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February 14, 2006

Dr. George Gray  
Assistant Administrator for Research and Development  
U.S. Environmental Protection Agency  
Office of Research and Development  
1200 Pennsylvania Avenue, NW  
Washington, DC 20460

Subject: Recommendations from the Board of Scientific Counselors' Workshop on  
Chapter 4 of the Staff Paper Entitled "An Examination of EPA Risk Assessment  
Principles and Practices"

Dear Dr. Gray:

The Board of Scientific Counselors (BOSC) of the Office of Research and Development (ORD) of the U.S. Environmental Protection Agency (EPA) was established to provide advice, information and recommendations to ORD concerning the management and scientific approaches used in the Agency's research program. When the staff paper entitled "An Examination of EPA Risk Assessment Principles and Practices" was completed by the Office of the Science Advisor, the BOSC was asked by Assistant Administrator Paul Gilman to host a workshop for the public and interested stakeholders that focused on a portion of the staff paper. Specifically, the BOSC was asked by Dr. Gilman to address issues in Chapter 4 of the staff paper, "Use of Default and Extrapolation Assumptions." Other professional societies were asked to provide feedback on the staff paper in the areas of probabilistic methods in risk assessment, methods of uncertainty analysis, and ecological risk assessment.

The staff paper described the current risk assessment practices of EPA. The purpose of the BOSC workshop, which was conducted on February 2-3, 2005 at the auditorium of the National Academy of Sciences (at 2101 Constitution Avenue, NW, in Washington, DC), 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. In each case, a speaker from EPA described the current practices and this was followed by three speakers who suggested refinements or alternative approaches that might be used in the future. Lively discussions were held at the end of each of the three workshop sessions.

The workshop was not intended to be a consensus workshop or a comprehensive survey and there was no attempt to develop a set of recommendations. Nonetheless, the BOSC members who organized the workshop believe that a few points should be brought to your attention.

First, the Office of the Science Advisor should be commended for preparing the staff paper on risk assessment practices, and for recommending best practices. EPA is a large organization that administers a number of laws, regulates a variety of activities and serves many stakeholders. It is in EPA's best interests to standardize its risk assessment practices as much as possible across its programmatic and regional offices. The staff paper is an important step towards standardization. EPA also tends to be viewed by other agencies, such as state environmental agencies, as a bellwether in risk assessment. It is likely that the staff paper will provide valuable guidance to these agencies as to what EPA believes to be best current approaches.

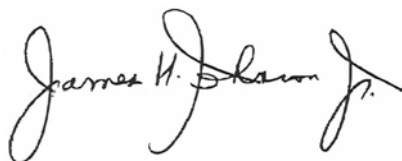
Toxicology and allied sciences have advanced considerably since risk assessment practices were first instituted and the pace of science continues to accelerate. With the advent of the genomics era, it is becoming possible to characterize in a quantitative way the relationships between effects at a molecular level and adverse outcomes on cell or organ function. This nascent science is an integral part of systems biology and it may be possible using these and related approaches to begin to experimentally test some of the fundamental assumptions in risk assessment, including the relevance of high-dose toxicity testing for predicting risks from limited exposures. The BOSC recognizes that it is part of the mandate 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 practice when feasible.

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. EPA has started to incorporate more of this kind of science into its risk assessments; in fact, the latest version of the Cancer Risk Assessment Guidelines provides a flexible model for the consideration of mode of action. We encourage EPA to continue to take a flexible approach to risk assessment so that the best science can be applied. 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. EPA should evaluate these suggestions and consider whether more in-depth studies and/or workshops are warranted to further explore them.

Finally, it was clear from the workshop that there continues to be high interest from many different stakeholder groups on the conduct and outcome of EPA's risk assessments. We encourage EPA to continue its transparent communications about risk assessment practices, including the rationale for choosing to use defaults or alternatives to defaults.

The BOSC was pleased to have the opportunity to conduct this workshop and we hope that the suggestions discussed there will be helpful to you and your staff as ORD continues to seek to improve the risk assessment process.

Sincerely,

A handwritten signature in black ink that reads "James H. Johnson, Jr." The signature is written in a cursive, flowing style.

James H. Johnson, Jr.  
Chair, Board of Scientific Counselors