August 10, 1999

EPA-SAB-CASAC-LTR-99-003

Honorable Carol M. Browner
Administrator
U.S. Environmental Protection Agency
401 M Street SW
Washington, DC 20460

RE: CASAC Review of the *Draft Document Air Quality Criteria for Carbon Monoxide* (EPA/600/P-99/001)

Dear Ms. Browner:

The Clean Air Scientific Advisory Committee (CASAC) of EPA's Science Advisory Board, supplemented by expert consultants (together referred to as the "Panel"), met on June 9, 1999 to review the February 1999 draft document, *Air Quality Criteria For Carbon Monoxide* (EPA/600/P-99/001), in a public meeting in Research Triangle Park, NC. This was the first draft of the new carbon monoxide (CO) Criteria Document since publication of the last CO Criteria Document in 1991, as part of the review of the National Ambient Air Quality Standards (NAAQS) for CO.

1. SUMMARY

As expected for a first draft of a Criteria Document, the Panel expressed the unanimous view that the document required revision and re-review by CASAC before it could constitute an adequate statement of the current scientific knowledge as a basis for reviewing the appropriateness of the existing CO NAAQS.

The Panel complimented EPA personnel (referred to as "Staff") for its good work in developing a high-quality first draft of a Criteria Document. Although attention must be given to numerous issues raised by the Panel in order for the document to be acceptable, the extent of the required revisions is modest and should be readily within the Staff's reach. The Panel especially complimented Staff for following through with the agreed-upon plan to focus on how new information might alter previous views of the effects of CO, rather than developing an exhaustive compilation of historic information.

The Panel recommended that information be added on the evolution of CO oximetry and its impact on interpretation of results, the implication for standard setting of the involvement of CO in ozone chemistry, interspecies differences in CO toxicokinetics, and potentially susceptible subpopulations. It noted the need for more analytical treatments of CO measurement methods, current health effects data, and uncertainties regarding both exposures and health risks. Additional recent literature on CO epidemiology and certain other topics was recommended for inclusion. The Panel questioned the emphasis given to information on acute high-level exposures and the health effects of CO poisoning, and the lack of justification given for its inclusion. It was

recommended that each chapter contain a summary of whether or not, and how, new information changes previously-held views of CO exposures and their health impacts. The Panel raised a broad range of other specific issues and editorial points that also need to be addressed

The Panel envisions no substantive barrier to the development of an acceptably revised CO Criteria Document and looks forward to the opportunity to review a revised document.

2. CHARGE TO CASAC

When queried at the end of the discussion of the document on June 9, Staff noted that it felt that the charge questions had been adequately addressed by the discussions and the Panel's comments. Accordingly, only selected summary responses to the charge questions are given here.

2.1 Coverage - *Are all pertinent issues adequately discussed? Are there any additional issues that should be addressed in the document?*

The coverage of general issues is complete. The Panel noted four specific issues that were either omitted, or discussed inadequately:

a) The potential effect of the evolution of technology for CO-oximetry and the variability in results among instruments on interpretation of the literature (Chapter 2).

b) The implications of the involvement of CO in ozone chemistry for standard setting; ie, justification for its inclusion in this document (Chapter 3).

c) Advances in our understanding of the amount and variability of contributions by vehicle emissions to general and roadside CO levels (Chapter 3).

d) The existence and implications of interspecies differences in CO pharmacokinetics (Chapter 5).

e) Potentially important susceptible subpopulations (Chapter 6).

2.2 Scientific Relevance - *Is the material focused and pertinent, given the subject matter and scope of the document? Does the material provide EPA with the kind of critical review and sound data useful for decisionmaking on the CO NAAQS?*

The material is relevant to consideration of the CO NAAQS, and is generally reasonably focused. Numerous of the Panelists' specific comments recommended improved focus on specific points. The Panel noted general needs for more analytical approaches to presenting information on measurement methodologies in Chapter 2 and on health effects in Chapter 6, and extracting key conclusions. With revisions adequately addressing the Panel's comments, the

document will provide a sound scientific basis for consideration of the appropriateness of the CO NAAQS.

2.3 Scientific Accuracy - *Is the material presented accurately, irrespective of other shortcomings?*

No circumstances of factually inaccurate material (other than points of minor editorial difficulties) were noted by the Panel. On the other hand, the Panel viewed the discussions in some areas as falling short of accurately portraying the nature and magnitude of current uncertainties. Points in this regard were raised in Chapters 3, 4, 5 and 6.

2.4 Literature Cited - *Are there any major or important omissions of pertinent literature?*

The panel recommended that Staff attempt to reduce the reliance on non-peer reviewed literature in Chapter 3. The extent to which appropriate peer-reviewed literature might have been overlooked was not clear. Specific suggestions were given for adding overlooked literature to Chapter 6.

2.5 Emphasis - *Is the length and level of detail appropriate, given the relative importance of the topic in the document?*

The length of the document is appropriate, and the Panel commends Staff for focusing on the extent to which recent findings alter views held at the time the last CO Criteria Document was written. The level of detail is generally appropriate, although additional detail on specific points is recommended in the Panel's comments. The Panel questions the emphasis given to high-level CO exposures and the effects resulting from acute CO "poisoning". It is not apparent that this information warrants the attention it received in the draft document.

2.6 Organization and Writing - *Is the document appropriately organized to address the key issues/topics covered? Is the document written clearly and concisely? If not, how might it be better organized or written?*

In general, the document is organized appropriately. Although minor organizational changes were recommended in specific places, the major sections and subsections follow in appropriate order. With revision to address the Panel's comments, the document will constitute an appropriately clear and concise summary of the current scientific knowledge regarding CO exposure and health risks.

The Panel recommends that, as the revisions are made, Staff review each chapter and integrative section to ensure that clear summary statements are made regarding whether, and how, new information has changed previously-held views of CO exposures and health risks.

3. COMMENTS BY CHAPTER

Only selected points are summarized below; no attempt is made to recapitulate all of the Panelist's comments. Numerous other points are raised in the comments of individual Panel members (Please see Appendix A) and the transcript of oral comments during the June 9, 1999 meeting. The appended comments are considered an integral part of the Panel's report, and Staff is urged to review them to develop a fuller understanding of the following points, and to note other issues which should also be given consideration, but are not summarized herein.

It should be noted that, although the following comments intentionally focus on criticisms and suggested changes, the Panel made numerous positive statements about the draft document, as reflected in both their written comments and the meeting transcript.

3.1 Chapter 1: Introduction

The Panel spent little time discussing the Executive Summary and Chapter 1. The structure and scope of these sections were considered appropriate. Some specific points were raised by individuals in written and oral comments. In general, these Sections appropriately introduce the document and portray appropriate summary information. It is anticipated that these sections will be reviewed carefully for changes needed to reflect revisions of the following material.

3.2 Chapter 2: Analytical Methods

Although the chapter contains a useful review of various measurement methods, it does not engage in an adequate evaluative comparison of the methods. Additional statements regarding the method(s) currently considered most effective for each measurement purpose would be useful. Comment on the utility of existing personal CO monitors and brief guidance for researchers conducting exposure assessments would be useful additions. Staff is advised to inquire about the status and potential usefulness of infrared-based remote sensing methods for obtaining average area concentrations for exposure assessment.

The subject material in Sections 2.2 and 2.4 seem duplicative, and might be combined.

There has been considerable development in CO-oximeter instrumentation over the years, and the different methods can yield different results. This issue should be described in chapter 2, and the type of instrument should be given throughout the document when "CO-Ox" results are presented.

3.3 Chapter 3: Sources, Emissions, and Concentrations

This chapter stands out from others in the document by citing numerous papers presented at meetings and unrefereed proceedings, as well as several technical reports of uncertain peer-review history. As an example, some important conclusions are drawn from the 1997 workshop proceedings published as an EPA document. Although this issue does not denigrate the accuracy

or usefulness of information communicated in proceedings, it would be best to rely on peer-reviewed publications to the extent possible, perhaps noting which, if any, of the material presented in meetings is in press in peer-reviewed journals.

It is not clear to the non-atmospheric scientist how "mixing ratio" differs from "concentration", or if it does not, why consistent terminology is not used throughout the document.

In the discussion of the potential reversal of the global decline in CO, the portrayal of the situation and its causes should be inclusive and tentative, taking care not to under-emphasize the uncertainty involved.

The discussion of the relative contributions of CO from human activity and other sources needs some clarification. From the information given, it is not clear that anthropogenic CO actually constitutes 80% of global CO as stated.

The context of the discussion of the involvement of CO in ozone chemistry is not clear. Although the chemistry facts are convincing, it is not clear what policy implications might extend from the relationship, or if none are intended, why so much space is dedicated to the discussion. The discussion of the atmospheric lifetime of CO could use clarification. The importances of temperature, deposition rates, and volumetric uptake by soil need clarification.

The considerable improvement since the last Criteria Document in our understanding of the contribution of engine emissions to general and roadside CO levels is not adequately portrayed. The relative contributions of different vehicle categories, the variability among in-use vehicles, and potential differences between predictions from certification testing and actual on-road emissions should be discussed in more detail.

The material in Section 3.4 is important, but the space given to the related material in Appendix 3A is questionable. The appendix might best be eliminated and the most relevant elements of that information moved into section 3.4 in condensed form.

It is not clear that the extensive discussion on indoor exposures warrants the relative weight given to the material in the chapter. Conversely, additional attention might be given to in-vehicle, roadway, and streetside microenvironments, in which people also spend a great deal of time. The CO exposures in these microenvironments is probably not well-represented by concentrations at area monitors, even though the CO sampled by are a monitors may be dominated by contributions from mobile sources.

3.4 Chapter 4: Population Exposure

Although the focus on information developed since the last Criteria Document is appropriate, it would be useful to present a succinct summary of historic population exposure levels in different environments as a jumping off point for the updated discussion. It would also

be useful to add some figures or tables to the subsequent sections to give perspective on actual contemporary exposure levels in different environments and among different segments of the population.

The basis for the considerable emphasis given to high-level CO exposures that lead to CO poisoning is not intuitive, and is not made clear. The relevance of these exposures to risks over which the Agency has some purview is questionable. If this pattern is to be followed for other pollutants, for example, one would expect discussions of occupational dust-induced pneumoconioses in the next particulate matter Criteria Document. These scenarios do not approach the significance of general indoor exposures in terms of person-hours. Similarly, the relevance of California's no-smoking policy is not made clear.

The discussion of exposure models presents the model components clearly, but does not adequately discuss where the inputs come from, the nature and magnitude of likely error, or the relative merits of different models.

3.5 Chapter 5: Pharmacokinetics and Mechanisms

The factors involved in the uptake and elimination of CO are described adequately, but the information on the distribution of the body burden of CO and the exchange between compartments needs strengthening. A table showing the distribution of CO mass in different compartments at an example exposure level would help place the contribution of endogenous CO and the tissue concentrations relative to blood concentration in a clearer context. The examples should be quantitative.

Although information in the chapter is drawn from both humans and animals, there is no mention of interspecies differences in CO uptake kinetics. The rate of uptake at a given exposure is known to differ considerably between rodents and humans, and this difference is certain to impact on the applicability of information from rodents to humans. This issue must be discussed.

The relevance of the information on mechanisms and effects given in Sections 5.7 and 5.8 to mechanisms and effects expected from ambient exposures is not stated, and should be discussed.

As described in detail in written comments and the meeting transcript, several points regarding the interrelationships among the pharmacokinetics of CO at ambient doses, physiological processes, and physiological clinical measurements need clarifying.

3.6 Chapter 6: Health Effects

Although the chapter appropriately avoids an exhaustive historical review of epidemiological studies, the review of more recent studies is not sufficiently complete. Four studies in particular, published during 1991 – 1999 and listed in Dr. Vedal's attached comments,

should be included. The inclusion of a table of epidemiology studies listing a few key features would help summarize the information. The present text descriptions of the studies vary considerably in their level of detail and the features they discuss. For both the epidemiological and non-epidemiological literature, the present text does not make it clear whether no more literature had been published since 1991, or additional literature existed but was not considered worthy to cite.

The description of the health effects data base is not sufficiently analytical. The validity of the studies with respect to our knowledge of CO health effects should be discussed, and the information should be placed in context regarding their utility in judging the adequacy of the CO standard. For example, some recent studies suggest that the epidemiological findings are not consistent and others appear to weaken the argument for specificity of effect. For some health effects, the present text does not adequately compare the strengths of the individual studies, or portray the balance of studies having positive and negative findings. There should be more discussion of the status of our ability to determine the extent to which the effects ascribed to CO may result from its being strongly correlated with other pollutants. More discussion of measurement error and its potential implications for interpreting the studies would be appropriate. Discussion of the biological plausibility of the relationship between ambient CO and non-cardiac effects should be included. The degree of uncertainty in our understanding of the effects of CO on the developing fetus is not adequately portrayed. Other examples of the need for a more analytical presentation are presented in the attached comments.

Several difficulties with the comparison of data from rats and humans in Figure 6-3 were raised and are noted in the individual comments and transcript. The Figure and accompanying explanation need either extensive revision or elimination.

3.7 Chapter 7: Integrative Summary and Conclusions

For many topics, this chapter does a reasonable job of integrating the foregoing information. Because this chapter is intended to integrate and summarize key aspects of preceding information, attention will need to be given to the extent to which changes influencing interpretations or conclusions in preceding chapters will necessitate changes here.

It is not apparent that the information presented in Sections 7.6 and 7.7 on health effects and susceptible populations represents the most appropriate summary and integration of the information presented in Chapter 6. The balance between presentation of acute, high-level effects and effects of lower ambient exposures is questionable. As noted before, it is not clear that the information on CO poisoning is central to understanding health risks from environmental exposures. The issue of susceptibility is raised in this chapter in greater detail than before. Although susceptibility is an important topic for integration, it would seem appropriate to include more detail on susceptible populations in Chapter 6, as a platform from which to extract key points in Chapter 7. The more detailed information in the preceding chapter could clarify the extent to which our current view of potential susceptible populations is speculative.

4. CONCLUSIONS

The Panel was unanimous in its opinion that the document needs revision and re-review by CASAC.

The Panel was complimentary of the document as a first review draft, and supportive of the focus of the present document on updating our information on exposures and health risks from CO since publication of the last Criteria Document. With revision along the lines suggested by the Panel's comments and discussions with Staff at the meeting, the document can represent an adequate synthesis of the present scientific information on CO, and serve as an adequate basis for the Agency's development of a Staff Paper focused on the appropriateness of the present CO NAAQS.

We appreciate the opportunity to review this draft document and to provide comments and advice to the Agency. We look forward to your response.

Sincerely,

Dr. Joe L. Mauderly, Chair
Clean Air Scientific Advisory Committee

U.S. Environmental Protection Agency
Science Advisory Board
Clean Air Scientific Advisory Committee (CASAC)
CASAC Carbon Monoxide Review Panel

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