

**Roger O. McClellan, DVM, MMS, DSc (Honorary),
Diplomate-ABT and ABVT
Fellow-ATS, SRA, AAAR, HPS, AAAS and Member-Institute of Medicine
Advisor, Toxicology and Human Health Risk Analysis
13701 Quaking Aspen Place N.E.
Albuquerque, NM 87111-7168
Tel: 505-296-7083
Cell: 505-850-9190
E-mail: roger.o.mcclellan@att.net**

February 23, 2015

TO: Albert Donnay

FROM: Roger O. McClellan



RE: Comments on your Draft Poster

Your e-mail of February 18, 2015 invited me and others to review and comment on your draft poster – “Re-analysis of Angina Study Cited by U.S. Environmental Protection Agency as a Primary Basis for National Ambient Air Quality Standards on Carbon Monoxide.” It is my understanding that the Poster will be presented at the Society of Toxicology meeting in San Diego, CA on March 26, 2015. You specifically asked that I review your draft Poster because I am identified by name in the Poster.

The draft Poster was also distributed to a number of other individuals with the memo of February 18th, specifically, copies to H. Vreman, W. Aranow, M. Pagano, C. Spino and D. Severson, apparently because they are mentioned by name in the draft Poster. In my opinion, the contents of the Poster are directed in part to the Health Effects Institute, the U.S. Environmental Protection Agency and the scientists who conducted the multi-center CO study. Thus, I was surprised that you did not provide those Institutions and individuals the opportunity to comment on the draft Poster. I am taking the liberty to send a copy of this memo to Dan Greenbaum at the HEI and Deirdre Murphy at the EPA.

In this memo I will address the specific question you addressed to me. In addition, I will offer some other comments on the contents of the draft Poster.

(1) Your draft Poster on the right side notes – “1992. EPA CASAC Chaired by Roger McClellan HEI CO Oversight Committee – then also President of SOT – endorses study as a primary for CO NAAQS.” This statement is rather confusing in the manner it links some factual statements; (a) I did serve on the HEI CO Oversight Committee (1983-1990); (b) I was Chair of CASAC (1987-1992); (c) I served as President of SOT (1989-1991); (d) The CASAC in 1992 did endorse the use of the results of the HEI CO Multi-Center study for setting the NAAQS for CO. The manner in which you present these four facts implies the facts are inter-related and inter-dependent.

The presentation would be much clearer if, under 1983 in the left side of the Poster, I was identified as a member of the HEI CO Oversight Committee. The fact that I served as SOT President in 1989-1990, Chair of CASAC in 1987-1992, and on the HEI Research Committee in 1981-1992, including membership on the HEI CO Oversight Committee from 1983-1991 when the last paper on the results of the study was published, are independent facts. My service on various EPA Science Advisory Board (SAB) Committees began soon after EPA was created and the SAB was created. Indeed, I was a Charter Member of the SAB. It would not have been possible for the SOT members to elect me as Vice President-Elect in early 1987 anticipating my becoming Chair of CASAC in 1987. Most certainly, the decisions made by CASAC when I served as Chair of CASAC were not influenced by my multiple roles in the HEI or SOT. Bottom line, a factual statement on your Poster would be – “1992. EPA CASAC, Chaired by Roger McClellan, endorses CO study as primary basis for CO NAAQS.”

I would note that your error in logic for this set of facts is repeated elsewhere in the Poster. The mere statement of two facts in juxta position does not mean the facts are linked and inter-dependent.

(2) As an over-arching statement – “It is my professional opinion, based on more than 50 years of experience conducting and interpreting research on air quality, that the HEI CO Multi-Center Study was planned, conducted, the findings analyzed and the results published in a scientifically appropriate manner.” Moreover, the results have been used in a scientifically appropriate manner to inform public policy decisions by the EPA Administrator on the setting of the NAAQS for CO.

I commend you for taking the time to review the conduct, analysis, and published results of the HEI CO Multi-Center study. As you note, you identified “over 150 examples of error,

misrepresentation and misconduct.” As you and I have discussed on multiple occasions, I would not have used the same language to describe your findings and conclusions. I would agree that in retrospect the HEI CO Multi-Center study did have some “warts and blemishes.” However, I think the core findings of the study remain sound.

The only serious finding you reported that is disappointing to me is my learning that the original study records were destroyed by the HEI in 2008. This is most disappointing to me because I view the HEI CO Multi-Center Study as a classic, one of a kind, study very well suited for re-analysis by multiple scientists and students. As you know, there has been much debate in recent years about preservation of scientific records and their availability for re-analysis by individuals other than the original researchers. I am on record as strongly supporting policies and practices that will require preservation of research records and their availability to other scientists while preserving the confidentiality of data on individuals. In my opinion, this is especially important for research conducted with public funding which addresses important societal issues such as the health effects of air pollutants. I strongly suspect that if HEI were faced with the same decision today on retention of records from the HEI CO Multi-Center Study, the decision would be to retain the records. That would certainly be the advice I would offer HEI today.

(3) In my opinion, you have done an admirable job of reconstructing the core data for the HEI CO Multi-Center Study. Indeed, I am sufficiently confident in your reconstruction of the data and re-analysis that I will accept your conclusions at the end of the Poster. I quote from your poster – “Most importantly for EPA Policy-making, 1-hour of exposure to CO at rest from 42 to 357 ppm had no significant effect and no dose-response effect on the mean times to angina or ST while exercising afterward in fresh air. % Change in time to angina and ST were not consistently correlated with Co, COHB, or each other [as shown at right], casting doubt on whether either is an indicator of myocardial ischemia as authors assumed a priori.”

I accept these scientific conclusions and endorse their use by the EPA Administrator in making the policy decisions required to set the NAAQS for CO. Thus, I see no basis for taking exception on scientific grounds to the EPA Administrator’s policy decision in 1994 and again in 2011 to re-affirm the NAAQS for CO as set in 1971.

(4) I urge you to carefully review your draft Poster focusing on presentation of key findings and recommendations for conducting and reporting results from similar studies in the

future. In revising your draft Poster I would remove the section you label – “Plagiarism.” As you and I have previously discussed, it is my opinion that you have misused and misinterpreted “plagiarism.” Using your very narrow interpretation of plagiarism, essentially every scientist who has ever submitted a required progress or final report to a government agency and published the same material in peer-reviewed papers would be viewed as guilty of “plagiarism.” Rubbish! Alternatively, I urge you to applaud the HEI approach to issuing detailed reports for most research studies HEI supports. In my professional opinion, such an approach should be strongly endorsed and other institutions and government agencies encouraged to follow suit. Indeed, if you did not have access to the detailed HEI report you would not have been able to do many of your re-analyses.

In summary, the HEI CO Multi-Center study planned, conducted and reported over an 8-year period (1983-1991) is the most robust study conducted to date of the short-term cardiac effects of brief exposure of human subjects to CO. Your detailed re-analysis of the study completed a quarter century after the results were originally reported, identifies how record keeping and analyses for this classic study might have been improved. Your analysis would not have been possible without access to the two peer-reviewed publications and the detailed HEI report. Each paper and the final detailed report had an important role. Your re-analysis emphasizes the importance of long-term maintenance of detailed records for studies of this kind.

A re-drafting of your Poster and preparation of a detailed manuscript focusing on recommendations for conducting similar studies in the future will be a valuable service to the scientific community and the public. When you revise your draft Poster it will be important to relate that the primary (health-based) NAAQS for carbon monoxide uses carbon monoxide as an indicator, an averaging time of 1 hour, a level of 35 ppm and the form is set as a maximum, not to be exceeded once in a year. This fact will provide a useful perspective for considering the level of carbon monoxide exposures used in the HEI CO Multi-Center Study.

xc: Dierdre Murphy, EPA
Dan Greenbaum, HEI
J. Brain
W. Aronow
N. E. Kaminski, SOT President

M. Pagano
S. Spino
D. Stevenson
P.L. Goering, SOT Vice President