



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
NATIONAL CENTER FOR ENVIRONMENTAL ASSESSMENT
WASHINGTON, DC 20460

OFFICE OF
RESEARCH AND DEVELOPMENT

April 9, 2009

MEMORANDUM

SUBJECT: CASAC Review of the Integrated Science Assessment for Carbon Monoxide:
First External Review Draft

FROM: John Vandenberg, Ph.D. /s/
Division Director
National Center for Environmental Assessment
Research Triangle Park Division (B243-01)

TO: Ellen Rubin, Ph.D.
Designated Federal Officer
Clean Air Scientific Advisory Committee
EPA Science Advisory Board Staff Office (1400F)

The draft *Integrated Science Assessment for Carbon Monoxide: First External Review Draft* (ISA) prepared by the Environmental Protection Agency's (EPA) National Center for Environmental Assessment – Research Triangle Park Division (NCEA –RTP) as part of EPA's ongoing review of the national ambient air quality standards (NAAQS) for carbon monoxide (CO) was released on March 12, 2009. The draft ISA will be reviewed by the Clean Air Scientific Advisory Committee (CASAC) CO NAAQS Review Panel (the CASAC CO Panel) at a public meeting to be held in Chapel Hill, NC on May 12-13, 2009. I am requesting that you forward the charge questions listed below to the CASAC CO Panel to prepare for that review.

The purpose of the draft ISA is to identify, evaluate, and summarize scientific information on the health and welfare effects associated with CO. The ISA is intended to “accurately reflect the latest scientific knowledge useful in indicating the kind and extent of identifiable effects on public health which may be expected from the presence of [a] pollutant in ambient air” (Clean Air Act, Section 108; 42 U.S.C. 7408). This first external review draft ISA integrates the scientific evidence for review of the NAAQS for CO and provides draft findings, conclusions and judgments on the strength, coherence and plausibility of the evidence. The draft ISA is supported by five Annexes that provide more comprehensive and detailed information on the relevant evidence available from the disciplines of atmospheric sciences and human exposure (Annex A), dosimetry (Annex B), epidemiology (Annex C), controlled human exposure studies (Annex D), and toxicology (Annex E). These Annexes are provided with the ISA for the Panel's information. The CASAC CO Panel is being asked to review the draft ISA. NCEA-RTP will also address comments received on supporting material in the Annexes, to the extent that Panel

members wish to review and provide comments on the Annexes.

Following the review of the draft ISA, NCEA-RTP staff will produce a second draft ISA, which will be released for CASAC and public review in early autumn 2009. Staff from the Office of Air Quality Planning and Standards will produce a Scope and Methods Plan for their risk and exposure assessment documents, which will be reviewed by CASAC and the public.

Charge to the CASAC CO Panel

We ask the Panel to focus on the following questions in their review:

1. The framework for causal determination presented in Chapter 1 was developed and refined in other ISAs (e.g., the PM ISA). During previous reviews, CASAC generally endorsed this framework in judging the overall weight of the evidence for health effects. Please comment on the extent to which Chapter 1 provides necessary and sufficient background information for review of the subsequent chapters of the CO ISA.
2. Chapter 2 presents the integrative summary and conclusions from the health effects evidence, with the evidence characterized in detail in subsequent chapters. What are the views of the Panel on the effectiveness of the integration of atmospheric science, exposure assessment, dosimetry, pharmacokinetics, and health effects evidence in the CO ISA?
3. To what extent are the atmospheric science and air quality analyses presented in Chapter 3 clearly conveyed and appropriately characterized? Is the information provided regarding CO source characteristics, CO chemistry, policy-relevant background CO, and spatial and temporal patterns of CO concentrations accurate and relevant to the review of the CO NAAQS?
4. How well do the choice and emphasis of exposure topics presented in Chapter 3 provide useful context for the evaluation of human health effects in the ISA? Is the discussion and evaluation of evidence regarding human exposure to ambient CO and sources of variability and error in CO exposure assessment presented clearly, succinctly, and accurately? The ISA concludes in section 3.7 that central-site monitor concentration is generally a good indicator for the ambient component of personal CO exposure. What are the views of the Panel on this conclusion and its supporting evidence?
5. The dosimetry and pharmacokinetics of CO are discussed in Chapter 4. Please comment on the presentation in the ISA of the current state of knowledge on the Coburn-Foster-Kane (CFK) model and model enhancements. Has the expected contribution of different exposure durations (1-24 h) to COHb levels been clearly and accurately conveyed?
6. The mode of action section in Chapter 5 presents information on both hypoxic and non-hypoxic mechanisms for CO health effects, with particular emphasis on recent studies evaluating the non-hypoxic effects at low to moderate CO levels. Please comment on the appropriateness of the focus, structure and level of detail in this discussion. For example,

is the evidence relating to the interaction between inhaled CO and endogenous CO properly characterized?

7. Chapter 5 presents information on cardiovascular, central nervous system, developmental, respiratory, and mortality outcomes following exposure to CO. To what extent are the discussion and integration of toxicological, clinical, and epidemiologic evidence for these health effects scientifically sound, appropriately balanced, and clearly communicated? Are the tables and figures presented in Chapter 5 appropriate, adequate, and effective in advancing the interpretation of these health studies?
 - a. For cardiovascular outcomes, controlled human exposure studies discussed in Chapter 5 and in previous assessments have identified cardiovascular effects in diseased individuals following exposures near the level of the current standards, while new epidemiologic studies provide evidence of cardiovascular effects at ambient concentrations. What are the opinions of the Panel on the treatment of factors influencing the interpretation of this evidence, such as the plausibility of cardiovascular effects occurring at ambient levels, the additive effect of ambient CO to baseline COHb resulting from endogenous and non-ambient CO, and the challenge of distinguishing effects of CO within a multipollutant mixture (e.g., motor vehicle emissions) in interpreting epidemiologic study results?
 - b. Please comment on the implementation, in Chapter 5, of the causal framework presented in Chapter 1. Does the integration of health evidence focus on the most policy-relevant studies and health findings?
8. What are the views of the Panel on the discussion of factors affecting susceptibility and vulnerability in Section 5.7?

We look forward to discussing these issues with the CASAC CO Panel at our upcoming meeting. Should you have any questions regarding the draft ISA, please feel free to contact Dr. Mary Ross (919-541-5170, ross.mary@epa.gov) or Dr. Thomas Long (919-541-1880, long.tom@epa.gov).

cc: Lynn Flowers, ORD/NCEA
Tom Long, ORD/NCEA
Karen Martin, OAR/OAQPS
Dave McKee, OAR/OAQPS
Ines Pagan, OAR/OAQPS
Peter Preuss, ORD/NCEA
Mary Ross, ORD/NCEA
Debra Walsh, ORD/NCEA
Lydia Wegman, OAR/OAQPS
Vanessa Vu, SAB, OA