



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON D.C. 20460

OFFICE OF THE ADMINISTRATOR
SCIENCE ADVISORY BOARD

June 10, 2014

EPA-CASAC-14-001

The Honorable Gina McCarthy
Administrator
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Washington, D.C. 20460

Subject: CASAC Review of the EPA's *Integrated Review Plan for the Primary National Ambient Air Quality Standards for Nitrogen Dioxide (External Review Draft)*

Dear Administrator McCarthy:

The Clean Air Scientific Advisory Committee (CASAC) Oxides of Nitrogen Primary National Ambient Air Quality Standards (NAAQS) Review Panel met on March 12, 2014, and May 7, 2014, to peer review the EPA's *Integrated Review Plan for the Primary National Ambient Air Quality Standards for Nitrogen Dioxide (External Review Draft)*, hereafter referred to as the Draft IRP. The Chartered CASAC approved this report during a public teleconference on May 7, 2014. The CASAC's consensus responses to the agency's charge questions and the individual review comments from the CASAC Oxides of Nitrogen Review Panel are enclosed.

Overall the CASAC finds the Draft IRP to be well written, well organized, and the topics are clearly presented. There are several recommendations for strengthening and improving the document highlighted below and detailed in the consensus responses. With the recommended revisions, the Draft IRP should serve its intended purpose in presenting the review plan, schedule, and process as well as the key policy-relevant science issues that will guide the Primary NAAQS for Nitrogen Dioxide (NO₂) review. A key purpose of the IRP is to present the key policy-relevant science issues that will inform the Integrated Science Assessment (ISA); thus, completion of the IRP should precede the completion of the Draft ISA, which was not the case for this review. Although the EPA did seek consultative advice on a portion of the IRP document from the CASAC Oxides of Nitrogen Panel in June 2013, the CASAC recommends that for future reviews, the IRP be completed and reviewed in its entirety prior to the completion of the First Draft ISA.

The CASAC recommends providing more detail and clarity regarding data from the new near-road monitoring network. The Draft IRP should indicate whether any of the near-road monitoring data will be obtained prior to the development of the Risk and Exposure Assessment (REA) document. The Draft IRP includes many of the key policy-relevant questions for consideration in the current NAAQS review. The CASAC identified a few additional policy-relevant questions that should be

included regarding important biological mechanisms and related modes of action, the assessment and use of exposure measurement and modeling error, and information on at-risk populations that live near NO₂ sources.

In the ambient environment, NO₂ exposures occur with those of copollutants. More attention should be given to NO₂ as a component of multi-pollutant mixture exposures. The Draft IRP needs to clearly frame the issue of copollutant exposures and clearly describe the plan for separating effects associated with NO₂ from effects associated with copollutants. The Draft IRP contains a list of questions that could be expanded to better assess the degree to which environmental pollutants, such as ozone or combustion-related copollutants (e.g., carbon monoxide, metals, black carbon, some organic species, fine particles and ultrafine particles) might act as confounders in epidemiological studies used in the ISA. Consideration also should be given to how these pollutants might act as effect modifiers in evaluations of mode of action or mechanisms and how the pollutants might interact in the atmosphere to alter spatial distributions and exposures. The near-road monitoring data may help inform these issues and there should be a discussion of how the data will be used.

The CASAC recommends including sensitivity analyses and formal uncertainty analyses (quantitative, when possible) in the plan for the Risk and Exposure Assessment (REA). These analyses would strengthen both the transparency and confidence in the REA and also might identify key gaps in the science related to oxides of nitrogen and inform both the research and regulatory community on future priorities.

The CASAC appreciates the opportunity to provide advice on the Draft IRP and looks forward to the EPA's response.

Sincerely,

/Signed/

Dr. H. Christopher Frey, Chair
Clean Air Scientific Advisory Committee

Enclosures

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Clean Air Scientific Advisory Committee
Oxides of Nitrogen Primary NAAQS Review Panel**

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Consensus Responses to Charge Questions on EPA's Integrated Review Plan for the Primary National Ambient Air Quality Standards for Nitrogen Dioxide (External Review Draft)

Overall Organization and Clarity

To what extent does the Panel find that the draft IRP clearly and appropriately communicates the plan for the current review of the primary NO₂ NAAQS and the key scientific and policy issues that will guide the review? To what extent are the decisions made in the last review, including the rationales for those decisions, clearly articulated?

The Draft IRP is very well organized and the plan for the current review is clearly presented. The history of the NO₂ NAAQS and the summary and rationale for the decisions made in the previous NO₂ NAAQS review are clear and concise. The summary of the previous review in section 1.1 may benefit from moving information related to legal aspects elsewhere, perhaps in footnotes, to improve readability.

Chapter 1 (Introduction) and Chapter 2 (Schedule)

To what extent does the Panel find that Chapters 1 and 2 clearly communicate the NAAQS legislative requirements, summarize the steps in the review process, summarize the history of the NO₂ NAAQS, and present the anticipated schedule for the current review?

Chapters 1 and 2 are well written and clearly communicate the NAAQS legislative requirements, the steps in the review process, the history of the NO₂ NAAQS, and the anticipated schedule for the current review. It would be helpful if Chapter 1 could note the start date for new literature considered for this review cycle (early 2008 as noted in section 3.1.1) and the anticipated end date of studies considered based on the current review schedule presented in Chapter 2.

There is some concern about the timing of the availability of sufficient NO₂ data from the near-road monitoring network relative to the need for these data to be used in the Risk and Exposure Assessment (REA) document (assuming an REA is developed for this review). An estimate of the number of near-road sites and amount (duration) of data from these sites that is expected to be available for use in the REA would be useful.

For near-road sites where the anticipated NO₂ design value is more than half of the NAAQS, there is a need for site descriptive information such as the proportion of truck traffic. Other traffic-related information, such as time-resolved traffic counts, and distance from the road would be helpful for a better understanding of the traffic factors that impact a specific site.

Chapter 3 – Key Policy-Relevant Issues

Building on key considerations and issues addressed in the last review, Chapter 3 presents a set of policy-relevant questions that will serve as a focus in this review. To what extent does the Panel find that these questions appropriately characterize the key scientific and policy issues for consideration in the current review? Are there additional issues that should be considered?

Chapter 3 presents a set of policy-relevant questions that will serve as a focus for the review of the NAAQS. Chapter 3 is well written and Figure 3-1 is particularly useful, as is the historical context summarized at the beginning of the chapter. In addition, the questions appropriately characterize many of the key scientific and policy issues for consideration in the current review.

The set of questions at the end of the chapter are overarching questions. The more specific questions in the other chapters of the IRP should be mapped to these overarching questions.

There are a few missing questions that should be added, including:

1. If new near-road monitoring data become available, how will they be used in the ensuing risk assessment?
2. What are the important biological mechanisms and related modes of action?
3. What are the important issues related to the assessment and use of exposure measurement and modeling error?
4. What information exists on at-risk populations near NO₂ sources?

Chapter 4 – Science Assessment

Chapter 4 describes the plan for the Integrated Science Assessment. Chapter 4 reflects revisions made to the Draft Plan for Development of the ISA for Nitrogen Oxides – Health Criteria, with consideration of comments received during the June 2013 consultation with CASAC.

To what extent does Chapter 4 clearly and adequately describe the scope, specific issues to be considered, and organization of the ISA? Please provide suggestions for any other issues that should be considered.

Chapter 4 provides the framework for the Integrated Science Assessment (ISA), highlighting the prior areas of identified uncertainty, and proposing an approach to assessing the new literature (and totality of evidence to date) related to oxides of nitrogen. The chapter is well written and provides a useful framework for the scientific questions that need to be addressed. There is some concern about the description of criteria for studies to be included in the literature review, and how decisions will be made with regard to the pertinence of studies to the questions at hand. More attention should be given to NO₂ as a component of multi-pollutant mixture exposures. The chapter contains a list of questions that could be expanded to better assess the degree to which environmental pollutants, such as ozone or combustion-related co-pollutants (for example, carbon monoxide, metals, black carbon, some organic species, fine particles and ultrafine particles) might act as positive or negative confounders in epidemiological studies used in the ISA. Consideration should also be given to how these pollutants might act as effect modifiers

in evaluations of mode of action or mechanisms and how the pollutants might interact in the atmosphere to alter spatial distributions and exposures.

With regard to animal research, will recent articles be held to new standards for reporting research, such as the *Animals in Research: Reporting In Vivo Experiments* (ARRIVE) guidelines (Kilkenny et al., 2010)?

Specific attention should be paid to the role of exposure assessment with regard to spatial and temporal variability and measurement error and how they relate to health effects. The discussion of measurement error starts well but does not discuss how measurement error will be handled in the ISA. A very important feature of error in exposure assessment is with respect to its adequacy for inference about health effects. This needs to be clearly discussed in the Draft IRP.

Please comment on the adequacy of the expanded discussion in Section 4.4 of issues that will be considered in the ISA related to: (a) spatial heterogeneity in ambient concentrations of oxides of nitrogen, particularly near- and on-road gradients, and implications for human exposures and (b) various factors to consider in the evaluation of health effects associated with ambient NO₂ exposure, including traffic, noise, indoor NO₂ exposures, and copollutant exposures.

In general the expanded discussion in Section 4.4 is adequate. However, the language concerning “multi-pollutant” exposures is inconsistent in the document. In non-experimental settings, it is difficult to disentangle effects associated with NO₂ exposure from effects associated with other near-combustion-source exposure. Moreover, source control measures that change NO₂ exposure are likely to have impacts on a suite of traffic-related air pollutants. The IRP should more clearly lay out the framework for how the EPA will separate out the effects associated with NO₂ from the effects associated with copollutants.

Other general concerns for this chapter

Chapter 4 would be further improved with an enhanced discussion of at-risk populations, including identification of additional at-risk groups that may have enhanced exposures to NO₂, including groups that have higher exposures as a result of their occupation, commuting exposures, and physical activity. Further, because exposures to oxides of nitrogen may be heavily influenced by time-in-traffic, the IRP should call for a specific focus on characterizing the exposures and response within the on-road microenvironment.

This section of the Draft IRP also lacks a discussion of socio-demographics of exposure, which may be an important consideration.

Chapter 5 – Quantitative Risk and Exposure Assessment

Chapter 5 summarizes the key risk and exposure analyses from the last review, including associated uncertainties, and discusses our planned approach to considering the potential for additional analyses in the current review. To what extent does Chapter 5 clearly and adequately describe the scope and specific issues, including the identification of the most important uncertainties, to be considered in developing the REA Planning Document for this review? To what extent is there additional information

that should be considered or additional issues that should be addressed in considering the potential for risk and/or exposure analyses in the current review?

Generally, Chapter 5 is well written and presents a reasonable series of approaches for conducting an REA for NO₂. The CASAC appreciates the manner in which the uncertainties from the 2008 REA are identified. Many of these uncertainties will serve as important topics for discussion in the upcoming REA planning document. In particular, a proper characterization of NO₂ spatial heterogeneity remains a key uncertainty and challenge in developing a future REA.

The CASAC recommends including sensitivity analyses and formal uncertainty analyses (quantitative, where possible) in the plan for the REA. Including sensitivity analyses of the primary modeled input parameters would strengthen both transparency and confidence in the REA. For example, the use of alternative or a range of plausible concentration-response functions for the epidemiology-based human health risk assessments would be useful (Page 5-17). Similarly, for both the air quality and human exposure components of the assessment, conducting formal uncertainty analyses or presenting propagation of error findings might identify key gaps in the science related to oxides of nitrogen and inform both the research and regulatory community on future priorities.

It is not clear how a future REA will utilize new methodological approaches, specifically with regard to hybrid and fused methods for estimating NO₂ spatiotemporal distributions. Models based on the AERMOD and Community Multi-scale Air Quality (CMAQ) models would generate refined near-roadway estimates, while accounting for potential chemistry and meteorological influences. For more details on new approaches that could be considered in an REA, see the individual comments by Dr. Georgopoulos.

The Draft IRP correctly cites the new near-road monitoring network as an important source of future information concerning NO₂ spatial distributions near roadways. Over time, these data hopefully will provide key information for use in exposure and risk analyses. Even in the absence of the near-road network data, however, more information currently exists concerning near-road NO₂ concentration gradients that could be utilized in a future REA. Individual comments from Dr. Sheppard note specifically that the Multi-Ethnic Study of Atherosclerosis and Air Pollution (MESA Air) study team has assembled geographic information on Air Quality System (AQS) sites that could be leveraged to inform questions on near-road NO₂.

The CASAC stresses the importance of the on-road microenvironment in contributing to total oxides of nitrogen exposure. Thus, modeling approaches used in the REA (i.e., Air Pollutants Exposure Model [APEX]) should pay specific attention to accurate characterizations of on-road and commuting exposures.

Although the focus of the REA should be on health risks associated with exposures to ambient NO₂, caution should be taken not to diminish the contribution to total exposure from indoor NO₂ sources, as well as the potential human health risks from these sources.

In the epidemiology-based REA approach, a major issue is whether the observed effects are from exposure to NO₂ alone, from other pollutants, or from the pollutant mixture. Although it is discussed within the context of uncertainty, this issue should receive greater emphasis. See individual comments from Dr. Zhang for further details.

Chapter 6 – Ambient Air Monitoring

To what extent does Chapter 6 clearly and appropriately communicate, for the purposes of this plan, the key aspects of measurement methods and surveillance network requirements for the NO₂ NAAQS?

The discussion in Chapter 6 about NO₂ measurement is useful and to the point with respect to NAAQS measurement of NO₂. The chapter can be strengthened by:

- Reviewing it for consistency with Chapter 4 (pp. 4-11 to 4-12 and the questions at the top of p. 3-15);
- Giving greater attention to an evaluation/discussion of other measurements that are key to interpreting the near-road network data; and
- Discussing two distinct purposes of observations (and their implications for network design):
 - to assess compliance with a NO₂ standard;
 - to better understand exposures and health effects of near road pollutants. This requires measurements in addition to NO₂ including nitric oxide, carbon monoxide, PM_{2.5}, and other non-NAAQS pollutants, such as black carbon and particle number concentration.

Chapter 7 – Policy Assessment and Rulemaking

To what extent does Chapter 7 clearly summarize the general process for the policy assessment and rulemaking phase of this review?

Chapter 7 is well written and covers the relevant topics. The CASAC has no recommended changes to this chapter.

References

Kilkenny, C., Browne, W. J., Cuthill, I. C., Emerson, M., and Altman, D. G. (2010). Improving bioscience research reporting: The ARRIVE guidelines for reporting animal research. *PLoS Biol*, 8(6):e1000412+.

Appendix A

Individual Comments by CASAC Oxides of Nitrogen Primary NAAQS Review Panel Members on EPA’s Integrated Review Plan for the Primary National Ambient Air Quality Standards for Nitrogen Dioxide (External Review Draft)

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Mr. George A. Allen

These comments focus on Chapters 1 and 2 (Introduction and Schedule) and Chapter 6 (Ambient Air Monitoring)

Charge Questions

Overall organization and clarity: To what extent does the Panel find that the draft IRP clearly and appropriately communicates the plan for the current review of the primary NO₂ NAAQS and the key scientific and policy issues that will guide the review? To what extent are the decisions made in the last review, including the rationales for those decisions, clearly articulated?

This draft of the IRP is very well organized. The plan for this current review is clearly presented. The history of the NO₂ NAAQS and the summary of the decisions and the rationale for them in the last review are clear and concise.

Introduction (Chapter 1) and Schedule (Chapter 2): To what extent does the Panel find that Chapters 1 and 2 clearly communicate the NAAQS legislative requirements, summarize the steps in the review process, summarize the history of the NO₂ NAAQS, and present the anticipated schedule for the current review?

These two chapters are well written, and meet the goals noted in this charge question.

Ambient Air Monitoring (Chapter 6): To what extent does Chapter 6 clearly and appropriately communicate, for the purposes of this plan, the key aspects of measurement methods and surveillance network requirements for the NO₂ NAAQS?

Section 6.1, Consideration of Sampling and Analysis Methods, provides a clear summary of existing and new methods for measurement of NO₂. Of most interest is the recent commercial availability of direct NO₂ measurement methods using the cavity attenuated phase shift (CAPS) technique. One commercially available CAPS instrument has an FEM designation, and a second is in the final stages of FEM approval at ORD. These instruments are expected to be a practical alternative (in terms of cost and operational effort) to the traditional CL-moly converter FRM monitor.

This section raises an important question regarding the potential of routine network deployment of CAPS or any other method that only measures NO₂ (e.g., does not measure NO). The potential loss of NO_x data is of concern, since NO_x is often the only widely available exposure surrogate for on-road pollutants. In addition, section 2.6.4.3 of the draft NO₂ ISA discusses the development of an “Integrated Mobile Source Indicator” to improve exposure assessment to on-road air pollutants. This “Indicator” uses CO, EC or BC, and NO_x as input parameters. The loss of NO_x data in routine ambient measurement networks would have a substantial impact on the performance of this indicator approach.

Section 6.2, Consideration of Air Monitoring Network Requirements.

This section is a concise summary of the existing and planned NO₂ monitoring networks. The Area-Wide and “susceptible and vulnerable communities” components of the monitoring network required by

the 2010 NO₂ rule are in place, since existing NO₂ monitors met these requirements. Section 6.2 also summarizes the design and requirements of the new near-road network component that has just recently begun to be deployed. This summary covers the number of sites and time line for deployment, but could benefit from additional detail on what other measurements are required at these sites. Some near-road sites require CO and PM_{2.5} along with (NO and) NO₂, and usually have optical black carbon and meteorological measurements also (some have particle number concentration too). These sites generate all the measurement inputs needed for the “Integrated Mobile Source Indicator” approach noted above and in the ISA. Other sites require only NO₂ measurements.

Most of the “NO₂ only” sites are in the third and final deployment phase, scheduled to be operational by January 2017. One of the near-road network goals is to support research; sites with only NO₂ measurements have minimal value in this context.

Section 6.2 ends with a sentence (Pg 6-5, lines 3-5) that suggests the minimum near-road network requirements promulgated in the 2010 rule could be re-evaluated during this review:

“Considering the availability of new near-road NO₂ monitoring data, the EPA may be in a position to re-evaluate the analyses underlying the minimum monitoring requirements promulgated in the 2010 revisions in this review.”

Since it is unlikely that EPA would increase the minimum requirements, this sentence could be taken to mean that when sufficient data is available, EPA may be able to justify reducing the final near-road network size by reducing or eliminating the third phase of near-road site deployment. This would be consistent with the continued downward trend of primary on-road NO₂ emissions due to both new (2010) controls on diesel emissions and the Tier 3 standards for both fuels (lower S gasoline) and automotive emissions controls that go into effect in 2017.

Thus, it is important that EPA commence to conduct analysis of NO₂ data from the near-road network as soon as it becomes available (later this or early next year).

Dr. Matthew Campen

Comments on Chapter 4

To what extent does Chapter 4 clearly and adequately describe the scope, specific issues to be considered, and organization of the ISA? Please provide suggestions for any other issues that should be considered.

Literature search – are all search-retrieved documents recorded and rationale for why they are considered/not considered also recorded?

Comment on page 4-8: “In addition, consideration will be given to studies that investigate exposure to oxides of nitrogen separately and in combination with other pollutants such as ozone, PM, and sulfur dioxide.”

It is generally understood that ozone and NO_x are mutually exclusive. That is, they will react out and thus tend not to co-exist. I would consider just dropping “ozone” from this sentence. Certainly, it is a sentence of hypothetical options, but all the same...

In 4.3.3, at the end regarding in vitro studies, I think a statement to anatomical relevance would be nice to see – that is, we should not be studying direct exposures of NO₂ on neurons or endothelial cells. Pretty much lung epithelia and other airway cells.

Comma after NAAQS review, bottom of 4-10 (very long sentence)

Please comment on the adequacy of the expanded discussion in Section 4.4 of issues that will be considered in the ISA related to:

(a) spatial heterogeneity in ambient concentrations of oxides of nitrogen, particularly near- and on-road gradients, and implications for human exposures and

There is strong language related to concerns about inadequacies of central site monitoring and an apparent appreciation for the roadway-associated nature of these exposures. I feel the approach is appropriate.

(b) various factors to consider in the evaluation of health effects associated with ambient NO₂ exposure, including traffic, noise, indoor NO₂ exposures, and copollutant exposures.

Certainly there are profound covariates to consider, but such is the case with most NAAQS pollutants. NO_x should be treated in a consistent manner with other recent ISAs.

Dr. Ronald C. Cohen

Comments on Chapter 6

The Chapter should be more strongly connected to the overview of "Atmospheric science and ambient concentrations" in CH4 pgs 4-11-4-12

The Chapter overemphasizes the question of loss of NO measurements and underemphasizes the benefits of new FEM methods that are specific to NO₂.

The substantial positive bias of the FRM NO₂ should be explicitly acknowledged on pg 6-1 near line 30
on pg 6-23 lines 1-4 and 6-13

The lack of positive bias from higher oxides of N (PAN, RONO₂ and HNO₃) should be explicitly mentioned for all three new instruments.

pg 6-2 line 18-20 The tone of the question presumes a negative. It would be more appropriate to ask what the balance between the benefits of having interference free measurements and the costs of losing NO measurements. Also, it would be appropriate to ask whether losing NO measurements is necessary.

pgs 6-3-6-5

some discussion of what concurrent measurements are needed to support isolating exposure effects to NO₂ as separate from other traffic related emissions would be pertinent here.

Dr. Philip M. Fine

Comments on Chapter 6 – Ambient Air Monitoring

To what extent does Chapter 6 clearly and appropriately communicate, for the purposes of this plan, the key aspects of measurement methods and surveillance network requirements for the NO₂ NAAQS?

The chapter provides a concise summary of the NO_x measurement methods and the existing and future national NO_x monitoring network. The last line of Chapter 6 anticipates that EPA may re-evaluate the analysis that underlies the minimum monitoring requirements for the NO_x near road network. A more detailed discussion may be appropriate regarding the criteria for evaluating the adequacy of the network relative to various monitoring objectives (NAAQS, health studies, public information). There is a potential divergence of opinions among stakeholders on this topic, and there should be plan for analyzing this issue carefully to help support any potential monitoring regulation changes in the future.

Page 6-1, Line 27

It is stated that the catalytic converter reduces ALL oxidized nitrogen species to NO. It may not be true that all oxidized nitrogen species are reduced, and the ISA discussion on this topic points to varying conversion efficiencies for different species, depending on temperature on other factors. The discussions in the two documents should be reconciled.

Dr. Panos G. Georgopoulos

Comments on Chapter 5

Chapter 5 (Quantitative Risk and Exposure Assessment) of “Integrated Review Plan for the Primary National Ambient Air Quality Standards for Nitrogen Dioxide” focuses on and describes the approach pursued during the prior review of 2008 (Section 5.1, pages 5-2 to 5-11). The consideration of “quantitative assessments for this review” is the subject of Section 5.2 (pages 5-11 to 5-12 and Tables 5-1 and 5-2). Section 5-1 includes a discussion of the uncertainties involved in the approach of the prior review, while Table 5-1, “Information (data, methods, models, etc.) identified as potentially important and/or newly available to inform the air quality characterization for the current review,” and Table 5-2, “Information (data, methods, models, etc.) identified as potentially important and/or newly available to inform the exposure assessment for the current review,” summarize, in the rightmost column, potential approaches for addressing components of the above uncertainties with this new information. However, it is not clear whether any of the methods for modeling air quality and exposure, which are applicable to oxides of nitrogen, that have evolved since the prior review, are going to be utilized in this context. For example, Özkaynak et al. (2013) summarized the findings of a series of presentations that took place at the International Society of Exposure Science 2011 Conference in Baltimore, MD. Symposium presenters considered a range of “alternative exposure metrics, including: central site or interpolated monitoring data, regional pollution levels predicted using the national scale Community Multiscale Air Quality model (CMAQ) or from measurements combined with local-scale (AERMOD) air quality models, hybrid models that included satellite data, statistically blended modeling and measurement data, concentrations adjusted by home infiltration rates, and population-based human exposure model (Stochastic Human Exposure and Dose Simulation, and Air Pollutants Exposure models) predictions.” (See also Özkaynak et al., 2014.) In another study that also used complementary air quality models (Beevers et al., 2013) employed both KCLurban, which gives source apportionment information, and the Community Multi-scale Air Quality model (CMAQ)-urban to characterize NO_x and NO₂ and evaluate the performance of the modeling approach. Given the fact that in recent years long-term (annual and multi-year) CMAQ simulations are becoming more commonly available for North America (e.g. Civerolo et al., 2010; Zhang et al., 2009), that can provide hourly estimates of NO and NO₂ concentrations at “background” level (typically 12x12 km resolution), it is strongly recommended that USEPA at least evaluate a hybrid modeling approach that would use a model such as AERMOD to “downscale” CMAQ estimates at point level (near-road, neighborhood, etc.) and use these estimates in conjunction with an exposure model such as APEX. It would also be useful, in such an enterprise, to consider dispersion models alternative to AERMOD, specifically CALPUFF which was used in the study of (Yu & Stuart, 2013), as this model may have more flexibility than AERMOD for applications relevant to the NO_x system, where nonlinearity of photochemical interactions poses particular challenges.

Another issue that should be addressed carefully in the context of exposure characterization is the issue of indoor NO_x emissions. The IRP document states on page 5-9 that “... in a limited set of targeted exposure analyses, exposures were also modeled considering indoor source emissions. The characterization of indoor source emissions of NO₂ and estimated air exchange rates used to simulate indoor microenvironments were considered an important uncertainty.” However, in footnote number 53 on the same page it is stated that “While potentially important in understanding health effects and the total exposure/health risk from NO₂, exposures resultant from indoor sources of NO₂ have limited

relevance in understanding health risk associated with ambient concentrations.” This statement should be modified/clarified in the context of the new review as it may be misleading with respect to the significance of indoor NO_x sources and exposures. In fact, improving indoor emission inventories of NO_x is needed in order to better characterize overall exposure and risk to these air pollutants.

References:

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Dr. Jack Harkema

No critical comments for Chapters 3 and 7. The plan is clearly stated with ample thoughtful and appropriate guiding questions for the review. The flow chart is helpful and could come earlier in the Chapter if so desired.

Dr. Michael T. Kleinman

The Integrated Review Plan provides an excellent overview of the process. For this preliminary evaluation I will focus on the charge questions related to Chapter 4.

Chapter 4 describes the scope and specific issues that will be considered in the ISA. The expanded discussion provides a very comprehensive listing of the topics that will be considered in the ISA and appropriately focuses on new information that can fill knowledge gaps identified in the previous 2008 ISA. The expanded discussion in section 4.4 appropriately identifies key issues related to spatial heterogeneity near heavily trafficked roads and near emission sources. While it is implied, it would be useful to discuss the direct consideration of demographics (i.e. what new information is available regarding the size of the population, its age distribution or its socioeconomic distribution) of the people residing or working near heavily trafficked roads or near other sources.

Dr. Timothy V. Larson

Overall organization and clarity:

The February 2014 draft IRP is well organized and clearly written. Overall, the questions posed cover the main issues. Tables 5-1 to 5-3 are especially informative. Along those lines, I have suggested a few additional questions that follow.

Schedule:

One issue not specifically mentioned in this particular section is the timing of the roll-out of the new near road monitoring network relative to the timing of the REA (It is discussed later in the document). We struggled with this issue last time and made decisions based on a limited set of near road measurements in a limited set of cities. A comprehensive data set of both traditional and near road monitoring would greatly enhance the final decisions on the form of the standard. Is there a more detailed roll out plan that optimizes the choice of sites and therefore the relevant monitoring information used in the REA?

Policy Relevant Issues:

- (1) The relevant averaging time is an issue given the results of the epidemiology. Will the consequences of such an averaging time(s) be examined?
- (2) In the 2008 REA analysis, possible alternative standards were evaluated in part by predictions of the resulting 1-hr on-road concentration estimates. Is this still the plan and, if so, will a uniform gradient be used across all sites to make such predictions?

Risk and Exposure Assessment:

- (1) Emphasis on U.S. and Canadian studies would presumably down weight the reported health associations from a number of European studies. Is this also true for the exposure information to help establish near-road gradients?
- (2) What information exists on at-risk populations who live near NO₂ sources?
- (3) The 2008 analysis pointed out the importance of on-road exposure estimates. Recent studies (e.g. Hudda et al Atmos. Environ. 59: 578-586, 2012; and Hudda and Fruin ES&T 47(19): 11048-11055, 2013) have shown, not surprisingly, that in-vehicle concentrations relative to those on the roadway are a strong function of the state of the cabin air circulation system (indoor air vs outdoor air setting) when windows are rolled up. Are the APEX model predictions consistent with the models derived from these recent studies?

Policy Assessment and Rulemaking:

The important issues related to the assessment and use of exposure measurement and modeling error need to be more clearly stated. In addition, the role of panel studies with respect to co-pollutant confounding needs to be given more emphasis.

Dr. Jeremy Sarnat

Comments on Chapter 4

Generally, I feel that the Science Assessment does an adequate job of describing the most important questions and uncertainties related to NO₂ exposure and health. The rewritten section 4.4 is strong, and properly stresses the importance of understanding the near-road environment. Data generated from the new near-road monitoring network should be able to address several key questions including gradients around roadways, associations between specific traffic species and NO₂ near traffic sources, and the relationship between noise and NO₂ in this microenvironment.

Understanding the specific role of NO₂ as either an independent predictor of health response or as a marker for a suite or source of pollution, is adequately recognized within the IRP. I believe statements similar to the following reflect major issues that should be considered in the ISA:

“What new information exists regarding oxides of nitrogen measurements in a multipollutant context? To what extent do NO₂ measurements serve as surrogates of exposure to other gaseous pollutants (e.g., carbon monoxide, nitrous acid), particle phase pollutants (e.g., ultrafine particles, black carbon, organic carbon, transition metals) generated by traffic or other combustion sources, or a mixture of traffic-related pollutants?”

As noted in my review of the ISA, there appears to be inconsistency with regard to the particular role of NO₂ as a traffic pollution surrogate. A more cohesive message should be developed linking the IRP directives to the ISA message.

Since total exposure to NO₂, for many people, occurs while commuting, there should be greater attention paid to characterizing exposures and response occurring within the on-road microenvironment (page 1-9 of ISA mentions this briefly).

Comments on Chapter 5

One approach for strengthening the risk assessment would be to include greater amount of sensitivity analyses of the primary modeled input parameters to enhance the robustness of the findings. Using alternative, realistic C-R functions for the epidemiologic-based human health risk assessments would be useful (Page 5-17). Similarly, for both the air quality and human exposure components to the assessment, conducting formal uncertainty analyses, or presenting propagation of error findings would potentially inform the research and regulatory community on the largest sources of uncertainty.

Dr. Richard Schlesinger

Comments on Chapter 4

p.4-5, lines 33-36. While clearly studies that reduce uncertainty need to be evaluated, this suggests that studies that may show novel results that may add some additional information about health effects that may not be totally consistent with other studies will not be evaluated. The description here needs to be retooled.

p.4-8, lines 23-26. It is not clear what is meant by intake dose. Is that exposure concentration? If not, intake dose is not necessarily available in these studies, so perhaps an additional focus that should be listed here is "exposure concentration."

p.4-14, lines 1-2. NO_x is also a direct acting irritant that can produce adverse health outcomes without production of secondary products.

p.4-14, line 18. Replace "internal NO₂" with "endogenous NO₂"

p.4-14, line 25. Should read, "...can be qualitatively and quantitatively compared...."

p.4-15, line 9 et seq. Many of these bullets are redundant and the list can be made more concise while not losing any of the concerns.

p.4-16, line 16. What is meant by other "disciplines?"

p. 4-15 to 4-17. Almost all of the bullets for short and long term exposures are the same, so the question is whether they need to be listed separately?

p.4-19, line 29. Is it not important to distinguish among risk due to intrinsic, acquired or extrinsic factors in determining relative susceptibility to exposure in different groups?

Dr. Elizabeth A. (Lianne) Sheppard

Overall this document is well-written and clear. I have some specific suggestions for the ISA (Chapter 4) and REA (Chapter 5) sections.

Comments on Chapter 4 – Science Assessment

I suggest that for evaluation of toxicological studies adherence to the ARRIVE guidelines also be considered.

The human exposure section is focusing on questions about human exposures with particular emphasis on epidemiological inference. The questions should be reviewed in the context of how relevant they are for epidemiology. This should be carried forward into the ISA itself (see my related comments on the ISA w.r.t. exposure assessment and exposure measurement error).

Regarding specific questions:

How have ambient models been merged with stochastic population exposure models recently to improve estimates of exposure?

Use of stochastic models is not appropriate for epidemiological inference. However, they are very valuable for risk assessment.

What new information exists regarding characterization of error in exposure assessment of oxides of nitrogen and how it influences personal-ambient exposure relationships?

I suggest that a very important consideration for error in exposure assessment is with respect to its adequacy for inference about epidemiological health effects. I think the question should be either rephrased or expanded to incorporate inference in epidemiological studies. (My related ISA comments may also help with rephrasing this question.)

What information is available regarding differences in exposure patterns for oxides of nitrogen and personal-ambient exposure relationships among various lifestages and populations?

I suggest the more relevant question is whether there are differences that might affect epidemiologic study inference or possibly risk assessment. Consideration of this question with respect to epidemiologic inference and risk assessment are distinct topics.

Comments on Chapter 5 – Quantitative Risk and Exposure Assessment

Scope and specific issues:

1. I agree overall with EPA's plan for the REA, specifically noting the plan to decide later how justified it is to conduct an exposure and risk assessment.

2. Dr. Sarnat’s comments on sensitivity analysis and other approaches to uncertainty analysis are well taken and should be included in the REA.

Identification of most important uncertainties:

3. I agree that spatial heterogeneity of NOx remains an important uncertainty.
4. Exposure occurs both on roads and near roads. Is there a way to incorporate both into the characterization? See below for some summaries of AQS data that may contribute to this.
5. Would evaluation of AERMOD in conjunction with existing AQS sites that are near roads but in cities other than Atlanta help address the AERMOD uncertainties?

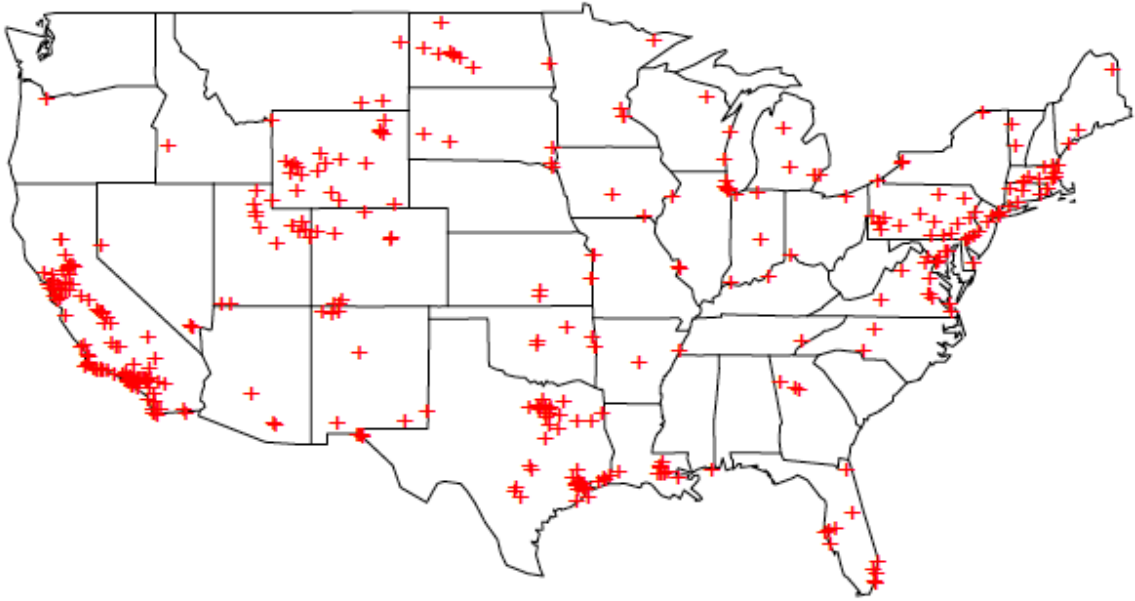
Additional information that should be considered:

6. The document states (p 5-6): “One of the most important uncertainties overall regards the spatial representation of the ambient monitors, ...” The existing AQS data may be able to address this uncertainty better than is appreciated. I insert below some data summaries based on compilation of AQS monitoring data that has been done at the University of Washington as part of our work for the MESA Air and NPACT studies. This (and additional potential data/analyses that could be provided) may help inform some of the existing uncertainties related to the ambient monitoring network. The following table characterizes how two geographic features are associated with all NOx monitors in the US. Pasted below is a map of the locations. In separate research, we have recent on-road data from a mobile monitoring network that might help summarize NOx.

Table: Characterization of 368 AQS monitoring locations that reported NOx in 2012 with respect to proximity to nearest road (A1, A2, A3) or nearest truck route. (Note: There are 30 additional locations that reported NO2 monitoring that are not included in this summary.)

Meters	To Road	To Truck Route
< 50	59 (16%)	5 (1%)
50 - 100	38 (10%)	7 (2%)
100 - 150	44 (12%)	6 (2%)
150 - 300	78 (21%)	18 (5%)
> 300	149 (40%)	332 (90%)

7. I think the use of APEX is a reasonable approach to estimating population exposures for risk assessment. Are there ways to use characterization of the current national network to address the biases identified in the past review from AERMOD? (p 5-16) Information is available that will help better characterize the existing national network (see above). Could this information be used to improve the AERMOD estimates?



Dr. Ronald E. Wyzga

I have relatively few comments on the plan as I believe that the devil is in the detailed implementation of the plan. In general it provides a good outline.

The Agency should use the 2011 NEI in its risk and exposure calculations. The significant reduction in NOx emissions since 2008 merits this change.

Some specific comments:

Comments on Chapter 3

p. 3-16: at the conclusion of the last review, CASAC recommended and EPA implemented a program to undertake monitoring near roadways. My understanding is that results from these monitors are not yet available; however, should there be any discussion about how these data are to be used in interpreting/extrapolating from health studies or in the risk assessment to be undertaken.

Comments on Chapter 4

p. 4-6: ll. 30-31: In the case of NOx it is important to learn whether NOx itself is responsible for the associated health effects or whether NOx is a surrogate for another pollutant. As such it is important that studies address this issue by considering copollutants as well. In particular the co-pollutants that appear to be of greatest interest are PM, CO, EC, and OC.

p. 4-7, ll. 15-27: This is important, but the document needs to address how or what it will do with respect to the exposure error issue. Although it is not the end-all, statistical significance is noteworthy and should be a factor that is noted in presenting study results.

Comments on Chapter 5

p. 5-3, ll. 19-21: This statement needs further elaboration.

p. 5-7, l. 4: My understanding is that AERMOD does not incorporate any chemistry; is there an alternative model that considers chemistry that could be used to replace/supplement AERMOD?

Dr. Junfeng (Jim) Zhang

The overall structure of the Integrated Review Plan for the Primary NAAQS for Nitrogen dioxide is well organized. The tabular and graphical presentations of information are particularly useful. For example, Figure 1-1 and Table 2.1 are very useful. I think the information presented in tables and figures along with figure/table captions are most easily conveyed to the reader. For this reason, I encourage the EPA authors to check whether they can further explain the tables and figures (in the captions) so the tables and figures can be readily understood even without the need to read the text.

My review focuses on Chapter 5 – Quantitative Risk and Exposure Assessment. Below are my comments on this chapter.

1. It is appropriate to use the three approaches to estimating exposures and health risks or REA. Each approach is well described in the chapter. I suggest that a section be added to explicitly describe how the information from the three approaches can be integrated to support an overall REA.
2. In the epidemiology-based REA approach, a major issue is whether the effects are of NO₂ or of other pollutants or the pollution mixture. This is discussed within the context of uncertainty. I think this issue shall be emphasized more strongly. It is well known that many epidemiological studies have used NO₂ concentrations as a surrogate of traffic-related pollution exposure. It would be useful to evaluate NO₂ correlations with PM and other pollutants in cited epidemiological studies. This should be independent from evaluating studies that have used two-pollutant models (presented in ISA).
3. In the evaluation of personal NO₂ exposure and the contribution from indoor sources, a useful parameter would be indoor-to-outdoor concentration (I/O) ratio. A table to summarize I/O ratios from the available literature will be useful. If I/O is smaller than 1, concentration-response relationships or risks derived from using outdoor concentrations may not be significantly affected by indoor source confounding. Then the issue will be how good the outdoor NO₂ concentration (measured or modeled) represents personal exposure. Approaches to addressing this issue are described and discussed well in this chapter.