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Keith McCoy

Vice President

Energy & Resources Policy

June 2, 2009

Information Quality Guidelines Staff (Mail Code 2811R)
United States Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Ariel Rios Building
Washington, D.C. 20460

Re: Request for Correction; Integrated Science Assessment - Oxides of Nitrogen

Dear Sir or Madam:

On behalf of the National Association of Manufacturers (NAM), I am submitting the attached Request for Correction (RFC) pursuant to Section 515(a) of the Treasury and General Government Appropriations Act for Fiscal Year 2001 (the Information Quality Act or IQA),[1] and the guidelines implementing the IQA issued by the United States Office of Management and Budget (OMB)[2] and the United States Environmental Protection Agency (EPA).[3] By way of background, the NAM is the nation's largest industrial trade association representing 11,000 small, medium and large manufacturers in all 50 states. The NAM is the leading voice of the manufacturing economy and its 12,700,000 workers in the United States.

As detailed below, in this RFC NAM requests correction of eight specific errors and omissions in EPA's final Integrated Science Assessment (ISA) for Oxides of Nitrogen (NO2),[4] as well as conforming changes to the final Risk and Exposure Assessment (REA) for the Primary NO_2 National Ambient Air Quality Standard (NAAQS),[5] and to any other EPA analyses, publications, or proposals predicated on information in the Final ISA that does not conform to EPA guidance and policy. If you have any questions related to the RFC, please contact Bryan Brendle at (202) 637-3176.

Sincerely,

Keith W. McCoy

Keith McCoy

cc: The Hon. Regina McCarthy, Assistant Administrator for Air and Radiation

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1 44 U.S.C. § 3516 (notes).

[2] OMB, Guidelines for Ensuring and Maximizing the Quality, Objectivity, Utility, and Integrity of Information Disseminated by Federal Agencies, 67 Fed. Reg. 8452 (Feb. 22, 2002), *available at* http://www.whitehouse.gov/omb/fedreg/reproducible2.pdf.

[3] EPA, Guidelines for Ensuring and Maximizing the Quality, Objectivity, Utility, and Integrity of Information Disseminated by the Environmental Protection Agency, EPA/260R-02-008 (Oct. 2002) (EPA Guidelines), *available at* http://www.epa.gov/QUALITY/informationguidelines/documents/EPA_InfoQualityGuidelines.pdf.

[4] EPA, Integrated Science Assessment for Oxides of Nitrogen -- Health Criteria, EPA/600/R-08/071 (July 2008) (Final ISA), *available at* http://oaspub.epa.gov/eims/eimscomm.getfile?p_download_id=475020.

[5] EPA, Risk and Exposure Assessment to Support the Review of the NO2 Primary National Ambient Air Quality Standard, EPA-452/R-08-008a (Nov. 2008) (Final REA), *available at* http://www.epa.gov/ttn/naaqs/standards/nox/data/20081121_NO2_ REA_final.pdf.

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Via E-Mail [to quality@epa.gov]

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As detailed below, in this RFC NAM requests correction of eight specific errors and omissions in EPA's final Integrated Science Assessment (ISA) for Oxides of Nitrogen (NO2),[4] as well as conforming changes to the final Risk and Exposure Assessment (REA) for the Primary NO_2 National Ambient Air

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4 EPA, Integrated Science Assessment for Oxides of Nitrogen -- Health Criteria, EPA/600/R-08/071 (July 2008) (Final ISA), *available at* http://oaspub.epa.gov/eims/eimscomm.getfile?p_download_id=475020.

Quality Standard (NAAQS),[5] and to any other EPA analyses, publications, or proposals predicated on information in the Final ISA that does not conform to EPA guidance and policy.

The NAM and its members are directly impacted by air quality regulations promulgated by the EPA and have a large stake in the transparency, consistency and science that forms the basis of the regulatory process. According to a 2008 study by the Manufacturing Institute, pollution abatement compliance costs amount to a 6.2 percent value-added tax on the domestic industrial sector, a rate which exceeds value-added burdens on all nine of the nation's major trading partners. Because of the cost disadvantage imposed by excessive regulation in the U.S., manufacturers advocate that objective, predictable and sound science be applied to all regulatory actions to avoid duplicative and unnecessary regulation. The NAM agrees with Congress that the Information Quality Act is an efficient tool with which to apply such standards in an evenhanded manner, not only with respect to the NAAQS process, but with all regulations promulgated by the EPA.

EXECUTIVE SUMMARY

In this RFC, NAM requests that EPA correct eight significant errors and omissions in the Final ISA for NO_2, and make conforming changes in the Final REA and in other EPA analyses that rely on the Final ISA. The corrections requested by NAM include the following:

- EPA's substantial reliance on an unpublished assessment described as a "meta-analysis" of the relation between NO_2 exposure and changes in airway responsiveness violates EPA Guidelines requiring "transparency about data and methods." EPA must prepare and release a report describing the methodology that was used and explaining how this document satisfies established scientific principles for conduct of a meta-analysis. EPA must then allow for proper scientific peer review and public comment concerning the methodology and use of this unpublished analysis.

- If EPA elects to retain the meta-analysis in the Final ISA, EPA must correct the Final ISA to resolve inconsistencies between the conclusions in the section on Airway Hyperresponsiveness and in the summary chapter.

- In the Final REA, EPA relied on a purported association between short-term NO_2 exposure and asthma from a study that was not properly reviewed in the Final ISA to support selection of a lower bound for potential short-term NO_2 standards. This use of a study that has not been fully reviewed by EPA scientists violates EPA Guidelines requiring use of the "best available science." The study in question did not find any association between asthma symptoms and NO_2 exposure after controlling for the effect of particulates. EPA must include a proper review of this study in the Final ISA, and must explain why it believes the study would provide any support for selection of a standard for NO_2.

- EPA assessments of several studies in the Final ISA differ materially from analyses of these same studies in EPA documents for prior NAAQS. Differing scientific evaluations

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[5] EPA, Risk and Exposure Assessment to Support the Review of the NO_2 Primary National Ambient Air Quality Standard, EPA-452/R-08-008a (Nov. 2008) (Final REA), *available at* http://www.epa.gov/ttn/naaqs/standards/nox/data/20081121_NO2_REA_final.pdf.

by EPA which appear to depend on the regulatory purpose for which data are being evaluated violate EPA Guidelines requiring "objectivity." EPA must either correct its current analyses to be consistent with its prior conclusions or explain why it believes those prior conclusions were incorrect.

I. INTRODUCTION

At the outset, NAM notes that the data and analyses appearing in the Final ISA are clearly "influential information" under several of the criteria given in the definition in the EPA Guidelines because the Final ISA was prepared and disseminated "in support of top Agency actions," the NO_2 NAAQS is an "economically significant action" as defined in Executive Order 12866, and peer review of the air quality criteria documents is expressly required by the Clean Air Act (CAA).[6] Because the information in the Final ISA is unquestionably "influential information" under the EPA Guidelines, it is required to "meet a higher standard of quality."[7]

In this RFC, NAM will identify eight specific errors and omissions in the Final ISA and request that these errors and omissions be corrected. One key omission that must be addressed involves the late addition to the Final ISA of data and conclusions based on an unpublished and undocumented assessment described as a "meta-analysis." This purported meta-analysis has never been released for public review and comment, nor has it been subjected to peer review by the Clean Air Science Advisory Committee (CASAC) or any other organization. Although it is difficult to reach any conclusions based on the sparse information provided by EPA, it appears that this unpublished analysis was compiled from existing data, and that it would not satisfy established scientific principles for conduct of a meta-analysis. EPA has materially based the conclusions in the Final ISA and the Final REA on this unpublished and unreleased analysis, and EPA is also developing future proposals concerning the NO_2 Primary NAAQS in reliance on the same material. These actions are not consistent with general IQA principles, or with the EPA Guidelines requiring "transparency about data and methods." EPA must prepare and release a written report describing the methodology used in this meta-analysis that includes an explanation and justification for its decision that it is scientifically valid to combine data from these diverse studies. EPA must also allow proper peer review and public comment concerning the methodology and use of this assessment.

The recent addition of material from the unpublished meta-analysis has also resulted in a serious contradiction and inconsistency in the Final ISA. The summary section of the Final ISA now includes a conclusion concerning the effect of short-term exposure to NO_2 on non-specific airway responsiveness that is inconsistent with the conclusions in the corresponding ISA chapter. This inconsistency must be corrected, because the EPA Guidelines require that information be "accurate" and "reliable."

The NAM also requests that EPA correct the Final ISA and the Final REA to properly address a study that EPA utilized in selecting the lower bound for potential short-term NO_2 standards. EPA did not evaluate this study in the Final ISA, and the Final REA characterizes the findings in the study in an inaccurate manner. EPA Guidelines requiring use of the "best available science" require that EPA do a proper scientific assessment of this study, and explain why EPA believes it has any relevance to selection of a short-term standard for NO_2.

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[6] EPA Guidelines at 19-20.

[7] EPA Guidelines at 19.

EPA must also reconcile its scientific conclusions in the Final ISA concerning three specific studies with the scientific assessments of these same studies in previous EPA documents prepared for other NAAQS. EPA's analysis is not "objective," as specifically required by the EPA Guidelines, because EPA's conclusions concerning the scientific meaning and value of particular studies differ materially based on the regulatory context in which they are considered.

II. THE NEW PROCESS FOR PERIODIC REVIEW OF NAAQS

EPA is required to list a particular pollutant under CAA Section 108 when it determines that emissions of that pollutant from numerous or diverse sources "may reasonably be anticipated to endanger public health or welfare."[8] After a pollutant is listed, EPA must develop air quality criteria for that substance that "accurately reflect the latest scientific knowledge useful in indicating the kind and extent of all identifiable effects on public health or welfare which may be expected from the presence of such pollutant in the ambient air, in varying quantities."[9] After issuance of air quality criteria for a listed pollutant, EPA must periodically review and revise such criteria.[10] This periodic review would normally be scheduled at five-year intervals, to coincide with the mandatory statutory schedule for review of the criteria and any necessary revision of the NAAQS themselves.[11]

In the past, periodic review of the NAAQS involved preparation of a voluminous Criteria Document, followed by issuance of a Staff Paper evaluating risk and exposure issues and making policy recommendations, and then a rulemaking to effect any needed revisions of the NAAQS. In December 2006, EPA decided to modify this process to make the evaluation of effects information and the assessment of risk and exposure more focused and concise, and to more clearly separate scientific analysis from policy judgments. Under this new process, which was revised in April 2007, EPA issues an ISA, which is intended to be a concise integration and synthesis of the science most pertinent to subsequent policy decisions, a REA that explains the key methodologies used, and a separate policy assessment issued in the form of an ANPR.[12]

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8 CAA § 108(a)(1), 42 U.S.C. § 7408(a)(1).

9 CAA § 108(a)(2), 42 U.S.C. § 7408(a)(2).

10 CAA § 108(c), 42 U.S.C. § 7408(c).

11 CAA § 109(d), 42 U.S.C. § 7409(d).

12 Memorandum from Marcus Peacock, EPA Deputy Administrator, to Dr. George Gray, Assistant Administrator, Office of Research and Development (ORD), and Bill Wehrum, Acting Assistant Administrator, Office of Air and Radiation (OAR), Re: Process for Reviewing National Ambient Air Quality Standards (Dec. 7, 2006) (2006 Peacock Memo), *available at* http://www.epa.gov/ttnnaaqs/memo_process_for_reviewing_naaqs.pdf; Memorandum from Marcus Peacock, EPA Deputy Administrator, to Dr. George Gray, Assistant Administrator, ORD, and Bill Wehrum, Acting Assistant Administrator, OAR, Re: Modifications to Process for Reviewing National Ambient Air Quality Standards (Apr. 17, 2007) (2007 Peacock Memo), *available at* http://www.epa.gov/ttnnaaqs/review.html.

In the case of the current periodic review for the NO_2 NAAQS, the generic five-year process for periodic review envisioned by the 2006/2007 policy was compressed to four years, and the anticipated 19 months between issuance of a draft ISA and the final ISA was reduced to 11 months.[13] When combined with EPA's decision to make late modifications and changes to the methodology EPA used for the ISA, this accelerated schedule has contributed to the deficiencies in information quality that are the subject of this RFC.

III. SUMMARY OF INFORMATION IN THE NITROGEN OXIDES ISA THAT DOES NOT CONFORM TO THE EPA GUIDELINES AND FOR WHICH NAM REQUESTS CORRECTIONS

A. EPA Conclusions in the Final ISA Based on an Unpublished and Undocumented Meta-Analysis

Late in the review process for the ISA, EPA added a new assessment which it described as a "meta-analysis" based on a diverse group of existing studies that considered the relation between NO_2 exposure and changes in airway responsiveness in asthmatics.[14] The process by which EPA prepared, adopted, and utilized this meta-analysis does not satisfy the EPA Guidelines concerning "transparency about data and methods." The meta-analysis in question was apparently prepared by or for EPA staff, using unspecified methodology, and has never been published, released to the public, presented to CASAC, or subjected to any other type of peer review process.

EPA's reliance on this unpublished and unreleased analysis violates a central tenet of the EPA Guidelines:

> It is important that analytic results for influential information have a higher degree of transparency regarding (1) the source of the data used, (2) the various assumptions employed, (3) the analytic methods applied, and (4) the statistical procedures employed.[15]

Rather than being transparent, the process by which EPA performed this meta-analysis is entirely opaque. The failure of EPA to provide any details concerning the methodology used to prepare this meta-analysis, or otherwise to subject the methodology it used to any form of scientific review, constitutes a severe violation of the EPA Guidelines. EPA's failure to disclose and justify the methodology utilized in this meta-analysis effectively prevents any meaningful peer review or public comment and must be corrected.

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13 *Compare* Generic NAAQS Review Process (Mar. 2007), attachment to the 2007 Peacock Memo, *available at* http://www.epa.gov/ttnnaaqs/peacock_4_17_07_attachment2.pdf, to the review schedule set forth in EPA, Integrated Review Plan for the Primary National Ambient Air Quality Standard for Nitrogen Dioxide (Aug. 2007) at 8, *available at* http://www.epa.gov/ttn/naaqs/standards/nox/data/20070823_nox_review_plan_final.pdf.

14 Final ISA at 3-16.

15 EPA Guidelines at 21.

There are established methodological problems with meta-analysis, which EPA itself has acknowledged elsewhere in the Final ISA. The validity of such analyses can be limited by "between-study heterogeneity and obvious publication bias,"[16] and "the heterogeneity of risk estimates seen in meta-analysis may also reflect the variation in analytical approaches across studies."[17] The failure of EPA to provide a description of the methodology it used for its unpublished meta-analysis precludes any meaningful scientific review by either CASAC or the public of the extent to which the meta-analysis is compromised by these well-recognized methodological problems.

Although it is not possible based on the material prepared and disclosed by EPA to review properly the purported "meta-analysis," the reported results indicate that EPA did not follow established scientific principles for performing a meta-analysis. EPA included results from studies utilizing a widely variable group of methodologies, including different methods of exposure, different exposure durations, different times between exposure and challenge, different challenge agents, and different measures of airway responsiveness. EPA excluded results from some other studies. EPA has provided no explanation or justification of the criteria used to include or exclude particular studies. There is no indication that EPA conducted any sensitivity analysis or used any of the established tests for heterogeneity. EPA also has not explained its selection of a test for statistical significance that considers only the frequency of response, but does not consider the magnitude of response or the causal relationship to NO_2 exposure. Due to the failure of EPA to disclose the methodology used in this assessment, none of these critical scientific concerns have been subject to proper public comment or scientific peer review.

EPA's unpublished and undocumented meta-analysis may profoundly influence the policy recommendations based on the Final ISA and the Final REA, because EPA is now suggesting for the first time that there is a statistically significant relationship between non-specific airway responsiveness and short-term exposure to 0.1 parts per million (100 parts per billion) NO_2. Thus, the inclusion of this information that does not conform to the EPA Guidelines may have a quite consequential impact on EPA policy concerning potential revisions of the NO_2 NAAQS.

The late insertion of this material has also resulted in a serious discrepancy between the conclusions concerning non-specific airway responsiveness in asthmatics that EPA reaches in the relevant chapter of the Final ISA and the conclusions on the same subject in the summary section of the Final ISA. In the section on Airway Hyperresponsiveness in the ISA chapter on Integrated Health Effects, EPA concludes:

> In general, small but significant increases in nonspecific airway responsiveness were observed in the range of 1.5 to 2.0 ppm for 3 h in healthy adults and between 0.2 and 0.3 ppm NO_2 for 30 min for asthmatics, but a wide range of responses were observed, particularly among asthmatics.[18]

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16 Final ISA at 3-23.

17 Final ISA at 3-49.

18 Final ISA at 3-17.

In contrast, the summary section of the Final ISA alters this conclusion by adding the phrase "and at 0.1 ppm NO_2 for 60-min exposures in asthmatics."[19] Since there is no support for the phrase added to the Final ISA conclusions in the individual studies previously evaluated by EPA, it is clear that this material alteration of EPA's basic conclusions is based exclusively on the new unpublished meta-analysis.

B. Substantial Reliance in the Final REA on Scientific Conclusions Concerning the Delfino (2002) Study That Are Not Supported by the ISA

To satisfy EPA Guidelines that require EPA to base its scientific conclusions concerning the effects of exposure to NO_2 on the "best available science," EPA must correct its decision to rely substantially in the Final REA on a study that was not properly reviewed in the Final ISA. IQA principles require that EPA base its analyses only on studies that have been thoroughly and objectively reviewed by EPA scientists. In the Final REA, EPA used a purported association from a study that was never subjected to any critical evaluation in the Final ISA to establish an NO_2 concentration of 50 ppb as the "lower end of the range" for potential short-term exposure standards.

The study by Delfino, *et al.* (2002)[20] is primarily an assessment of the effects of particulate air pollution, and it was barely mentioned during preparation of the Final ISA. References to this study appear only in two tables in the Final ISA[21] and in one table in the accompanying comprehensive ISA Annexes.[22] In contrast to many other epidemiologic studies, there is no narrative discussion of this study in the Final ISA, nor is there any indication that EPA scientists did any critical analysis of the study while preparing the Final ISA.

The study by Delfino, *et al.* (2002) was a study of the relation between air pollution and asthmatic symptoms in 22 asthmatic children. Careful evaluation of this study establishes that it does not support any association between short-term NO_2 exposure and asthmatic symptoms. There was no statistically significant association between asthma symptoms and 1-hour exposure to NO_2, and no significant association even for 8-hour exposure to NO_2 when using a multi-pollutant model that controlled for the effects of PM_{10}. EPA acknowledges that the effects of NO_2 were not statistically significant for this study in a multi-pollutant model in one of the footnotes in the Final REA.[23]

Although a critical review of the Delfino, *et al.* (2002) study would establish that this study does not support an association between either short-term or long-term NO_2 exposure and asthma symptoms,

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19 Final ISA at 5-11; *see also* Final REA at 33.

20 Delfino, R. J., Zeiger, R. S., Seltzer, J. M., Street, D. H., McLaren, C. E. (2002). Association of asthma symptoms with peak particulate air pollution and effect modification by anti-inflammatory medication use. *Environ. Health Perspect*. 110: A607-A617.

21 Final ISA at 5-8 and 5-17

22 EPA, Integrated Science Assessment for Oxides of Nitrogen -- Health Criteria, Annexes, EPA/600/R-08/072 (July 2008), at 6-22, *available at* http://oaspub.epa.gov/eims/eimscomm.getfile?p_download_id=475024.

23 Final REA at 52, note 6.

EPA bases one of its most important policy determinations in the Final REA on the existence of such an association. EPA requested additional ambient air exposure data from the investigators in the Delfino, *et al.* (2002) study, and that data showed that the maximum short-term NO_2 concentrations to which the subjects were exposed were relatively low (50 ppb at the 98th percentile and 53 ppb at the 99th percentile).[24]

Based on an incorrect premise that the Delfino, *et al.* (2002) study provides "evidence for associations between short-term ambient NO_2 concentrations and respiratory morbidity," the Final REA concludes "that it is appropriate to base the lower end of the range of alternative standard levels on this study."[25] The significance of the decision of EPA staff to utilize the Delfino, *et al.* (2002) study for this purpose is made quite clear in the final chapter of the REA, which states:

> The study by Delfino et al., (2002) provides evidence for associations between short-term ambient NO_2 concentrations and respiratory morbidity in a location where NO_2 concentrations were well below the levels in most other key epidemiologic studies.[26]

Just as in the case of the unpublished meta-analysis, it appears that EPA scientists manipulated the data to support a lower standard, rather than performing an objective and defensible appraisal of what standards the data will support. This sort of selective use of the data is even more troubling because the study on which EPA is basing its recommendation was never subjected to careful scientific scrutiny during the preparation of the Final ISA. Like the unpublished meta-analysis, EPA first made use of this information so late in the review process that meaningful peer review or comment opportunity was not possible. The substantial reliance of EPA in the Final REA on a study that was not carefully considered in the Final ISA constitutes a clear violation of IQA principles.

C. Inconsistent Scientific Conclusions in Differing EPA Documents Concerning the Same Studies

To satisfy the EPA Guidelines requiring "objectivity," the NAM also requests that EPA correct substantive assessments of particular studies in the Final ISA that differ materially from assessments of the same studies done by EPA in prior NAAQS documents. Differing scientific evaluations by EPA which appear to depend on the regulatory purpose for which data are being evaluated are inconsistent with the required objectivity. In particular, it is not appropriate for EPA to sequentially attribute all of the observed effects in a study to differing pollutants. EPA must use models and methods which are designed to separate the contributions of individual pollutants, and must account properly for confounding and surrogacy whenever it considers epidemiologic studies involving exposure to multiple pollutants. When EPA fails properly to evaluate the potential contributions of each pollutant to any observed effects, this also is contrary to its obligation under the CAA to include in air quality criteria:

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[24] Final REA at 53.

[25] Final REA at 54.

[26] Final REA at 303.

> [T]he types of air pollutants which, when present in the atmosphere, may interact with such pollutants to produce an adverse effect on public health or welfare.[27]

Study by Krewski, *et al.* (2002)

In the Final ISA, EPA cites the Krewski, *et al.* (2000) study[28] as evidence of a significant association between NO_2 exposure and mortality.[29] Although EPA acknowledges that exposure to NO_2 was "highly correlated" with other pollutants, including $PM_{2.5}$ and SO_2,[30] EPA does not consider the analysis of the respective contributions of single pollutants in the same study that EPA included in its prior Staff Paper for Particulate Matter. In that document, EPA stated: "In single-pollutant models, none of the gaseous co-pollutants was significantly associated with mortality except SO_2."[31] If EPA has not altered its scientific views concerning this study as expressed in the PM Staff Paper, it is entirely inappropriate for EPA to suggest that the Krewski, *et al.* (2000) study provides any evidence of an association between NO_2 exposure and mortality.

Study by Schildcrout, *et al.* (2006)

Another example of how EPA has reached different scientific conclusions in the Final ISA than in prior NAAQS documents is provided by the Schildcrout, *et al.* (2006) study.[32] In the Final ISA, EPA includes an extensive discussion of this study of asthmatic children and the relationship purportedly found in this study between NO_2 and various respiratory symptoms.[33] In contrast, as part of the NAAQS review for ozone, EPA expressly declined to rely on this same study because of specific limitations in the study

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27 CAA § 108(a)(2)(B), 42 U.S.C. § 7408(a)(2)(B).

28 Krewski, D., Burnett, R.T., Goldberg, M.S., Hoover, K., Siemiatycki, J., Jerrett, M., Abrahamowicz, M., White, W.H. (2000). Reanalysis of the Harvard Six Cities study and the American Cancer Society study of particulate air pollution and mortality: a special report of the Institute's Particle Epidemiology Reanalysis Project. Cambridge, MA: Health Effects Institute, *available at* http://pubs.healtheffects.org/view.php?id=6.

29 Final ISA at 3-74.

30 *Id.*

31 EPA, Review of the National Ambient Air Quality Standards for Particulate Matter: Policy Assessment of Scientific and Technical Information, OAQPS Staff Paper, EPA-452/R-05-005 (Dec. 2005) at 3-17 (PM Staff Paper), *available at* http://www.epa.gov/ttn/naaqs/standards/pm/data/pmstaffpaper_20051221.pdf.

32 Schildcrout, J.S., Sheppard, L., Lumley, T., Slaughter, J.C., Koenig, J.Q., Shapiro, G.G. (2006). Ambient air pollution and asthma exacerbations in children: an eight-city analysis. *Am. J. Epidemiol.* 164: 505-517.

33 Final ISA at 3-23 to 3-26, 5-11.

design. Among the limitations EPA cites were the fact that the Schildcrout, *et al.* (2006) study included "children in which the severity of their asthma was not clearly identified," and the use of a study population that was "not comparable to other large multi-city studies."[34] EPA must explain why it chose to discount the value of the Schildcrout, *et al.* (2006) study when evaluating the effects of ozone, but has relied on it extensively in the Final ISA for NO_2.

PEF and the Mortimer, *et al.* (2002) Study

A third example of how EPA has reached differing scientific conclusions depending on the regulatory context is the way that EPA has used studies of self-reported peak expiratory flow (PEF), particularly the large multi-city trial by Mortimer, *et al.* (2002).[35] In the rulemaking to revise the NAAQS for ozone, EPA placed considerable reliance on a finding in the Mortimer, *et al.* (2002) study of statistically significant associations between increased ozone levels and morning PEF, which remained significant even when concentrations exceeding 0.08 ppm were excluded from the analysis.[36] This reported association with lung function decrements was only positive for ozone. The discussion of this study in the final ozone criteria document states: "Of all the pollutants examined, including O_3, PM_{10}, NO_2, and SO_2, only O_3 was found to be associated with morning PEF."[37]

In contrast to its findings for ozone, EPA evaluated nine different studies of NO_2 exposure and PEF, and concluded that *none* of the nine studies showed any significant association with ambient NO_2 exposure.[38] Despite the significance that EPA assigned to PEF as a measure of lung function in the rulemaking for the ozone NAAQS, the Final ISA for NO_2 concludes:

> Recent epidemiologic studies provided somewhat inconsistent evidence on short-term exposure to NO_2 and inflammatory responses in the

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[34] EPA, Responses to Significant Comments on the 2007 Proposed Rule on the National Ambient Air Quality Standards for Ozone, Docket No. EPA-HQ-OAR-2005-0172 (Mar. 14, 2008) at A-4 to A-5, *available at* http://www.epa.gov/ttnnaaqs/standards/ozone/s_o3_cr_rc.html.

[35] Mortimer, K. M., Neas, L. M., Dockery, D. W., Redline, S., Tager, I. B. (2002). The effect of air pollution on inner-city children with asthma. *Eur. Respir. J.* 19: 699-705.

[36] EPA, National Ambient Air Quality Standards for Ozone, Proposed Rule, 72 Fed. Reg. 37818, 37828-29 (July 11, 2007), *available at* http://www.epa.gov/ttn/naaqs/standards/ozone/data/frnotice_07-11-07.pdf; EPA, National Ambient Air Quality Standards for Ozone, Final Rule, 73 Fed. Reg. 16436, 16445 (Mar. 27, 2008), *available at* http://www.epa.gov/fedrgstr/EPA-AIR/2008/March/Day-27/a5645.pdf.

[37] EPA, Air Quality Criteria for Ozone and Related Photochemical Oxidants, EPA 600/R-05/004aF (Feb. 2006), at 8-35, *available at* http://oaspub.epa.gov/eims/eimscomm.getfile?p_download_id=456384**.**

[38] Final ISA at 3-28.

> airways, as well as for associations with lung function decrements. The epidemiologic evidence for these effects can be characterized as consistent, in that associations are reported in studies conducted in numerous locations with a variety of methodological approaches.[39]

The second sentence is this quote is very misleading, because multiple studies found no association at all between one of the principal measures of impaired lung function previously utilized by EPA and NO_2 exposure.

IV. SPECIFIC CORRECTIONS THAT NAM REQUESTS TO THE FINAL ISA AND ALL SUBSEQUENT EPA DOCUMENTS THAT RELY ON CORRECTED INFORMATION

Based on the foregoing analysis, NAM requests that EPA make eight specific corrections to the Final ISA, as well as conforming corrections to the Final REA, the ANPR currently in preparation, and to any other EPA analyses, publications, or proposals predicated on corrected information in the Final ISA. The Final ISA is unquestionably "influential information" and the corrections requested by NAM are essential to satisfy the EPA Guidelines issued under the IQA. The specific corrections requested by NAM are itemized in Table 1 (appended).

EPA must prepare and release a report that includes a detailed description and justification of the methodology used in the unpublished "meta-analysis" of the relationship between short-term NO_2 exposure and non-specific airway responsiveness, including the specific criteria employed in including or excluding particular studies, all sensitivity analyses or other tests for heterogeneity, and any evaluation or test for publication bias. EPA must also subject this report to proper peer review by CASAC, and afford an opportunity for review and comment by other interested members of the public. These actions are essential to satisfy the EPA requirement for "transparency about data and methods." If EPA ultimately elects to retain this meta-analysis in the Final ISA and other documents after it have been properly reviewed and critiqued, EPA must revise the Final ISA to reconcile the differing conclusions in the section on Airway Hyperresponsiveness and in the summary chapter.

EPA must also revise the Final ISA to eliminate concerns about "objectivity" resulting from inconsistencies in its scientific assessment of particular studies. EPA's determination of what the "best available science" establishes should not be altered by the regulatory purpose of the analysis or by the policy objectives favored by the analysts. If EPA intends to rely materially on the Delfino, *et al* (2002) study in selecting the lower bound concentration for potential short-term NO_2 standards, EPA must conduct a proper scientific assessment of this study and incorporate that assessment in the Final ISA. EPA must also clearly explain why it believes that this study has any pertinence to selection of a short-term NO_2 standard, even though there was no significant association with NO_2 when the investigators controlled for the effect of particulate matter.

EPA must also fully reconcile the differing conclusions in the Final ISA and in the scientific analyses EPA previously prepared for other NAAQS. For each affected study or subject, EPA must either correct the analysis in the Final ISA to be fully consistent with its prior analyses, or it must clearly explain why it now believes that the scientific determination in the prior NAAQS documents was erroneous.

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[39] Final ISA at 3-42.

CONCLUSION:

The NAM appreciates the opportunity to submit this RFC and urges EPA to make the requisite corrections to the Final ISA and the related documents for the NO_2 NAAQS as promptly as practicable. While some of the necessary corrections will require time to accomplish, the NAM believes that all of the requested corrections are essential both to satisfy the EPA Guidelines and to complete a proper and defensible review of the NO_2 NAAQS under the CAA.

If you have any questions concerning this submission, please contact Bryan Brendle at (202) 637-3176 or bbrendle@nam.org.

EPA Information Quality Guidelines Staff
June 2, 2009
Table 1

Table 1

Item	Action Requested	IQA Concern
1	Prepare and release a report that includes a detailed description and justification of the methodology for the unpublished "meta-analysis" of short-term NO_2 exposure and non-specific airway responsiveness included in the Final ISA.	Transparency about data and methods
2	Submit the report on methodology for the "meta-analysis" for peer review by CASAC and public comment.	Peer review
3	If the "meta-analysis" is retained in the Final ISA, revise the Final ISA to reconcile differing conclusions in the section on "Airway Hyperresponsiveness" and in the summary chapter.	Accuracy
4	Either eliminate reliance on the Delfino, *et al.* (2002) study in the Final REA or include a proper scientific assessment of this study in the Final ISA.	Objectivity
5	If the Final REA continues to rely on the Delfino, *et al.* (2002) study, explain why this study is relevant to short-term NO_2 exposure when there was no significant association with NO_2 after controlling for particulate matter.	Best available science
6	Reconcile inconsistent conclusions concerning the Krewski, *et al.* (2000) study in the Final ISA and the Staff Paper for the NAAQS for Particulate Matter.	Consistency
7	Reconcile inconsistent conclusions concerning the Schildcrout, *et al.* (2006) study in the Final ISA and the rulemaking for the NAAQS for ozone.	Consistency
8	Reconcile inconsistent treatment of studies of self-reported peak expiratory flow (PEF) such as Mortimer, *et al.* (2002) in the Final ISA and the rulemaking for the NAAQS for ozone.	Consistency