



## THE ADMINISTRATOR OF THE ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

SEP - 4 2013

H. Christopher Frey, Ph.D.  
Chair  
Clean Air Scientific Advisory Committee  
Science Advisory Board  
U.S. Environmental Protection Agency  
1200 Pennsylvania Avenue, NW  
Washington, D.C. 20460

Dear Dr. Frey:

Thank you for your June 4, 2013, letter in which you provided the Clean Air Scientific Advisory Committee's comments and recommendations on the U.S. Environmental Protection Agency's *Integrated Science Assessment for Lead, Third External Review Draft*, released in November 2012 for public comment and peer review. The EPA greatly appreciates your hard work.

My staff carefully considered the panel's comments and recommendations and those we received from the public. We made revisions, which include adding recently published papers you identified, to address the panel's consensus and individual comments as well as the public's comments.

The CASAC panel recommended that the EPA revise the causal determination for reduced kidney function from "likely to be a causal relationship" to "suggestive of a causal relationship." The EPA thoroughly evaluated the evidence for reduced kidney function as it relates to the EPA's framework for causal determinations. After considering the totality of the toxicological and epidemiologic evidence, with a particular focus on the potential for reverse causation to influence study findings, the EPA agreed with CASAC's recommendation to revise the causal determination for reduced kidney function to "suggestive of a causal relationship."

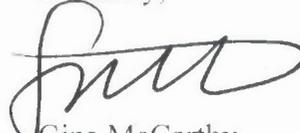
The panel noted that previous revisions successfully enhanced the clarity and transparency of the application of the causal framework by defining specific endpoint groupings around which conclusions would be formed. The panel offered additional advice to refine certain health-outcome categories to increase their specificity, appropriately categorize several nervous-system endpoints, adopt standard naming conventions for behavioral outcomes and enhance the evaluation of individual studies and the display of summary information. The EPA implemented these recommendations throughout the document by including new figures such as those showing various ecological effects as a function of exposure concentration, by identifying and clarifying attributes of the key evidence considered in forming conclusions and by documenting the limitations and uncertainties of that evidence.

The CASAC recognized that the draft ISA integrated "an extraordinary amount of information about at-risk populations and employs a useful framework" for evaluation of potential at-risk populations and lifestyles and recommended that the EPA add a table to include information on the relative magnitude of the effect modification from various risk factors. My staff compiled and evaluated quantitative risk

estimates from health studies and found that there were few studies, and their results were not always comparable; thus, the information was incorporated in the text of the document where possible, rather than as a table. Given the characteristics of the available data we think this is an appropriate way to convey this information.

I once again extend my sincerest thanks to you and the panel members for your hard work. We are grateful for your independent critical reviews to help us ensure that the EPA uses the best science to protect public health and the environment.

Sincerely,



Gina McCarthy