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

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OFFICE OF
RESEARCH AND DEVELOPMENT

Dr. James H. Johnson, Jr.
Chair, Board of Scientific Counselors
Dean, College of Engineering, Architecture, and Computer Sciences
Howard University
2366 6th Street, NW
Washington, DC 20059

Dear Dr. Johnson:

The Office of Research and Development (ORD) would like to take this opportunity to thank you and the members of the Board of Scientific Counselors (BOSC) for organizing and participating in the February 2005 workshop on Chapter 4 of the Staff Paper on EPA Risk Assessment Principles and Practices. We especially thank Drs. Henderson, Stuart, Daston, and Duke for co-authoring a paper summarizing the workshop.

Enclosed with this letter is our response to the points raised in your Letter Report of February 14, 2006. Please feel free to contact me if further information is needed.

We are pleased that the BOSC was very supportive of our efforts in this area. Again, thank you for your advice to ORD.

Best regards,

George Gray
Assistant Administrator

Enclosure

Office of Research and Development (ORD)
Response to the Board of Scientific Counselors (BOSC)
February 2006 Risk Assessment Workshop Letter Report

BOSC Risk Assessment Workshop Workgroup:
Dr. Rogene Henderson, Lead
Dr. George Daston
Dr. Clifford Duke
Dr. John Giesy

Submitted:
William Sette, PhD
Toxicologist
Office of the Science Advisor

ORD Response to Board of Scientific Counselors (BOSC) Review of the EPA Staff Paper Entitled "An Examination of EPA Risk Assessment Principles and Practices" in February 2005

The BOSC conducted a workshop on February 2-3, 2005 in Washington, DC that focused on Chapter 4 of EPA's staff paper, "Use of Default and Extrapolation Assumptions." The purpose of the BOSC workshop was to first present the current practices of EPA, and then have speakers provide constructive feedback for refining EPA's current practices, or suggesting alternative approaches for default and extrapolation assumptions that might be used in the future. Three topics were covered in detail: (1) use of default assumptions and uncertainty factors, (2) extrapolation from high to low doses, and (3) extrapolation between species. The BOSC transmitted a letter report on the workshop to ORD in February 2006. The following is a narrative response to the points raised in the letter report. The committee's comments are written in italics and ORD's response follows in regular type.

BOSC COMMENTS FOLLOWED BY ORD'S RESPONSE

1. With the advent of the genomics era, it is becoming possible to characterize in a quantitative way the relationships between effects at a molecular level and adverse outcomes on cell and organ function.

ORD agrees. The Agency has a Genomics Workgroup with several subgroups focused on quality assessment, data submission, management, and analysis, microbial source tracking, and training. The most recent effort for this workgroup has been to develop interim guidance for Microarray-based assays for regulatory and risk assessment applications. A draft document is undergoing internal review by the Science Policy Council and we hope to begin external peer review this summer.

2. The BOSC recognizes that it is part of EPA's Computational Toxicology Program to participate in research and model development in systems biology. This activity needs to continue to be supported and its results incorporated into risk assessment practices when feasible.

ORD is continuing its work in this area. Our next activity related to the Staff Paper will involve a consultation with the SAB this fall to discuss a number of our key follow up activities and plans in risk assessment practices. Current plans call for systems biology as one key area of focus for this meeting.

3. Many of the participants in the workshop provided examples of how advances in science can provide a foundation for risk assessment based on mode of action and of the replacement of default uncertainty factors with empirical data.

ORD agrees. Recent efforts related to mode of action analyses include internal communications to support implementation of mutagenic mode of action analyses for carcinogenicity, and most recently, EPA has begun internal review of a paper from a Risk Assessment Forum technical panel intended to assist EPA risk assessors in determining whether data support

a finding of a mutagenic mode of action for carcinogenicity. Efforts to use empirical data to replace uncertainty factors continue on a case by case basis, wherever possible.

4. Some of the presenters at the workshop suggested that changes in toxicity test designs and quantitative risk assessment approaches need to be considered at this point.

With respect to toxicity test design, EPA, with ORD support, has a contract with the National Academies of Science to review recent scientific advances and determine how they can be most effectively used to develop new testing strategies for conducting toxicity assessments. The committee will release a second report in the fall of 2006 that will provide a long-range vision and strategy for advancing the practices of toxicity testing and human health assessment of environmental contaminants. In its planned SAB consultation, we are currently planning to discuss probabilistic risk assessment for human health, expert elicitation, and possibly other new initiatives to advance the practice of quantitative risk assessment.

5. We encourage EPA to continue its transparent communications about risk assessment practices.

As briefly noted above, EPA is currently planning a consultation with the SAB for this fall to review its follow up activities to the entire Risk Assessment Task Force Staff Paper, with a focus on a number of key issues, including as now planned, systems biology, and a number of approaches to elements of quantitative risk assessment. As plans for this meeting evolve, we will keep you updated.