

Children's Health Protection Advisory Committee

November 17, 2011

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

RE: Prenatal Exposures and Children's Environmental Health

Dear Administrator Jackson:

As requested by the Office of Children's Health Protection (OCHP), the Children's Health Protection Advisory Committee (CHPAC) has considered issues related to prenatal exposures to environmental contaminants and their implications for the Environmental Protection Agency (EPA). Largely as a result of research conducted over the last decade, we now understand that environmental exposures can profoundly affect children even before they are born. Prenatal exposures, including pre-conception exposures, contribute to infant mortality, pregnancy loss, birth defects, and conditions and diseases throughout the lifespan, creating significant social and economic burdens. These exposures occur in the home, in the workplace, and in the community.

Many or most EPA methods and policies were adopted before the significance of prenatal exposures was understood so it is important to revisit current policies and practices to address this emerging knowledge. Building on past CHPAC recommendations¹ and previous work by OCHP to reduce risks from exposures during the prenatal period, we present specific recommendations for your consideration and summarize key observations from our discussions. As you know, CHPAC includes representatives with a variety of perspectives and backgrounds related to children's environmental health; consequently, we offer recommendations in four diverse areas.

CHPAC recommends that EPA:

1. update policies and practices to address the prenatal period;
2. incorporate social determinants of health and environmental justice into programs and policies;
3. design and disseminate messages through diverse partnerships; and
4. address the prenatal period, key outcomes and mechanisms in research priorities.

It is helpful to reflect briefly on key advances in knowledge about the prenatal period. Biomonitoring using umbilical cord blood shows many

¹ CHPAC letters of Dec 20, 2011; March 3, 2011; and October 21, 2010 at http://yosemite.epa.gov/ochp/ochpweb.nsf/content/CHPAC_Comments.htm

chemical compounds cross the placenta from mother to the developing child. The prenatal period can be the period most sensitive to chemical exposures because growth and development occur rapidly, and structures and systems are formed. Small perturbations can have lasting impacts. Effects of prenatal exposures can take a toll throughout the life span. We are concerned about disease in childhood but prenatal exposures also increase the likelihood, severity or acceleration of the onset of diseases later in life. Reducing prenatal exposures improves health over the long term.

CHPAC acknowledges EPA's essential contributions to the development of the knowledge base.² Along with the National Institute of Environmental Health Sciences (NIEHS), EPA has supported Children's Environmental Health Research Centers that draw upon expertise in the research community. Consequently, in just over a decade, the centers have produced significant findings about many topics including the significance of prenatal exposures. This has been a highly effective return on the small investment.³ Knowledge of new toxicants and potential adverse health outcomes can emerge rapidly. EPA has the ability to and should respond in a timely manner to these new threats by conducting research and creating public health messaging in these areas.

Exposures during the prenatal period need to be systematically addressed in environmental health policies and analyses. While knowledge has increased, the evidence base is far from complete. Studies have been published for only a few agents and a few outcomes. CHPAC concludes that actions are needed while research continues.

Our recommendations are presented below.

I. Update Policies and Practices to Address the Prenatal Period

CHPAC recommends that EPA update its policies and practices throughout the agency to address the prenatal period.

- a. CHPAC recommends that EPA and its federal partners expand biomonitoring for the prenatal period and use such data to identify chemicals that require attention.**

Neither the prenatal nor early childhood periods are included in the national biomonitoring program at the Centers for Disease Control and Prevention (CDC). The national biomonitoring program should be capable of detecting prenatal exposures to chemicals in broad use and those in children's environments, as part of a program to ensure chemical safety. Consideration of chemicals detected in maternal blood would provide an additional useful perspective.

- b. CHPAC recommends that EPA consistently consider the prenatal period when developing standards and guidelines for allowable concentrations of chemicals in environmental or exposure media and when adopting toxicity values such as reference doses or cancer risk values. Further, CHPAC recommends that EPA**

² A Decade of Children's Environmental Health Research, EPA Office of Research and Development, December 2007 http://epa.gov/ncer/publications/research_results_synthesis/ceh_report_508.pdf

³ CHPAC July 2007 letter on EPA/NIEHS Children's Centers and attached report Review of the Research Translation of the EPA/NIEHS Children's Research Centers: Accomplishments and Opportunities for the Future http://yosemite.epa.gov/ochp/ochpweb.nsf/content/CHPAC_Comments.htm

adopt methods to protect against potential effects of prenatal exposures in cases where data are lacking to fully assess the significance of such exposures.

When sufficient data are not available, it may be appropriate for EPA to adopt adjustment factors to account for the uncertainties of the database and for concerns about exposure, vulnerability, or sensitivity. CHPAC believes that the significance of exposures during the prenatal period is not adequately addressed by the current use of adjustment and uncertainty factors.

c. CHPAC recommends that EPA improve the knowledge base for prenatal exposures to support chemical safety assessment.

Strategies are needed to improve the knowledge base for assessment of the safety of environmental agents during the prenatal period for use by the agency and the public. EPA should incorporate data streams relevant to prenatal exposures in chemical assessment and prioritization. One example is human bioaccumulation, which leads to maternal body burdens and then to prenatal exposures. For agents commonly present in environments and relevant to prenatal exposure, chemical safety testing is critical. EPA should require testing for chemicals or agents that are found in environments that contribute to prenatal exposures.

d. CHPAC recommends that EPA consider all of the hazards and associated health endpoints in chemical screening and assessment that result from prenatal exposure.

EPA and other entities emphasize reproductive and developmental effects as sole outcomes that are important for children. Such an approach will miss other important adverse health outcomes. Prenatal exposure can contribute to a variety of conditions and diseases during childhood including effects on neurodevelopment, lung development, respiratory function, immune function, and hormonal systems. These exposures can also contribute to increased risk of diseases later in life.

e. CHPAC recommends that EPA consistently include the prenatal period in methods for safety testing of chemicals, including traditional methods that rely on whole animals, as well as the "robot" methods that rely on high or medium throughput strategies and testing of narrow responses. CHPAC also recommends that EPA ensure that the validation for any of the newer "robot" or high throughput or other such methods include the prenatal period as well as the perturbation or endpoints that may occur as a result of prenatal exposures.

While ToxCast and other high throughput testing strategies will yield a great deal of information, it is important to ensure that these techniques have the capability to detect effects of prenatal exposures. CHPAC is concerned that the current approach to validation of ToxCast and related "robot" or high throughput methods does not adequately reflect either exposures during the prenatal period nor all of the kinds of perturbations or endpoints that may occur as a result of prenatal exposures. Consequently, they may produce false negatives and allow chemicals where prenatal effects may be important to be viewed as "safe." One approach would be to require whole animal, multigenerational toxicity studies in order to develop a robust source of prenatal toxicity data for comparing, correlating, and interpreting results from the next

generation of toxicity testing developed by EPA and its partners. Perhaps there are other options as well. A robust option that addresses the prenatal period is needed, and, so far as CHPAC has been able to determine, has not yet been identified.

- f. CHPAC recommends that EPA develop criteria for use of screening tests that account for the limitations of the tests for identifying chemicals that may adversely affect the prenatal life stage.**

It is important that the implications of screening results be carefully considered. We understand that EPA intends to use a positive result (i. e., showing an effect) in a screening test to refer a chemical for additional testing using broader methods. Conversely, agents found to be negative (i.e. lacking any effect) during screening would receive no further testing in this paradigm. EPA would fail to follow up on false negatives. CHPAC is concerned that under this approach EPA may not recognize false negatives and, consequently, not be protective for children; particularly for results of prenatal exposures because of the lack of complete coverage of early life stages by the newer, faster screening methods.

- g. CHPAC recommends that EPA develop metrics to account for the combined burden of prenatal exposure.**

Such metrics could then be used to help track and study the overall burden of exposure during the prenatal period and its effects. The combination of chemicals that may accumulate during the prenatal period is a concern. It is not just individual chemicals but the burden of all these chemicals acting together that will affect the development of a child and contribute to health effects.

- h. CHPAC recommends that EPA work with the National Institute for Occupational Safety and Health (NIOSH), the Occupational Safety and Health Administration (OSHA), and industry to develop mechanisms to assure protection of men and women in the workplace from exposures that may impact the workers during the preconception and prenatal period.**

II. Incorporate Social Determinants of Health and Environmental Justice into Programs and Policies

- a. CHPAC recommends that EPA begin to quantify and incorporate social determinants of health into its programs and policies, including risk assessment and risk management.**

Health disparities are closely linked with social and economic disadvantage. The influence of social determinants, including income, education, occupation, race/ethnicity, and an individual's environment, begins even before birth. The unequal distribution of environmental exposures and resulting burden of disease is inextricably linked to social determinants of health. For example, the effects of social determinants such as stress, on birth weight, one common metric for the prenatal period, are well established. Emerging research on the role of stress in environmentally related health condition underscores the need to fully consider the social determinants of health.

Research has shown how a woman's health during pregnancy affects her newborn's life chances and long-term health risks and how social characteristics such as income, education, race/ethnicity, and occupation can significantly impact health. Some of the adverse effects that develop from exposures in early stages of human development are difficult to overcome later on in life. Social conditions also have an impact on life-long health, including that of future generations and, therefore, need to be more thoughtfully researched as well as integrated into policy decisions.

- b. CHPAC recommends that OCHP work in collaboration with the Office of Environmental Justice on issues of research, policy and action to address health disparities, specifically in the prenatal period.**

Creating a more comprehensive, sustainable framework to achieve environmental justice will require public participation and building on existing science and successful partnerships. EPA's Plan EJ 2014⁴ outlines a number of strategies to empower disenfranchised communities. This Plan can be used to expand the definition of vulnerable populations to include women who are or may become pregnant, infants, children, and the unborn. Linking environmental justice priorities for action with the OCHP's mission to protect children from environmental risks would leverage resources and expertise to reduce health disparities and promote environmental justice throughout life.

III. Design and Disseminate Messages through Diverse Partnerships

CHPAC recommends that OCHP lead EPA in creating and implementing an agency-wide, nationally consistent outreach and communications plan about prenatal environmental exposures.

EPA should engage with diverse partners including professional health care provider organizations, community-based organizations, and academic partners to create effective messaging for the public. Information can empower the public so they can participate in the development of public policies related to the environment and health and take individual actions to avoid or reduce harmful exposures (e.g., metals, pesticides, solvents, plastics, air pollutants, tobacco smoke). Models for messaging about reducing risks during the prenatal period have been created by the March of Dimes⁵ and past efforts of EPA⁶. EPA can build upon these effective examples, leveraging resources through collaborations with organizations that produce and disseminate health messages for pregnant women.

- a. CHPAC recommends that EPA partner with experts in public health education and social marketing to create effective agency-wide communication strategies that produce culturally sensitive messages for health providers and women and their families.**

⁴ <http://www.epa.gov/compliance/ej/plan-ej/>

⁵ Staying Safe, http://www.marchofdimes.com/pregnancy/stayingsafe_indepth.html

⁶ Promoting Good Prenatal Health: Air Pollution and Pregnancy,
[http://yosemite.epa.gov/ochp/ochpweb.nsf/content/OCHP_Prenatal_FS_7_10.htm/\\$File/OCHP_Prenatal_FS_7_10.pdf](http://yosemite.epa.gov/ochp/ochpweb.nsf/content/OCHP_Prenatal_FS_7_10.htm/$File/OCHP_Prenatal_FS_7_10.pdf)

Partnerships between EPA and other federal agencies such as the Maternal Child Health Bureau provide opportunities for cross-disciplinary development of messages about how to prevent prenatal exposures.

- b. **CHPAC recommends that EPA use existing partnerships and create new ones to effectively disseminate messages to women who are or may become pregnant, their families and their providers.**

Integration of messages with existing networks such as the National Healthy Homes, Healthy Babies Coalition⁷ and electronic media such as text4baby⁸, Health 2.0⁹, Fish-Facts.org¹⁰, and other web-based and new media approaches would offer opportunities to reach targeted populations efficiently. Public health professionals, health care providers and especially Pediatric Environmental Health Specialty Unit (PEHSU) staff are key messengers who can identify at-risk populations, provide anticipatory guidance and education about environmental exposures, and empower communities to take precautionary action. Messaging efforts could replicate strategies used in successful public health campaigns such as the stop smoking campaigns to raise awareness and provide action steps.

Partnerships between EPA and community-centered care would present another opportunity for dissemination of messages by health care providers in diverse and underserved settings, including urban, rural, and tribal communities.

Peer-reviewed publications that discuss clinical approaches to the translation of research findings into practice through the identification and management of environmental health issues pre-conceptually and prenatally would also provide a means for reaching public health professionals and health care providers.

- c. **CHPAC recommends that EPA evaluate the effectiveness of its communication messaging.**

Evaluation should include whether the message was culturally sensitive, if the message was disseminated through media appropriate for the targeted audience, and if knowledge and behavior of individuals and communities, as well as policies were modified to reduce or eliminate prenatal environmental hazards. Empowering the public with information on these environmental hazards can create a constituency that demands public policy that protects the environment and the health of future generations.

IV. Address the prenatal period, key outcomes, and mechanisms in research priorities

CHPAC recommends that EPA continue to conduct, fund, and promote research on the effects of prenatal exposures, through continued support for the EPA/NIEHS Children's Environmental Health Research Centers, its own research, and partnerships with other research funding entities.

⁷ <http://www.hmhb.org/>

⁸ <http://www.text4baby.org/>

⁹ <http://www.health2con.com/>

¹⁰ <http://www.fish-facts.org/>

a. CHPAC recommends conducting research on the effects of pre-conception exposures.

The pre-conception time period has received limited research attention, though there is evidence that metals such as chromium III can have effects after pre-conception exposure in mice, including epigenetic changes, increased cancer risk, and hormonal changes. Other agents to be studied include those that bioaccumulate or have long half-lives in the body, such as some metals (e.g., lead, mercury) and halogenated compounds (e.g., PCBs, dioxins).

b. CHPAC recommends that EPA focus research attention on epigenetic effects resulting from prenatal exposures.

Epigenetics changes are potentially heritable changes to the genome that do not involve changes in DNA sequence, including DNA methylation, histone modification, and microRNA changes. These changes can suppress or stimulate gene expression, which can lead to changes in health endpoints. Epigenetic mechanisms may explain how environmental toxicants impact the genome early in fetal life and program future disease development in current and future generations. For example, increased DNA placental methylation patterns have been associated with abnormal fetal growth and environmental factors may influence DNA methylation during the prenatal period.

c. CHPAC recommends that EPA support and conduct research that accounts for mixture effects, to investigate how multiple contaminant exposures occurring during pre-conception and prenatal periods affect biological systems and lead to disease development.

Research priorities should recognize that humans experience multiple exposures to multiple chemicals, often at low dose levels, throughout all life stages, including the pre-conception and prenatal stages. For example, data show that women are exposed to multiple phthalate chemicals. In animal studies, prenatal exposures to mixtures of phthalate chemicals leads to compounded health outcomes as compared to single agent exposures.

d. CHPAC recommends that EPA focus research attention on chronic diseases that are increasingly observed in children including but not limited to neurodevelopmental disorders, obesity, and allergies/asthma.

We need to know what exposures contribute to these disorders and how effects occur. The prevalence of neurodevelopmental disorders including autism, ADHD, and anxiety is increasing in children without known cause. Early life programming of brain development is extremely important for cognition and neurologic function throughout life. The neurologic system starts to develop in fetal life and continues with important periods of vulnerability throughout early childhood, later childhood, and adolescence.

Childhood obesity is at epidemic proportions in the United States. While exercise and diet play a large role in metabolic programming, many physicians and scientists recognize that some individuals have different metabolic set points that predispose them to gain weight and store fat. Programming of these set points is thought to occur in utero

because infants born small or large for gestational age are both at increased risk for obesity later in life.

Both genetic and environmental factors such as dust and pollen contribute to allergic (IgE mediated) disease development, but little is known about how emerging environmental toxicants may contribute to disease development. Childhood allergies, asthma, and eczema are considered atopic diseases that consistently lead to physician visits and/or hospital admission. Maternal history of allergies and asthma is directly linked to infant outcomes and may reflect both genetic and environmental exposures during the prenatal period. With the rise in these diseases, other environmental factors such as changing pollen concentrations due to climate change, new toxicants found in dust, or exposure to nanoparticles may be contributing to disease development.

- e. **CHPAC recommends that EPA engage with populations that are most burdened by environmental exposures and increased disease prevalence in its research activities.**

A growing body of research suggests that there are benefits to conducting environmental health research in partnership with communities. Specifically, low income, underserved communities with disproportionate burdens of environmental exposures and disease should be a priority. Community based participatory research (CBPR) can expand social structures and processes that contribute to the ability of community members to improve health and may enhance translation of research findings into actions to reduce exposures to environmental toxicants and improve public health overall.

We applaud EPA for the continued support for the EPA Community Action for a Renewed Environment (CARE) Program that offers innovative ways for communities to take the lead in research activities, organize, and act to reduce exposures. This program should serve as a model program that can be replicated and expanded.

CHPAC concludes that greater investment in research regarding prenatal exposures and its associated health effects, along with greater dissemination and public discussion of these findings are essential to the development of sound policies and practices. CHPAC is aware that EPA is being harshly criticized for carrying out its fundamental responsibility to protect public health. Groups focused on children's health and allied areas could bring attention to the extensive public benefits of sound environmental protection policies and particularly the opportunities to make kids healthier and smarter by taking care of their early environments. CHPAC urges EPA to consider these recommendations in its efforts to advance the agency's policies, practices, and research agenda related to the prenatal period.

Thank you for your commitment to children's health.

Sincerely,

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

cc: Peter Grevatt, Director, Office of Children's Health Protection, Office of the Administrator