Children's Health Protection Advisory Committee

October 21, 2010

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

RE: Upcoming EPA staff discussions of the NRC report *Science and Decisions: Advancing Risk Assessment*

Dear Administrator Jackson:

During the July 2010 meeting of the Children's Health Protection Advisory Committee (CHPAC) members learned that U.S. Environmental Protection Agency (EPA) staff will come together this month to discuss risk assessment issues and advice contained in three recent National Academy of Sciences (NAS) reports to EPA. One of those reports, *Science and Decisions: Advancing Risk Assessment* (NRC, 2009), describes the Academy's review of the EPA's current risk assessment approaches and practices and provides recommendations for improvements with the intent of providing the public with improved protection from environmental contaminants. It is an important role of the Agency to consider new practices as they become available. CHPAC urges the EPA to review its current risk assessment practices in light of the report's recommendations to take into consideration background exposure, vulnerable populations, and mode of action information in developing health standards. CHPAC anticipates that implementation of these recommendations will result in reductions in health disparities and greater protections for vulnerable groups, including children. CHPAC recommends that EPA staff scientists participating in the upcoming discussions bring the concern of early life stage exposure and sensitivity to the conversations that will take place concerning optimizing risk assessment practice.

Early life stages of concern to CHPAC include the prenatal period, infancy, and early childhood through adolescence. CHPAC is especially concerned that risk assessment practices may not be fully developed for the prenatal period, which represents one of the most vulnerable periods of development. Prenatal exposures can have adverse effects on the fetus, which may manifest at birth, during childhood, or later in life as poor birth outcome, disease, or other effects (such as reduced IQ). CHPAC recommends that the EPA fully and consistently take into account the risks from exposures during the prenatal period, as well as exposures occurring during infancy and throughout childhood, when developing health protective exposure limits for chemicals and other agents.

[1] National Research Council. Science and Decisions: Advancing Risk Assessment. Washington, DC: National Academies Press, 2009. http://books.nap.edu/catalog.php?record_id=12209.

Science and Decisions acknowledges previous reviews and recommendations regarding Agency risk assessment practices conducted by the NAS and others. During the upcoming discussions, CHPAC recommends that the participants also consider a conceptual framework for assessing risks to children from exposure to environmental agents (Daston, et. al., 2004)[2] developed as a result of a 2001 workshop sponsored by the EPA. This conceptual framework, which specifically addresses issues associated with assessing risks to children, contains many elements that are consistent with several of the recommendations made in the *Science and Decisions* report. Utilizing the conceptual framework would be one measure EPA could take to consider all of the best available science when implementing the recommendations presented in *Science and Decisions*. While the authors of *Science and Decisions* acknowledge that implementation could take many years and, importantly, could take a significant level of research prior to adopting their recommendations, it seems an important time to look at the science being developed for assessing risks in early life stages.

A significant recommendation of the *Science and Decisions* report is that the Agency move away from its current practice of assuming for non-cancer endpoints that a threshold dose exists below which no toxicity will occur toward an approach which considers background exposures, vulnerable groups/life stages and mode-of-action information in choosing between three conceptual models for dose response assessment[3]. As stated in the report, "Threshold determinations should not be made in isolation inasmuch as other chemical exposures and biologic factors that influence the same adverse effect can modify the dose response relationship and therefore should be considered" (NRC, 2009).

As EPA considers this particular recommendation from *Science and Decisions*, CHPAC suggests that it may be helpful to discuss chemicals for which information on the increased sensitivity of children to the toxic effects are available. Examples for which information on interactions with nutritional status, genetics, background exposures to chemicals with similar toxicities, non-chemical stressors, or other factors is available would likely be especially instructive. Lead and arsenic are two such chemicals. In the context of EPA's discussions of the NAS recommendations, CHPAC encourages the Agency to consider whether the current health standards for lead and arsenic, as well as other chemicals, adequately take into account early life stage exposures. CHPAC also urges EPA to discuss appropriate risk limits or increments that would need to be used in cases where linear models of risk are employed.

EPA's current risk assessment practice does not explicitly take into account prenatal carcinogen exposures when estimating cancer risk. CHPAC recommends that in the course of the upcoming discussions EPA consider how best to take into account exposures to carcinogens during the prenatal period. Additionally, both CHPAC[4] and the *Science and Decisions* report recommend the extension of the application of default Age Dependent Adjustment Factors (ADAFs) beyond mutagenic carcinogens unless there is sufficient information indicating that use

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[2] Daston, G., Faustman, E., Ginsberg, G., Fenner-Crisp, P., Olin, S., Sonawane, B., Bruckner, J., and Breslin, W. 2004. A framework for assessing risks to children from exposure to environmental agents. Environmental Health Perspectives 112(2):238-256.

[3] The models are described in Chapter 5 of *Science and Decisions* (NRC, 2009).

[4] CHPAC letter to the previous administrator, dated December 14, 2007, contains greater detail concerning the use of ADAFs when there is doubt concerning the mode of carcinogenic action (http://yosemite.epa.gov/ochp/ochpweb.nsf/content/12142007.htm/$file/12142007.pdf).

of the default ADAF is not appropriate[5]. We urge the EPA to consider these recommendations in the course of the upcoming discussions.

In summary, CHPAC views the upcoming EPA discussions as one of many opportunities to discuss potential sensitive life stages/populations and how improvements in the Agency's risk assessment practices can offer vulnerable groups appropriate protection from environmental exposures. CHPAC asks you to direct staff scientists to more fully and consistently consider early life stage susceptibility (sensitivity and exposure) and latent effects from early life exposure as staff discuss implementing recommendations contained in the NAS report. Early life stage susceptibility is an area of emerging science, and CHPAC suggests that staff consider ways to rapidly integrate new information as it develops.

Sincerely,

/Signed/

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

cc: Paul Anastas, Assistant Administrator, EPA Office of Research and Development
Kathryn Gallagher, Executive Director, EPA Risk Assessment Forum
Peter Grevatt, Director, EPA Office of Children's Health Protection
Edward Ohanian, Chair, EPA Risk Assessment Forum

[5] This recommendation is consistent with the EPA Science Advisory Board 2004 review of EPA's cancer supplemental guidance related to risks resulting from early life exposure which concluded: "Certain groups of non-mutagenic carcinogens with known modes of action serve as important examples in support of applying a default factor to non-mutagenic carcinogens when the mode of action is unknown. The Review Panel suggests that the Agency reconsider limiting the application of adjustment factors only to mutagenic agents and instead apply a default approach to both mutagenic and to non-mutagenic chemicals for which mode of action remains unknown or insufficiently characterized." EPA-SAB-04-003 found at www.epa.gov/sab/.