



THE ADMINISTRATOR OF THE ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OCT 30 2015

Ana Diez Roux, M.D., Ph.D.
Chair
H. Christopher Frey, Ph.D.
Immediate Past Chair
Oxides of Nitrogen Primary NAAQS Review Panel
Clean Air Scientific Advisory Committee
Science Advisory Board
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington, D.C. 20460

Dear Drs. Diez Roux and Frey:

Thank you for your September 9, 2015, letter providing the Clean Air Scientific Advisory Committee Oxides of Nitrogen Review Panel's comments and recommendations on the U.S. Environmental Protection Agency's *Integrated Science Assessment (ISA) for Oxides of Nitrogen – Health Criteria (Second Review External Review Draft – January 2015)*. We at the EPA greatly appreciate the panel's thorough review and constructive comments. My staff is carefully considering your advice and the comments we received from the public. We are making revisions to address both consensus and individual Clean Air Scientific Advisory Committee comments.

The CASAC panel concurred with the causal determinations made in the second draft ISA for relationships between nitrogen-dioxide exposure and the array of evaluated health effects but recommended we more clearly communicate the reasoning behind the causal determination for respiratory effects from long-term exposure. Specifically, we are clarifying our reasoning for strengthening the determination from "suggestive, but not sufficient, to infer a causal relationship" in the 2008 ISA to "likely to be a causal relationship" in the current ISA. Guided by the ISA's causal framework, we are more explicitly linking new epidemiologic evidence with previous animal toxicological and controlled human-exposure evidence in a potential mode of action by which nitrogen-dioxide exposure could lead to asthma development.

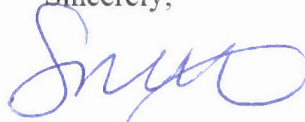
The discussion in the second draft ISA of spatial and temporal patterns in ambient nitrogen-dioxide concentrations was well-received by the CASAC panel. For the final ISA we are addressing the panel's advice to add details by including data on nitrogen-dioxide concentrations from the new U.S. near-road monitoring network and other sites close to emissions sources for more cities and for longer time periods. Further, description of near-road nitrogen-dioxide concentration gradients is being improved by delineating information for longer (e.g., weekly) and shorter (e.g., hourly) duration measurements.

The CASAC panel acknowledged the improved integration between nitrogen-dioxide-exposure assessment and epidemiology in characterizing potential exposure measurement error and confounding by co-pollutants.

Based on advice to refine the evaluations of the strength of the health-effects evidence, we are providing a more complete and balanced discussion of the strengths and limitations of various nitrogen-dioxide exposure assessment methods to represent personal exposure. We are using this information to more explicitly assess the adequacy of exposure assessment in individual epidemiologic studies rather than make broad generalizations about a particular method. We are also more consistently noting the extent to which key epidemiologic studies have assessed potential confounding by co-pollutants highly correlated with nitrogen-dioxide ambient concentrations and exposures, in particular, those related to traffic.

We recognize that our efforts to protect the environment can only be as good as the science upon which it is based. Independent critical reviews, such as those by CASAC, help ensure that we use the best science to protect our nation's environment and public health. Please accept my appreciation for your hard work and thoughtful review.

Sincerely,



Gina McCarthy