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

EPA-SAB-CASAC-91-015

July 17, 1991

OFFICE OF
THE ADMINISTRATOR

The Honorable William K. Reilly
Administrator
U.S. Environmental Protection Agency
401 M Street, SW
Washington, DC 20460

Dear Mr. Reilly:

At a public meeting held on April 30, 1991, the Clean Air Scientific Advisory Committee (CASAC) completed its review of the draft EPA Air Quality Criteria for Carbon Monoxide dated March 1990. The Committee unanimously concluded that this document, with minor revisions (currently being incorporated by ECAO Staff), provides a scientifically balanced and defensible summary of the current knowledge of the effects of this pollutant and provides an adequate basis for the EPA to make a decision as to the appropriate primary NAAQS for carbon monoxide.

The first external review draft of this document was released for public comment on April 30, 1990 with the comment period ending on July 31, 1990. CASAC is pleased with the responsiveness of ECAO in producing a comprehensive, well-written document to support Agency decision-making. For the record, I have attached brief responses to the major issues which were addressed in the Committee charge.

The CASAC is ready to review the Staff Paper on Carbon Monoxide as soon as it is available. The Committee urges the Agency to move forward as rapidly as possible with completion of the Staff Paper and, ultimately, the issuance of a reaffirmed or revised NAAQS for carbon monoxide based on the current scientific data.

We appreciate the opportunity to present our views on this important environmental health issue.

Sincerely,

Roger O. McClellan
Chairman, Clean Air
Scientific Advisory Committee

Attachment

Clean Air Scientific Advisory Committee
Review of
Draft Air Quality Criteria for Carbon Monoxide

On April 30, 1991, the Clean Air Scientific Advisory Committee convened to review the draft document Air Quality Criteria for Carbon Monoxide, dated March 1990. Development of this document stems from requirements of section 108 of the Clean Air Act. This section requires that the Administrator identify pollutants that may reasonably be anticipated to endanger public health or welfare and to issue air quality for them. These criteria must incorporate the latest scientific information available to indicate the type and extent of identifiable effects that may occur from exposure to the pollutant in ambient air.

Section 109 of the Act requires periodic review/revision of existing criteria and standards. If the Administrator concludes that the revised criteria make appropriate the proposal of new standards, such standards are to be promulgated in accordance with section 109(b). Conversely, if the Administrator concludes that the revisions to the standards are unnecessary, they remain unchanged.

In accordance with the Clean Air Act, EPA's Environmental Criteria and Assessment Office is revising the criteria for carbon monoxide, incorporating new data which have become available since the completion of the last criteria document (1979) and the addendum to that document (1984).

The draft carbon monoxide document review consisted of a chapter by chapter review and focused on addressing the following issues:

1) What method of analysis of blood carboxyhemoglobin levels, optical or gas chromatography, should be used to determine lowest observed adverse effect levels for CO? Should end-exposure or end-exercise COHb levels be used as an input to the exposure models of COHb formation developed by Coburn, Foster and Kane?

Due to the large amount of variability in spectroscopic measurement of carboxyhemoglobin by CO oxymeters, gas chromatography should be the method of choice.

Coburn-Foster-Kane-based models yield the expectant net increase in COHb for a given exposure to CO (concentration and duration), and the level of activity/exercise (alveolar ventilation and diffusing lung capacity for CO). Input to the model requires the preexposure COHb level, with the post exposure level

predicted by the model. The model does not accurately predict the rate of appearance of COHb at the blood sampling point because of the lag in the delivery of CO due to lung washing and blood circulation factors.

2) How important is tissue action of CO, given the likelihood of typical ambient exposures of the population to low levels of CO for 1 to 8 hours in duration?

Although it is difficult to expand on the information contained within the document, it should be noted that elevated levels of CO, particularly from bolus exposures, may potentially affect the electron transport chain. Also, some studies conclude that CO dissolved in plasma is more dangerous than elevated COHb levels. Low levels of dissolved CO may be significant in cellular respiration.

3) What fraction of the total population with ischemic heart disease (IHD) is represented by the study populations used in the recent key clinical investigations of Sheps, et al. (1987), Adams et al. (1988), Kleinman et al. (1989) and Allred et al. (1989)?

The study by Allred et al. and the Coronary Artery Surgery Study (CASS) provide a wide representation of patients with ischemic heart disease., and the CASS study is a good source of information on the variability of characteristics of IHD (almost 25,000 patients enrolled). All subjects studied for the effects of CO fall within this variability.However, since no Coronary Artery Disease (CAD) registry was developed for the CO studies, coupled with the change in characterization of CAD in recent years, it is difficult to assess the representativeness of the study populations.

4) Were appropriate statistical analyses used in the key studies on subjects with IHD? Should there be a more rigorous comparison of statistical approaches , including discussion of primary versus secondary analyses, use of trimmed or non-trimmed means, and choice of one- or two-tailed tests of significance? Could other formal techniques (meta-analysis) be used to provide a better assessment of data?

The analyses provided in the document were adequate and appropriate. In general statistical analyses need not be uniform, but should be tailored to the data being collected, and the distinction between one- and two-tailed tests is insignificant. Meta-analysis is useful, but graphic presentations such as those provided in figure 10-2 are satisfactory. However, error bars should be highlighted and made a common basis for data presentation.

5) Could differences in the study designs utilized in the key studies on the subjects with Ischemic Heart Disease account for some of the differences in the results?

It is unlikely that variations in study design resulted in variations in results. The protocols for each study are described in sufficient detail and the authors have done an excellent job of presenting and interpreting the results.

6) Are the small changes reported in the key studies on subjects with Ischemic Heart Disease of clinical significance? What is the definition of an adverse health effect in this population?

There is a wide distribution of opinion concerning this issue. The panel agrees that the effects observed at these levels are small performance decrements and that they are consistent across the populations studied. It is important to note that the ST segment changes and decrements in the time to onset of angina appear to be a consistent response to low levels of CO exposure. Among health professionals there is a range of views as to the clinical significance of these changes with the dominant view being that the changes should be considered as adverse or a harbinger of adverse effects.