

**Summary Minutes of the
U.S. Environmental Protection Agency (EPA)
Science Advisory Board (SAB) Staff Office
Clean Air Scientific Advisory Committee (CASAC)
Oxides of Nitrogen Primary NAAQS Review Panel
Public Meeting
May 1-2, 2008**

Committee Members: (See Roster – Attachment A)

Scheduled Date and Time: From 8:30 a.m. to 5:30 p.m. (Eastern Time) on May 1, 2008; and from 8:30 a.m. to 2:00 p.m. (Eastern Time) on May 2, 2008. (See Federal Register Notice, Attachment B)

Location: Marriott at Research Triangle Park, 4700 Guardian Drive, Durham, NC, 27703

Purpose: To conduct a peer review of EPA's Integrated Science Assessment (ISA) for Oxides of Nitrogen – Health Criteria (Second External Review Draft, August 2007) and to conduct a consultation on the EPA's Nitrogen Dioxide Health Assessment Plan: Scope and Methods for Exposure and Risk Assessment (September 2007 Draft).

Attendees:

Chair: Dr. Rogene Henderson.

Panel Members:

- Dr. Ed Avol
- Dr. John R. Balmes (by phone)
- Dr. Ellis B. Cowling
- Dr. James Crapo
- Dr. Douglas Crawford-Brown (by phone)
- Dr. Terry Gordon (05-01-08 only)
- Dr. Dale Hattis
- Dr. Donna Kenski
- Dr. Patrick Kinney (by phone 05-02-02; in person, 05-01-08)
- Dr. Steven Kleeberger (in person, 05-01-08; by phone 05-02-02)
- Dr. Timothy Larson (by phone)
- Dr. Kent Pinkerton
- Dr. Edward Postlethwait
- Dr. Armistead (Ted) Russell
- Dr. Jonathan Samet (by phone) (in person, 05-01-08; by phone 05-02-02)
- Dr. Christian Seigneur
- Dr. Elizabeth A. (Lianne) Sheppard
- Dr. Frank Speizer
- Dr. George Thurston
- Dr. James Ultman,
- Dr. Ronald Wyzga

SAB Staff Office: Dr. Angela Nugent, EPA SAB Staff Office,
Designated Federal Officer (DFO)

Dr. Vanessa Vu, Director of the EPA SAB Staff
Office

EPA Participants Listed on the Agenda

Dr Ila Cote (EPA ORD)Development (ORD)Staff]

Dr. Mary Ross (EPA ORD)

Dr, Dennis J. Kotchmar (EPA ORD)

Dr Qingyu Meng (EPA ORD)

Dr. Thomas Luben (EPA ORD)

Dr. Stephen Graham (EPA OAR)

Mr. Harvey Richmond (EPA OAR)

Dr. Scott Jenkins (EPA OAR)

Meeting Summary – May 1, 2008

The discussion addressed the topics included in the Proposed Meeting Agenda (See Meeting Agenda - Attachment C) and roughly followed the sequence summarized below.

Opening of Public Meeting

Dr. Angela Nugent, Designated Federal Officer (DFO) for the CASAC Oxides of Nitrogen Primary NAAQS Review Panel, opened the public meeting at 8:35 a.m

Dr. Vanessa Vu welcomed CASAC panel members and thanked them for their work. She acknowledged EPA Staff from ORD and OAR and the efforts of the DFO. Dr. Rogene Henderson thanked members for the pre-meeting comments and asked panel members present and on the telephone to introduce themselves.

Introduction to Draft ISA for Oxides of Nitrogen – Health Criteria

Dr. Ila Cote, Division Director for EPA's National Center for Environmental Assessment – Research Triangle Park (RTP) (NCEA) provided a brief slide presentation overview of the second draft ISA (Attachment D). She summarized ORD's response to CASAC's comments on the first draft ISA, listed the charge questions, and summarized the major conclusions in the ISA. She particularly welcomed CASAC comments on the framework for causal determinations. She introduced Dr Qingyu Meng and Dr. Thomas Luben, who spoke about the challenges presented by the atmospheric chemistry of nitrogen oxides (NO_x), particularly the difficulties of relating personal exposures and ambient concentrations, choosing an appropriate averaging time, and addressing the problem of spatial variation of nitrogen dioxide (NO₂) in urban areas.

First Public Comment Period

Dr. Angela Nugent introduced three members of the public who requested the opportunity to provide public comment. Dr. Christopher Long from Gradient Corporation presented comments on behalf of the Utility Air Regulatory Group (UARG). His major comments are provided in Attachment E. Mr. Jon Heuss from Air Improvement Resource, Inc. spoke on behalf of the Alliance of Automobile Manufacturers and referred panel members to his written comments. He noted a need for more consistency in the application of the causal framework and a more balanced treatment of studies. He stated that he would provide additional written comments identifying specific articles omitted from the ISA. Mr. Ted Steichen presented public comments on behalf of the American Petroleum Institute. He noted that the second draft ISA relies on epidemiological studies which he stated were not sufficient to establish health effects for NO_x. He noted that he will follow up with more detailed written comments for the docket. He stated a concern that the accelerated schedule for NO_x development provides too short a timeframe for EPA's science review.

After the public comments were complete, the panel proceeded to discuss and deliberate on the charge questions related to the ISA.

Discussion and Response to Agency Charge Question 1: What are the views of the Panel on the characterization of the search strategy for identifying literature, criteria for study selection, the the framework for scientific evaluation of studies and causality determination?

Dr. Jonathan Samet, the primary lead discussant, noted substantial improvements over the first draft ISA. He suggested that EPA in the future provide a response to comments memorandum that would inform the CASAC of changes made in response to previous comments. He made several suggestions to improve the document. He suggested that the ISA cite and quote technical literature more carefully. He suggested that EPA use and not change or rename the Bradford Hill guidelines for assessing causality. He called on EPA to be more consistent in applying the Bradford Hill guidelines throughout the ISA and to address the issue of publication bias in the use of studies that address multiple pollutants where NO₂ is found with other chemicals. Other members agreed, but cautioned EPA should use the factors as a guide to professional judgment and not as a checklist. One member noted that he had checked EPA's literature search and found a large number of recent articles, described well. Another member commended EPA for its balanced, unbiased description of the epidemiological database related to NO₂. He noted a strong evidence of epidemiological effects at ambient levels and a gap between the epidemiological and toxicology data, because the toxicology data shows evidence of effects only at higher levels. He advised EPA to provide more discussion of interactions between particles and gases. He emphasized the importance of a 1964 paper published by Boren discussing carbon particles and their effects. He observed that particles may not be confounders for NO₂ toxicity; they might be co-conspirators, assisting NO₂ in reaching inside the lungs.

The chair noted with approval that EPA had identified policy-relevant questions early in the draft ISA and in the concluding chapter. She noted the need for EPA to address those questions explicitly either in the ISA or the policy assessment document at a later stage.

Agency Charge Question 2: To what extent are the atmospheric chemistry and air quality characterizations clearly communicated, appropriately characterized, and relevant to the review of the primary NO₂ NAAQS? Are the properties of ambient oxides of nitrogen appropriately characterized, including spatial and temporal patterns and relationships between ambient oxides of nitrogen and human exposure? Does the information in Chapter 2 provide a sufficient atmospheric science and exposure basis for the evaluation of human health effects presented in later chapters?

Dr. Armistead Russell, the primary lead discussant, noted many improvements in the second draft ISA's discussion of atmospheric chemistry. He advised EPA to include a brief list of sources in the final ISA and not relegate the information to the annex. He encouraged EPA to discuss sources such as airports and railroads as well as mobile sources. He noted that the ISA provided good coverage of available models. He called for a discussion of the likely limitations and uncertainties of the models either in the ISA or the risk and exposure assessment (REA) document. He would like to see a brief discussion of the models and formulas used and the science supporting them. He also suggested that EPA should better characterize the extent of interferences with monitors because the document incorrectly communicates that interference is a major barrier. For endpoints of concern, for example, for peak concentrations of NO₂, the document conveys the sense that interference could be as high as 50%, but the 50% estimate is likely derived from a Mexican study and a Swiss study, at times of the day and year not relevant to the United States. He advised EPA to be more consistent in its evaluation of available air monitoring data.

Other panel members agreed that the second draft ISA had an improved discussion of atmospheric chemistry. Additional comments from panel members included the following suggestions:

- Provide information about contributions of NO_x species.
- Provide a more effective summary and identification of conclusions in chapter 2.
- Section 2.5.4 on-road contributions should be additionally supported by some analysis of on-road or near-road concentrations, making use of type of analysis described in the Stephen Graham memorandum circulated to panelists.
- Include a discussion in ISA (not the annex) of extrapolating long-term average to short-term intense exposures and options for addressing this issue and make use of recent references to integrated models used in confined urban areas.
- When discussing exposures surrounding monitors, include an analysis of population concentrations nearby.
- Provide a more balanced evaluation of CMAQ, AIRMOD, and alternative models.
- Present data in way that contour points can be reproduced in black and white.
- Ensure that analytical decisions are not driven by data availability, but instead by important issues related to human health. Extend calculations so they estimate hours of exposure estimated from animal studies using some simple anthropometric extrapolation, to allow for consideration of whether exposures

may be in range of level that caused a toxicological effect shown in animal studies.

- Describe in ISA how dosimetry can be estimated from on-road exposures, so the description in the Risk and Exposure Assessment can be strengthened.
- Focus on the problem of monitor siting, exposure assessments, and interpretation of epidemiological studies because wind interferences affecting NO_x exposures could result in “huge differences” in health effects.
- Provide easier cross referencing between the ISA and annexes, especially to get access to formulas.
- Provide a more thorough analysis of correlations of annual and seasonal data.
- Provide more explicit discussion of co-pollutant issues.
- Distinguish more clearly between personal and population exposures, perhaps providing data in separate tables.
- Address issues associated with the use of a central monitoring site. If a monitor is at a hot spot, results will not correlate well with population models. Epidemiologists do not use hot spots, they use community-based monitors. EPA should look at hospital admissions, focusing on unscheduled admissions and excluding scheduled admissions. EPA should average results from community-based monitors to derive population effects and apply general practices in epidemiology to the analysis.

Agency Charge Question 3: To what extent is the discussion and integration of evidence from the animal toxicology and controlled human exposure studies and epidemiologic studies technically sound, appropriately balanced, and clearly communicated? What are the views of the Panel on the conclusions drawn in the draft ISA regarding the strength, consistency, coherence and plausibility of NO₂-related health effects?

Dr. James Crapo, the primary lead discussant, began the discussion by noting his agreement with the “global overall decision” in the ISA that there are health effects associated with short-term exposures that raise the need to re-examine the form of the current National Ambient Air Quality Standard (NAAQS). He stated that ISA should use the Bradford Hill guidelines to evaluate the science relating to the appropriate form and level for a new standard.

He noted that the document did not provide a clear analysis of the science related to choosing alternative levels as a basis for the Risk and Exposure Assessment. He saw the need for information and analysis that would inform decisions about the levels to test per population exposed. He notes that the ISA derived levels (200, 250, 300 ppb) by focussing on two studies discussed on page 318 regarding airways responsiveness for a sensitive population, allergen-challenged individuals. He argued that use of these two studies from a single institution using the same technology does not meet the Bradford Hill guidelines and that the inflammatory response found did not represent a significant effect that would be convincing to a decision maker.

Dr. Crapo observed that alternative information was available in table 5.3-2 on page 510, focusing on epidemiological studies that demonstrate effects. That information, however, is

mixed. Animal experiments do not show effects at the low levels where epidemiological studies show effects.

Dr. Crapo called for a more balanced and complete analysis of the total database of epidemiological, clinical, and toxicology studies to examine the appropriate range for the REA, which might be a very broad range (to assess effects at low levels as well as higher levels).

A committee discussion followed. Panel members generally agreed with Dr. Crapo that charge questions 2 and 3 were linked and that EPA should more “sharply” address the science relating to whether effects occur within the range of interest. Panel members also made the following additional points:

- The ISA discussion of longer term exposures was reasonably presented and communicated.
- Chapter 3 should systematically apply causal framework to discussion of different long- and short-term effects.
- Figure 3.1.1 needs to be corrected.
- the ISA should provide a more careful discussion of epidemiological data related to long term exposures to NO₂. Panelists spoke of the high quality of the children’s health studies and Mexico City study.
- EPA should address the issue of co-pollutants and the discrepancies between the toxicology and epidemiology data. The presence of particles may not “confound” analysis of NO_x exposures; particles may facilitate NO_x reaching the lung. EPA should explore biological plausibility of effects at lower levels.
- EPA should improve the discussion on pages 398-399 to integrate discussion of asthma prevalence, respiratory, and epidemiology studies more fully into the document.
- EPA should improve figures and legends so they can be understood separately from the text.
- EPA should include discussion of updated controlled exposure animal toxicology literature, which shows effects at a lower level.
- The ISA should clearly state that susceptible populations (adult asthmatics and children with physician-diagnosed asthma) are critical to the risk assessments.
- The Australian studies are critical--they show significant effects at 1-hour peak level at 40 to 80 ppb range, critical studies.
- EPA should evaluate whether it is appropriate to equally weight toxicology, epidemiology, and clinical studies.
- The ISA should identify research needed to discern NO_x from PM effects, updating the research conducted by Boren (Boren, Hollis. 1964. *Carbon as a Carrier Mechanism for Irritant Gases*. Archives of Environmental Health. The Sixth Annual Air Pollution Medical Conference. Vol 8 pp. 119-124.
- The ISA should provide additional information on studies that “do not inform” analysis.

Agency Charge Question 4: What are the views of the Panel on the characterization of groups likely to be susceptible or vulnerable to NO₂ and the potential public health impact of NO₂ exposure?

Dr. John Balmes, the primary lead discussant, noted that the draft ISA did a good job on this question. The ISA notes that individuals with pre-existing respiratory disease may be most susceptible to NO_x. He disagreed, however, with the ISA conclusion that younger boys were more susceptible than girls to asthma and suggested that the ISA delete this conclusion.

Other panel members agreed that EPA provided a good treatment of susceptibility. Other members suggested that additional susceptible groups (in addition to children and asthmatics) be considered, and that EPA should create a table of likely susceptible groups and evaluate the related evidence. Members identified the following other conditions that may enhance susceptibility: obesity (inflammation and airways susceptibility), very low birthweight infants (susceptibility to infections, more at risk in terms of responsiveness to viral infections), and infants (because of the relationship shown between NO₂ and SIDS). Panel members added that such a table should also identify research needs.

Members also made the following points:

- The ISA should include a discussion of endogenous generation of reactive nitrogen species by asthmatics.
- The ISA should address the public health significance of NO₂ effects. If health problems of allergen-challenged populations are exacerbated by NO₂, what is the increased public health burden. This information should be integrated into the summary.
- The ISA should identify the numbers of people who live near highways and high exposures to identify populations of vulnerable people.
- Both the ISA and the Risk and Exposure Assessment should use terms “susceptibility” and “vulnerability” consistently.

Agency Charge Question 5: What are the Panel’s views on the adequacy of this second external review draft ISA to provide support for future exposure and policy assessments?

Dr. Douglas Crawford Brown and Dr. Jonathan Samet provided initial remarks as primary lead discussants. Dr. Crawford Brown noted that the conclusion of the ISA does a good job of summarizing key points in earlier chapters and related literature findings. It does not, however, provide clear conclusions to guide the exposure and risk assessor. It does not provide a synthesis of information related to averaging time or measurement.

Dr. Samet noted that the NO_x ISA was a model for ISAs in EPA’s revised NAAQS process. He agreed that the ISA should provide more integration. He encouraged EPA to revise the document so it addresses the framing questions that open Chapter 5 and describes the relationship between the ISA and the risk and exposure assessment.

Other panel members agreed that the conclusion should provide a more integrated synthesis of information and describe a clear relationship to the risk and exposure assessment. Panel members made the following additional points:

- The conclusion should summarize evidence for an effects threshold for different effects.
- The conclusions should summarize evidence related to NO₂ effects *per se* or conclusions about NO₂ viewed as an index.
- Conclusions in current ISA not clear to the reader – whether the clinical studies and related effects are key or whether the epidemiological studies are the key focus in the risk and exposure assessment.
- Epidemiological evidence shows that NO₂ plays a role in causing disease. the effects are difficult to discern from those of co-pollutants, but NO₂ is “an important player.”
- Since the epidemiological studies provide the basis for causality, the exposure levels associated with the epidemiological studies should be discussed more prominently, along with levels for the clinical and toxicology studies.

Summary of Next Steps

Dr. Henderson concluded the discussion of ISA charge questions by asking primary lead discussants to summarize the deliberations of the panel for their charge questions and provide draft text to her and the DFO by May 9, 2008.

Introduction to EPA’s draft Risk and Exposure Assessment

Mr. Harvey Richmond from EPA’s OAR introduced OAR Staff, Drs. Scott Jenkins and Stephen Graham and contractor support for the draft Risk and Exposure Assessment (REA), Ms. Arlene Rosenbaum from ICF. OAR staff provided a slide presentation overview of the draft REA provided in Attachment F.

Second Public Comment Session

Dr. Anne Smith from CRA International provided a slide presentation (Attachment G) and oral comments on behalf of the Utilities Air Regulatory Group.

Air Quality Information and Analyses (Initial discussion)

Dr. Christian Seigneur, the primary lead discussant, began the panel’s deliberation of air quality monitoring by voicing a concern about possible significant underestimation of exposures to NO_x in EPA’s Philadelphia assessment. He suggested that EPA identify the cause of the underprediction and check to see if the inventory could be corrected or if the model is lacking. EPA’s contact responded that the Philadelphia assessment only modeled hot spots and did not attempt to be comprehensive. Dr. Seigneur noted that adjustments to the model should be specific to the receptor in question. He suggested that EPA should increase modeling results where a larger effect would be expected through data fusion, rather than by a constant factor.

Other members agreed with this suggestion.

Dr. Seigneur also noted that EPA should describe the sources of uncertainty and variability due to model specification and provide a quantitative or semi-quantitative discussion of the most important sources of uncertainty.

Other members made the following points:

- EPA should compare modeling results for model of on-road exposures with available data from on-road or near-road monitors and report results of the comparison to build confidence in the estimates
- EPA's chosen locations to model may not be representative. Philadelphia, with its small central downtown area may not be representative of most cities and does not appear as a likely worst case. The APEX model depends on monitors far from locations where most people live.
- In response to a request for advice on which cities should be modeled next, one member noted that Los Angeles may be most interesting. Cities should be chosen that provide the most promising "geometry" that would provide highest exposures to NO_x and provide a richer picture of NO_x exposures.
- EPA should change the exponential decay adjustment used for on-road concentration so that NO_2 decay would not be constantly calculated downward. EPA should use a Gaussian modeling adjustment.
- EPA should clarify the extrapolation method used for on-road concentrations because the current description of the methodology is difficult to follow. A member suggests that EPA include some of the basic conclusions, equations, and key exposures be included in the ISA
- EPA should compare ratios for off-road and on-road concentrations and use data to validate the ratios. EPA could compare on-road extrapolations for air quality and simulated spatial distributions for exposure.
- EPA should clarify if the air quality models include residents or commuters and consider the exposures experienced by commuters.
- EPA should precede the air quality modeling discussion with an overview of the "cascade of models and assumptions" to convey the big picture of the air quality modeling effort.
- EPA must provide a stronger analysis and supporting documentation to convince the reader that it has identified the extremes of distributions, because the Agency's exposure strategy depends on "counting exceedances," which is more difficult than counting averages
- The summarization of data is based on exceedances at an hourly level and so EPA most rigorously evaluate the high values, the extremes, that it is simulating.
- Figures 9, 10, and 11 estimating risks for certain exceedances are key tables. EPA should provide an estimate of confidence around those modeled air quality values. If the confidence intervals are extremely large for the very few cities for which it is practical to model air quality, it may not be useful for EPA to expend resources to look at additional cities.
- Literature on air quality conditions in Danish Street canyons may be of use to EPA. Dr. Timothy Larson agreed to provide citations to this literature.

Conclusion of Discussion on May 1, 2008

At the chair's request, the Designated Federal Officer adjourned the meeting at 5:15 p.m.

Meeting Summary – May 2, 2008

The DFO opened the meeting at 8:30. The chair determined that there was no need to continue the discussion of air quality information and analyses and asked the panel to begin its deliberation of the exposure analysis in the first draft REA.

Exposure Analysis

Dr. Patrick Kinney, the primary lead discussant, noted that the approach was technically sound, the assessment was well written, and that the focus on asthmatics was appropriate. He asked whether the prevalence used in the Philadelphia assessment should be based on local asthma rates and whether prevalence rates used should be geographic-specific. He also asked whether exposures should include sidewalk commutes for students and workers in cities. He observed that EPA had chosen the micro-environments well and that pedestrian micro-environments should be included. He concurred with the EPA staff decision to use results from human chamber studies as the benchmarks for the exposure assessment.

Other panel members made the following observations:

- The identification of the relevant ambient concentration to use in the exposure assessment is problematic. Monitoring results are an alternative way of getting at exposures of populations based on ambient exposures. Several panel members advised EPA to derive both estimates, compare them against each other, and use the comparison as a kind of uncertainty analysis. The goal would be to identify what fraction of the population is above some ambient concentration of interest.
- Several members voiced concern about whether the level of sophistication required for characterizing the fraction of the population above the ambient concentration of interest is beyond EPA's current capabilities and whether it was appropriate to invest the resources necessary to achieve such a sophisticated analysis
- EPA should carefully address how indoor concentrations may change as it makes adjustments to modeled results for outdoor concentrations.
- If EPA is attempting to model exceedences, then it must account for the great variability reflected in monitor sitings, variation in house designs, cooking events that do not match the 1-hour cooking event default, and other model variability issues that are necessary to model the extremely high tail of the exposure distribution.
- Monitor siting does not align well with population distribution. EPA should acknowledge the major differences in monitoring siting in counting exceedences and how that aligns with population in a gross sense.

- EPA should examine full-plot histograms for modeled and monitored diurnal data for a selected site and compare daily, weekly, and annual data.

Several panel members noted that EPA faced major challenges in exposure modeling for NO_x, based on the endpoint chosen. They argued that, given such challenges, EPA's REA should consider the epidemiological endpoints for which there are strong data and incorporate relevant exposure analyses. Those members stated that the REA should not focus only on exposure levels relevant to chamber studies of asthmatics. Given the limited time to develop the REA, several members suggest that EPA assess whether it can develop a prediction of ambient exposures that captures variability. If it is not confident that variability can be captured, EPA should develop an assessment based on the effects identified in the epidemiology literature.

Characterization of Health Risks

Professor Ed Avol, primary lead discussant, led the discussion with his initial comments. He noted that both susceptible and vulnerable populations are at risk from NO₂ exposure. He advised EPA to provide a richer discussion of people's proximity to roadways and susceptibilities related to obesity, chronic obstructive pulmonary disorder, diabetes, genetic predisposition, social-economic status, and smokers to describe the much larger universe of at-risk populations.

He advised EPA to expand the chapters on health risks to focus on other factors than airways responsiveness and to evaluate risks from short-term exposures, long-term exposures, and mortality. He noted the biological plausibility regarding NO_x effects provided by animal toxicology data. He stated that the health risks were clear and needed to be more clearly discussed. In regard to charge question 5, he noted that the epidemiological findings should be given more measure and stature in the REA.

Other members provided comments. They generally agreed that the body of evidence suggests that NO₂ exposure causes short-term respiratory health effects and that the epidemiological data were more convincing than the controlled human exposure data, which did not meet the Bradford Hill guidelines. Members noted that the controlled human exposure data were not clinically significant or statistically valid. Individual members then made the following additional points:

- Asthma-related epidemiology data derived from hospital admissions would be more likely to be compelling to decision makers than the controlled human data involving small changes in airways responsiveness.
- The benchmark values chosen by the Agency appear reasonable, but the rationale for deriving them (i.e., the controlled human exposure data) was not.
- Epidemiological literature suggests that a change in respiratory morbidity occurs with a 20 ppb drop in daily average NO₂ concentration. [I did not understand the sentence I deleted. If it can be clarified, add it back. RFH]
- A public health-protective approach would acknowledge, and not discount, effects if co-pollutants were involved.

- If EPA is selecting the asthmatic population as the most sensitive group, the analysis should identify how many of them are exposed and then describe and assess the risks for those exposed
- Australian data show effects below 100 ppb.
- Use of the epidemiological studies as a basis for the NO₂ assessment is more difficult than for ozone or particulate matter because of the atmospheric chemistry of NO₂. The effects of NO₂ cannot be “teased out” with multi-variable models. The REA must make a stronger case based on the epidemiological, toxicological, and controlled human exposure data to develop a bounding estimate.
- The REA should clarify the distinctions between vulnerable and susceptible populations and use those terms consistently
- The REA should identify analytical needs to guide future research or to provide specific suggestions for how to redesign NO₂ monitoring networks.
- The REA would be strengthened by investing resources in developing an analysis combining the epidemiological, toxicological, and controlled human exposure data, rather than conducting air quality modeling for additional cities.
- EPA should consider undertaking a national epidemiology assessment and providing an estimate of risks and uncertainties. The results would be more useful and practical than conducting detailed air quality modeling of several additional studies.

After members provided their comments, Dr. Karen Martin provided several comments. She noted that although OAR had not designed the draft REA around the epidemiological data, OAR planned to provide a qualitative discussion of the epidemiological data in the policy assessment that would be part of the Advance Notice of Public Rulemaking (ANPR). She requested specific advice from the panel that would assist EPA with addressing the specific challenges presented by developing an epidemiologically-based quantitative risk assessment for NO₂. She noted that the NO₂ database did not have the multi-city studies that facilitated assessments for ozone and particulate matter; that the atmospheric chemistry for NO₂ presented monitoring challenges; and that there wasn't the “breadth and depth” of epidemiology studies finding independent effects for NO₂ in single and multiple pollutant models. She asked for advice that would help EPA relate the peak averaging times from clinical and toxicological analyses with longer term averages used in epidemiology studies.

Members responded that the current draft REA did not provide a convincing assessment of the risks associated with short term exposures to NO₂ or cogent information about the health impacts of alternative standards. Members observed that the assessment based on the epidemiology studies should not wait for release of the ANPR. One member observed that multi-city studies were important but not the “gold standard” for epidemiology. A few members noted that EPA could make use of daily exposure information and hospital admissions for quantitative assessment of NO₂ impacts. Use of daily (24-hour) emission data would reduce uncertainties and would be merited, since the health data driving the analysis make epidemiological findings compelling. It may be more important to develop a compelling rationale for a short-term standard, based on the most defensible available data, than to split hairs over whether the short-term standard should be a 24-hour or 1-hour standard. One member commented that it would be acceptable to focus on 24-hour exposures, because it would not

cause a “huge major impact” to assess effects that accumulate over 24 hours, rather than to focus on peak 1-hour effects. EPA could develop 24-hour averages from an aggregation of hourly predictions. Members suggested that the current Federal reference standard could facilitate this estimate. A member also suggested that EPA could link the exposure and risk assessment to the epidemiological findings by analyzing both 24-hour averages and peak exposures, using ambient data. EPA could add an analysis of APEX model, process-related, central site 24-hour average and distribution of personal exposures. [I guessed at what this sentence means and tried to clarify it. Did I get it right? RFH] Such an analysis would relate personal exposures to site data. EPA could build its analysis on available data related to 24-hour exposures and identify a research need for effects related to 1-hour peak exposures. A member suggested that EPA should identify points at which a significant proportion of the population have a 20 ppb decrease from “as is” levels (based on 24-hr average). Another member suggested that EPA analyze epidemiology studies that address peak NO₂ exposures to see if there are correlation between hourly peaks and 24-hour averages.

A member suggested that EPA could use national Medicare data to analyze relative risks of hospital emissions for asthma. Hospital admission data are available for every state. Another member noted that concentration-response ratios developed for one city could be applied to other cities, with an evaluation of the reasonableness of the assumption involved. Yet another member, however, voiced caution that it would be too risky to conduct a new analysis to derive a NO₂ based on existing Medicare data, given the Agency’s time constraints for developing the REA.

Some members emphasized that an assessment based on endpoints identified in the epidemiological literature should use population-oriented (central site) monitors. They suggested that EPA contact authors of epidemiology studies to determine if they linked exposures and health effects to central site monitors and if they excluded hot spots. One member advised EPA to identify cities that linked 1-hour and 24-hour monitors. He noted that specific studies exist on this topic for Atlanta.

Members discussed issues related to EPA’s possible use of European studies that rely on monitors that are sited and operate very differently from monitors in the United States. If EPA were to use European data, it would systematically underestimate coefficients. One member advised EPA to create a table showing effects shown by the literature (e.g., respiratory effects, hospital emissions) drawn from the ISA and the available literature that shows the type and quality of exposure data used.

Summary of Next Steps Related to the Review of the draft Risk and Exposure Assessment

The Chair concluded the meeting with a general summary of the discussion and identification of next steps for the panelists. She acknowledged the special challenges presented by the NO₂ REA. She asked primary lead discussants to provide responses to the charge questions in their areas of responsibility to her and the DFO by May 9, 2008. She asked that this draft text reflect the panel discussion. She noted that she would work with the DFO to circulate a draft letter by May 16, 2007 for panel comment and finalization by May 21, 2008, and that the

chartered CASAC would have the opportunity to review and approve the letter during a public teleconference on June 11, 2008. The panel was scheduled to provide advice on the second draft REA during a public meeting on September 9-10, 2008.

At the chair's request, the Designated Federal Officer adjourned the meeting at 12:15 p.m.

Respectfully Submitted:

/Signed/

Angela Nugent
Designated Federal Officer

Certified as True:

/Signed/

Rogene Henderson
Chair

NOTE AND DISCLAIMER: The minutes of this public meeting reflect diverse ideas and suggestions offered by committee members during the course of deliberations within the meeting. Such ideas, suggestions, and deliberations do not necessarily reflect definitive consensus advice from the panel members. The reader is cautioned to not rely on the minutes to represent final, approved, consensus advice and recommendations offered to the Agency. Such advice and recommendations may be found in the final advisories, letters, or reports prepared and transmitted to the EPA Administrator following the public meetings.

Attachments

Attachment A	Roster
Attachment B	Federal Register Notice
Attachment C	Meeting Agenda
Attachment D	Presentation: Integrated Science Assessment for Oxides of Nitrogen – Health Criteria 2nd External Review Draft, Presentation by Dr. Ila Cote, EPA/ORD/NCEA
Attachment E	Comments on the Integrated Science Assessment (ISA) for Oxides of Nitrogen- Health Criteria (March 2008 Draft) On Behalf of the Utility Air Regulatory Group (UARG), Presentation by Dr. Christopher M. Long, Gradient Corporation
Attachment F	Presentation: Overview of the First Draft Risk and Exposure Assessment to Support the NO ₂ Primary NAAQS
Attachment G	Presentation from Dr. Anne Smith on behalf of UARG: Comments on First Draft of EPA’s Risk and Exposure Assessment to Support the Review of the NO ₂ Primary NAAQS

Attachment A: Roster

U.S. Environmental Protection Agency Clean Air Scientific Advisory Committee (CASAC) Oxides of Nitrogen Primary NAAQS Review Panel

CHAIR

Dr. Rogene Henderson, Scientist Emeritus, Lovelace Respiratory Research Institute, Albuquerque, NM

CASAC MEMBERS

Dr. Ellis B. Cowling, University Distinguished Professor At-Large, Emeritus, Colleges of Natural Resources and Agriculture and Life Sciences, North Carolina State University, Raleigh, NC

Dr. James Crapo, Professor of Medicine, Department of Medicine , National Jewish Medical and Research Center, Denver, CO

Dr. Douglas Crawford-Brown, Professor and Director, Department of Environmental Sciences and Engineering, Carolina Environmental Program, University of North Carolina at Chapel Hill, Chapel Hill, NC

Dr. Donna Kenski, Data Analyst, Lake Michigan Air Directors Consortium, Des Plaines, IL

Dr. Armistead (Ted) Russell, Professor, Department of Civil and Environmental Engineering , Georgia Institute of Technology, Atlanta, GA

Dr. Jonathan M. Samet, Professor and Chair of the Department of Epidemiology, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD

CONSULTANTS

Dr. Ed Avol, Professor, Preventive Medicine, Keck School of Medicine, University of Southern California, Los Angeles, CA

Dr. John R. Balmes, Professor, Department of Medicine, Division of Occupational and Environmental Medicine, University of California, San Francisco, CA

Dr. Terry Gordon, Professor, Environmental Medicine, NYU School of Medicine, Tuxedo, NY

Dr. Dale Hattis, Research Professor, Center for Technology, Environment, and Development, George Perkins Marsh Institute, Clark University, Worcester, MA

Dr. Patrick Kinney, Associate Professor, Department of Environmental Health Sciences, Mailman School of Public Health, Columbia University, New York, NY

Dr. Steven Kleeberger, Professor, Lab Chief, Laboratory of Respiratory Biology, National Institute of Environmental Health Sciences, National Institutes of Health, Research Triangle Park, NC

Dr. Timothy V. Larson, Professor, Department of Civil and Environmental Engineering, University of Washington, Seattle, WA

Dr. Kent Pinkerton, Professor, Regents of the University of California, Center for Health and the Environment, University of California, Davis, CA

Dr. Edward Postlethwait, Professor and Chair, Department of Environmental Health Sciences, School of Public Health, University of Alabama at Birmingham, Birmingham, AL

Dr. Richard Schlesinger, Associate Dean, Department of Biology, Dyson College, Pace University, New York, NY

Dr. Christian Seigneur, Vice President, Atmospheric & Environmental Research, Inc., San Ramon, CA

Dr. Elizabeth A. (Lianne) Sheppard, Research Professor, Biostatistics and Environmental & Occupational Health Sciences, Public Health and Community Medicine, University of Washington, Seattle, WA

Dr. Frank Speizer, Edward Kass Professor of Medicine, Channing Laboratory, Harvard Medical School, Boston, MA

Dr. George Thurston, Associate Professor, Environmental Medicine, NYU School of Medicine, New York University, Tuxedo, NY

Dr. James Ultman, Professor, Chemical Engineering, Bioengineering Program, Pennsylvania State University, University Park, PA

Dr. Ronald Wyzga, Technical Executive, Air Quality Health and Risk, Electric Power Research Institute, Palo Alto, CA

SCIENCE ADVISORY BOARD STAFF

Dr. Angela Nugent, Designated Federal Officer, 1200 Pennsylvania Avenue, NW 1400F, Washington, DC, Phone: 202-343-9981, Fax: 202-233-0643, (nugent.angela@epa.gov)

Attachment B: Federal Register Notice

Science Advisory Board Staff Office; Clean Air Scientific Advisory Committee (CASAC);
Notification of a Public Advisory Committee Meeting of the CASAC
Oxides of Nitrogen Primary NAAQS Review Panel and Public
Teleconference of the CASAC
PDF Version (3 pp, 104K, About PDF)

[Federal Register: April 11, 2008 (Volume 73, Number 71)]

[Notices]

[Page 19835-19837]

From the Federal Register Online via GPO Access [wais.access.gpo.gov]

[DOCID:fr11ap08-53]

ENVIRONMENTAL PROTECTION AGENCY

[FRL-8553-2]

Science Advisory Board Staff Office; Clean Air Scientific
Advisory Committee (CASAC); Notification of a Public Advisory Committee
Meeting of the CASAC Oxides of Nitrogen Primary NAAQS Review Panel and
Public Teleconference of the CASAC

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice.

SUMMARY: The Environmental Protection Agency (EPA) Science Advisory Board (SAB) Staff Office announces a public meeting of the Clean Air Scientific Advisory Committee's (CASAC) Oxides of Nitrogen Primary NAAQS Review Panel (Panel) to conduct a peer review of EPA's Integrated Science Assessment for Oxides of Nitrogen--Health Criteria (Second External Review Draft) (EPA/600/R-07/093aB and EPA/600/R-07/903bB, March 2008) and to conduct a review of the EPA's Risk and Exposure Assessment to Support the Review of the NO₂ Primary National Ambient Air Quality Standard: First Draft and Risk and Exposure Assessment to Support the Review of the NO₂ Primary National Ambient Air Quality Standard: Draft Technical Support Document (TSD). The chartered CASAC will review and approve the Panel's report by teleconference.

[[Page 19836]]

DATES: The meeting will be held from 8:30 a.m. (Eastern Time) on Thursday, May 1, 2008 through 2 p.m. (Eastern Time) on Friday, May 2,

2008. The chartered CASAC will meet by public teleconference from 3 p.m. to 5 p.m. on June 11, 2008 (Eastern Time).

Location: The May 1-2, 2008 meeting will take place at the Marriott at Research Triangle Park, 4700 Guardian Drive, Durham, NC 27703, telephone: (919) 941-6200.

FOR FURTHER INFORMATION CONTACT: Any member of the public who wishes to submit a written or brief oral statement (5 minutes or less) or wants further information concerning this meeting must contact Dr. Angela Nugent, Designated Federal Officer (DFO), EPA Science Advisory Board (1400F), U.S. Environmental Protection Agency, 1200 Pennsylvania Avenue, NW., Washington, DC 20460; via telephone/voice mail: (202) 343-9981; fax: (202) 233-0643; or e-mail at: nugent.angela@epa.gov. For information on the CASAC teleconference on June 11, 2008, please contact Mr. Fred Butterfield, Designated Federal Officer (DFO), at the above listed address, via telephone/voice mail: (202) 343-9994 or e-mail at: butterfield.fred@epa.gov. General information concerning the CASAC and the CASAC documents cited below can be found on the EPA Web site at: <http://www.epa.gov/casac>.

SUPPLEMENTARY INFORMATION: Background: The Clean Air Scientific Advisory Committee (CASAC) was established under section 109(d)(2) of the Clean Air Act (CAA or Act) (42 U.S.C. 7409) as an independent scientific advisory committee. CASAC provides advice, information and recommendations on the scientific and technical aspects of air quality criteria and national ambient air quality standards (NAAQS) under sections 108 and 109 of the Act. The CASAC is a Federal advisory committee chartered under the Federal Advisory Committee Act (FACA), as amended, 5 U.S.C., App. The Panel will comply with the provisions of FACA and all appropriate SAB Staff Office procedural policies.

Section 109(d)(1) of the CAA requires that the Agency periodically review and revise, as appropriate, the air quality criteria and the NAAQS for the six "criteria" air pollutants, including oxides of nitrogen (NO_x). EPA is in the process of reviewing the primary NAAQS for nitrogen dioxide (NO₂) as an indicator for NO_x. Primary standards set limits to protect public health, including the health of "sensitive" populations such as asthmatics, children, and the elderly.

EPA previously released an integrated plan for all aspects of this review of the primary NO₂ standard, Integrated Review Plan for the Primary National Ambient Air Quality Standard for Nitrogen Dioxide (August 2007), which reflected advice provided by CASAC through a consultation, which resulted in the CASAC letter, Scientific Advisory Committee's (CASAC) Consultation on the Draft Integrated Plans for Review of the Primary NAAQS for NO₂ and SO₂ EPA-CASAC-07-005. The CASAC also previously peer reviewed EPA's Integrated

Science Assessment for Oxides of Nitrogen--Health Criteria (First External Review Draft) (EPA/600/R-07/093, August 2007) and issued a peer review report, Clean Air Scientific Advisory Committee's (CASAC) Peer Review of EPA's Integrated Science Assessment (ISA) for Oxides of Nitrogen--Health Criteria (First External Review Draft, August 2007), EPA-CASAC-08-002. The CASAC also provided consultative advice on the EPA's Nitrogen Dioxide Health Assessment Plan: Scope and Methods for Exposure and Risk Assessment and issued a consultation letter, Clean Air Scientific Advisory Committee's (CASAC) Consultation on EPA's Nitrogen Dioxide Health Assessment Plan: Scope and Methods for Exposure and Risk Assessment (September 2007 Draft), EPA-CASAC-08-001.

As the next step in that review process, EPA's Office of Research and Development (ORD) has completed a draft document, Integrated Science Assessment for Oxides of Nitrogen--Health Criteria (Second External Review Draft) (EPA/600/R-07/093aB and EPA/600/R-07/903bB, March 2008) and has requested that CASAC review the document. EPA's Office of Air and Radiation (OAR) has also completed two draft documents entitled (1) Risk and Exposure Assessment to Support the Review of the NO₂ Primary National Ambient Air Quality Standard: First Draft and (2) Risk and Exposure Assessment to Support the Review of the NO₂ Primary National Ambient Air Quality Standard: Draft Technical Support Document (TSD). OAR has requested that CASAC review this assessment of human exposure and health risk for nitrogen dioxide (NO₂). After the panel has drafted its reports, the chartered CASAC will meet by conference call to review and approve the drafts.

Technical Contact: Any questions concerning EPA's Integrated Science Assessment for Oxides of Nitrogen--Health Criteria (Second External Review Draft) (EPA/600/R-07/093aB and EPA/600/R-07/903bB, March 2008) should be directed to Dr. Dennis Kotchmar, ORD (by telephone: (919) 541-4158, or e-mail: Kotchmar.dennis@epa.gov). Any questions concerning EPA's Risk and Exposure Assessment To Support the Review of the NO₂ Primary National Ambient Air Quality Standard: First Draft and Risk and Exposure Assessment To Support the Review of the NO₂ Primary National Ambient Air Quality Standard: Draft Technical Support Document (TSD) should be directed to Dr. Scott Jenkins, OAR (by telephone: (919) 541-1167, or e-mail: jenkins.scott@epa.gov).

Availability of Meeting Materials: EPA-ORD's Integrated Science Assessment for Oxides of Nitrogen--Health Criteria (Second External Review Draft) can be accessed on EPA's National Center for Environmental Assessment Web site at: <http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=189147>. EPA-OAR's Risk and Exposure Assessment To Support the Review of the NO₂ Primary National Ambient Air Quality Standard: First Draft and Risk and Exposure Assessment To Support the Review of the NO₂ Primary National Ambient Air Quality Standard: Technical Support Document (TSD) will be accessible via the Agency's Office of Air Quality Planning and Standards Web site at: <http://>

www.epa.gov/ttn/naaqs/standards/nox/s_nox_cr_rea.html. Agendas and materials in support of the meeting and teleconference will be placed on the SAB Web site at: <http://www.epa.gov/casac> in advance.

Procedures for Providing Public Input: Interested members of the public may submit relevant written or oral information for the CASAC Panel to consider during the advisory process. **Oral Statements:** In general, individuals or groups requesting an oral presentation at a public meeting will be limited to five minutes per speaker, with no more than a total of one hour for all speakers. Interested parties should contact Dr. Angela Nugent, DFO, in writing (preferably via e-mail) by April 24, 2008 at the contact information noted above to be placed on the public speaker list for this meeting. To be placed on the public speaker list for the June 11, 2008 teleconference, interested parties should notify Mr. Fred Butterfield, DFO, by e-mail no later than June 6, 2008. Oral presentations will be limited to a total of 30 minutes for all speakers.

Written Statements: Written statements for the public meeting should be received by Dr. Angela Nugent at the contact information above by April 24, 2008, so that the information may be made available to

[[Page 19837]]

the Panel for their consideration prior to this meeting. Written statements for the teleconference should be received by Mr. Fred Butterfield, DFO, by June 6, 2008. Written statements should be supplied to the appropriate DFO by June 6, 2008. Written statements should be supplied to the appropriate DFO in the following formats: one hard copy with original signature (optional), and one electronic copy via e-mail (acceptable file format: Adobe Acrobat PDF, MS Word, MS PowerPoint, or Rich Text files in IBM-PC/Windows 98/2000/XP format).

Accessibility: For information on access or services for individuals with disabilities, please contact Dr. Nugent at the phone number or e-mail address noted above, preferably at least ten days prior to the meeting, to give EPA as much time as possible to process your request.

Dated: April 7, 2008.
Anthony F. Maciorowski,
Deputy Director, EPA Science Advisory Board Staff Office.

Attachment C: Meeting Agenda

U.S. Environmental Protection Agency – Science Advisory Board (SAB) Staff Office
Clean Air Scientific Advisory Committee (CASAC)
Oxides of Nitrogen (NO_x) Primary Review Panel
Public Meeting
May 1-2, 2008
Marriott at Research Triangle Park, 4700 Guardian Drive, Durham, NC, 27703

Meeting Agenda

Purpose: to conduct a peer review of EPA's *Integrated Science Assessment (ISA) for Oxides of Nitrogen – Health Criteria (Second External Review Draft, August 2007)* and to conduct a review of the EPA's *Risk and Exposure Assessment to Support the Review of the NO₂ Primary National Ambient Air Quality Standard: First Draft*.

May 1, 2008

8:30 a.m.	Welcome	Dr. Angela Nugent, EPA SAB Staff Office, Designated Federal Officer Dr. Vanessa Vu, EPA, SAB Staff Office
8:40 a.m.	Introduction of Members, Review of Agenda and Agency Charge Questions for the Peer Review of the Second Draft ISA	Dr. Rogene Henderson, Chair
8:50 a.m.	Introduction to Draft ISA for Oxides of Nitrogen – Health Criteria	Dr Ila Cote Dr. Mary Ross Dr, Dennis J. Kotchmar Dr Qingyu Meng Dr. Thomas Luben EPA Office of Research and Development Staff
9:20 a.m.	Public Comments	To be announced

Members' Discussion and Deliberations

9:35 a.m.	Agency Charge Question 1	<i>Discussants:</i> <u>Dr. Jonathan M. Samet</u> Dr. Dale Hattis Dr. Elizabeth A. (Lianne) Sheppard Dr. George Thurston
10:15 a.m.	Agency Charge Question 2	<i>Discussants:</i> <u>Dr. Armistead (Ted) Russell</u> Dr. Donna Kenski Dr. Timothy V. Larson (by phone) Dr. Christian Seigneur

Dr. James Ultman

10:55 a.m.	BREAK	
11:15 a.m.	Agency Charge Question 3	<i>Discussants:</i> <u>Dr. James Crapo</u> Dr. Ed Avol Dr. John R. Balmes (by phone) Dr. Terry Gordon Dr. Kent Pinkerton Dr. Jonathan M. Samet Dr. Richard Schlesinger Dr. George Thurston
12:00 p.m.	LUNCH	
1:00 p.m.	Agency Charge Question 4	<i>Discussants:</i> <u>Dr. John R. Balmes (by phone)</u> Dr. Steven Kleeberger Dr. Edward Postlethwait
1:40 p.m.	Agency Charge Question 5	<i>Discussants:</i> <u>Dr. Douglas Crawford-Brown (by phone)</u> <u>Dr. Jonathan M. Samet</u> Dr. Frank Speizer Dr. Ronald Wyzga
2:45 p.m.	Summary of Next Steps	Dr. Rogene Henderson
3:00 p.m.	BREAK	
3:15 p.m.	Introduction to EPA's draft <i>Risk and Exposure Assessment</i>	Dr. Stephen Graham Mr. Harvey Richmond, Dr. Scott Jenkins EPA Office of Air and Radiation
3:45 p.m.	Public Comments	To be announced
<i>Members' Discussion and Deliberations</i>		
4:00 p.m.	Air Quality Information and Analyses (Initial Discussion)	<i>Discussants:</i> <u>Dr. Christian Seigneur</u> Dr. Donna Kenski Dr. Timothy V. Larson (by phone) Dr. Armistead (Ted) Russell Dr. James Ultman

4:55 p.m.	Review of Agenda for May 2, 2008	Dr. Rogene Henderson
5:00 p.m.	Adjourn Meeting	Dr. Angela Nugent

May 2, 2008

8:30 a.m.	Reconvene the Panel Meeting	Dr. Angela Nugent
8:35 a.m.	Air Quality Information and Analyses (Continuation)	<i>Discussants:</i> <u>Dr. Christian Seigneur</u> Dr. Donna Kenski Dr. Timothy V. Larson (by phone) Dr. Armistead (Ted) Russell Dr. James Ultman
9:15 a.m.	Exposure Analysis	<i>Discussants:</i> <u>Dr. Patrick Kinney</u> Dr. Douglas Crawford-Brown (by phone) Dr. Dale Hattis Dr. Elizabeth A. (Lianne) Sheppard
10:30	BREAK	
10:45 a.m.	Characterization of Health Risks	<i>Discussants:</i> <u>Dr. Ed Avol</u> Dr. John R. Balmes (by phone) Dr. James Crapo Dr. Terry Gordon (by phone) Dr. Patrick Kinney Dr. Steven Kleeberger Dr. Kent Pinkerton Dr. Edward Postlethwait Dr. Jonathan M. Samet (by phone) Dr. Richard Schlesinger Dr. Frank Speizer Dr. George Thurston Dr. Ronald Wyzga
12: 15 p.m.	LUNCH	
1:00 p.m. .	Continued Discussion of Characterization of Health Risks	Panel
1:45 p.m.	Summary of Next Steps Related to the Review of the draft <i>Risk and Exposure Assessment</i>	Dr. Rogene Henderson
2:00 p.m.	Adjourn the Meeting	Dr. Angela Nugent

Attachment D Presentation Integrated Science Assessment for Oxides of Nitrogen – Health Criteria 2nd External Review Draft, Presentation by Dr. Ila Cote, EPA/ORD/NCEA

*Integrated Science Assessment for
Oxides of Nitrogen – Health Criteria*
2nd External Review Draft

**Clean Air Science Advisory
Committee Meeting
May 1, 2008**

Dr. Ila L. Cote
Acting Division Director
National Center for Environmental Assessment
US EPA Office of Research and Development

Charge Question 1

What are the views of the Panel on the characterization of the search strategy for identifying literature, criteria for study selection, the framework for scientific evaluation of studies and causality determination?

RESEARCH & DEVELOPMENT
Building a scientific foundation for sound environmental decisions

New Framework for Causal Determinations

Establish uniform language concerning causality and improve specificity of our findings:

- assess the separate and combined lines of evidence from epidemiology, clinical, animal and in vitro toxicology studies
- classify and characterize the data to evaluate causality

Adapted from the Surgeon General's Smoking Reports and the NAS/IOM document, "Improving the Presumptive Disability Decision-Making Process for Veterans" (2007)

RESEARCH & DEVELOPMENT
Building a scientific foundation for sound environmental decisions

Hill's Factors for Judging Causality

- Consistency of the observed association
- Strength of the observed association
- Specificity of the observed association
- Temporal relationship of the observed association
- Biological gradient (exposure-response relationship)
- Biological plausibility
- Coherence
- Experimental evidence (from human populations)
- Analogy

RESEARCH & DEVELOPMENT
Building a scientific foundation for sound environmental decisions

New Framework for Causal Determinations

A two-step approach is used to judge the scientific evidence about exposure to criteria pollutants and risks to public health.

The first step is to determine causality

- Sufficient to infer a *causal relationship*.
- Sufficient to infer a *likely causal relationship* (i.e., more likely than not).
- *Suggestive but not sufficient* to infer a causal relationship.
- *Inadequate to infer the presence or absence* of a causal relationship.
- *Suggestive of no causal relationship*.

The second step is further evaluation of the population response (e.g. the shape of concentration-response, susceptibility differences, ambient levels and exposure time periods at which effects are observed).

RESEARCH & DEVELOPMENT
Building a scientific foundation for sound environmental decisions

NCEA-RTP NOx TEAM ISA IN SUPPORT OF THE PRIMARY STANDARD

Dr. Ila Cote – Acting Division Director
Dr. Mary Ross – Branch Chief

Dr. Dennis Kotchmar - NOx Team Leader

Dr. Jeffrey Arnold
Dr. James Brown
Dr. Barbara Buckley
Ms. Rebecca Daniels
Dr. Jee Young Kim
Dr. Ellen Kirrane
Dr. Thomas Long
Dr. Thomas Luben
Dr. Qingyu Meng
Dr. Joseph Pinto
Dr. Paul Reinhart
Mr. Jason Sacks
Dr. David Svendsgaard
Dr. Lori White
Dr. William Wilson

RESEARCH & DEVELOPMENT
Building a scientific foundation for sound environmental decisions

Response to CASAC Review

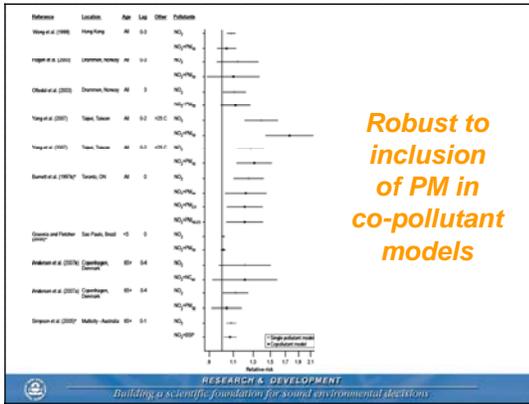
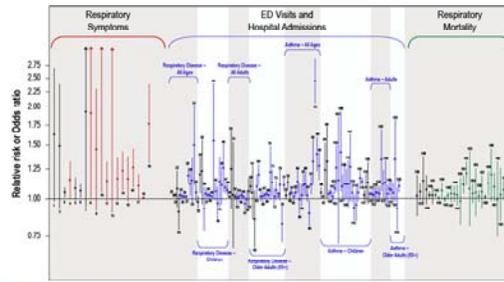
Ambient NO₂ is a component of a mixture of combustion-related pollutants, making it difficult to distinguish and quantify the individual effect of NO₂ in observational studies

Evidence for an independent effect:

- Consistent, coherent, and biologically plausible respiratory effects
- Robust to inclusion of additional criteria pollutants in copollutant models

Current ambient NO₂ exposures can result in adverse impacts to public health at ambient concentrations below the current standard

Consistent and Coherent Results



Key Conclusions

Short-term Exposure

- Respiratory Morbidity: *sufficient to infer a likely causal relationship*
- Cardiovascular Morbidity: *inadequate to infer the presence or absence of a causal relationship*
- Mortality: *suggestive but not sufficient to infer a causal relationship*

Long-term Exposure

- Respiratory Morbidity: *suggestive but not sufficient to infer a causal relationship*
- Other Morbidity: *inadequate to infer the presence or absence of a causal relationship*
- Mortality: *inadequate to infer the presence or absence of a causal relationship*

Attachment E: Comments on the Integrated Science Assessment (ISA) for Oxides of Nitrogen- Health Criteria (March 2008 Draft) On Behalf of the Utility Air Regulatory Group (UARG), Presentation by Dr. Christopher M. Long, Gradient Corporation

Comments on the Integrated Science Assessment (ISA) for Oxides of Nitrogen- Health Criteria (March 2008 Draft)

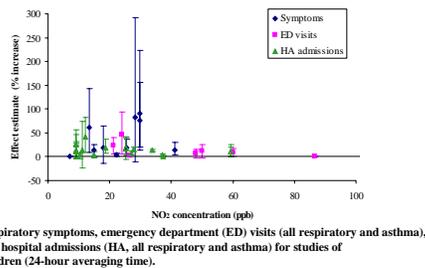
On Behalf of the Utility Air Regulatory Group (UARG)

Christopher M. Long, Sc.D.
Peter A. Valberg, Ph.D.
Gradient Corporation
May 1, 2008

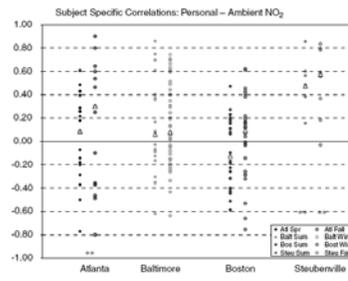
Overarching Comments

- Chapter 5 does not provide sufficient integration and analysis of the different lines of NO_x health-effects evidence
 - By disregarding the NO₂ concentrations at which health effect associations have been observed, Figure 5.3-1 gives an incomplete and misleading picture of the epidemiological evidence for short-term exposure NO₂ health effects.
 - The association between ambient NO₂ concentrations and personal NO₂ exposures is complex and remains poorly understood, raising questions regarding the proper interpretation of the reported NO₂ epidemiologic associations.
 - US EPA does not sufficiently consider the fact that NO₂ may be acting as a surrogate for other pollutants.
 - US EPA should quantitatively contrast the dose levels typical of ambient NO₂ epidemiological studies versus those used in human controlled exposure studies.

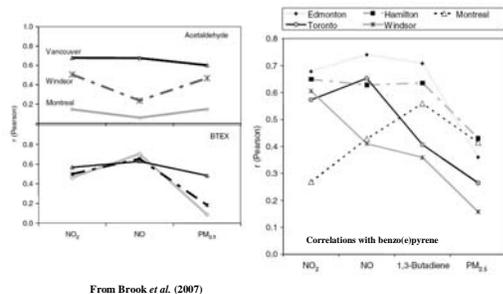
Figure 5.3-1 Disregards a Key Factor for Assessing the Consistency and Coherence of the Epidemiologic Evidence, Namely Dose-Response



Ambient NO₂ vs. Personal NO₂ Correlations Are Poor and Vary Widely



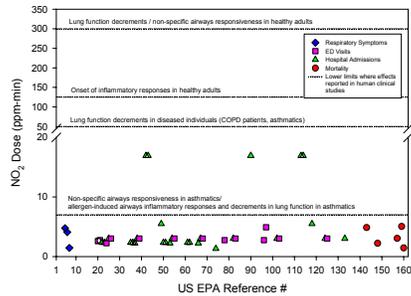
Recent Studies Provide Compelling Evidence for Ambient NO₂ Acting as a Surrogate



Available Multi-Pollutant Model Results Are Limited and Conflicting

- Of the two-pollutant model results provided in Figures 3.1-10 and 3.1-11 for NO₂ and respiratory-related HA or ED:
 - only one model adjusting for particle concentrations was for PM_{2.5}, with most adjusting instead for PM₁₀.
 - only two studies included adjustment for a gaseous pollutant other than O₃ or SO₂.
 - None adjusted for aldehydes, PAHs, or particle-bound organics.
 - None of the cited studies are for U.S. locations.
- Recently published multi-pollutant model results (*e.g.*, Tolbert *et al.*, 2007; McCreanor *et al.*, 2007; Delfino *et al.*, 2008) contradict the EPA conclusion that ambient NO₂ is robust in multi-pollutant models.

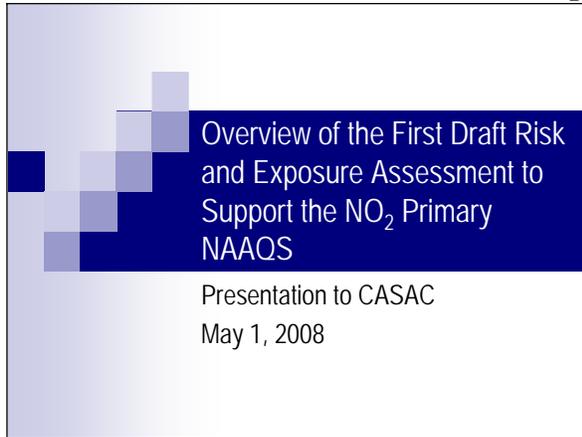
Epidemiologic Associations Are Generally Reported for NO₂ Doses Far Below Human Clinical Toxicology No-Effect Levels



Recommendations for EPA

- Merely acknowledging uncertainties is not sufficient. Uncertainties must be quantified, and affect the weight that is placed on particular study findings or particular lines of evidence.
- The supportive (or non-supportive) role of clinical and experimental studies at the specific ambient concentrations in question should be directly addressed.
- Chapter 5 needs to be less of an introduction of ideas and recitation of selected study findings, and more of an integrative synthesis that can inform policy-makers.

Attachment F Presentation: Overview of the First Draft Risk and Exposure Assessment to Support the NO₂ Primary NAAQS



Overview of the First Draft Risk and Exposure Assessment to Support the NO₂ Primary NAAQS

Presentation to CASAC
May 1, 2008

Overview of Presentation

- Background
 - Timeline of current review
 - Purpose and scope of documents
- Overview of Approaches
 - Exposure
 - Risk
- Risk characterization based on air quality assessment
- Risk characterization based on exposure assessment

2

Timeline for Review

Major Milestones		Projected Completion Date	Projected CASAC Review Date
Integrated Review Plan	Draft Final	April 2007 June 2007	May 2007
Integrated Science Assessment	First Draft Second Draft Final	August 2007 March 2008 July 2008	October 2007 May 2008
Risk/Exposure Assessment	Plan First Draft Second Draft Final	September 2007 March 2008 August 2008 November 2008	October 2007 May 2008 September 2008
Rulemaking	ANPR Proposed Final	December 2008 May 2009 December 2009	January 2009

*Indicates that a single CASAC meeting will address both documents

3

Purpose and Scope of Documents

- Purpose
 - Convey the approach taken to characterize exposures and risks associated with ambient NO₂
 - Present results of those assessments
 - **Inform the rulemaking process**
- Scope
 - First draft documents consider recent NO₂ levels and levels associated with just meeting the current standard
 - Exposure assessment in single location (Philadelphia County)
 - Subsequent drafts will also address levels associated with just meeting potential alternative standards
 - Exposure assessment will include additional locations

4

Overview of Approaches Used to Estimate Exposures and Characterize Risks

- Exposure characterization
 - Air quality analysis: Ambient levels of NO₂ derived from a combination of ambient monitors and modeling of levels on roadways
 - Exposure analysis: Considers time spent in different microenvironments, with each microenvironment characterized by a unique NO₂ concentration
- Risk characterization
 - Estimates of population exposure compared to potential benchmark levels (0.20, 0.25, 0.30 ppm)
 - Levels identified from the controlled human exposure literature on airways responsiveness in asthmatics
 - Epidemiological literature will be used as part of an evidence-based approach to assessing the adequacy of potential alternative standards

5

Air Quality Analysis and Risk Characterization

- Selection of locations
 - AQS monitoring data used (1995-2006)
 - Locations chosen if they had high annual average and/or 1-hour levels
 - Annual average \geq 90th percentile and/or 1-hour levels above 200 ppb
- Scenarios evaluated
 - Ambient air quality as-is
 - Ambient air quality adjusted upwards such that levels of NO₂ in each location just meet the current standard
 - On-road levels of NO₂ modeled based on ambient air quality as-is
 - On-road levels of NO₂ modeled based on ambient air quality adjusted upwards such that levels of NO₂ in each location just meet the current standard
- Risk characterization
 - Number of exceedances of potential benchmark values estimated for each area

6

Estimated Number of Benchmark Exceedances

Estimated Mean (and 98th percentile) Number of Benchmark (200 ppb) Exceedances Per Year* by Location

Location	Ambient		On-Road		Location	Ambient		On-Road	
	As-Is	Roll-Up	As-Is	Roll-Up		As-Is	Roll-Up	As-Is	Roll-Up
Boston	0 (0)	0 (5)	1 (8)	87 (753)	Atlanta	0 (0)	8 (56)	1 (16)	335 (1647)
Chicago	0 (0)	1 (15)	10 (142)	176 (1022)	El Paso	0 (0)	7 (27)	1 (9)	389 (1604)
Cleveland	0 (0)	1 (4)	3 (36)	387 (1322)	Jacksonville	1 (2)	31 (72)	3 (23)	607 (1642)
Denver	0 (0)	2 (7)	8 (69)	277 (1233)	Las Vegas	0 (0)	1 (12)	1 (15)	278 (1929)
Detroit	1 (12)	8 (45)	5 (44)	440 (1444)	Phoenix	0 (0)	0 (1)	3 (44)	149 (1172)
Los Angeles	0 (0)	0 (5)	11 (131)	106 (788)	Provo	0 (0)	88 (526)	70 (662)	516 (1966)
Miami	0 (3)	17 (69)	0 (7)	406 (1345)	St. Louis	0 (0)	0 (5)	1 (7)	182 (1100)
New York	0 (0)	0 (2)	9 (90)	84 (709)	Other CMSA	0 (0)	0 (3)	0 (5)	64 (569)
Philadelphia	0 (0)	1 (25)	1 (14)	174 (973)	Not MSA	0 (0)	3 (44)	0 (4)	101 (874)
Washington	0 (0)	0 (5)	1 (14)	208 (1171)					

*Mean estimated exceedances per year based on the years 2001-2006

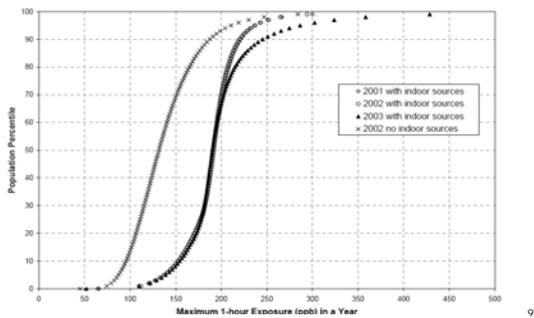
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Exposure Analysis and Risk Characterization

- Probabilistic approach was used to estimate population exposures
- Approach considers the time people spend in different microenvironments and variable NO₂ concentrations that occur within these microenvironments
- Estimates of exposure were compared to potential health benchmark values
- Initial focus was on Philadelphia
 - Additional locations will be evaluated for subsequent drafts

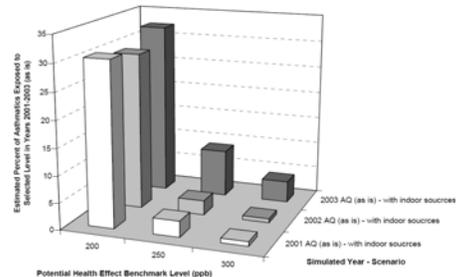
8

Estimated 1-hour NO₂ Exposures: Air Quality As-Is



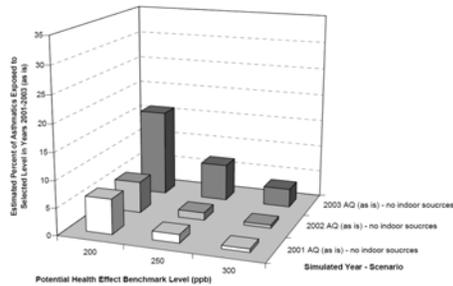
9

Percent of Asthmatics with at Least One Exceedance: Air Quality As-Is



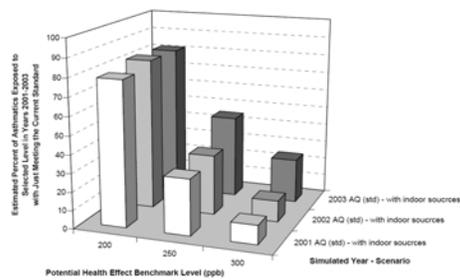
10

Percent of Asthmatics with at Least One Exceedance (No Indoor Sources): Air Quality As-Is



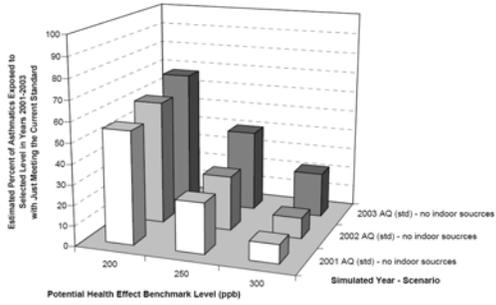
11

Percent of Asthmatics with at Least One Exceedance: Just Meeting Current Standard



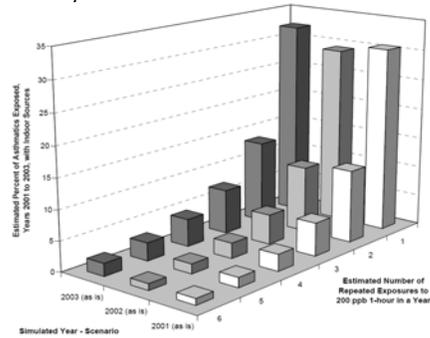
12

Percent of Asthmatics With at Least One Exceedance (No Indoor Sources): Just Meeting Current Standard



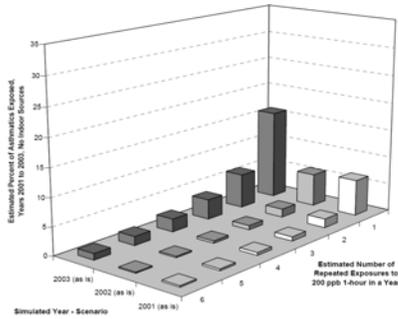
13

Percent of Asthmatics With Repeated Exceedances: Air Quality As-Is



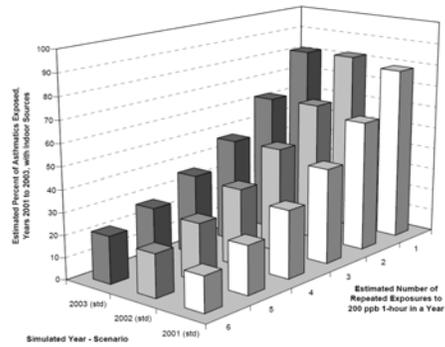
14

Percent of Asthmatics With Repeated Exceedances (No Indoor Sources): Air Quality As-Is



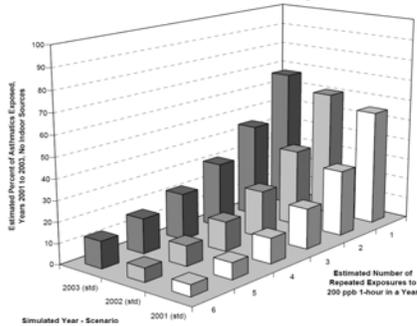
15

Percent of Asthmatics With Repeated Exceedances: Just Meeting Current Standard



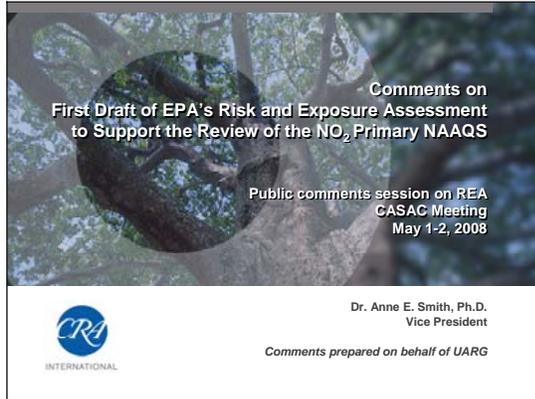
16

Percent of Asthmatics With Repeated Exceedances (No Indoor Sources): Just Meeting Current Standard



17

Attachment G: Presentation from Dr. Anne Smith on behalf of UARG: Comments on First Draft of EPA's Risk and Exposure Assessment to Support the Review of the NO₂ Primary NAAQS



Several Key Issues with REA

I address the first 2 issues in these slides. (The 3rd and 4th issues are addressed in the written comments I have also provided for CASAC)

1. REA does not establish a linkage between its "benchmark exposure levels" and evidence of enhanced risks
 - No apparent basis for using a benchmark of 200 ppb
 - Linkages between REA and ISA are not clear
2. Selection of cities in REA is not representative
3. "Roll up" to simulate exposures at current standard is far too extreme to provide any useful information
4. Concern that the Exposure Analysis and the Air Quality Characterization are inconsistent with each other.

CRA INTERNATIONAL

Risk Assessment Needs Clear Linkage of Scientific Evidence of Risk

- No "concentration-response" relationship attempted
- Uses "benchmarks" of 200 ppb, 250 ppb and 300 ppb
 - ➔ **WHAT DO THESE MEAN IN TERMS OF "RISK"?**
 - The "lower- middle- and upper end of the range identified in the ISA as the lowest levels at which controlled human exposure studies have provided sufficient evidence for the occurrence of NO₂-related airway responsiveness"
 - Relevant studies identified in Table 1 of REA

CRA INTERNATIONAL

Table 1 of REA Is Supposed to Support Choice of Benchmark Levels in Range of 200 to 300 ppb

Study	NO ₂ Exposure Level	Exposure Duration	Health Endpoints	Population	Study Design	Matrix Used	Number of Subjects	Statistical Significance	Health Study Peer Reviewed
Chen, 2004	0.4	3 hours	Cardiorespiratory	Children	Controlled	Airways	8	Yes	Yes
Chen, 2005	0.4	3 hours	Cardiorespiratory	Children	Controlled	Airways	8	Yes	Yes
Chen, 2007	0.4	3 hours	Cardiorespiratory	Children	Controlled	Airways	8	Yes	Yes
Chen, 2008	0.4	3 hours	Cardiorespiratory	Children	Controlled	Airways	8	Yes	Yes
Chen, 2009	0.4	3 hours	Cardiorespiratory	Children	Controlled	Airways	8	Yes	Yes
Chen, 2010	0.4	3 hours	Cardiorespiratory	Children	Controlled	Airways	8	Yes	Yes
Chen, 2011	0.4	3 hours	Cardiorespiratory	Children	Controlled	Airways	8	Yes	Yes
Chen, 2012	0.4	3 hours	Cardiorespiratory	Children	Controlled	Airways	8	Yes	Yes
Chen, 2013	0.4	3 hours	Cardiorespiratory	Children	Controlled	Airways	8	Yes	Yes
Chen, 2014	0.4	3 hours	Cardiorespiratory	Children	Controlled	Airways	8	Yes	Yes
Chen, 2015	0.4	3 hours	Cardiorespiratory	Children	Controlled	Airways	8	Yes	Yes
Chen, 2016	0.4	3 hours	Cardiorespiratory	Children	Controlled	Airways	8	Yes	Yes
Chen, 2017	0.4	3 hours	Cardiorespiratory	Children	Controlled	Airways	8	Yes	Yes
Chen, 2018	0.4	3 hours	Cardiorespiratory	Children	Controlled	Airways	8	Yes	Yes
Chen, 2019	0.4	3 hours	Cardiorespiratory	Children	Controlled	Airways	8	Yes	Yes
Chen, 2020	0.4	3 hours	Cardiorespiratory	Children	Controlled	Airways	8	Yes	Yes
Chen, 2021	0.4	3 hours	Cardiorespiratory	Children	Controlled	Airways	8	Yes	Yes
Chen, 2022	0.4	3 hours	Cardiorespiratory	Children	Controlled	Airways	8	Yes	Yes
Chen, 2023	0.4	3 hours	Cardiorespiratory	Children	Controlled	Airways	8	Yes	Yes
Chen, 2024	0.4	3 hours	Cardiorespiratory	Children	Controlled	Airways	8	Yes	Yes
Chen, 2025	0.4	3 hours	Cardiorespiratory	Children	Controlled	Airways	8	Yes	Yes
Chen, 2026	0.4	3 hours	Cardiorespiratory	Children	Controlled	Airways	8	Yes	Yes
Chen, 2027	0.4	3 hours	Cardiorespiratory	Children	Controlled	Airways	8	Yes	Yes
Chen, 2028	0.4	3 hours	Cardiorespiratory	Children	Controlled	Airways	8	Yes	Yes
Chen, 2029	0.4	3 hours	Cardiorespiratory	Children	Controlled	Airways	8	Yes	Yes
Chen, 2030	0.4	3 hours	Cardiorespiratory	Children	Controlled	Airways	8	Yes	Yes

A table like this does not exist in the ISA

CRA INTERNATIONAL

Table 1 Re-Ordered by Exposure Levels:

Shows No Risk-Related Basis for a Benchmark of 200 ppb

Study	NO2(ppm)	Duration	Significant?
Roger, 1990	0.15	1.25-hr	NO
Jenkins, 1999	0.2	6-hr	NO
Jörres, 1990	0.25	30-min	
Jörres, 1991 (*)	0.25	30-min	NO
Barck, 2005	0.26	15-min (3x in 2days)	NO
Barck, 2005	0.26	15-min (3x in 2days)	
Strand, 1997	0.26	30-min	
Barck, 2002	0.26	30-min	
Strand, 1996	0.26	30-min	
Strand, 1998	0.26	30-min (4x/day)	
Bylin, 1985	0.3	20-min	
Rubenstein, 1990	0.3	30-min	NO
Tumnicliffe, 1994	0.4	1-hr	
Witten, 2005	0.4	3-hr	NO
Jenkins, 1999	0.4	3-hr	
Witten, 2005	0.4	3-hr	NO
Devalia, 1994	0.4	6-hr	NO
Mohsenin, 1987	0.5	1-hr	
Roger, 1990	0.6	1.25-hr	NO

Exposures ~200 ppb

Exposures ~250 ppb

Exposures ≥ 300 ppb

5 (*) Table 1 of REA has 2 identical entries for Jörres, 1991. The apparent duplicate was deleted in the above.



Selection Criteria for Cities Creates an Unrepresentative Characterization of US Exposure Levels

For Air Quality Characterization:

- Cities with a monitor whose annual average NO₂ is among the worst 10% of all US NO₂ monitors, or with at least one reading above 200 ppb (1995-2006)

For Exposure Modeling:

- Cities with a monitor whose annual average NO₂ is among the worst 10% of all US NO₂ monitors, and with at least one reading above 200 ppb (2001-2006)
 - Philadelphia and Los Angeles
- Add the city with greatest number of hours above 200 ppb
 - Detroit
- Add cities with a worst-10% average or exceedances earlier
 - Atlanta and Phoenix



Summary

- **The combined effect of**
 1. BENCHMARKS AT WHICH EFFECTS ARE NOT DOCUMENTED
 2. ANALYSIS OF ONLY THE WORST-CASE CITIES**produces a characterization of NO₂ exposures that overstates the magnitude of the potential risks**
- **This is exacerbated by the 2 other concerns discussed in my written comments (handout), i.e.,**
 - Unreasonable "roll up" of NO₂ data to simulate current NAAQS
 - Apparent inconsistencies in NO₂ data in the 2 parts of the REA



Extrapolations to Simulate 53 ppb Annual Average NO₂ Are Extremely Large

