



U.S. Environmental Protection Agency
Clean Air Scientific Advisory Committee
Oxides of Nitrogen Primary NAAQS Review Panel
Public Meeting

Review of the Integrated Science Assessment for Oxides of
Nitrogen – Health Criteria,
First External Review Draft

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Durham, NC
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Timeline for the ISA for Oxides of Nitrogen

Science and Policy Issue Workshop	February 29-March 1, 2012
Draft Plan for Development of the ISA	May 3, 2013
CASAC/public consultation on draft plan of ISA	June 5, 2013
Peer Input Workshop	June 11, 2013
First external review draft ISA	November 22, 2013

CASAC/public review of first draft ISA	March 12-13, 2014
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Second external review draft ISA	August 2014
CASAC/public review of second draft ISA	October 2014
Final ISA	February 2015

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Content of the ISA for Oxides of Nitrogen

Preamble

Preface: Legislative Requirements and History of the NAAQS for NO₂

Executive Summary

Chapter 1. Integrative Synthesis of the ISA

Chapter 2. Atmospheric Chemistry and Exposure to Oxides of Nitrogen

Chapter 3. Dosimetry and Modes of Action for Inhaled Oxides of Nitrogen

Chapter 4. Integrated Health Effects of Short-term Exposure to Oxides of Nitrogen

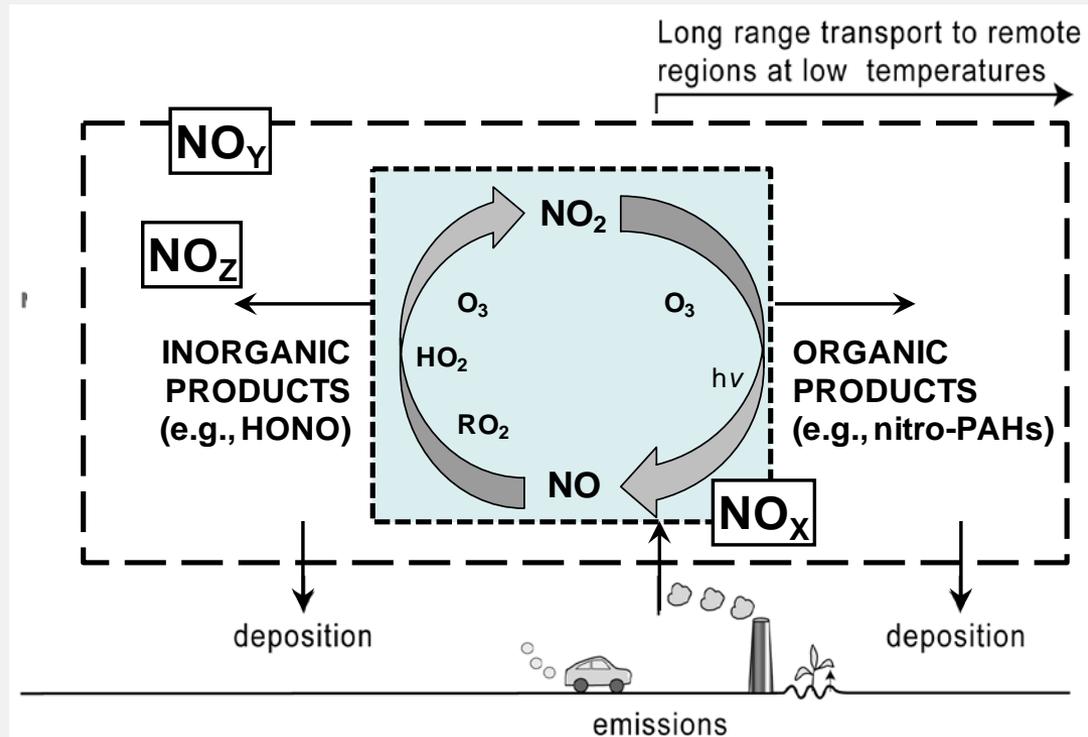
Chapter 5. Integrated Health Effects of Long-term Exposure to Oxides of Nitrogen

Chapter 6. Populations Potentially at Increased Risk for Health Effects related to Exposure to Oxides of Nitrogen

Scope of the ISA for Oxides of Nitrogen

- Scientific foundation to inform the review of the current primary (health-based) National Ambient Air Quality Standards (NAAQS) for nitrogen dioxide (NO_2)

- Oxides of nitrogen include all oxidized forms of nitrogen
 - Gaseous and Particulate: NO_Y
- This ISA evaluates:
 - Gaseous oxides of nitrogen: NO_2 , nitric oxide (NO), NO_X ($\text{NO}_2 + \text{NO}$), others
 - Health effects



Modified from Figure 2-1 of the ISA for Oxides of Nitrogen – Health Criteria, First External Review Draft

- Not included in this ISA:
 - Particulate species (e.g., nitro-PAHs) – evaluated in ISA for Particulate Matter
 - Welfare and ecological effects – evaluated as part of the review of the secondary NAAQS for oxides of nitrogen and sulfur

Charge – Chapter 2

Sources, atmospheric chemistry, air quality characterization, and human exposure to oxides of nitrogen

- To what extent is the information presented regarding characteristics of sources, chemistry, monitoring concentrations, and human exposure accurate, complete, and relevant to the review of the NO₂ NAAQS?
- To what extent are the analyses of air quality presented clearly conveyed, appropriately characterized, and relevant to the review of the NO₂ NAAQS?
- How effective are the source category groupings and the discussion of source emissions in understanding the importance and impacts of oxides of nitrogen from different sources on both national and local scales?

U.S. Sources of NO_x Emissions

Groupings in the 1st draft ISA 2008 National Emissions Inventory

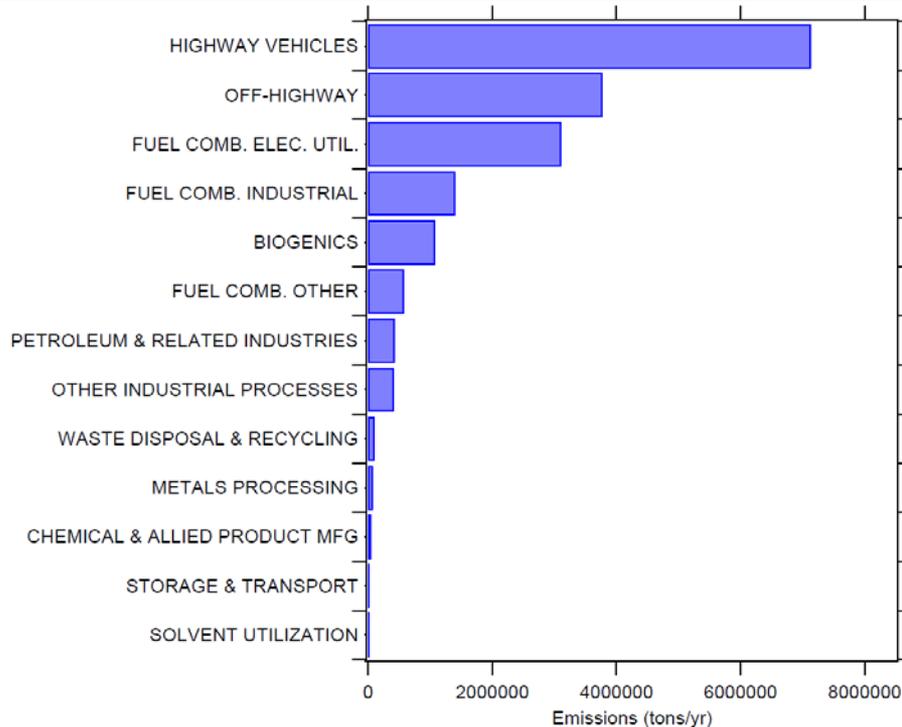
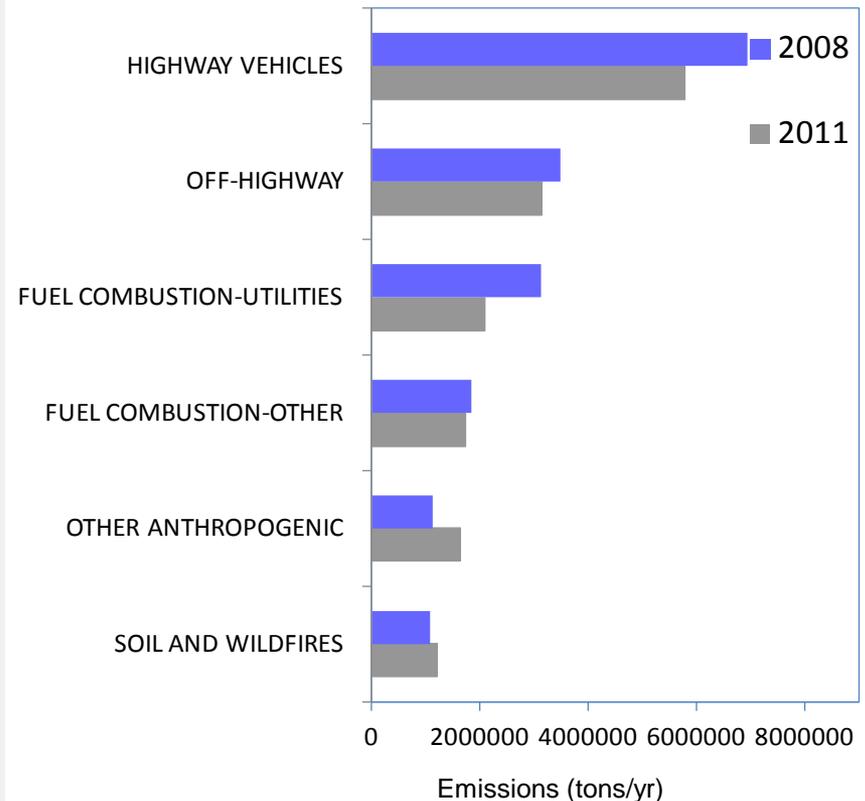


Figure 2-2 of the ISA for Oxides of Nitrogen – Health Criteria, First External Review Draft

Proposed groupings for 2nd draft ISA with 2011 National Emissions Inventory



Charge – Chapter 2 (cont'd)

- Please comment on the extent to which available information on the [spatial and temporal trends of ambient oxides of nitrogen at various scales has been adequately and accurately described](#).
- Please comment on the accuracy, level of detail, and completeness of the [discussion regarding exposure assessment and the influence of exposure error on effect estimates](#) in epidemiologic studies of the health effects of NO₂.

Charge – Chapter 3

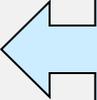
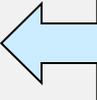
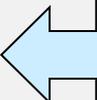
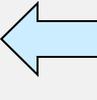
Dosimetry and modes of action for NO₂ and NO

- Given the ubiquity of reactive substrates and reaction rate of NO₂ with these substrates, it appears unlikely NO₂ itself will penetrate through the lung lining fluid to the epithelium (see Table 3-1). **Please comment on the adequacy of the discussion of NO₂ uptake and reactivity in the respiratory tract.**
- Since existing dosimetric models for NO₂ do not consider the probability of oxidants/cytotoxic products reaching target sites, it was concluded that these **models are inadequate for within or cross species comparisons. Please comment on the validity of this conclusion** and identify and comment on the validity of any alternative conclusions.
- Please comment on the **adequacy of the discussion of endogenously occurring NO₂ and NO** and their reaction products in comparison to that derived from ambient inhalation.
- To what extent are the **discussion and integration of the potential modes of action underlying the health effects of exposure to oxides of nitrogen presented accurately and in sufficient detail**? Are there additional modes of action that should be included in order to characterize fully the underlying mechanisms of oxides of nitrogen?

Causal Determinations from the 2008 and First Draft ISA for Oxides of Nitrogen

Health Effect Category	2008 ISA	First Draft ISA
Short-term NO₂ Exposure		
Respiratory Effects	Likely to be a Causal Relationship	Causal Relationship
Cardiovascular Effects	Inadequate to Infer a Causal Relationship	Likely to be a Causal Relationship
Total Mortality	Suggestive of a Causal Relationship	Likely to be a Causal Relationship
Long-term NO₂ Exposure		
Respiratory Effects	Suggestive of a Causal Relationship	Likely to be a Causal Relationship
Cardiovascular Effects	Inadequate to Infer a Causal Relationship	Suggestive of a Causal Relationship
Reproductive and Developmental Effects	Inadequate to Infer a Causal Relationship	Fertility, Reproduction, and Pregnancy Suggestive of a Causal Relationship Adverse Birth Outcomes Suggestive of a Causal Relationship Postnatal Development Suggestive of a Causal Relationship
Total Mortality	Inadequate to Infer a Causal Relationship	Suggestive of a Causal Relationship
Cancer	Inadequate to Infer a Causal Relationship	Suggestive of a Causal Relationship

Framework for Causal Determinations

Causal relationship	Evidence is sufficient to conclude that there is a causal relationship with relevant pollutant exposures (e.g., doses or exposures generally within one to two orders of magnitude of current levels). That is, the pollutant has been shown to result in health effects in studies in which chance, confounding, and other biases could be ruled out with reasonable confidence. For example: (1) controlled human exposure studies that demonstrate consistent effects; or (2) observational studies that cannot be explained by plausible alternatives or that are supported by other lines of evidence (e.g., animal studies or mode of action information). Generally, the determination is based on multiple high-quality studies conducted by multiple research groups.	 <p>Rule out chance, confounding, and other biases Consistency, coherence, biological plausibility, high-quality studies</p>
Likely to be a causal relationship	Evidence is sufficient to conclude that a causal relationship is likely to exist with relevant pollutant exposures. That is, the pollutant has been shown to result in health effects in studies where results are not explained by chance, confounding, and other biases, but uncertainties remain in the evidence overall. For example: (1) observational studies show an association, but copollutant exposures are difficult to address and/or other lines of evidence (controlled human exposure, animal, or mode of action information) are limited or inconsistent; or (2) animal toxicological evidence from multiple studies from different laboratories demonstrate effects, but limited or no human data are available. Generally, the determination is based on multiple high-quality studies.	 <p>Multiple, high-quality studies show effects Uncertainty remains</p>
Suggestive of a causal relationship	Evidence is suggestive of a causal relationship with relevant pollutant exposures, but is limited. For example, (1) at least one high-quality epidemiologic study shows an association with a given health outcome although inconsistencies remain across other studies that are or are not of comparable quality; or (2) a well-conducted toxicological study, such as those conducted in the National Toxicology Program (NTP), shows effects relevant to humans in animal species.	 <p>Evidence is limited. Association found in at least one high-quality study Or, results show some inconsistency</p>
Inadequate to infer a causal relationship	Evidence is inadequate to determine that a causal relationship exists with relevant pollutant exposures. The available studies are of insufficient quantity, quality, consistency, or statistical power to permit a conclusion regarding the presence or absence of an effect.	 <p>Evidence is of insufficient quantity, quality, consistency</p>
Not likely to be a causal relationship	Evidence indicates there is no causal relationship with relevant pollutant exposures. Several adequate studies, covering the full range of levels of exposure that human beings are known to encounter and considering at-risk populations and lifestages, are mutually consistent in not showing an effect at any level of exposure.	 <p>Multiple studies consistently show no effect across exposure concentrations</p>

Charge – Chapters 4 and 5

Assessments of the health effects associated with short-term and long-term exposure to oxides of nitrogen, respectively. Organized by health effect category, outcome, and scientific discipline.

- To what extent do the discussions in this chapter accurately reflect the body of evidence from epidemiologic, controlled human exposure, and toxicological studies?
- Please comment on the balance of discussion of evidence from previous and recent studies in informing the causal determinations.
- Please comment on the adequacy of the discussion of the strengths and limitations of the evidence in the text and tables within Chapters 4 and 5 and in the evaluation of the evidence in the causal determinations.

Charge – Chapters 4 and 5 (cont'd)

- What are the views of the panel on the [integration of epidemiologic, controlled human exposure, and toxicological evidence](#), in particular, on the balance of emphasis placed on each source of evidence? Please comment on the adequacy with which [issues related to exposure assessment and mode of action are integrated in the health effects discussion](#). Please provide recommendations on information in other chapters of the ISA that would be useful to integrate with the health effects discussions in these chapters.
- Please comment on the appropriateness of [using experimental and epidemiologic evidence for morbidity effects to inform the biological plausibility of total mortality](#) associated with short-term (Section 4.4) and long-term (Section 5.5) NO₂ exposure and in turn, to inform causal determinations.

Charge – Chapter 4 (cont'd)

NO₂ and airways responsiveness – Section 4.2.2

Main focus is an [updated EPA meta-analysis](#) of airways responsiveness data for individuals with asthma from controlled human exposure studies.

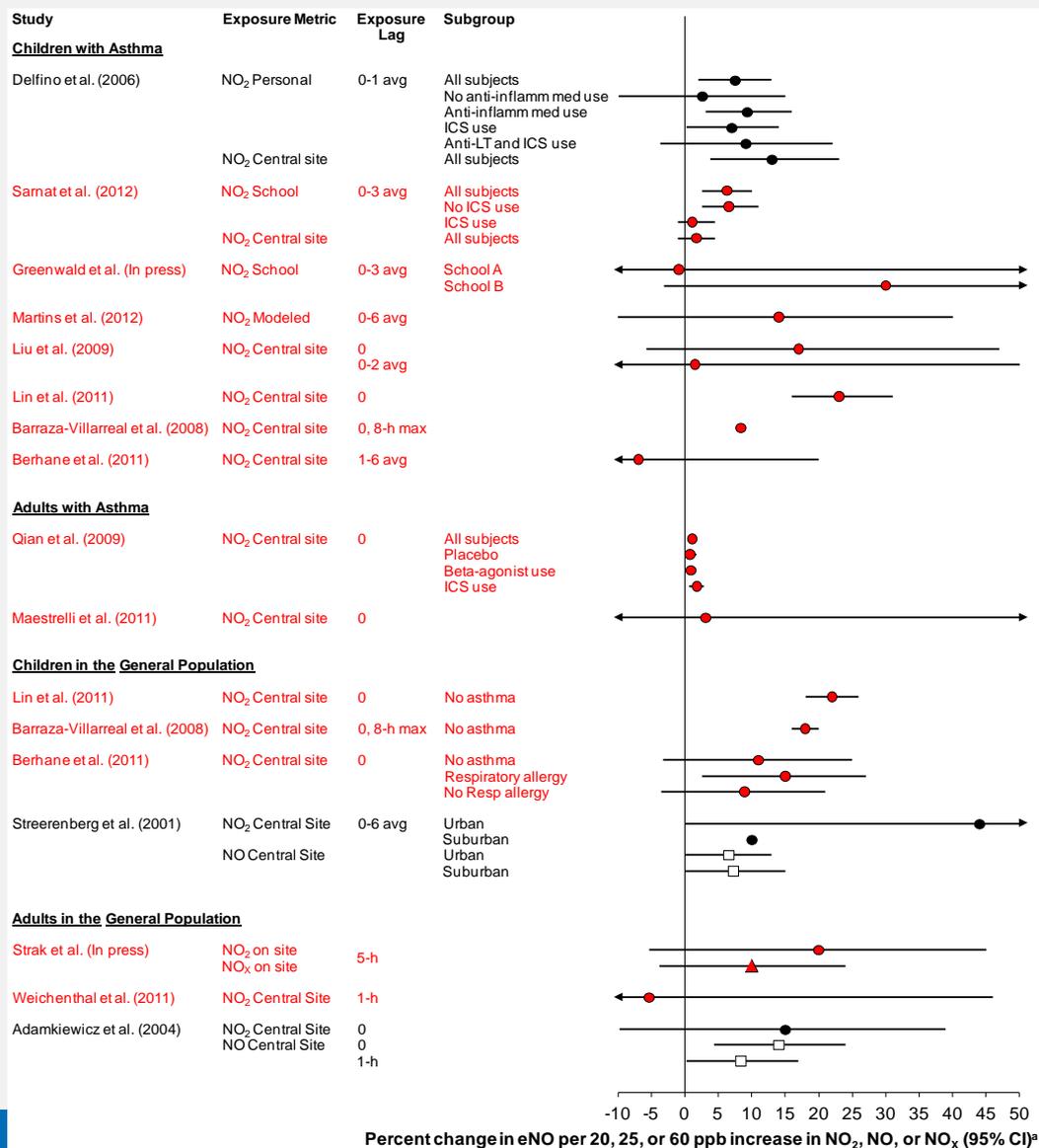
Extension of analyses by Folinsbee (1992), 2008 ISA, and 1993 Air Quality Criteria Document.

- This material presently is unpublished, and we ask the Panel to [provide the peer review for the analysis](#), in particular, to comment on the appropriateness of the methodology utilized for the meta-analysis, the conclusions reached based on this analysis, and its use in the draft ISA.
- With regard to [factors potentially affecting airways responsiveness, please comment on the adequacy of this discussion](#). Are there other modifying factors that should be considered?

Charge – Chapters 4 and 5 (cont'd)

- The 2008 ISA for Oxides of Nitrogen stated that one of the largest uncertainties was the potential for health effects observed in association with NO₂ exposure to be confounded by correlated copollutants.
 - To what extent has evidence that informs independent effects of NO₂ been adequately discussed in Chapters 4 and 5 and appropriately interpreted as reducing uncertainty (for example, evaluation of copollutant model results)? Has the current draft ISA appropriately considered recent epidemiologic findings regarding potential copollutant confounding in causal determinations?
 - Please provide comments specifically for respiratory effects, cardiovascular effects, and total mortality of short-term NO₂ exposure.
- What are the views of the panel regarding the clarity and effectiveness of figures and tables in conveying information about the consistency of evidence for a given health endpoint? In particular, was the use of the tables and figures in both the text and online in the HERO database effective in providing additional information on the studies evaluated? Are there tables and figures in the ISA that would be more appropriate to include as a resource in the HERO database?

Summary Figure of Associations between Oxides of Nitrogen and Exhaled Nitric Oxide



- Effect estimates standardized to a 20 ppb increase in 24-h average NO₂ or NO, 30 ppb increase in 1-h max NO₂ or NO, 40 ppb increase in 24-h avg NO_x, and 60 ppb increase in 1-h max NO_x
- Increments for NO₂ based on differences between U.S. nationwide 95th percentile and median
- Increments for NO and NO_x based on NO₂ distribution and the ratios of annual average NO or NO_x (only data available) to annual average NO₂

Legend

Black = studies from 2008 ISA
 Red = recent studies
 Circles = NO₂
 Squares = NO
 Triangles = NO_x

Charge – Chapters 4 and 5 (cont'd)

- To what extent is the **causal framework transparently applied** to evidence for each of the health effect categories evaluated to form causal determinations?
- How **consistently was the causal framework applied** across the health effect categories?
- Do the **text and tables in the summaries and causal determinations clearly communicate how the evidence was considered** to form causal determinations?

Weight of Evidence Tables accompanying Causal Determinations

Table 4-23 Summary of evidence supporting a causal relationship between short-term NO₂ exposure and respiratory effects.

Rationale for Causal Determination ^a	Key Evidence ^b	Key References ^b	NO ₂ Concentrations Associated with Effects ^c
Asthma morbidity			
Consistent associations from multiple, high quality epidemiologic studies at relevant concentrations	Increases in asthma hospital admissions, ED visits in diverse populations in association with 24-h avg and 1-h max NO ₂ , lags 0 and 3 to 5-day avg in additional recent studies of all ages and children.	Strickland et al. (2010) , Villeneuve et al. (2007) , Ko et al. (2007b) , Son et al. (2013) , Ito et al. (2007) , Li et al. (2011b) Section 4.2.7.3, Figure 4-4	Overall study mean 24-h avg: 15.7-28.5 ppb Overall study mean 1-h max: 22.0-44.4 ppb
	No association in recent Canadian multicity study of all ages	Stieb et al. (2009)	Mean 24-h avg: 22.7 ppb
	Coherence with increases in respiratory symptoms in children with asthma in diverse populations in association with 24-h avg, 2-4 avg NO ₂ , 1-h max, lags 0, 3 to 6-day avg in previous and recent studies	U.S. multicity studies: Mortimer et al. (2002) , Schildcrout et al. (2006) , Gent et al. (2003) , Mann et al. (2010) , Section 4.2.6.1, Figure 4-3	Overall study mean 24-h avg: 14.2-28.6 ppb Overall study mean 1-h max: 37.4-66 ppb

Weight of Evidence Tables accompanying Causal Determinations (cont'd)

Rationale for Causal Determination ^a	Key Evidence ^b	Key References ^b	NO ₂ Concentrations Associated with Effects ^c
<p>Chance, confounding, and other biases can be ruled out with reasonable confidence in part, by evidence from controlled human exposure studies</p>	<p>NO₂-induced increases in AHR in adults with asthma exposed at rest following nonspecific or allergen challenge in several individual previous studies and meta-analyses.</p>	<p>Folinsbee (1992) Section 4.2.2, Table 4-3, Table 4-4, Table 4-5</p>	<p>100 ppb for 1 h 200-300 ppb for 30 min</p>
<p>Some evidence describes key events to inform mode of action</p>	<p>Increases in eosinophil activation, IgE, Th2 cytokines in adults and rats and guinea pigs</p>	<p>Barck et al. (2005a); Barck et al. (2002), Gilmour et al. (1996), Ohashi et al. (1994) Table 4-11, Table 4-11, Table 4-12, Sections 3.3.2.6, and 4.2.4.3</p>	<p>Humans: 260 ppb 15-30 min Rats/guinea pigs: 3,000 ppb for 2 weeks, 5,000 ppb for 3 h</p>
<p>Initiation of inflammation</p>	<p>No consistent effect on pulmonary clearance</p>	<p>Section 4.2.5.2</p>	<p>1,500-3,500 ppb for 2-6 h</p>
<p>Initiation of inflammation</p>	<p>Increases in PMNs and prostaglandins in healthy adults</p>	<p>Section 4.2.4.1</p>	<p>5,000 ppb for 3 h</p>

Causal Determinations from the 2008 and First Draft ISA for Oxides of Nitrogen

Health Effect Category	2008 ISA	First Draft ISA
Short-term NO₂ Exposure		
Respiratory Effects	Likely to be a Causal Relationship	Causal Relationship
Cardiovascular Effects	Inadequate to Infer a Causal Relationship	Likely to be a Causal Relationship
Total Mortality	Suggestive of a Causal Relationship	Likely to be a Causal Relationship
Long-term NO₂ Exposure		
Respiratory Effects	Suggestive of a Causal Relationship	Likely to be a Causal Relationship
Cardiovascular Effects	Inadequate to Infer a Causal Relationship	Suggestive of a Causal Relationship
Reproductive and Developmental Effects	Inadequate to Infer a Causal Relationship	Fertility, Reproduction, and Pregnancy Suggestive of a Causal Relationship Adverse Birth Outcomes Suggestive of a Causal Relationship Postnatal Development Suggestive of a Causal Relationship
Total Mortality	Inadequate to Infer a Causal Relationship	Suggestive of a Causal Relationship
Cancer	Inadequate to Infer a Causal Relationship	Suggestive of a Causal Relationship

Progression of Assessment of At-risk Lifestages and Populations across ISAs



Terminology
and definitions

Susceptible
Innate or acquired
factors

Vulnerable
Extrinsic factors or
elevated exposure

Susceptible
Populations with greater
likelihood of health
effects related to air
pollutant exposure

At-risk

Groups with characteristics that increase the risk of
air pollutant-related health effect
Risk could be due to:

- intrinsic factors
- extrinsic factors
- increased dose
- increased exposure

Explicit
methods for
assessment

No

Yes

Yes

Yes

Epidemiologic or controlled human exposure analyses stratified on a factor
Experimental studies of a specific health condition or disease model

Framework for
conclusions

No

No

No

Yes

ISA where
used

Oxides of Nitrogen
Final, Jul 2008

Carbon Monoxide
2nd draft, Sep 2009

Ozone
2nd draft, Sep 2011

Ozone
Final, Feb 2013

Oxides of Sulfur
Final, Sep 2008

Particulate Matter,
Final, Dec 2009

Lead
2nd draft, Feb 2012

Lead
Final, Jun 2013

Framework for Classifying Evidence for Factors that may Characterize At-risk Lifestages and Populations

Classification	Weight of Evidence for Health Effects
----------------	---------------------------------------

Adequate evidence	There is substantial, consistent evidence within a discipline to conclude that a factor results in a population or lifestage being at increased or decreased risk of air pollutant-related health effect(s) relative to some reference population or lifestage. Where applicable this includes coherence across disciplines. Evidence includes multiple high-quality studies.
Suggestive evidence	The collective evidence suggests that a factor results in a population or lifestage being at increased or decreased risk of an air pollutant-related health effect relative to some reference population or lifestage, but the evidence is limited due to some inconsistency within a discipline or, where applicable, a lack of coherence across disciplines.
Inadequate evidence	The collective evidence is inadequate to determine if a factor results in a population or lifestage being at increased or decreased risk of an air pollutant-related health effect relative to some reference population or lifestage. The available studies are of insufficient quantity, quality, consistency, and/or statistical power to permit a conclusion to be drawn.
Evidence of no effect	There is substantial, consistent evidence within a discipline to conclude that a factor does not result in a population or lifestage being at increased or decreased risk of air pollutant-related health effect(s) relative to some reference population or lifestage. Where applicable this includes coherence across disciplines. Evidence includes multiple high-quality studies.

Consistency within discipline
Coherence across disciplines

Limited evidence
Inconsistency within discipline
Lack of coherence across disciplines

Insufficient quantity, quality, consistency, statistical power

Studies consistent in showing no effect within discipline and across disciplines

Modified from Table III of the Preamble to the ISA

Conclusions regarding Factors that may Characterize At-risk Lifestages and Populations

Evidence Classification	Potential At-risk Factor
Adequate evidence	Lifestage: Children Older Adults
Suggestive evidence	Genetic background Asthma Chronic Obstructive Pulmonary Disease Socioeconomic status Sex Diet
Inadequate evidence	Cardiovascular disease Diabetes Race/Ethnicity Obesity Smoking Residential Location (urban/nonurban)
Evidence of no effect	-

Time windows of exposure:
NO₂ exposure during prenatal period or infancy

Chapter 1: potential inter-relationships among factors that may better inform public health impact

Examples:

- Older adults with pre-existing disease
- Children of low SES and pre-existing disease

Charge – Chapter 6

Factors that may modify exposure to NO₂, physiological responses to NO₂ exposure, or risk of health effects associated with NO₂ exposure. Consistent with the final ISAs for ozone and lead, conclusions inform at-risk lifestages and populations.

- How effective are the categories of at-risk factors in providing information on potential at-risk lifestages and populations? Is there [information available on other key at-risk factors that is not included](#) in the first draft ISA and should be added?
- To what extent do the discussions in this chapter [accurately reflect the body of available evidence](#) from epidemiologic, controlled human exposure, and toxicological studies, including the extent to which evidence indicates that the effects of NO₂ exposure are independent of other traffic-related copollutants?
- Please comment on the [consistency and transparency with which the framework for drawing conclusions about at-risk factors](#) has been applied in this ISA.
- To what extent is available scientific evidence on [factors that modify exposure to NO₂ discussed in the chapter and adequately considered in conclusions](#) for at-risk lifestages or populations?

Charge – Chapter 1

Key information about process for ISA development, integrative summary of the ISA, characterization of available scientific information on policy-relevant issues

- Please comment on the usefulness and effectiveness of the summary presentation. Please provide [recommendations on approaches that may improve the communication of key ISA findings to varied audiences and the synthesis of available information across subject areas.](#)
- What are the Panel's thoughts on the [application of the Health and Environmental Research Online \(HERO\) system](#) to support a more transparent assessment process?
- To what extent does Chapter 1 [communicate the key scientific information](#) on sources, atmospheric chemistry, ambient concentrations, exposure, and health effects of oxides of nitrogen as well as at-risk lifestages and populations? What information should be added or is more appropriate to leave for discussion in the subsequent detailed chapters?

Charge – Chapter 1 (cont'd)

- What are the Panel's thoughts on the rationale presented for forming causal determinations for NO₂ exposure only and considering epidemiologic results for associations between NO_x and health effects in causal determinations for NO₂ (Sections 1.4.1 and 1.4.3)?
- Based on individual Panel member recommendations on the *Draft Plan for the Development of the Integrated Science Assessment for Nitrogen Oxides – Health Criteria* (May 2013), Chapter 1 presents an integrated evaluation of various epidemiologic lines of evidence that inform the independent effects of NO₂ exposure (Section 1.5).
 - Please comment on the extent to which this discussion is informative in describing how the evidence of independent effects of NO₂ is evaluated in this ISA. Does the discussion accurately reflect the available evidence? If this discussion is informative, what information could be added or removed to improve the discussion?
 - Should the discussion remain in Chapter 1 or should it be moved to another part of the ISA?
- Please comment on the extent to which the discussion of various policy-relevant considerations is clearly described and integrates relevant information (Section 1.6). Please identify any other relevant information that would be useful to include.

Charge – Executive Summary

Concise synopsis of the key findings and conclusions of the ISA for a broad range of audiences

- **Please comment on the clarity with which the Executive Summary communicates the key information from the ISA.**
- **Please provide recommendations on information that should be added or information that should be left for discussion in the subsequent chapters of the ISA.**

HERO

Health and Environmental Research Online

- Facilitates complete, sustainable and effective assessment development

HERO internal page: www.epa.gov/heronet

- Provides transparency to stakeholders and the public

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The HERO Database

The Health and Environmental Research Online (HERO) database provides an easy way to view the scientific literature behind EPA science assessments.

The database includes more than 300,000 scientific articles from the peer-reviewed literature used by EPA to develop its Integrated Science Assessments (ISA) that feed into the NAAQS review. It also includes references and data from the Integrated Risk Information System (IRIS), a database that supports critical agency policymaking for chemical regulation. Risk assessments characterize the nature and magnitude of health risks to humans and the ecosystem from pollutants and chemicals in the environment.

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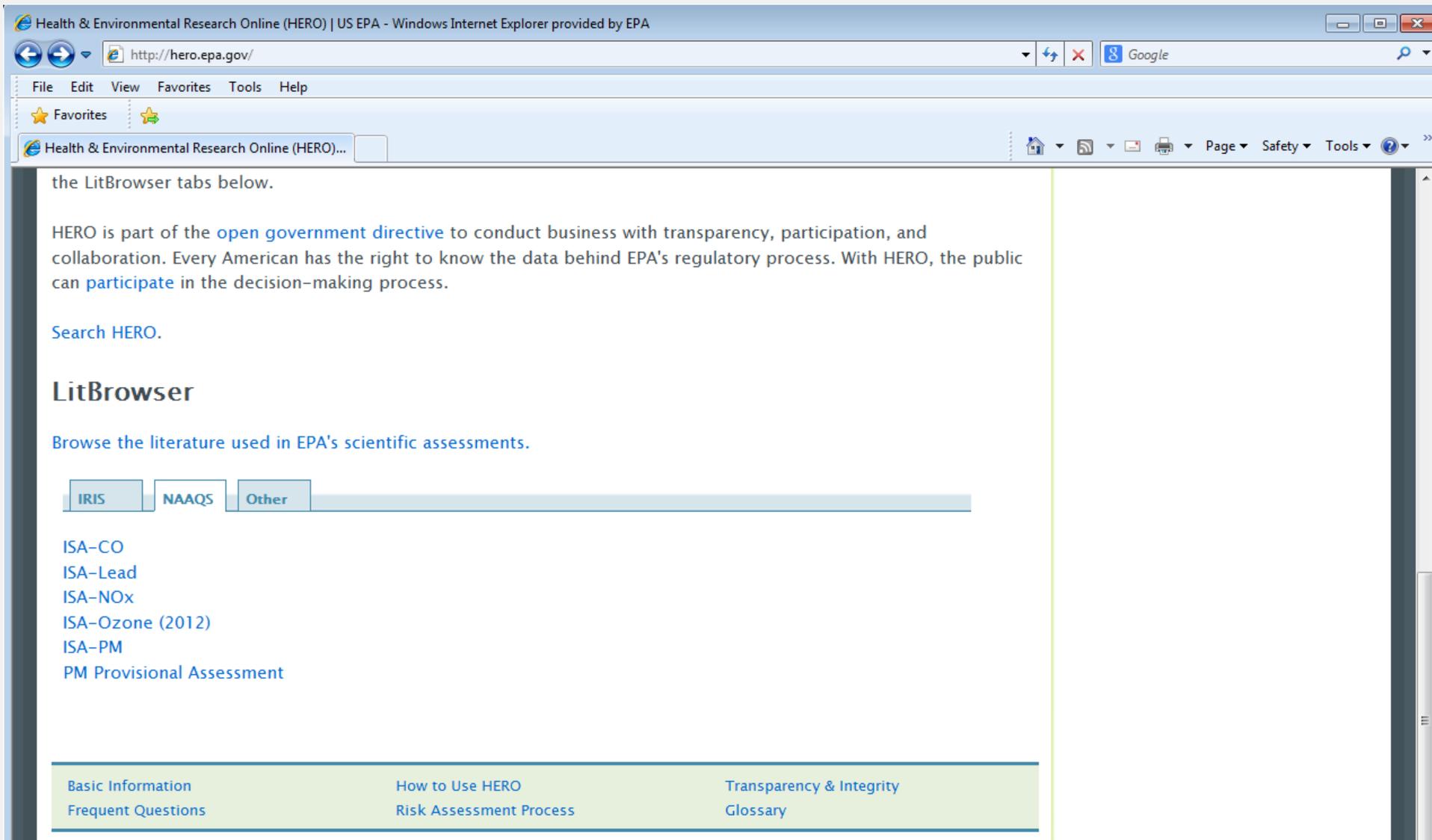
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- ISA-Lead
- ISA-NOx
- ISA-Ozone (2012)
- ISA-PM
- PM Provisional Assessment

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What is HERO?

The Health and Environmental Research Online is a database of scientific studies and other references used to develop EPA's risk assessments aimed at understanding the health and environmental effects of pollutants and chemicals. It is developed and managed in EPA's Office of Research and Development (ORD) by the [National Center for Environmental Assessment \(NCEA\)](#).

What data does HERO provide?

For each reference, HERO contains:

- Reference type
- Citation elements: authors, title, year of publication, source. Depending on the type of reference, the citation will also include volume, page numbers, URL, etc.
- Abstract or brief description
- Topic areas that describe the reference (e.g., carbon monoxide, asthma)
- Assessment(s) in which the reference was used, if relevant. Note that HERO contains references *considered for use* in assessment development, not just those references actually used.
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HERO ID

679693

Reference Type

Journal Article

Title

Respiratory effects of commuters' exposure to air pollution in traffic

Author(s)

Zuurbier, M; Hoek, G; Oldenwening, M; Meliefste, K; van den Hazel, P; Brunekreef, B

Year

2011

Journal

Epidemiology

ISSN: 1044-3983

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Issue

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Page Numbers

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21228698

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[10.1097/EDE.0b013e3182093693](https://doi.org/10.1097/EDE.0b013e3182093693)

Web of Science Id

WOS:000286970700013

Abstract

BACKGROUND: : Much time is spent in traffic, especially during rush hours, when air pollution concentrations on roads are relatively high. Controlled exposure studies have shown acute respiratory effects of short, high exposures to air pollution from motor vehicles. Acute health effects of lower real-life exposures in traffic are unclear. METHODS: : Exposures of 34 healthy, nonsmoking adult volunteers were repeatedly measured while commuting for 2 hours by bus, car, or bicycle. Particle number (PN), particulate matter (PM2.5 and PM10), and soot exposures were measured. Lung function and airway resistance were measured directly before, directly following, and 6 hours after exposure. Exhaled nitric oxide (NO) was measured directly before and 6 hours after exposure. Inhaled doses were estimated

Public Landing Page for ISA for Oxides of Nitrogen – Health Criteria

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ISA-NOx

November 2013: EPA released the *ISA for Oxides of Nitrogen - Health Criteria (first external review draft)*. Evidence from recent studies of the health effects, atmospheric science (source, concentration, and fate and transport), exposure, dosimetry and modes of action of oxides of nitrogen was reviewed, evaluated, and integrated with the evidence that was included in the previous ISA for Oxides of Nitrogen and Air Quality Criteria Documents. Literature searches were conducted to identify studies published since the 2008 ISA.

This page provides access to references cited in the first external review draft ISA, as well as those considered for inclusion.

All References for ISA-NOx (sorted by author)

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1.



Workshop on assessment of health science for the review of the NAAQS for nitrogen (NOx) and sulfur oxides (SOx)

(2007)

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Lower detectable limit--(1) technical definition

U.S. EPA (2006)

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Remaining Meeting Agenda

Wednesday March 12	
2:15 p.m.	EPA Presentation on Draft Integrated Science Assessment
3:00 p.m.	Public Comments
3:30 p.m.	Break
3:45 p.m.	Discussion of Charge Questions – Chapter 2 Atmospheric Chemistry and Exposure – Chapter 3 Dosimetry and Modes of Action
5:30 p.m.	Recess
Thursday March 13	
8:00 a.m.	Convene Meeting
8:05 a.m.	Discussion of Charge Questions – Chapter 4 Health Effects of Short-term Exposure – Chapter 5 Health Effects of Long-term Exposure
10:00 a.m.	Break
10:15 a.m.	Discussion of Charge Questions – Chapter 4 Health Effects of Short-term Exposure – Chapter 5 Health Effects of Long-term Exposure – Chapter 6 Populations Potentially at Increased Risk
12:00 p.m.	Lunch
1:15 p.m.	Discussion of Charge Questions – Chapter 6 Populations Potentially at Increased Risk – Executive Summary – Chapter 1 Integrative Synthesis of ISA
3:00 p.m.	Clarifying Public Comments
3:15 p.m.	Summary and Action Items
3:30 p.m.	Adjourn