Comments submitted during public review

1) Assessment of whether the Current Intelligence Bulletin has fully included all relevant material in its evaluation that is pursuant to its aims

No comments requiring a response.

2) Evaluation of whether the presentation and summarization of that material is fair and unbiased

See 3) below.

3) Determination of whether the overall conclusions are accurate and supportable, including those relating to support for the 1995 conclusions and recommendations

Bruce Watzman

Mr. Watzman submitted extensive comments on behalf of the National Mining Association. These are provided in detail in Appendix 1.

In summary, Mr. Watzman:

1) Was concerned about the peer-review process for the CIB (and, by implication, the CCD);

2) Was concerned with issues of data quality in the research upon which the CCD and CIB were based;

3) Indicated that there were many scientists and others who felt that the findings cited in the CCD and CIB were unreliable.

With respect to 1) the CIB was subject to review and public comment following procedures that comply with Office of Management and Budget (OMB) and the Department of Health and Human Services guidelines and procedures. The review steps included:
1) Internal review by division supervisors and scientists, as well as NIOSH experts;
2)Formal peer review by two independent experts with knowledge of coal mining worker health and stakeholder review by an expert associated the coal industry;
3)Public review by formal posting for 60 days using a NIOSH docket for organization of comments received http://wwwlink.cdc.gov/niosh/docket/archive/docket210.html ;
4)Advanced posting on the HHS Peer Review Agenda for highly influential scientific documents: http://www.cdc.gov/niosh/review/peer/HISA/expandashealth-pr.html5) Formal response to peer reviewers and public comments (including this document).

The CCD was produced prior to the issuance of the OMB guidelines but still complied with NIOSH standards for peer review and public comment. Those procedures are consistent with current Office of Management and Budget (OMB) and the Department of Health and Human Services guidelines and procedures. The review steps included:

1) Internal review by division supervisors and scientists, as well as NIOSH experts;
2)Formal peer review by independent experts with knowledge of coal mining worker health and stakeholder review by coal industry and labor representatives (see page xxii of the CCD).
3)Public review by formal posting for 60 days using a NIOSH docket for organization of comments received.
4) Endorsement by the Secretary of Labor's Advisory Committee on the Elimination of Pneumoconiosis Among Coal Mine Workers, a chartered committee of independent experts.

Each review stage was followed by document revision as required.

The material presented in the CIB is all drawn from published studies peer-reviewed as part of journal submission.

In his second main point, Mr. Watzman focuses on the increase in coal workers' pneumoconiosis that has been observed in recent years and questions whether it is real. This is actually not the major thrust of the CIB, which has as its aim the evaluation of post-1995 information with the intent of determining whether the new information substantially modifies the CCD recommendations. In the event, no information was uncovered that contradicted the CCD recommendations. Rather the observed increase in CWP strengthened the need for action.

In relation to his second point, Mr. Watzman has an extensive critique suggesting that miners with pneumoconiosis are more likely to select for examination in the coal miner surveillance program. This would imply that miners are aware of their radiologic status. Yet, given that miners with early stages of the disease do not generally have symptoms of their disease, this assertion is not very tenable. In some states, such as Kentucky, there are actual negative financial consequences in terms of future compensation, for participating if one has, or feels they may have, CWP.

Mr. Watzman also questioned the years of potential life lost analysis cited in the CIB. He states that causes of death noted on the death certificate often do not represent reality, being assigned to help coal miners obtain compensation. However, if the determination of pneumoconiosis or COPD on the death certificate is spurious, and therefore does not represent actual disease (and by implication no impairment or disability), there would be no excess loss in years of potential life lost. However, we found there were such losses. The findings are entirely consistent with prior mortality analyses showing that death rates from pneumoconiosis or COPD increase with increasing coal mine dust exposure.

Finally with respect to 2), among other things Mr. Watzman questions the data used for control of smoking in the analyses (of lung function and symptoms). This criticism really applies to studies that were cited in the CCD, since little has been published on this topic since then. Those data were obtained by interview with the miner using a standardized respiratory symptoms and smoking questionnaire based on a accepted standard international questionnaire that is used extensively in epidemiologic research. Such information has been validated, among other ways, by comparison with lung function and death certificate data.

In reply to Mr. Watzman's third point, our intent was to take into account all peer-reviewed scientific data and findings that relate to the document's aim. Mr. Watzman states that there is much controversy and doubt over the published findings from NIOSH. However he did not cited any peer-reviewed findings or data for consideration that make this point. The NIOSH findings are consistent with those from overseas, particularly from Britain, where for 50 years or so an extensive epidemiologic study has been underway. This British study not only benefitted from dust measurements collected for epidemiologic purposes but also had high worker participation rates, among other positive attributes.

One peer reviewer commented on the comments of Mr. Watzman. Those thoughts are provided in Appendix 2.

4) Evaluation of whether the organization and format of the material as presented is satisfactory for the intended purpose

No comments requiring a response.

5) Other comments

James Weeks

Glossary.

Aerodynamic Diameter: I suggest using the definition in the 1995 Criteria Document.

Accepted.

Chronic Obstructive Pulmonary Disease (COPD). A final sentence should read, "The diagnosis is confirmed by spirometry." This sentence is taken from:
NHLBI/WHO Global Initiative for Chronic Obstructive Lung Disease, Workshop Summary." Am J Respir Crit Care Med 163:1256-76, 2001.
This supports using spirometry as a necessary part of medical surveillance.

Accepted.

Coal Workers' Pneumoconiosis (CWP). This should include surface as well as underground miners and should read, "... employment in a coal mine" without limiting it to an underground mine. Surface coal miners get CWP too.

Accepted.

Crystalline Silica. The last sentence should read, "The predominant form of silica exposure is quartz." without limiting it to coal mines or even to mining.

Accepted.

on p 10, the document states, "Unfortunately, there is a lack of data on working hours . . " This is not quite true. Number of workers and working hours, from which one can derive hours per worker, per mine is reported for each mine under 30 CFR Part 50 and is available at

http://www.cdc.gov/niosh/mining/data/

under the accident and injury files from 1983 to 2008. Since these data are annual (quarterly, actually) for each mine, you should be able to link hours worked to the CWP research files for each subject in the file via their employment history and approximately adjust each miner's exposure. (This assumes you have the mine where the subject worked and for how long.) And in any event, you should include hours worked prospectively.

The text was revised to make it clear that the context related to the specific availability for individual workers required for epidemiologic research.

on p 15, Sec. 5.3 Compliance Policy & Procedures.

It is important to recognize the importance of longer work shifts and how it affects each miner's exposure. But you should take it a step further and show how it could affect compliance. Because of longer work shifts, there is a need to adjust the concentration limit of respirable dust in order to achieve the equivalent cumulative exposure that is provided for in the current 2 mg/m^3 8-hour standard. For example, for a ten-hour shift, the concentration limit combined with shift length should result in the same cumulative exposure as does the 2 mg/m^3 standard for 8 hours. This is a cumulative exposure of 2 mg/m^3 x 8 hours = 16 $mg\text{-}hrs/m^3$. For a ten-hour shift, the concentration limit should be 2 mg/m^3 x (8/10) = 1.6 mg/m^3 so that the cumulative exposure would be the same: 10 hrs x 1.6 mg/m^3 = 16 $mg\text{-}hrs/m^3$. Or, more generally, conc x time = constant. This is a well-established adjustment in industrial hygiene. (See for example, Armstrong et al., Occ Exposure Limits: an approach and calculation aid for extended work schedule adjustments. J Occup Environ Hyg 2005. 2(11):600-607.)

This suggestion is beyond the scope of the document, which is intended to be a review of new information and not a commentary on how the recommendations should be used.

One peer reviewer commented on the comments of Dr. Weeks. Those thoughts are provided in Appendix 3.

Appendix 1: Comments of Mr. Watzman

The following comments are submitted on behalf of the National Mining Association (NMA) in response to the draft document titled, "A Review of Information Published Since 1995 on Coal Mine Dust Exposures and Associated Health Outcomes" (the Post-1995 Report).

Over many years, NMA and its members have demonstrated their commitment to working with MSHA, CDC and NIOSH to ensure a safe and healthy working environment for all miners. In particular, NMA and its members agree that dust-related diseases in America's coal mines should be eliminated and support the industry and regulatory efforts, grounded in valid science, to accomplish that goal. NMA welcomes the opportunity to participate in this latest effort to evaluate the significance of newly evolving data, to best employ that data to maximize the effectiveness of dust control methodologies and to pursue a course toward the best health outcomes for America's coal miners.

NMA suggests that at this stage, a new approach is called for that will address the scientific controversies that have confounded the dust standards debate and facilitate any comprehensive action that may be needed. That new approach is set forth in the peer review requirements of the Information Quality Act, 44 U.S.C. § 3516, note. (IQA).

The IQA was enacted in 2001, after publication of the Criteria for a Recommended Standard Occupational Exposure to Respirable Coal Mine Dust (1995 Criteria Document), and was inapplicable to the 1995 Criteria Document. The IQA, however, is applicable to the draft and final Post-1995 Report addressed in these comments. IQA compliance is mandatory for all covered agencies and its application to the Post-1995 Report is not in doubt.

Generally, the IQA requires the Office of Management and Budget (OMB) to publish guidelines applicable to federal agencies "for ensuring and maximizing the quality, objectivity, utility and integrity of information (including statistical information) disseminated by Federal agencies". 67 Fed. Reg. 8452 (2002). Each covered agency also is required to publish its own guidelines and "establish administrative mechanisms allowing affected persons to seek and obtain correction of information maintained and disseminated by the agency that does not comply with the [OMB] guidelines." Id. On Sept. 9, 2010, the U.S. Department of Health and Human Services issued comprehensive agency-wide guidelines to implement the IQA. Part II D contains the sub-agency specific guidelines applicable to the Centers for Disease Control and Prevention and Agency for Toxic Substances and Disease Registry including the National Institute for Occupational Safety and Health, DHHS Guidelines, Part II D(I). Of equal importance and applicability is OMB's Bulletin for Peer Review, which was adopted to more fully and rigorously implement the language and intent of the IQA. 70 Fed. Reg. 2664-2667 (Jan. 14, 2005) (OMB Bulletin). Because of the high probability that the Post-1995 Report is comprised of highly influential scientific information that

may serve as a basis for regulatory action, the Post-1995 Report may also invoke the standards requiring additional peer review in accordance with paragraph III of the OMB Bulletin. 70 Fed. Reg. 2675. The OMB Bulletin also expressly provides that publication for public comment is not a substitute for peer review and does not satisfy the requirements of the bulletin.

For the reasons that follow, NMA believes that careful attention to IQA principles reflected in all applicable guidelines and a comprehensive, unbiased peer review process will provide a better, more useful and more universally acceptable analysis of the health effects that are attributable to coal mine dust exposures in our nation's coal mines.

In the 1995 Criteria Document, the authors favored a recommended exposure level for all coal mines of 1 mg/m3 as a time-weighted average for up to 10 hr/day during a 40-hour work-week measured according to current MSHA methods. The improvement of other protective strategies was recommended as well. Feasibility and cost were not considered at any length in the 1995 Criteria Document although it was understood that this recommendation would be both costly and difficult to achieve.
The 1995 Criteria Document did not, in the minds of many in the coal mining industry, make a strong or persuasive case that the applicable 2 mg/m3 permissible exposure limit was inadequately protective or that a reduction would have made a significant or measurable difference in the elimination or maximum achievable control of dust-related diseases. Much of the research relied upon in the 1995 Criteria Document was based on subject populations that worked for most or all of their careers in much dustier conditions than allowed by the 2 mg/m3 limit.

At the same time, the Work-Related Lung Disease Surveillance System data showed a dramatic decrease in the incidence of CWP (ILO 1/0 or greater) in the period from 1985-1994. This period also showed a significant decrease in the numbers of miners interested in participating in the surveillance programs, suggesting that the decline in the prevalence of disease in the larger populations of miners was even greater. Also, almost all of the Chronic Obstructive Pulmonary Disease (COPD) data was collected from study participants with little or no exposure to less dusty conditions mandated after 1972, and the COPD studies seemed to do a very poor job controlling for smoking and other non-occupational causes of COPD. This is particular relevant in that smoking prevalence has been documented to be particularly acute in the Appalachian region. Many have challenged the COPD studies for poor study design and for assumptions that were not justified by known science. In the opinion of some, the 1995 case seeking a more restrictive 1 mg/m3 standard was more theoretical and aspirational than it was grounded in sound science.

The draft Post-1995 Report, like its predecessor, seems to NMA to raise more questions than it answers and again shows less concern for documented confounding factors than NMA believes is warranted.

The centerpiece for the 2010 draft is a reported increase in the prevalence of pneumoconiosis among underground coal miners in the periods from 2000-2004 and 2005-2009 over the percentage of miners showing some level of CWP in the periods from 1990-1994 and 1995-1999. The 2005-2009 data showed a slight overall decline from the 2000-2004 period even though the more recent period reflects a targeted study. The study itself states: "the recent CWXSP findings may be upwardly biased, with the implication that the apparent rise in prevalence may be an artifact". The data reported do not show the degree of severity or advancement of CWP in these study groups, or compare severity with prior study groups.

The Post-1995 Report also reports that miners are developing CWP at earlier ages; that there has been an increase in years of potential life lost (YPLL) for currently exposed miners; and that new research confirms earlier findings that coal mine dust may produce clinically significant levels of chronic airways obstruction in miners independent of and perhaps additive to the effects of cigarette smoking. Perhaps, most troubling is a reported significant increase in prevalence of progressive massive fibrosis (PMF) in populations of longer term miners in the 2005-2009 period.

When the 1995 Criteria Document was publicly disseminated, it generated controversy in the mining and scientific community. The Post-1995 Report will do little to quell the ongoing controversy. Instead, it raises many questions that seem to be glossed over or deemed irrelevant in the pursuit of the Post-1995 Report's principal recommendation for a reduction in the PEL to 1 mg/m3 of coal mine dust and the development of a new separate PEL for crystalline silica.

For example, the conclusion that the periods from 2000-2004 and 2005-2009 show a meaningful and permanent increase in prevalence compared to earlier periods is a difficult claim to prove given the changing populations of miners examined; the likelihood that recent exposures would not significantly alter surveillance results for subjects whose work history occurred principally before the 2000-2004 and 2005-2009 time frames; and the lack of any longitudinal consistency in the self-selecting miner population. It does not seem that these confounding factors can easily be ironed out by standard statistical conventions, even though the draft claims to have largely eliminated serious bias. That claim is not convincing and questions of reproducibility and transparency remain unanswered.

The same concerns are present in the reported increases in PMF. After very steep declines in the prevalence of PMF, the reported uptick, especially in the 2005-2009 period, merits much more critical investigation and verification than it gets in the Post-1995 Report. PMF often is misdiagnosed even by B readers and the causes are still not well understood. Because the numbers of cases are few, even considering an increase in prevalence, and because typically the less healthy miners select into the surveillance programs and that effect is magnified by a targeted surveillance program, any conclusion that there is a PMF epidemic is premature and perhaps mistaken. It seems highly unlikely that PMF prevalence would so rapidly start creeping up to 1975-1985 levels when the subject populations had much more significant exposures to respirable

dust for most of their mining careers. A more rigorous peer reviewed investigation certainly is warranted in this connection.

In the same regard, the YPLL data is, in our opinion, entirely unreliable. In many coal mining communities, and certainly in eastern Appalachia, death certificates of former coal miners very frequently include a reference to pneumoconiosis or COPD as an "underlying" or even principal cause of death in order to help with a black lung claim. Indeed, in the litigation of black lung claims, the law has evolved to give little or no weight to death certificates in determining the cause of a miner's death.
The COPD analysis in the report is also quite controversial. Almost all of the principal research cited in the original 1995 Criteria Document involve miners with exposure histories pre-dating the 2 mg/m3 federal dust standard or foreign studies that are often difficult to evaluate or compare with U.S. data. In many of these studies, both from the U.S. and elsewhere, cigarette smoking histories are not very well documented, other causes of chronic airways obstruction, like asthma, are ignored and study design is subject to question in important respects.

The Post-1995 Report does not suggest that there is an increase in chronic obstructive lung disease or that the prediction of researchers cited in the original 1995 Criteria Document that the 2 mg/m3 standard would substantially reduce the risk of dust related COPD was incorrect. The post-1995 studies cited are very difficult to evaluate, have not all been peer-reviewed, and in many ways, seem to reflect the conviction of many of the pre-1995 researchers that they were correct in the first place -- broadly implicating coal mine dust in severe COPD, notwithstanding the views of critics.
For these and other reasons, many pulmonary scientists and others remain unconvinced that the CDC/NIOSH publications and research conclusions on coal mine dust are sufficiently reliable and scientifically rigorous to be considered authoritative.
The forward to the draft Post-1995 Report states:
A principal intent [of the Report] is to determine whether the 1995 recommendations remain valid in light of the new findings and whether they need to be updated or supplemented . . .

NMA does not conduct medical research, but many of its members are understandably concerned whether decision makers, whose research has a significant impact on them, are basing their analyses on the best possible science that is untainted by bias and outcome-driven studies and whether such science has been subjected to peer-review. The IQA should have a significant role to play in addressing those concerns and testing the validity of the scientific conclusions reached. NMA believes also that OMB's Final Information Quality Bulletin for Peer Review should be employed to ensure that the data and new research relied upon in the Post-1995 Report are appropriately disseminated to the public and regulators in keeping with the new requirements imposed by the IQA and the Bulletin for Peer Review.

NMA understands that CDC and NIOSH are very familiar with the requirements of the IQA and OMB's Bulletin for Peer Review. Because the 1995 Criteria Document was not subject to IQA requirements, it would be appropriate that the Post-1995 Report now

should be subject to a full peer review exercise. The Post-1995 Report presents new data and analysis and assumes the correctness of the analyses disseminated in the original 1995 Criteria Document without having also subjected it to peer review. There is no doubt that the Post-1995 Report proposes to disseminate influential scientific information as defined in Part II of the Peer Review Bulletin and it may well satisfy the requirements of Part III of the bulletin pertaining to Highly Influential Scientific Assessments.

Several peer review requirements stand out as being particularly noteworthy in this setting. First, NMA believes that special attention should be paid to the requirements of "independence" of reviewers and "rotation" of reviewers. NMA is concerned that the failure to include critics of the most controversial conclusions noted here suggests that the authors and researchers are not totally independent and unbiased. Following OMB's Peer Review Bulletin will help to gain industry acceptance of the final Post-1995 Report and better cooperation as the dust standard debate continues.
It is noted further that a certification of the administrative record of the peer review proceeding is required if there is an intent to use the Post-1995 Report in support of regulatory action.

Independent of the peer review process, NMA urges the drafters of the final report to pay special attention to IQA quality criteria. The essential principles of information quality according to the IQA statute, OMB and CDC guidelines are "utility," "objectivity" and "integrity." CDC Guidelines V.A. OMB and CDC guidelines further provide: "With regard to analysis of risks to human health, safety and the environment maintained or disseminated by the agencies, agencies shall either adopt or adapt the quality principles applied by Congress to risk information used and disseminated pursuant to the Safe Drinking Water Act Amendments of 1996 (SDWA) (42 U.S.C. 3009-1(b)(3)(A) and (D)." Id. § VII. The exacting risk assessment principles of the SDWA are set forth in § VII of CDC's guidelines.

Looking at the key elements of the information quality assessment, the objectivity standard is most directly implicated in an IQA review of the Post-1995 Report. Under OMB and CDC guidelines, "objectivity" requires that covered information be "accurate, clear, complete and unbiased . . ." and include the disclosure of "errors sources, affecting data quality . . . "67 Fed. Reg. 8459. The agency may ensure that the information reported is "accurate, reliable and unbiased" and that the "original and supporting data shall be generated and the analytic results shall be developed using sound statistical and research methods." Id. Agency compliance and the IQA are satisfied by "1) clearly identifying the limitations inherent in the information dissemination product (e.g., possibility of errors, degree of reliability and validity) so users are fully aware of the quality and integrity of the information . . ., 2) taking reasonable steps to remove the limitations inherent in the information, and 3) reconsidering [the delivery of] the information . . . ." Memorandum M-05-04 for the Heads of Executive Departments and Agencies (Dec. 17, 2004) http://whitehouse.gov/sites/default/files/omb/assets/omb/memoranda/fy2005/m05-04.pdf.

The COPD and chronic obstructive airways analyses, the meaning of new prevalence data and statistical relevance and validity of that data, viewed in light of study design and study populations; the relevance of any conclusion across all segments of the coal mining industry, including surface and Western mining operations; and the significance properly accorded to market data cited will all be better understood and accepted following rigorous peer review according to the OMB criteria, and the overall application of IQA quality standards where, as here, influential scientific information has been submitted for public dissemination and regulatory action. Federal science authorities have an obligation to satisfy the new requirements discussed in these comments.

For the reasons noted in this letter and, in particular, in light of the considerable controversy that has persisted for decades in the dissemination and utilization of information concerning the health hazards of coal mine dust, it is time to subject the research data to the best possible analysis to seek a consensus among all stakeholders for the future.

Appendix 2. Response of one peer reviewer to Mr. Watzman's comments

1) Need for IQA (Information Quality Act) peer review: This appears to be a legal/regulatory argument which is questioning the process by which NIOSH peer reviews its bulletins and documents and asserts that this document cannot be published without a separate peer review process including the OMB's Bulletin for Peer Review.

I am not qualified to render a legal opinion as to whether or not the NIOSH process is appropriate, however I would note that this document is not presenting new data that has yet to undergo peer review. Instead, this article is a review of data that has been extensively peer reviewed and published in the medical literature since 1995. There is no reference to any data or studies that have not been peer reviewed internally in NIOSH and externally prior to publication as full manuscripts in peer reviewed journal.

There is one exception to this and that is reference #24 which is data that is to be presented at his year's APHA conference. Consideration may be given to removing this reference from the update since the data has not been reviewed and published in manuscript form.

2) Watzman then goes on to criticize the 1995 criteria document, stating that it relied on pre 1972 data. He also states that there was little data on lung function and COPD from the post 1972 era, thus questioning its validity. This is incorrect, and not relevant to the current update as well. The 1995 CCD did include data from NSCWP after 1972 as well as much other later data. These data formed the main foundation of the document's arguments. Clearly data from before this time was discussed as it does inform our understanding of the health effects of coal mine dust.

Watzman makes several generalities regarding the 1995 CCD including stating that there was poor control of smoking histories in the COPD studies and that research relied upon in the CCD was challenged by "some" as having poor designs. He does not refer to any published critiques of the CCD or allege that the data was not appropriately peer reviewed.

I do not think these comments are particularly relevant to the current document, other than to criticize the original CCD and its conclusions, undermining the basis for affirming those conclusions.

Watzman then moves on criticize the Surveillance Data – Section 2.1 of the update. He seems to question the NIOSH surveillance data showing an increase in the prevalence of CWP. He ignores the plateau in CWP prevalence first reported in 2003 (as well as concerning increases in some subsets of miners). He then attributes subsequent reports of increases in prevalence to the focused enhanced surveillance program. This criticism was explicitly and convincingly discussed in the update. There was a detailed discussion of this bias in the update which essentially rules out an upward bias. He is also not convinced by the author's discussion of weighting state specific prevalence of disease by participation rates, but does not state why. He also seems to discount or

ignore the entire issue of hotspots of rapidly progressive and severe disease which were uncovered as part of the enhanced surveillance program.

Mr. Watzman also criticizes the reported increases in prevalence of CWP reported from CWXSP and the enhanced program because the populations are self selected, however the methodology of the regular program did not change and there is no data to support the notion that the population would change their pattern of self selection.

Mr. Watzman questions the data showing an increase in the prevalence of PMF, stating that it is often misdiagnosed, however there is no reason to assume that the rate of misdiagnosis would somehow be changing among the panel of NIOSH B-readers. There is also no evidence that the pattern of self selection of less healthy miners would somehow change as well. In addition, a targeted program only means that the geographic areas were targeted, not those sicker miners were somehow targeted thereby falsely elevating the prevalence of this disease.

In addition, examination of other data sources – such as the West Virginia OP data [See Wade et al. http://chestjournal.chestpubs.org/content/early/2010/09/28/chest.10-1326, have confirmed the findings in the NIOSH surveillance data.

Watzman also criticizes the YPPL due to the unreliability of death certificate data. He cites the propensity of authors of death certificates to note black lung in order to help black lung claims, however this tendency would not be expected to have changed recently, and therefore the trend would not be affected.

Watzman finally makes broad criticisms of the data in the update relating coal mine dust to COPD. He incorrectly states that the articles in this section were not peer reviewed when they were and notes that there have been "critics" of these studies, however there are no citations to published data contradicting these findings.

Watzman concludes by reiterating his concerns that the document be peer reviewed by the IQA process noted above.

In summary, I am not persuaded that Watzman has raised any significant issues related to the quality of the articles reviewed and included in this update. He has not identified any peer-reviewed literature that was not included in this review, has not cited any literature which has been published which contradicts the conclusions of the articles in this review or is a valid criticism of the published literature.

There is only one reference that I noted that has not been published as a full peer reviewed manuscript, but has been peer reviewed for presentation at the APHA meetings.

In order to avoid any criticism in this regard, removing this reference may be expedient.

Appendix 2. Response of one peer reviewer to Dr. Weeks' comments

One peer reviewer commented on the suggestions of Dr. Weeks as follows: "I agree with Dr. Weeks that the inclusion of spirometry as an essential component of the diagnosis of COPD is necessary. I would update the reference that he gave to use the GOLD COPD document of 2009. "A clinical diagnosis of COPD should be considered in any patient who has dyspnea, chronic cough, or sputum production, and/or a history of exposure to risk factors for the disease. The diagnosis should be confirmed by spirometry." Page 33. [Global Initiative For Chronic Obstructive Lung Disease. Updated 2009.

I think Dr. Weeks' other suggestions are quite useful."