminated foods for example, including certain fish, dairy products, eggs and plants.

Chemicals that are shown or predicted to be persistent or to bioaccumulate should be reviewed for sources and means of control, giving particular priority to those with health and safety concerns. These criteria are of particular relevance to consider in efforts to eliminate health disparities. When health and safety data are not available, EPA should obtain such data, particularly when means of control or alternatives are not available or being implemented.

In the absence of health and safety data, EPA should make predictions based on what is known about the toxicity of structurally similar chemicals and the chemical's physical and chemical properties.

2. Occurrence in Environments Relevant to Children

Is the chemical present in

- Indoor air?
- House dust?
- Outdoor soil, other outdoor ground surfaces, and outdoor structures where children may play, crawl, and engage in hand-to-mouth behavior?
- Foods, water and other beverages that represent a significant percentage of those that infants, children, and pregnant and lactating women consume?
- Products designed or marketed for use by pregnant or nursing women?
- Baby products, children's products, or toys?
- Homes or products commonly used in the home?
- Day-care/pre-school settings, after-school care settings, or schools or products commonly used in these settings?
- Occupational settings where pregnant women, nursing women, women and men of child-bearing age, parents and children work. Resulting in *in utero*, preconception, lactational, 'take home', or direct exposures.

Chemicals that are reported in these environments should be reviewed for health and safety data. When such data are not available, EPA should obtain such data.

In the absence of health and safety data, EPA should make predictions based on what is known about the toxicity of structurally similar chemicals and the chemical's physical and chemical properties.

Attention to availability of safer alternatives and to control measures is warranted for those chemicals that are predicted or found to have health and safety concerns.

3. Occurrence in Humans

Is the chemical likely to or known to

- Occur in human tissues (e.g., fat, bone, brain), blood (including cord blood), or other body fluids (e.g., breast milk, amniotic fluid, urine)?
- Cross the placenta?
- Cross the blood-brain barrier?

Review of health and safety data may be warranted for many of the chemicals that are known or predicted to occur in humans. When health and safety data are not available, EPA should obtain such data.

In the absence of health and safety data, EPA should make predictions based on what is known about the toxicity of structurally similar chemicals and the chemical's physical and chemical properties.

Chemicals[1] that are detected in human biomonitoring or biomarker studies should be reviewed for sources and means of control. Detection in individuals of any age, including adults, is relevant to children. This is because i) occurrence in adults suggests likely occurrence in children, and ii) occurrence in mothers and fathers has implications for children, whether it be as a result of parental exposures occurring prior to conception, during pregnancy, or while nursing.

For chemicals that are known or predicted to cross the placenta or blood-brain barrier and for chemicals that are predicted to be present in tissues, blood, and other body fluids (especially those detected or predicted to be in cord blood, amniotic fluid or breast milk), attention to availability of safer alternatives and to control measures is warranted.

4. Ubiquitous Chemicals

Is the chemical

- Ubiquitous in the environments (indoor or outdoor), foods, or products people encounter in the U.S.?
  Examples of ubiquitous chemicals include bisphenol A and several phthalate compounds. Biomonitoring data indicate widespread frequent exposure of the U.S. population to bisphenol A and several phthalates, which each have short-biological half-lives and are non-persistent and non-bioaccumulative.

Ubiquitous chemicals should be reviewed for health and safety data. When such data are not available, EPA should obtain such data.

In the absence of health and safety data, EPA should make predictions based on what is known about the toxicity of structurally similar chemicals and the chemical's physical and chemical properties. Attention to availability of safer alternatives and to control measures is warranted.

5. Toxicities of Particular Concern for Children

Is the chemical likely to

- Cause developmental toxicity or developmental neurotoxicity?
- Cause reproductive toxicity?
- Interfere with natural hormone synthesis, secretion, transport, binding, action, or elimination (e.g., disrupt normal hormone function)?
- Alter normal lung development, structure, and function or cause respiratory toxicity?
- Cause immunotoxicity?
- Cause cancer?
- Be genotoxic and/or mutagenic?
- Have effects (epigenetic or genetic) on the child as a result of preconception exposure to either parent or in utero exposure?

Chemicals that cause such effects should be reviewed for sources and means of control or phase out. When health and safety data are not available, EPA should obtain such data.
In the absence of health and safety data, EPA should make predictions based on what is known about the toxicity of structurally similar chemicals and the chemical's physical and chemical properties.

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[1] Exceptions may include chemicals for which intake is intentional, e.g., for nutritional or therapeutic purposes.

In conclusion, we appreciate the opportunity to recommend actions that EPA can take to protect children's health, and to provide these criteria for identifying chemicals of concern for children.

Prevention of harmful exposures early in life has positive impacts throughout one's life. Thus, investment in actions to reduce hazards for children will pay dividends for society as a whole.

Thank you for your consideration of our recommendations and suggestions.

Sincerely,

/Signed/

Pamela Shubat, Ph.D.
Chair
Children's Health Protection Advisory Committee

cc: Steve Owens, Assistant Administrator, Office of Chemical Safety and Pollution Prevention
Peter Grevatt, Director, Office of Children's Health Protection
Wendy Cleland-Hamnett, Director, Office of Pollution Prevention and Toxics