Cancer Guidelines

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

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OFFICE OF
RESEARCH AND DEVELOPM

J. Routt Reigart, MD
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Protection Advisory Committee
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Dear Dr. Reigart:

Thank you for your letter of May 30, 2002, to the Administrator, expressing the Children's Health Protection Advisory Committee's (CHPAC) continuing interest in the Agency's efforts to revise the 1986 Guidelines for Carcinogen Risk Assessment. I know that the Committee has provided the Agency with constructive suggestions in the past in the area of children's cancer risk. The issues that you have identified are central to our revisions of the Guidelines. In the Agency's recent *Federal Register* notice soliciting further public comment on the draft Guidelines, the topic of assessing children's cancer risk was highlighted and we requested information on the public's experience in applying the draft Guidelines and any relevant scientific studies that the Agency should consider in formulating the final Guidelines. Since this has been an area of long-standing controversy, a diversity of opinions was expressed. Presently, the scientific issues to which your recommendations refer are actively being discussed by the Agency's scientific staff and the Science Policy Council and I welcome your latest perspectives.

In your current communication, as well as in earlier correspondence, the Committee has pointed out that the revised guidelines should address the following topics relative to children's risk: (1) information needed to determine a mode of carcinogenic action and to deviate from a linear default dose-response relationship; (2) whether cancer modes of action differ between children and adults; and (3) consideration of exposure during the childhood period and the view that these exposures can have a disproportionate impact on risk as compared to adult exposures. Your letter correctly points out that there are many unresolved scientific issues regarding the causes of children's cancer. We see publication of the revised Guidelines not as an end in the Agency's efforts to develop guidance on assessing children's cancer risk but as an evolutionary step to be followed by additional, more specific guidance, as our experience and scientific understanding improve. I agree with your position, which is also consistent with the Science Advisory Board's (SAB) recommendation, that the Agency move forward to finalize the Guidelines at this time and I encourage the Committee's continuing involvement.

There are four principles that are guiding our efforts to revise the 1986 Guidelines:

- **The Guidelines must be based on sound science.** Toward this end, we have had three Science Advisory Board reviews of earlier drafts and separate SAB reviews of chloroform and atrazine risk assessments which illustrated application of aspects of the Guidelines (e.g., establishing a mode of action and assessing its applicability to early life-stages). Although a consensus was not reached by the SAB on the best way to approach children's cancer risk in the Guidelines, they did provide many useful recommendations that the Agency is now considering. Your recommendation that we actively engage other organizations like the National Toxicology Program and CalEPA is a good one. In April 2000, the Agency cosponsored a workshop with the National Institute of Environmental Health Sciences to explore informational needs to address children's cancer risk. CalEPA staff has submitted comments on the Guidelines in response to the Agency's recent *Federal Register* notice and these are being considered in finalizing the Guidelines.

- **The Guidelines must provide a flexible framework.** Our understanding of the mechanisms underlying cancer has increased considerably since 1986 and will continue to do so. So too have the types of studies (e.g., genomics and transgenics) that may provide data critical to understanding these mechanisms. These advances will improve our ability to assess children's cancer risk in the future. The emphasis that the Guidelines give to understanding an agent's mode of action is critical to identifying life-stages or susceptible subpopulations that are at increased risk. Of great importance also is the application of the Guidelines to chemical-specific situations and the associated peer reviews will ensure that the Agency's assessments reflect the most up-to-date science. Thus, I agree with your recommendation that the Agency makes an effort to include experts in children's health on peer review committees for chemical-specific carcinogen potency assessments.

- **The Guidelines must explicitly address early life-stages and sensitive subpopulations.** Throughout the Guidelines, risk assessors will be given guidance to explicitly consider sensitive life-stages and subpopulations in each component of the risk assessment. Although the science and available methods may be currently limited to fully address all aspects of the considerations your Committee identified, the Guidelines will provide the basis for incorporating mechanistic, life-stage specific information.

- **The Guidelines must utilize public health protective default options when significant data gaps exist.** In keeping with EPA's mission and long-standing approach to risk assessment, the Guidelines will incorporate a set of default options (both qualitative and quantitative) to bridge critical methodological and information gaps that are designed to be protective of public health. The National Academy of Sciences in their *Science and Judgment* report supported the

Agency's continued use of default options in its risk assessments. The Guidelines will be explicit in identifying these defaults and provide guidance as to their use. Your letter makes recommendations in this area which will be considered by the Agency.

I would like to reiterate that the Agency welcomes CHPAC's perspectives on the revisions to the Guidelines and would like to pursue continued dialogue. Based upon where we are presently in our internal deliberations and understanding that the CHPAC Science and Regulatory workgroup is planning to meet in October, I suggest that the Agency provides a briefing at that time on our efforts and plans for outreach. A follow-up briefing might also be in order when the full CHPAC meets in December.

Sincerely yours,

Paul Gilman

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