



# **Integrated Review Plan for the Primary National Ambient Air Quality Standards for Nitrogen Dioxide**

**External Review Draft**

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# **Integrated Review Plan for the Primary National Ambient Air Quality Standards for Nitrogen Dioxide**

## **External Review Draft**

### **U. S. Environmental Protection Agency**

National Center for Environmental Assessment  
Office of Research and Development  
and  
Office of Air Quality Planning and Standards  
Office of Air and Radiation

Research Triangle Park, North Carolina

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## **DISCLAIMER**

This draft integrated review plan serves as a public information document and as a management tool for the U. S. Environmental Protection Agency's National Center for Environmental Assessment and Office of Air Quality Planning and Standards in conducting the review of the national ambient air quality standards for nitrogen dioxide. The approach described in this draft plan may be modified for presentation in the final plan to reflect review by the Clean Air Scientific Advisory Committee and public comments. Subsequent modifications to the plan may result from information developed during this review, and in consideration of advice and comments received from the Clean Air Scientific Advisory Committee and the public during the course of the review. Mention of trade names or commercial products does not constitute endorsement or recommendation for use.

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## LIST OF ACRONYMS/ABBREVIATIONS

AADT	Annual Average Daily Traffic
AMMS	Air Monitoring and Methods Subcommittee
ANPR	Advanced notice of proposed rulemaking
APEX	Air Pollutants Exposure model
AQCD	Air Quality Criteria Document
AQI	Air Quality Index
AQS	EPA's Air Quality System
CAA	Clean Air Act
CASAC	Clean Air Scientific Advisory Committee
CBSA	Core Based Statistical Area
CFR	Code of Federal Regulations
CO	Carbon monoxide
COPD	Chronic obstructive pulmonary disease
C-R	Concentration-response
CV	Cardiovascular
CVD	Cardiovascular disease
ED	Emergency department
EPA	Environmental Protection Agency
FEM	Federal Equivalent Method
FEV <sub>1</sub>	Forced expiratory volume in one second, volume of air exhaled in first second of exhalation
FR	Federal Register
FRM	Federal Reference Method
GAM	Generalized Additive Models
HA	Hospital admissions
HERO	Health and Environmental Research Online
HONO	Nitrous acid
HRV	Heart rate variability
HNO <sub>3</sub>	Nitric acid
IRP	Integrated Review Plan
ISA	Integrated Science Assessment
IUGR	Intrauterine growth restriction, intrauterine growth retardation
Km	Kilometer
LC	Local conditions
LML	Lowest measured level
m	Meters
MSA	Metropolitan Statistical Area
NAAQS	National Ambient Air Quality Standards
NCEA	National Center for Environmental Assessment
NCore	National Core Monitoring Network
NO	Nitric oxide
NO <sub>2</sub>	Nitrogen dioxide
NO <sub>3</sub> <sup>-</sup>	Nitrate
NO <sub>x</sub>	NO+NO <sub>2</sub>
NO <sub>y</sub>	Total oxides of nitrogen (NO <sub>x</sub> + NO <sub>z</sub> )

NO <sub>z</sub>	Reactive oxides of nitrogen (e.g., HNO <sub>3</sub> , HONO, PAN, particulate nitrates)
O <sub>3</sub>	Ozone
OAQPS	Office of Air Quality Planning and Standards
OAR	Office of Air and Radiation
OMB	Office of Management and Budget
ORD	Office of Research and Development
PA	Policy Assessment
PAN	Peroxyacetyl nitrate
PM	Particulate matter
ppb	Parts per billion
ppm	Parts per million
PRB	Policy-relevant background
QA	Quality assurance
QMP	Quality Management Plan
REA	Risk and Exposure Assessment
RIA	Regulatory Impact Analysis
RTP	Research Triangle Park
SES	Socioeconomic status
SLAMS	State and local air monitoring stations
SO <sub>2</sub>	Sulfur dioxide
TBD	To be determined



# 1 INTRODUCTION

The U.S. Environmental Protection Agency (EPA) is conducting a review of the primary (health-based) national ambient air quality standards (NAAQS) for nitrogen dioxide (NO<sub>2</sub>). This draft Integrated Review Plan (IRP) presents the planned approach for the review. This review will provide an integrative assessment of relevant scientific information for oxides of nitrogen and will focus on the basic elements that define the NAAQS: the indicator,<sup>1</sup> averaging time,<sup>2</sup> form,<sup>3</sup> and level.<sup>4</sup> The EPA Administrator will consider these elements collectively in evaluating the protection to public health afforded by the primary standards.

This document is organized into eight chapters. Chapter 1 summarizes the legislative requirements for the review of the NAAQS (section 1.1), summarizes the review process (section 1.2), provides an overview of past reviews of the primary NO<sub>2</sub> NAAQS (section 1.3), and outlines the scope of the current review (section 1.4). Chapter 2 presents the status and schedule for the current review. Chapter 3 provides background on the key issues and uncertainties that informed the final decisions in the last review and presents a set of policy-relevant questions that will serve to focus this review on the critical scientific and policy issues. Chapters 4 through 7 discuss the planned scope and organization of key assessment documents, the planned approaches for preparing the documents, plans for scientific and public review of the documents, and specific ambient air quality monitoring considerations. Complete reference citations are provided in chapter 8.

## 1.1 LEGISLATIVE REQUIREMENTS

Two sections of the Clean Air Act (CAA) govern the establishment, review, and revision of the NAAQS. Section 108 (42 U.S.C. 7408) directs the Administrator to identify and list certain air pollutants and then to issue air quality criteria for those pollutants. The Administrator is to list those air pollutants that in her “judgment, cause or contribute to air pollution which may reasonably be anticipated to endanger public health or welfare;” “the presence of which in the ambient air results from numerous or diverse mobile or stationary sources;” and “for which . . . [the Administrator] plans to issue air quality criteria...” Air quality criteria are intended to

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<sup>1</sup> The “indicator” of a standard defines the chemical species or mixture that is measured in determining whether an area attains the standard. Nitrogen dioxide (NO<sub>2</sub>) is the indicator for the oxides of nitrogen.

<sup>2</sup> The “averaging time” defines the time period over which ambient measurements are averaged (e.g., 1-hour, 8-hour, 24-hour, annual).

<sup>3</sup> The “form” of a standard defines the air quality statistic that is compared to the level of the standard in determining whether an area attains the standard. For example, the form of the current 1-hour NO<sub>2</sub> standard is the three-year average of the 98<sup>th</sup> percentile of the annual distribution of 1-hour daily maximum NO<sub>2</sub> concentrations.

<sup>4</sup> The “level” defines the allowable concentration of the criteria pollutant in the ambient air.

1 “accurately reflect the latest scientific knowledge useful in indicating the kind and extent of all  
2 identifiable effects on public health or welfare which may be expected from the presence of [a]  
3 pollutant in the ambient air . . .” 42 U.S.C. 7408(b). Section 109 (42 U.S.C. 7409) directs the  
4 Administrator to propose and promulgate “primary” and “secondary” NAAQS for pollutants for  
5 which air quality criteria are issued.<sup>5</sup> Section 109(b)(1) defines a primary standard as one “the  
6 attainment and maintenance of which in the judgment of the Administrator, based on such  
7 criteria and allowing an adequate margin of safety, are requisite to protect the public health.”<sup>6</sup> A  
8 secondary standard, as defined in section 109(b)(2), must “specify a level of air quality the  
9 attainment and maintenance of which, in the judgment of the Administrator, based on such  
10 criteria, is requisite to protect the public welfare from any known or anticipated adverse effects  
11 associated with the presence of [the] pollutant in the ambient air.”<sup>7</sup>

12 The requirement that primary standards provide an adequate margin of safety was  
13 intended to address uncertainties associated with inconclusive scientific and technical  
14 information available at the time of standard setting. It was also intended to provide a reasonable  
15 degree of protection against hazards that research has not yet identified. See *Lead Industries*  
16 *Association v. EPA*, 647 F.2d 1130, 1154 (D.C. Cir 1980); *American Petroleum Institute v.*  
17 *Costle*, 665 F.2d 1176, 1186 (D.C. Cir. 1981); *American Farm Bureau Federation v. EPA*, 559  
18 F. 3d 512, 533 (D.C. Cir. 2009); *Association of Battery Recyclers v. EPA*, 604 F. 3d 613, 617-18  
19 (D.C. Cir. 2010). Both kinds of uncertainties are components of the risk associated with pollution  
20 at levels below those at which human health effects can be said to occur with reasonable  
21 scientific certainty. Thus, in selecting primary standards that provide an adequate margin of  
22 safety, the Administrator is seeking not only to prevent pollution levels that have been  
23 demonstrated to be harmful but also to prevent lower pollutant levels that may pose an  
24 unacceptable risk of harm, even if the risk is not precisely identified as to nature or degree. The  
25 CAA does not require the Administrator to establish a primary NAAQS at a zero-risk level or at  
26 background concentration levels, see *Lead Industries v. EPA*, 647 F.2d at 1156 n.51, *Mississippi*  
27 *v. EPA*, 723 F. 3d 246, 255, 262-63 (D.C. Cir. 2013), but rather at a level that reduces risk  
28 sufficiently so as to protect public health with an adequate margin of safety.

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<sup>5</sup> As discussed in section 1.4 below, this document describes the review of the *primary* NO<sub>2</sub> standards. The *secondary* NO<sub>2</sub> standard will be separately reviewed in conjunction with review of the secondary SO<sub>2</sub> standard.

<sup>6</sup>The legislative history of section 109 indicates that a primary standard is to be set at “the maximum permissible ambient air level . . . which will protect the health of any [sensitive] group of the population,” and that for this purpose “reference should be made to a representative sample of persons comprising the sensitive group rather than to a single person in such a group.” S. Rep. No. 91-1196, 91st Cong., 2d Sess. 10 (1970).

<sup>7</sup> Welfare effects as defined in section 302(h) (42 U.S.C. 7602(h)) include, but are not limited to, “effects on soils, water, crops, vegetation, man-made materials, animals, wildlife, weather, visibility and climate, damage to and deterioration of property, and hazards to transportation, as well as effects on economic values and on personal comfort and well-being.”

1 In addressing the requirement for an adequate margin of safety, the EPA considers such  
2 factors as the nature and severity of the health effects involved, the size of the sensitive group(s),  
3 and the kind and degree of uncertainties. The selection of any particular approach to providing an  
4 adequate margin of safety is a policy choice left specifically to the Administrator's judgment.  
5 See *Lead Industries Association v. EPA*, 647 F.2d at 1161-62; *Mississippi v. EPA*, 723 F. 3d at  
6 265.

7 In setting standards that are "requisite" to protect public health and welfare, as provided  
8 in section 109(b), the EPA's task is to establish standards that are neither more nor less stringent  
9 than necessary for these purposes. In so doing, the EPA may not consider the costs of  
10 implementing the standards. See generally, *Whitman v. American Trucking Associations*, 531  
11 U.S. 457, 465-472, 475-76 (2001). Likewise, "[a]ttainability and technological feasibility are not  
12 relevant considerations in the promulgation of national ambient air quality standards." *American*  
13 *Petroleum Institute v. Costle*, 665 F. 2d at 1185.

14 Section 109(d)(1) requires that "not later than December 31, 1980, and at 5-year intervals  
15 thereafter, the Administrator shall complete a thorough review of the criteria published under  
16 section 108 and the national ambient air quality standards . . . and shall make such revisions in  
17 such criteria and standards and promulgate such new standards as may be appropriate . . ."  
18 Section 109(d)(2) requires that an independent scientific review committee "shall complete a  
19 review of the criteria . . . and the national primary and secondary ambient air quality standards. . .  
20 and shall recommend to the Administrator any new . . . standards and revisions of existing  
21 criteria and standards as may be appropriate . . . ." Since the early 1980s, this independent  
22 review function has been performed by the Clean Air Scientific Advisory Committee (CASAC).<sup>8</sup>

## 23 **1.2 OVERVIEW OF THE NAAQS REVIEW PROCESS**

24 The current process for reviewing the NAAQS includes four major phases: (1) planning,  
25 (2) science assessment, (3) risk/exposure assessment, and (4) policy assessment and rulemaking.  
26 Figure 1-1 provides an overview of this process, and each phase is described in more detail  
27 below.<sup>9</sup>

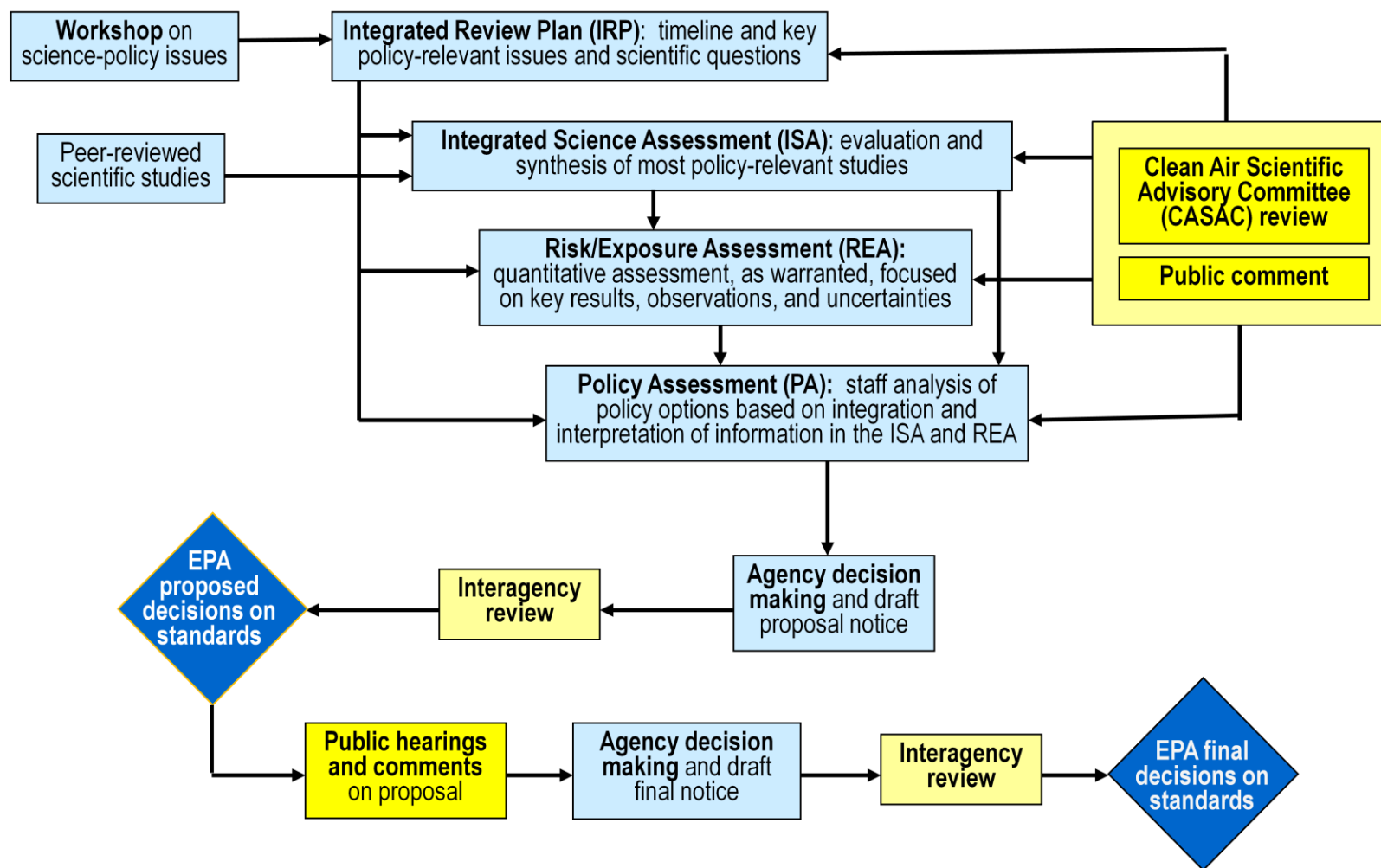
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<sup>8</sup>Lists of CASAC members and of members of the CASAC Oxides of Nitrogen Primary NAAQS Review Panel are available at:

<http://yosemite.epa.gov/sab/sabproduct.nsf/WebCASAC/CommitteesandMembership?OpenDocument>.

<sup>9</sup>The EPA maintains a website on which key documents developed for NAAQS reviews are made available (<http://www.epa.gov/ttn/naaqs/>). The EPA's NAAQS review process has evolved over time (Jackson, 2009).

Information on the current process is available at: <http://www.epa.gov/ttn/naaqs/review.html>. As discussed in section 1.3 below, this process was generally followed in the primary NO<sub>2</sub> NAAQS review completed in 2010 with the exception that there was not a separate Policy Assessment document issued. Rather, the Risk and Exposure Assessment (U.S. EPA, 2008b) included a policy assessment chapter (i.e., Chapter 10).



**Figure 1-1. Overview of the NAAQS review process.**

1 The planning phase of the NAAQS review process begins with a science policy  
2 workshop, which is intended to identify issues and questions to frame the review. Drawing from  
3 the workshop discussions, a draft IRP is prepared jointly by EPA's National Center for  
4 Environmental Assessment (NCEA), within the Office of Research and Development (ORD),  
5 and EPA's Office of Air Quality Planning and Standards (OAQPS), within the Office of Air and  
6 Radiation (OAR).<sup>10</sup> The draft IRP is made available for CASAC review and for public comment.  
7 The final IRP is prepared in consideration of CASAC and public comments. This document  
8 presents the current plan and specifies the schedule for the entire review, the process for  
9 conducting the review, and the key policy-relevant science issues that will guide the review.

10 The second phase of the review, science assessment, involves the preparation of an  
11 Integrated Science Assessment (ISA) and supplementary materials. The ISA, prepared by  
12 NCEA, provides a concise review, synthesis, and evaluation of the most policy-relevant science,  
13 including key science judgments that are important to the design and scope of exposure and risk  
14 assessments, as well as other aspects of the NAAQS review. The ISA (and any supplementary  
15 materials that may be developed) provides a comprehensive assessment of the current scientific  
16 literature pertaining to known and anticipated effects on public health and welfare associated  
17 with the presence of the pollutant in the ambient air, emphasizing information that has become  
18 available since the last air quality criteria review in order to reflect the current state of  
19 knowledge. As such, the ISA forms the scientific foundation for each NAAQS review and is  
20 intended to provide information useful in forming judgments about air quality indicator(s),  
21 form(s), averaging time(s) and level(s) for the NAAQS. The current review process generally  
22 includes production of a first and second draft ISA, both of which undergo CASAC and public  
23 review prior to completion of the final ISA. Chapter 4 below provides a more detailed  
24 description of the planned scope, organization, and assessment approach for the ISA and any  
25 supporting materials that may be developed.

26 In the third phase, the risk/exposure assessment phase, OAQPS staff considers  
27 information and conclusions presented in the ISA, with regard to support provided for the  
28 development of quantitative assessments of the risks and/or exposures for health and/or welfare  
29 effects. As an initial step, staff prepares a planning document (REA Planning Document) that  
30 considers the extent to which newly available scientific evidence and tools/methodologies  
31 warrant the conduct of quantitative risk and exposure assessments. As discussed in Chapter 5

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<sup>10</sup>In this review of the primary NAAQS for NO<sub>2</sub>, a draft plan for development of the ISA was prepared by NCEA prior to development of this draft IRP. The draft plan for development of the ISA was made available for public comment and was the subject of a consultation with CASAC (78 FR 26026; 78 FR 27234). Comments received during that consultation have been considered in preparation of chapter 4 in this draft IRP. Further comments received on this draft IRP will be considered in developing a final IRP and a second draft ISA.

1 below, the REA Planning Document focuses on the degree to which important uncertainties in  
2 the last review may be addressed by new information available in this review. Specifically, the  
3 document considers the extent to which newly available data, methods, and tools might be  
4 expected to appreciably affect the assessment results, or address important gaps in our  
5 understanding of the exposures and risks associated with NO<sub>2</sub>. To the extent warranted, this  
6 document outlines a general plan, including scope and methods, for conducting assessments. The  
7 REA Planning Document is generally prepared in conjunction with the first draft ISA<sup>11</sup> and is  
8 presented for consultation with CASAC and for public comment. When an assessment is  
9 performed, one or more drafts of each risk and exposure assessment document (REA) undergoes  
10 CASAC and public review. The REA provides concise presentations of methods, key results,  
11 observations, and related uncertainties. Chapter 5 below discusses consideration of potential  
12 quantitative human health-related assessments for this review.

13 The review process ends with the policy assessment and rulemaking phase. The Policy  
14 Assessment (PA) is prepared prior to issuance of proposed and final rules. The PA provides a  
15 transparent presentation of OAQPS staff analyses and conclusions regarding the adequacy of the  
16 current standards and, if revision is considered, what revisions may be appropriate. The PA  
17 integrates and interprets the information from the ISA and REA to frame policy options for  
18 consideration by the Administrator. Such an evaluation of policy implications is intended to help  
19 “bridge the gap” between the Agency’s scientific assessments, presented in the ISA and  
20 REA(s), and the judgments required of the EPA Administrator in determining whether it is  
21 appropriate to retain or revise the NAAQS. In so doing, the PA is also intended to facilitate  
22 CASAC’s advice to the Agency and recommendations to the Administrator on the adequacy of  
23 the existing standards and, as pertinent, on revisions that may be appropriate to consider, as  
24 provided for in the CAA. In evaluating the adequacy of the current standards and, as appropriate,  
25 a range of potential alternative standards, the PA considers the available scientific evidence and,  
26 as available, quantitative risk and exposure analyses together with related limitations and  
27 uncertainties. The PA focuses on the information that is most pertinent to evaluating the basic  
28 elements of national ambient air quality standards: indicator, averaging time, form, and level.  
29 One or more drafts of a PA are released for CASAC review and public comment prior to  
30 completion of the final PA.

31 Following issuance of the final PA and consideration of conclusions presented therein,  
32 the Agency develops and publishes a notice of proposed rulemaking that communicates the  
33 Administrator’s proposed decisions regarding the standards review. A draft notice undergoes

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<sup>11</sup>The current review of the primary NO<sub>2</sub> standards is an exception to this. As indicated in Table 2-1 below, the draft REA planning document will be made available for public comment and consultation with CASAC subsequent to the CASAC review of the first draft ISA.

1 interagency review involving other federal agencies prior to publication.<sup>12</sup> Materials upon which  
2 the proposed decision is based, including the documents described above, are made available to  
3 the public in the regulatory docket for the review.<sup>13</sup> A public comment period, during which  
4 public hearings are generally held, follows publication of the notice of proposed rulemaking.  
5 Taking into account comments received on the proposed rule,<sup>14</sup> the Agency develops a final rule  
6 which undergoes interagency review prior to publication to complete the rulemaking process.  
7 Chapter 7 below discusses the development of the PA and the rulemaking steps for this review.

### 8 **1.3 REVIEW OF AIR QUALITY CRITERIA FOR OXIDES OF** 9 **NITROGEN AND STANDARDS FOR NITROGEN DIOXIDE**

10 In 1971, the EPA added nitrogen oxides to the list of criteria pollutants under section  
11 108(a)(1) of the CAA and issued the initial air quality criteria (36 FR 1515, January 30, 1971;  
12 U.S. EPA, 1971). Based on these air quality criteria, the EPA promulgated NAAQS for nitrogen  
13 oxides using NO<sub>2</sub> as the indicator (36 FR 8186, April 30, 1971). Both primary and secondary  
14 standards were set at 100 µg/m<sup>3</sup> (equal to 0.053 parts per million (ppm)), annual average. Since  
15 then, the Agency has completed multiple reviews of the air quality criteria and primary  
16 standards, as summarized in Table 1-1.  
17

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<sup>12</sup> Where implementation of the proposed decision would have an annual effect on the economy of \$100 million or more (e.g., by necessitating the implementation of emissions controls), the EPA develops and releases a draft regulatory impact analysis (RIA) concurrent with the notice of proposed rulemaking. This activity is conducted under Executive Order 12866. The RIA is conducted completely independent of the rulemaking process and, by statute, is not considered in decisions regarding the review of the NAAQS.

<sup>13</sup> All documents in the docket are listed in the [www.regulations.gov](http://www.regulations.gov) index. Publically available docket materials are available either electronically at [www.regulations.gov](http://www.regulations.gov) or in hard copy at the Air and Radiation Docket and Information Center. The docket ID number for this review is EPA-HQ-OAR-2013-0146.

<sup>14</sup> When issuing the final rulemaking, the Agency responds to all significant comments on the proposed rule.

**Table 1-1. Primary national ambient air quality standards for oxides of nitrogen since 1971.**

Final Rule/Decision	Indicator	Averaging Time	Level	Form
1971  36 FR 8186 Apr 30, 1971	NO <sub>2</sub>	1 year	53 ppb <sup>15</sup>	Annual arithmetic average
1985  50 FR 25532 Jun 19, 1985	Primary NO <sub>2</sub> standard retained, without revision.			
1996  61 FR 52852 Oct 8, 1996	Primary NO <sub>2</sub> standard retained, without revision.			
2010  75 FR 6474 Feb 9, 2010	NO <sub>2</sub>	1 hour	100 ppb	3-year average of the 98 <sup>th</sup> percentile of the annual distribution of daily maximum 1-hour concentrations
	Primary annual NO <sub>2</sub> standard retained, without revision.			

The EPA retained the primary and secondary NO<sub>2</sub> standards, without revision, in reviews completed in 1985 and 1996 (50 FR 25532, June 19, 1985; 61 FR 52852, October 8, 1996). In the latter of the two decisions, the EPA concluded that “the existing annual primary standard appears to be both adequate and necessary to protect human health against both long- and short-term NO<sub>2</sub> exposures” and that “retaining the existing annual standard is consistent with the scientific data assessed in the Criteria Document (U.S. EPA, 1993) and the Staff Paper (U.S. EPA, 1995) and with the advice and recommendations of CASAC” (61 FR 52854, October 8, 1996).<sup>16</sup>

<sup>15</sup> The initial standard level of the annual NO<sub>2</sub> standard was 100 µg/m<sup>3</sup> which is equal to 0.053 ppm or 53 parts per billion (ppb). The units for the standard level were officially changed to ppb in the final rule issued in 2010 (75 FR 6531, February 9, 2010).

<sup>16</sup> In presenting the rationale for the final decision, the EPA noted that “a 0.053 ppm annual standard would keep annual NO<sub>2</sub> concentrations considerably below the long-term levels for which serious chronic effects have been observed in animals” and that “[r]etaining the existing standard would also provide protection against short-term peak NO<sub>2</sub> concentrations at the levels associated with mild changes in pulmonary function and airway responsiveness observed in controlled human [exposure] studies” (60 FR 52874, 52880, October 11, 1995).



1 The last review of the air quality criteria for oxides of nitrogen (health criteria) and the  
2 primary NO<sub>2</sub> standard was initiated in December 2005 (70 FR 73236, December 9, 2005).<sup>17,18</sup>  
3 The Agency's plans for conducting the review were presented in the *Integrated Review Plan for*  
4 *the Primary National Ambient Air Quality Standard for Nitrogen Dioxide* (2007 IRP, U.S. EPA,  
5 2007a), which included consideration of comments received during a CASAC consultation as  
6 well as public comment on a draft IRP. The scientific assessment for the review was described in  
7 the 2008 *Integrated Science Assessment for Oxides of Nitrogen – Health Criteria* (2008 ISA,  
8 U.S. EPA, 2008a), multiple drafts of which received review by CASAC and the public. The EPA  
9 also conducted quantitative human risk and exposure assessments, after consultation with  
10 CASAC and after receiving public comment on a draft analysis plan (U.S. EPA, 2007b). These  
11 technical analyses were presented in the *Risk and Exposure Assessment to Support the Review of*  
12 *the NO<sub>2</sub> Primary National Ambient Air Quality Standard* (2008 REA, U.S. EPA, 2008b),  
13 multiple drafts of which received CASAC and public review.

14 Over the course of the last review, the EPA made several changes to the NAAQS review  
15 process. An important change was the discontinuation of the Staff Paper, which traditionally  
16 contained staff evaluations to bridge the gap between the Agency's science assessments and the  
17 judgments required of the EPA Administrator in determining whether it was appropriate to retain  
18 or revise the NAAQS.<sup>19</sup> In the course of reviewing the second draft REA, however, CASAC  
19 expressed the view that the document would be incomplete without the addition of a policy  
20 assessment chapter presenting an integration of evidence-based considerations and risk and  
21 exposures assessment results. CASAC stated that such a chapter would be "critical for  
22 considering options for the NAAQS for NO<sub>2</sub> (Samet, 2008a). In addition, within the period of  
23 CASAC's review of the second draft REA, the EPA's Deputy Administrator indicated in a letter  
24 to the CASAC chair, addressing earlier CASAC comments on the NAAQS review process, that  
25 the risk and exposure assessment would include "a broader discussion of the science and how  
26 uncertainties may effect decisions on the standard" and "all analyses and approaches for  
27 considering the level of the standard under review, including risk assessment and weight of  
28 evidence methodologies" (Peacock, 2008, p. 3). Accordingly, the final 2008 REA included a  
29 policy assessment chapter that considered the scientific evidence in the 2008 ISA and the

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<sup>17</sup>Documents related to the current review as well as reviews completed in 2010 and 1996 are available at:  
[http://www.epa.gov/ttn/naaqs/standards/nox/s\\_nox\\_index.html](http://www.epa.gov/ttn/naaqs/standards/nox/s_nox_index.html).

<sup>18</sup>The EPA conducted a separate review of the secondary NO<sub>2</sub> NAAQS jointly with a review of the  
secondary SO<sub>2</sub> NAAQS. The Agency retained those secondary standards, without revision, to address the direct  
effects on vegetation of exposure to gaseous oxides of nitrogen and sulfur (77 FR 20218, April 3, 2012).

<sup>19</sup>Initial changes to the NAAQS review process included a policy assessment document reflecting Agency  
(rather than staff) views published as an advanced notice of public rulemaking (ANPR). Under this process, the  
ANPR would have been reviewed by CASAC (Peacock, 2006).

1 exposure and risk results presented in other chapters of the 2008 REA as they related to the  
2 adequacy of the then current primary annual NO<sub>2</sub> standard and potential alternative standards for  
3 consideration (U.S EPA, 2008b, chapter 10).<sup>20</sup> CASAC discussed the final version of the 2008  
4 REA, with an emphasis on the policy assessment chapter, during a public teleconference on  
5 December 5, 2008 (73 FR 66895, November 12, 2008). Following that teleconference, CASAC  
6 offered comments and advice on the primary NO<sub>2</sub> standard in a letter to the Administrator  
7 (Samet, 2008b).

8 As discussed in more detail in section 3.1 below, after considering an integrative  
9 synthesis of the body of evidence on human health effects associated with the presence of NO<sub>2</sub> in  
10 the air and the exposure and risk information, the Administrator determined that the existing  
11 primary NO<sub>2</sub> NAAQS, based on an annual arithmetic average, was not sufficient to protect the  
12 public health from the array of effects that could occur following short-term exposures to  
13 ambient NO<sub>2</sub>. In so doing, the Administrator particularly noted the potential for adverse health  
14 effects to occur following exposures to elevated NO<sub>2</sub> concentrations that can occur around major  
15 roads (75 FR 6482). In a notice published in the *Federal Register* on July 15, 2009, the EPA  
16 proposed to supplement the existing primary annual NO<sub>2</sub> standard by establishing a new short-  
17 term standard (74 FR 34404). In a notice published in the *Federal Register* on February 9, 2010,  
18 the EPA finalized a new short-term NO<sub>2</sub> standard with a level of 100 ppb, based on the 3-year  
19 average of the 98<sup>th</sup> percentile of the annual distribution of daily maximum 1-hour concentrations.  
20 The EPA also retained the existing primary annual NO<sub>2</sub> standard with a level of 53 ppb, annual  
21 average (75 FR 6474). The Agency's final decision included consideration of CASAC (Samet,  
22 2009) and public comments on the proposed rule.

23 Revisions to the NAAQS were accompanied by revisions to the data handling procedures,  
24 the ambient air monitoring and reporting requirements, and the Air Quality Index (AQI).<sup>21</sup> As  
25 described in section 6.2 below, one aspect of the new monitoring network requirements included

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<sup>20</sup> Subsequent to the completion of the 2008 REA, EPA Administrator Jackson called for additional key changes to the NAAQS review process including reinstating a policy assessment document that contains staff analysis of the scientific bases for alternative policy options for consideration by senior Agency management prior to rulemaking (Jackson, 2009). As discussed in Chapter 7 of this document, a Policy Assessment will be developed for this review.

<sup>21</sup> The current federal regulatory measurement methods for NO<sub>2</sub> are specified in 40 CFR part 50, Appendix F and 40 CFR part 53. Consideration of ambient air measurements with regard to judging attainment of the standards is specified in 40 CFR part 50, Appendix S. The NO<sub>2</sub> monitoring network requirements are specified in 40 CFR part 58, Appendix D, section 4.3. The EPA revised the AQI for NO<sub>2</sub> to be consistent with the revised primary NO<sub>2</sub> NAAQS as specified in 40 CFR part 58 Appendix G. Guidance on the approach for implementation of the new standard was described in the *Federal Register* notices for the proposed and final rules (74 FR 34404; 75 FR 6474).

1 requirements for States to locate monitors near heavily trafficked roadways in large urban areas  
2 and in other locations where maximum NO<sub>2</sub> concentrations can occur. Subsequent to the 2010  
3 rulemaking, the EPA revised the deadlines by which the near-road monitors are to be operational  
4 in order to implement a phased deployment approach (78 FR 16184, March 14, 2013). As  
5 discussed in section 6.2 below, the near-road NO<sub>2</sub> monitors will become operational between  
6 January 1, 2014 and January 1, 2017.

## 7 **1.4 SCOPE OF THE CURRENT REVIEW**

8 Section 108(c) of the CAA specifies that the air quality criteria relating to NO<sub>2</sub> include  
9 consideration of nitric and nitrous acids, nitrites, nitrates, nitrosamines, and other derivatives of  
10 oxides of nitrogen, including multiple gaseous and particulate species. This includes gases such  
11 as NO<sub>2</sub> and nitric oxide (NO) as well as their gaseous and particulate reaction products (e.g.,  
12 organic and inorganic nitrates and nitrites, nitro-polycyclic aromatic hydrocarbons) (U.S. EPA,  
13 2013b, section 2.2, Figure 2-1). Collectively, we refer to this set of species as NO<sub>y</sub>. *Id.* As in  
14 previous reviews, this review will focus on effects associated with the gaseous NO<sub>y</sub> species.  
15 Effects associated with the particulate species (e.g., nitrate) are addressed in the review of the  
16 NAAQS for particulate matter (PM) (78 FR 30866, January 15, 2013; U.S. EPA, 2009).<sup>22</sup>

17 Consistent with the review completed in 2010, this review is focused on the *primary*  
18 standards and as such will only consider relevant scientific information related to potential health  
19 effects associated with exposure to oxides of nitrogen. The EPA is separately reviewing the  
20 secondary standard for oxides of nitrogen in conjunction with a review of the secondary SO<sub>2</sub>  
21 standard (78 FR 53452, August 29, 2013).<sup>23</sup>

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<sup>22</sup> When referring to the group of gaseous oxidized nitrogen compounds as a whole, the ISA and other assessment documents developed in this review will use the term “oxides of nitrogen.” Based on the definition commonly used in the scientific literature, the abbreviation NO<sub>x</sub> will refer specifically to the sum of NO<sub>2</sub> and NO concentrations (U.S. EPA, 2013b, section 2.2).

<sup>23</sup> Additional information on the ongoing review of the secondary NO<sub>2</sub> and SO<sub>2</sub> standards is available at: <http://www.epa.gov/ttn/naaqs/standards/no2so2sec/index.html>.

## 2 STATUS AND SCHEDULE

In February 2012, the EPA announced the initiation of the current periodic review of the air quality criteria for oxides of nitrogen and the primary NO<sub>2</sub> NAAQS and issued a call for information in the *Federal Register* (77 FR 7149, February 10, 2012). Also, as an initial step in the NAAQS review process described in section 1.1 above, the EPA invited a wide range of scientific experts (from EPA and outside organizations) to participate in a workshop to discuss the policy-relevant science to inform the development of this draft IRP. *Id.* These experts represented a variety of scientific disciplines, including epidemiology, human and animal toxicology, statistics, risk/exposure analysis, and atmospheric science. This workshop was held February 29 to March 1, 2012 in Research Triangle Park, NC and provided an opportunity for the participants to broadly discuss the key policy-relevant issues around which the EPA would structure this review of the primary NO<sub>2</sub> NAAQS and the most meaningful new science that would be available to inform our understanding of these issues.<sup>24</sup> Based in part on the workshop discussions, the EPA developed the *Draft Plan for Development of the Integrated Science Assessment (ISA) for Nitrogen Oxides – Health Criteria* (U.S. EPA, 2013a)<sup>25</sup> and this draft IRP outlining the schedule, the process, and the policy-relevant science issues identified as key to guiding the evaluation of the air quality criteria for oxides of nitrogen and the review of the primary NO<sub>2</sub> NAAQS.

Table 2-1 outlines the schedule under which the Agency is currently conducting this review. The scope of the review and the key documents to be prepared during the review are discussed throughout the rest of this document.

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<sup>24</sup> Workshop materials are available in the rulemaking docket accessible through <http://www.regulations.gov>, Docket ID number EPA-HQ-OAR-2013-0146.

<sup>25</sup> The EPA released a draft plan outlining the plans for developing the ISA for CASAC consultation and public review (78 FR 26026, May 3, 2013). The EPA held a consultation with CASAC on this draft plan during a public teleconference on June 5, 2013 (78 FR 27234, May 9, 2013). CASAC and public comments on the draft plan were considered in developing Chapter 4 of this draft IRP.

**Table 2-1. Anticipated schedule for the current review.**

Stage of Review	Major Milestone	Target Date
<b>Integrated Review Plan (IRP)</b>	Literature Search	Ongoing
	<i>Federal Register</i> Call for Information	February 10, 2012
	Workshop on science/policy issues	February 29 – March 1, 2012
	Draft plan for developing ISA	May 2013
	CASAC consultation on draft ISA plan	June 5, 2013
	Draft IRP	February 2014
	CASAC review of draft IRP	March 12-13, 2014
	Final IRP	June 2014
<b>Integrated Science Assessment (ISA)</b>	First draft ISA	November 2013
	CASAC public meeting for review of first draft ISA	March 12-13, 2014
	Second draft ISA	August 2014
	CASAC/public review of second draft ISA	October 2014
	Final ISA	February 2015
<b>Risk/Exposure Assessment (REA)</b>	REA Planning Document	September 2014
	CASAC consultation/public review of REA Planning Document	October 2014
	If warranted, First draft REA	TBD
	CASAC/public review of first draft REA	
	Second draft REA	
	CASAC/public review of second draft REA	
<b>Policy Assessment (PA)/Rulemaking</b>	Final REA	
	First draft PA	January 2015
	CASAC/public review of first draft PA	February 2015
	Second draft PA <sup>26</sup>	October 2015
	CASAC/public review of second draft PA	November 2015
	Final PA	April 2016
	Notice of proposed rulemaking	September 2016
	Notice of final rulemaking	June 2017

<sup>26</sup> The anticipated schedule presented in Table 2-1 includes preparation of two draft PAs for CASAC and public review. However, in NAAQS reviews where a new REA is not developed and where staff preliminarily conclude in a first draft PA that it is appropriate to consider retaining the current standards, without revision, the EPA may decide that there is no new substantive information that we would intend to add that would provide a basis for preparing a second draft PA. In NAAQS reviews in which the newly available information calls into question the adequacy of the current standard(s), a second draft PA is typically prepared to include staff consideration of potential alternative standards. If the Agency determines that a second draft PA is not warranted, CASAC and public comments on the first draft PA will be considered in preparing the final PA and the schedule adjusted accordingly.

### 3 KEY POLICY-RELEVANT ISSUES

In each NAAQS review, an initial step is to address the following overarching question:

- **Does the currently available scientific evidence and exposure/risk-based information support or call into question the adequacy of the protection afforded by the current standard(s)?**

As appropriate, reviews also address a second overarching question:

- **What alternative standards, if any, are supported by the currently available scientific evidence and exposure/risk-based information, and are appropriate for consideration?**

To inform our evaluation of these overarching questions in the current review, we have identified key policy-relevant issues to be considered. These key issues reflect aspects of the health effects evidence, air quality information, and exposure/risk information that, in our judgment, are likely to be particularly important to informing the Administrator's decisions. They build upon the key issues that were important in previous reviews.

Section 3.1 below describes the key considerations and conclusions from the last review with regard to the adequacy of the primary NO<sub>2</sub> standards (section 3.1.1), and with regard to the elements for a revised suite of standards judged in that review to provide requisite public health protection (section 3.1.2). Section 3.2 summarizes our general approach for reviewing the primary NO<sub>2</sub> standards in the current review and outlines the key policy-relevant issues. These issues are presented as a series of questions that will frame our approach to considering the extent to which the available evidence and information support retaining or revising the current primary standards for NO<sub>2</sub>.

#### 3.1 CONSIDERATIONS AND CONCLUSIONS IN LAST REVIEW

The last review of the primary NO<sub>2</sub> NAAQS was completed in 2010 (75 FR 6474). In consideration of health effects evidence and air quality and exposure/risk information available in that review, the EPA established a new short-term standard to provide increased public health protection, including for asthmatics and other at-risk populations,<sup>27</sup> against an array of adverse

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<sup>27</sup> As used here and similarly throughout this document, the term *population* refers to persons having a quality or characteristic in common, such as a specific pre-existing illness or a specific age or lifestage, with lifestage referring to a distinguishable time frame in an individual's life characterized by unique and relatively stable behavioral and/or physiological characteristics that are associated with development and growth. Identifying at-risk populations includes consideration of intrinsic (e.g., genetic or developmental aspects) or acquired (e.g., disease or smoking status) factors that increase the risk of health effects occurring with exposure to oxides of nitrogen as well as extrinsic, nonbiological factors such as those related to socioeconomic status, reduced access to health care, or exposure.

1 respiratory health effects that had been linked to short-term NO<sub>2</sub> exposures (75 FR 6498 to 6502,  
2 February 9, 2010; U.S. EPA, 2008a, sections 3.1.7 and 5.3.2.1; Table 5.3-1) (75 FR 6502).  
3 Specifically, EPA established a short-term standard defined by the 3-year average of the 98<sup>th</sup>  
4 percentile of the yearly distribution of daily maximum 1-hour NO<sub>2</sub> concentrations, with a level  
5 of 100 ppb. In addition to setting the new 1-hour standard, EPA retained the annual standard of  
6 53 ppb (75 FR 6502). Together, the two standards were concluded to provide protection for  
7 susceptible groups against adverse respiratory health effects associated with short-term  
8 exposures to NO<sub>2</sub> and effects potentially associated with long-term exposures. As discussed  
9 further in section 6.2 below, in conjunction with the revised primary NO<sub>2</sub> NAAQS the EPA also  
10 established a two-tiered monitoring network composed of: (1) near-road monitors which would  
11 be placed in locations of expected maximum 1-hour NO<sub>2</sub> concentrations near heavily trafficked  
12 roads in urban areas and (2) monitors located to characterize areas with the highest expected NO<sub>2</sub>  
13 concentrations at the neighborhood and larger spatial scales (also referred to as “area-wide”  
14 monitors) (75 FR 6505 to 6506, February 9, 2010).

15 Key policy-relevant aspects of the Administrator’s decisions with regard to need to revise  
16 the primary NO<sub>2</sub> NAAQS, and with regard to the elements of the revised standard, are described  
17 below in sections 3.1.1 and 3.1.2, respectively. Areas of uncertainty identified in the last review  
18 are noted in section 3.1.3.

### 19 **3.1.1 Need for Revision**

20 The 2010 decision to revise the existing primary NO<sub>2</sub> standard was based on the extensive  
21 body of evidence published through early 2008 and assessed in the 2008 ISA (U.S. EPA, 2008a),  
22 including the assessment of the policy-relevant aspects of that evidence;<sup>28</sup> the quantitative  
23 exposure and risk analyses presented in the REA (U.S. EPA, 2008b); the advice and  
24 recommendations of CASAC (Samet, 2008b); and public comments (U.S. EPA, 2010). The  
25 scientific evidence included controlled human exposure studies providing evidence of airway  
26 hyperresponsiveness in asthmatics following short-term exposures to NO<sub>2</sub> concentrations as low  
27 as 100 ppb, and epidemiological studies reporting associations between short-term NO<sub>2</sub> and  
28 respiratory effects in locations that would have met the annual standard. The quantitative  
29 analyses presented in the 2008 REA included exposure and risk estimates for air-quality adjusted  
30 to just meet the annual standard. Based on the evidence and exposure/risk information, and based  
31 on CASAC’s advice that “the current NAAQS does not protect the public’s health and that it  
32 should be revised” (Samet, 2008b, p. 2), the Administrator concluded that the existing primary

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<sup>28</sup> As noted in section 1.3 above, due to changes in the NAAQS process, the last review of the NO<sub>2</sub> NAAQS did not include a separate Policy Assessment. Rather, the REA for that review included a Policy Assessment chapter.

1 annual NO<sub>2</sub> standard alone was not sufficient to protect public health from the array of  
2 respiratory effects that had been reported following short-term exposures to oxides of nitrogen  
3 (75 FR 6488 to 6490, February 9, 2010).

4 As an initial consideration in reaching this decision, the Administrator noted that the  
5 evidence relating short-term (minutes to hours) NO<sub>2</sub> exposures to respiratory morbidity was  
6 judged in the ISA to be “sufficient to infer a likely causal relationship” (75 FR 6489; U.S. EPA,  
7 2008a, sections 3.1.7 and 5.3.2.1).<sup>29</sup> This evidence included a large body of epidemiological  
8 studies reporting associations between short-term NO<sub>2</sub> concentrations measured at central-site  
9 monitors and respiratory-related symptoms, emergency department visits, and hospital  
10 admissions. Overall, the 2008 ISA characterized the epidemiological evidence as *consistent*, in  
11 that associations were reported in studies conducted in numerous locations with a variety of  
12 methodological approaches, and *coherent*, in that the studies reported associations with  
13 respiratory health outcomes that were logically linked together. In addition, a number of these  
14 associations were statistically significant, particularly the more precise effect estimates (U.S.  
15 EPA, 2008a, section 5.3.2.1). In studies that evaluated concentration-response (C-R)  
16 relationships, they appeared linear within the observed range of data with “little evidence of any  
17 effect threshold” (U.S. EPA, 2008a, sections 4.2 and 5.3.2.9). In considering the epidemiological  
18 evidence, the Administrator acknowledged that the interpretation of the studies is complicated by  
19 the fact that on-road vehicle exhaust emissions are a nearly ubiquitous source of combustion  
20 pollutant mixtures than include NO<sub>2</sub>, but additionally noted ISA analyses of co-pollutants  
21 generally found that NO<sub>2</sub> associations remained robust in multi-pollutant models (75 FR 6489).

22 The evidence also included controlled human exposure studies that evaluated airway  
23 hyperresponsiveness in asthmatics following short-term (30-minute to 2-hour) exposures to NO<sub>2</sub>  
24 concentrations at or above 100 ppb, as well as supporting evidence from animal toxicological  
25 studies (U.S. EPA, 2008a, sections 3.1.3 and 5.4). The EPA drew two broad conclusions  
26 regarding airway responsiveness in asthmatics following NO<sub>2</sub> exposures. First, that NO<sub>2</sub>  
27 exposure may enhance the sensitivity to allergen-induced decrements in lung function and  
28 increase the allergen-induced airway inflammatory response following 30-minute exposures of  
29 asthmatic adults to NO<sub>2</sub> concentrations as low as 260 ppb. (U.S. EPA, 2008a, section 5.3.2.1,  
30 Figure 3.1-2). Second, that exposure to NO<sub>2</sub> resulted in small but significant increases in  
31 nonspecific airway hyperresponsiveness in healthy and asthmatic adults. In asthmatics, the ISA  
32 concluded that such increases were observed following 1-hour exposures to 100 ppb NO<sub>2</sub> (U.S.

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<sup>29</sup>In contrast, the evidence relating long-term (weeks to years) NO<sub>2</sub> exposures to adverse health effects was judged to be either “suggestive but not sufficient to infer a causal relationship” (respiratory morbidity) or “inadequate to infer the presence or absence of a causal relationship” (mortality, cancer cardiovascular effects, reproductive/developmental effects) (75 FR 6478).



1 EPA, 2008a, sections 3.1.3.2; 5.3.2.1). The EPA further concluded that the majority of  
2 asthmatics may experience NO<sub>2</sub>-related airway hyperresponsiveness following short-term NO<sub>2</sub>  
3 exposures between 100 and 300 ppb (U.S. EPA, 2008a, Table 3.1-3; U.S. EPA, 2008b, p. 283).  
4 Enhanced airway responsiveness could have important clinical implications for asthmatics since  
5 transient increases in airway responsiveness following NO<sub>2</sub> exposure have the potential to  
6 increase symptoms and worsen asthma control (74 FR 34415, July 15, 2009; U.S. EPA, 2008a,  
7 sections 5.3.2.1 and 5.4). An update to a meta-analysis of data for nonspecific airway  
8 responsiveness that had been considered in the previous review provided support to the  
9 conclusions on exposure concentrations eliciting effects (Folinsbee, 1992; U.S. EPA, 1993, 60  
10 FR 52818, October 11, 1995; U.S. EPA, 2008a, section 3.1.3.2, Tables 3.1-2 and 3.1-3).<sup>30</sup>

11 The exposure-and risk-based information further informed the Administrator's decisions  
12 regarding adequacy of the then-existing NO<sub>2</sub> primary standard. The Administrator took note of  
13 the REA conclusion that risks estimated for air quality adjusted upward to simulate just meeting  
14 the current standard could reasonably be concluded to be important from a public health  
15 perspective, while additionally recognizing the uncertainties associated with adjusting air quality  
16 in such analyses (75 FR 6489).<sup>31</sup> For air quality adjusted to just meet the existing annual  
17 standard, the REA findings given particular attention by the Administrator included the  
18 following: "a large percentage (8-9%) of respiratory-related ED visits in Atlanta could be  
19 associated with short-term NO<sub>2</sub> exposures; most asthmatics in Atlanta could be exposed on  
20 multiple days per year to NO<sub>2</sub> concentrations at or above 300 ppb, and most locations evaluated  
21 could experience on-/near-road NO<sub>2</sub> concentrations above 100 ppb on more than half of the days  
22 in a given year" (75 FR 6489; U.S. EPA, 2008b, section 10.3.2).<sup>32</sup> The 2008 REA additionally

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<sup>30</sup>The changes made to the analysis were to remove the results of one allergen study and to add the results from a non-specific responsiveness study, and to discuss results for an additional exposure concentration (i.e., 100 ppb) (U.S. EPA, 2008a, section 3.1.3.2).

<sup>31</sup> As described further in chapter 5 below, the 2008 REA considered air quality data from the existing network of ambient monitors as well as data from controlled human exposure studies and epidemiological studies to model exposure to NO<sub>2</sub> and to estimate health risks associated with short-term exposures. Additionally, recognizing that large segments of the public live, work, go to school, or travel on or near roads, the 2008 REA also estimated exposures that would occur in these particular locations.

<sup>32</sup> Estimates were developed for: (1) an "as-is" scenario in which it estimated the health risks associated with short-term exposure to NO<sub>2</sub> at actual recent air-quality concentrations, which were lower than what was permitted by the then current annual NO<sub>2</sub> standard; (2) a "just meets" scenario in which it estimated the health risks associated with air quality adjusted upward to simulate just meeting the then current annual standard; and (3) other scenarios for potential alternative standards. The 2008 REA's health risk estimates were based on actual or modeled ambient concentrations at pre-2010 air quality monitors. Those monitors primarily measured NO<sub>2</sub> concentrations that were representative of a broad geographic area (e.g., area-wide ambient measurements ) rather than concentrations at specific locations where the highest concentrations of NO<sub>2</sub> were likely to be found (e.g., maximum or peak ambient measurements including near major roadways).

Area-wide monitors are defined as those sited at neighborhood, urban, and regional scales, as well as those monitors sited at either a micro- or middle-scale that are representative of many such locations in the same Core

found that, under the “as is” scenario (i.e., recent air quality concentrations), individuals spending time on or near roads could expect to experience short-term NO<sub>2</sub> exposures above health effect benchmark levels of concern<sup>33</sup> multiple times per year.

In reaching the conclusion on adequacy of the then-existing standard, the Administrator also considered advice received from CASAC. In their advice, CASAC agreed that the primary concern in the review was to protect against health effects that have been associated with short-term NO<sub>2</sub> exposures. CASAC also agreed that the annual standard alone was not sufficient to protect public health against the types of exposures that could lead to these health effects. As noted in their letter to the EPA Administrator, “CASAC concurs with EPA’s judgment that the current NAAQS does not protect the public’s health and that it should be revised” (Samet, 2008b).

Based on the considerations summarized above, the Administrator concluded that the then-existing NO<sub>2</sub> primary NAAQS was not requisite to protect public health with an adequate margin of safety and that the standard should be revised in order to provide increased public health protection against respiratory effects associated with short-term exposures, particularly for susceptible populations such as asthmatics, children, and older adults (75 FR 6490). Upon consideration of approaches to revising the standard, the Administrator concluded that it was appropriate to set a new short-term standard, as described below.

### **3.1.2 Elements of Revised Standard**

In considering appropriate revisions in the last review, each of the four basic elements of the NAAQS (indicator, averaging time, level, and form) was evaluated. The rationale for decisions on those elements is summarized below.

#### **3.1.2.1 Indicator**

In previous reviews, the EPA focused on NO<sub>2</sub> as the most appropriate indicator for oxides of nitrogen because the available scientific information regarding health effects was largely indexed by NO<sub>2</sub>. In the review completed in 2010, controlled human exposure studies and animal toxicological studies provided specific evidence for health effects following exposures to NO<sub>2</sub>. In addition, epidemiological studies typically reported effects associated with NO<sub>2</sub> concentrations though the degree to which monitored NO<sub>2</sub> reflected actual NO<sub>2</sub> concentrations,

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Based Statistical Area (CBSA) (40 CFR 58.1). The introduction and first use of the term “area-wide” was in the final rule for the last primary NO<sub>2</sub> NAAQS review as part of the NO<sub>2</sub> minimum monitoring requirements (75 FR 6504, February 9, 2010). The term was formally defined in the final rule for the most recent PM NAAQS review (78 FR 3235 and 3281 to 3282, January 15, 2013). The underlying spatial scales are defined in 40 CFR part 58 Appendix D, section 1.2(b).

<sup>33</sup> Health effect benchmark levels evaluated in the 2008 REA ranged from 100 to 300 ppb based on increased airway hyperresponsiveness in asthmatics (from controlled human exposure studies) (U.S. EPA, 2008b, section 6.2).

1 as opposed to NO<sub>2</sub> plus other gaseous oxides of nitrogen, was recognized as an uncertainty (75  
2 FR 6490, February, 9, 2010; U.S. EPA 2008b, section 2.2.3).

3 Based on the information available in the last review, and consistent with the views of  
4 CASAC (Samet, 2008b, p.2; Samet, 2009, p.2), the Agency concluded it was appropriate to  
5 continue to use NO<sub>2</sub> as the indicator for a standard that was intended to address effects associated  
6 with exposure to NO<sub>2</sub>, alone or in combination with other gaseous oxides of nitrogen. In so  
7 doing, the EPA recognized that measures leading to reductions in population exposures to NO<sub>2</sub>  
8 will also reduce exposures to other oxides of nitrogen (75 FR 6490).

### 9 **3.1.2.2 Averaging times**

10 In considering the most appropriate averaging time for the NO<sub>2</sub> primary NAAQS, the  
11 Administrator noted the available scientific evidence as assessed in the ISA, the air quality  
12 analyses presented in the REA, the conclusions of the policy assessment chapter of the REA,  
13 CASAC recommendations, and public comments received (75 FR 6490). Her key considerations  
14 are summarized below.

15 When considering averaging time, the Administrator first noted that the evidence relating  
16 short-term (minutes to hours) NO<sub>2</sub> exposures to respiratory morbidity was judged in the ISA to  
17 be “sufficient to infer a likely causal relationship” (U.S. EPA, 2008a, section 5.3.2.1) while the  
18 evidence relating long-term (weeks to years) NO<sub>2</sub> exposures to adverse health effects was judged  
19 to be either “suggestive but not sufficient to infer a causal relationship” (respiratory morbidity)  
20 or “inadequate to infer the presence or absence of a causal relationship” (mortality, cancer,  
21 cardiovascular effects, reproductive/developmental effects) (U.S. EPA, 2008a, sections 5.3.2.4-  
22 5.3.2.6). The Administrator concluded that these judgments most directly supported an  
23 averaging time that focused protection on short-term exposures to NO<sub>2</sub>.

24 As had been done in previous reviews of the NO<sub>2</sub> NAAQS, the Administrator next noted  
25 that it is instructive to evaluate the potential for a standard based on annual average NO<sub>2</sub>  
26 concentrations, as was the existing standard at the time of the 2010 review, to provide protection  
27 against short-term NO<sub>2</sub> exposures. To this end, the Administrator considered REA analyses that  
28 indicated a relatively large degree of variability in ratios of short-term (i.e., 1-hour and 24-hour)  
29 NO<sub>2</sub> concentrations to annual average concentrations, suggesting that a standard based on annual  
30 average NO<sub>2</sub> concentrations would not likely be an effective or efficient approach to focus  
31 protection on short-term NO<sub>2</sub> exposures. For example, these analyses indicated that in some  
32 areas the existing annual standard could allow 1-hour daily maximum NO<sub>2</sub> concentrations of  
33 about 400 ppb, while in other areas the annual standard could limit 1-hour daily maximum NO<sub>2</sub>  
34 concentrations to about 150 ppb. Thus, for purposes of protecting against the range of 1-hour  
35 NO<sub>2</sub> exposures, the Administrator agreed with the REA conclusion that a standard based on

1 annual average concentrations would likely require more control than necessary in some areas  
2 and less control than necessary in others, depending on the standard level selected.

3 In next considering the level of support available for specific short-term averaging times,  
4 the Administrator noted that the policy assessment chapter of the REA considered evidence from  
5 both experimental and epidemiologic studies. Controlled human exposure studies and animal  
6 toxicological studies provided evidence that NO<sub>2</sub> exposures from less than 1-hour up to 3-hours  
7 can result in respiratory effects such as increased airway responsiveness and inflammation (ISA,  
8 section 5.3.2.7). She specifically noted the ISA conclusion that exposures of asthmatic adults to  
9 100 ppb NO<sub>2</sub> for 1-hour can result in small but significant increases in nonspecific airway  
10 responsiveness (U.S. EPA, 2003a, section 5.3.2.1). In addition, the epidemiologic literature  
11 provided support for short-term averaging times ranging from approximately 1-hour up to 24-  
12 hours (U.S. EPA, 2003a, section 5.3.2.7). Based on this, the Administrator concluded that a  
13 primary concern with regard to averaging time is the degree of protection provided against 1-  
14 hour NO<sub>2</sub> concentrations. Based on REA analyses of ratios between 1-hour and 24-hour NO<sub>2</sub>  
15 concentrations, she further concluded that a standard based on 1-hour daily maximum NO<sub>2</sub>  
16 concentrations could also be effective at protecting against 24-hour NO<sub>2</sub> exposures.

17 Based on the above, the Administrator judged that it was appropriate to set a new NO<sub>2</sub>  
18 standard with a 1-hour averaging time. She concluded that such a standard can effectively limit  
19 short-term (i.e., 1- to 24-hours) exposures that have been linked to adverse respiratory effects.  
20 She also retained the existing annual standard to continue to provide protection for effects  
21 potentially associated with long-term exposures to oxides of nitrogen (75 FR 6502). These  
22 decisions were consistent with CASAC advice to establish a primary short-term standard for  
23 oxides of nitrogen based on using 1-hour maximum NO<sub>2</sub> concentrations and to retain the current  
24 annual standard<sup>34</sup> (Samet, 2008b, p. 2; Samet, 2009, p. 2).

### 25 **3.1.2.3 Levels**

26 With consideration of the available health effects evidence, exposure and risk analyses,  
27 and air quality information, the Administrator set the level of the new 1-hour NO<sub>2</sub> standard at  
28 100 ppb. This standard was focused on limiting the *maximum* 1-hour NO<sub>2</sub> concentrations in  
29 ambient air, including in locations near major roadways where the highest ambient NO<sub>2</sub>

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<sup>34</sup> CASAC advised that “the findings of the REA do not provide assurance that a short-term standard based on the one-hour maximum will necessarily protect the populations from long-term exposures at levels potentially leading to adverse health effects” therefore, it recommended retaining the existing annual standard (Samet, 2008b, p. 2).

1 concentrations can occur in urban areas (75 FR 6474).<sup>35</sup> In establishing this new standard, the  
2 Administrator emphasized the importance of protecting against exposures to peak concentrations  
3 of NO<sub>2</sub>, such as those that can occur around major roadways. Available evidence and  
4 information suggested that roadways account for the majority of exposures to peak NO<sub>2</sub>  
5 concentrations and, therefore, are important contributors to NO<sub>2</sub>-associated public health risks.

6 In setting the level of the new 1-hour standard at 100 ppb, the Administrator noted that  
7 there is no bright line clearly directing the choice of level. Rather, the choice of what is  
8 appropriate is a public health policy judgment entrusted to the Administrator. This judgment  
9 must include consideration of the strengths and limitations of the evidence and the appropriate  
10 inferences to be drawn from the evidence and the exposure and risk assessments.

11 The Administrator judged that the existing evidence from controlled human exposure  
12 studies supported the conclusion that the NO<sub>2</sub>-induced increase in airway responsiveness at or  
13 above 100 ppb presents a risk of adverse effects for some asthmatics, especially those with more  
14 serious (i.e., more than mild) asthma. The Administrator noted that the risks associated with  
15 increased airway responsiveness cannot be fully characterized based on available controlled  
16 human exposure studies, and thus she was not able to determine whether the increased airway  
17 responsiveness experienced by asthmatics in these studies is an adverse health effect. However,  
18 the Administrator concluded that asthmatics, particularly those suffering from more severe  
19 asthma, warrant protection from the risk of adverse effects associated with the NO<sub>2</sub>-induced  
20 increase in airway responsiveness. Therefore, the Administrator concluded that the controlled  
21 human exposure evidence supported setting a standard level no higher than 100 ppb to reflect a  
22 cautious approach to the uncertainty regarding the adversity of the effect. However, those  
23 uncertainties led her to also conclude that this evidence did not support setting a standard level  
24 lower than 100 ppb.

25 The Administrator also considered the more serious health effects reported in NO<sub>2</sub>  
26 epidemiologic studies. She noted that a new standard focused on protecting against maximum 1-  
27 hour NO<sub>2</sub> concentrations in ambient air anywhere in an area, with a level of 100 ppb and an  
28 appropriate form (as discussed below), would be expected to limit area-wide<sup>36</sup> NO<sub>2</sub>  
29 concentrations to below those in locations where epidemiologic studies had reported associations  
30 with respiratory-related hospital admissions or emergency department visits. The Administrator

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<sup>35</sup>In conjunction with this new standard, the Administrator established a 2-tiered monitoring network that included monitors sited to measure the maximum NO<sub>2</sub> concentrations near major roadways, as well as monitors sited to measure maximum area-wide NO<sub>2</sub> concentrations (section 6, below).

<sup>36</sup>As discussed above, area-wide concentrations refer to those measured by monitors that have been sited to characterize ambient concentrations at the neighborhood and larger spatial scales (see also section 6, below).

1 also concluded that such a 1-hour standard would be consistent with the REA conclusions based  
2 on the NO<sub>2</sub> exposure and risk information.

3         Given the above considerations and the comments received on the proposal, the  
4 Administrator judged it appropriate to set a 1-hour standard focused on limiting the maximum  
5 allowable NO<sub>2</sub> concentrations that can occur anywhere in an area, with a level of 100 ppb.  
6 Specifically, she concluded that such a standard, with an appropriate form as discussed below,  
7 would provide a significant increase in public health protection compared to that provided by the  
8 annual standard alone and would be expected to protect against the respiratory effects that have  
9 been linked with NO<sub>2</sub> exposures in both controlled human exposure and epidemiologic studies.  
10 This includes limiting exposures at and above 100 ppb for the vast majority of people, including  
11 those in at-risk groups, and maintaining area-wide NO<sub>2</sub> concentrations well below those in  
12 locations where key U.S. epidemiologic studies had reported that ambient NO<sub>2</sub> is associated with  
13 clearly adverse respiratory health effects, as indicated by increased hospital admissions and  
14 emergency department visits. The Administrator also noted that a standard level of 100 ppb was  
15 consistent with the consensus recommendation of CASAC.

16         In setting the standard level at 100 ppb rather than a lower level, the Administrator also  
17 acknowledged the uncertainties associated with the scientific evidence. She noted that a 1-hour  
18 standard with a level lower than 100 ppb would only result in significant further public health  
19 protection if, in fact, there is a continuum of serious, adverse health risks caused by exposure to  
20 NO<sub>2</sub> concentrations below 100 ppb and/or associated with area-wide NO<sub>2</sub> concentrations well-  
21 below those in locations where key U.S. epidemiologic studies had reported associations with  
22 respiratory-related emergency department visits and hospital admissions. Based on the available  
23 evidence, the Administrator did not believe that such assumptions were warranted. Taking into  
24 account the uncertainties that remained in interpreting the evidence from available controlled  
25 human exposure and epidemiologic studies, the Administrator noted that the likelihood of  
26 obtaining benefits to public health with a standard set below 100 ppb decreases while the  
27 likelihood of requiring reductions in ambient concentrations that go beyond those that are needed  
28 to protect public health increases.

#### 29         **3.1.2.4 Forms**

30         The “form” of a standard defines the air quality statistic that is to be compared to the level of  
31 the standard in determining whether an area attains the standard. The Agency recognizes that for  
32 short-term standards, concentration-based forms which reflect consideration of a statistical  
33 characterization of an entire distribution of air quality data with a focus on a single statistical metric,  
34 such as the 98<sup>th</sup> or 99<sup>th</sup> percentile, can better reflect pollutant-associated health risks than forms based  
35 on expected exceedances. This is the case because concentration-based forms give proportionally  
36 greater weight to days when pollutant concentrations are well above the level of the standard than to

1 days when the concentrations are just above the level of the standard.<sup>37</sup> In addition, when averaged  
2 over three years, these concentration-based forms are judged to provide an appropriate balance  
3 between limiting peak pollutant concentrations and providing a stable regulatory target, facilitating  
4 the development of stable implementation programs (75 FR 6492).

5 In the last review, the EPA considered two specific concentration-based forms (i.e., the 98<sup>th</sup>  
6 and 99<sup>th</sup> percentile concentrations), averaged over 3 years, for the new 1-hour NO<sub>2</sub> standard. The  
7 focus on the upper percentiles of the distribution was based, in part, on evidence of health effects  
8 associated with short-term NO<sub>2</sub> exposures from experimental studies which provided information on  
9 specific exposure concentrations that were linked to respiratory effects. The Agency proposed to  
10 adopt either a 99<sup>th</sup> percentile or a 4<sup>th</sup> highest form, averaged over 3 years and also solicited comment  
11 on both 98<sup>th</sup> percentile and 7<sup>th</sup> or 8<sup>th</sup> highest forms (74 FR 34430, July 15, 2008). Given the potential  
12 for instability in the higher percentile concentrations and the absence of data from the proposed  
13 two-tier monitoring network (e.g., around major roadways), CASAC, in a letter to the Administrator  
14 following issuance of the Agency's proposed rule, recommended a form based on the 3-year average  
15 of the 98<sup>th</sup> percentile of the distribution of 1-hour daily maximum NO<sub>2</sub> concentrations (Samet, 2009,  
16 p. 2).

17 In reaching her final decision in the last review, the Administrator recognized that the public  
18 health protection provided by the new 1-hour NO<sub>2</sub> standard was based in large part on: (1) the  
19 approach used to set the standard and (2) the level of the standard in conjunction with the form of the  
20 standard (75 FR 6493, February 9, 2010). Given that the EPA set a new primary 1-hour NO<sub>2</sub> standard  
21 that focused on limiting the *maximum* allowable NO<sub>2</sub> concentration in ambient air, the Agency  
22 agreed with CASAC that an appropriate consideration with regard to form was the extent to which  
23 specific statistics could be unstable at locations where maximum NO<sub>2</sub> concentrations are expected  
24 (e.g., including near major roads).

25 Given the limited available information on the variability in peak NO<sub>2</sub> concentrations near  
26 important sources of NO<sub>2</sub> such as near major roadways, and given the recommendation from CASAC  
27 of the potential for instability in the 99<sup>th</sup> percentile concentrations, the Administrator judged it  
28 appropriate to set the form based on the 3-year average of the 98<sup>th</sup> percentile of the annual  
29 distribution of daily maximum 1-hour NO<sub>2</sub> concentrations. *Id.* In addition, consistent with CASAC  
30 advice (Samet, 2008b, p. 2; Samet, 2009, p.2), the EPA retained the form of the annual standard (75  
31 FR 6502).

### 32 **3.1.3 Areas of Uncertainty**

33 While the available scientific information informing the last review was stronger and  
34 more consistent than in previous reviews, and provided a strong basis for decision making in that

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<sup>37</sup> Compared to an exceedance-based form, a concentration-based form reflects the magnitude of the exceedance of a standard level not just the fact that such an exceedance occurred.

review, the Agency recognized that areas of uncertainty remained. These were generally related to: (1) understanding the role of NO<sub>2</sub> in the complex ambient mixture which includes a range of co-occurring pollutants (e.g., PM<sub>2.5</sub>, ozone, CO, SO<sub>2</sub>); (2) understanding the extent to which monitored ambient NO<sub>2</sub> concentrations used in epidemiological studies reflect exposures in study populations and the range of ambient concentrations over which we continue to have confidence in the health effects observed in the epidemiological studies; (3) understanding the extent to which the magnitude and potential adversity of NO<sub>2</sub>-induced respiratory effects reported in controlled human exposures studies can be characterized; (4) understanding the NO<sub>2</sub> concentration gradients around important sources, such as major roads, and relating those gradients to broader ambient monitoring concentrations; and (5) an improved characterization of NO<sub>2</sub> exposures and risk including alternative approaches for estimated risks associated with air quality simulated to just meet current or alternative standards.

### **3.2 GENERAL APPROACH FOR THE CURRENT REVIEW**

The approach for this review builds on the substantial body of work done during the course of the last review, taking into account the more recent scientific information and air quality data now available to inform our understanding of the key policy-relevant issues. The approach described below is most fundamentally based on using the EPA's assessment of the current scientific evidence and associated quantitative analyses to inform the Administrator's judgments regarding primary standards for oxides of nitrogen that are requisite to protect public health with an adequate margin of safety. This approach will involve translating scientific and technical information into the basis for addressing a series of key policy-relevant questions using both evidence- and exposure/risk-based considerations.<sup>38</sup>

Figure 3-1 summarizes the general approach, including consideration of the policy-relevant questions which will frame the current review. The ISA, REA (if warranted), and PA developed in this new review will provide the basis for addressing the key policy-relevant questions and will inform the Administrator's judgment as to the adequacy of the current primary NO<sub>2</sub> standards and decisions as to whether to retain or revise these standards. This approach recognizes that the available health effects evidence generally reflects a continuum, consisting of ambient concentrations at which scientists generally agree that health effects are likely to occur, through lower concentrations at which the likelihood and magnitude of the response become increasingly uncertain. Furthermore, this approach is consistent with the requirements of the NAAQS provisions of the CAA and with how the EPA and the courts have historically interpreted the CAA. As discussed in section 1.1 above, these provisions require the

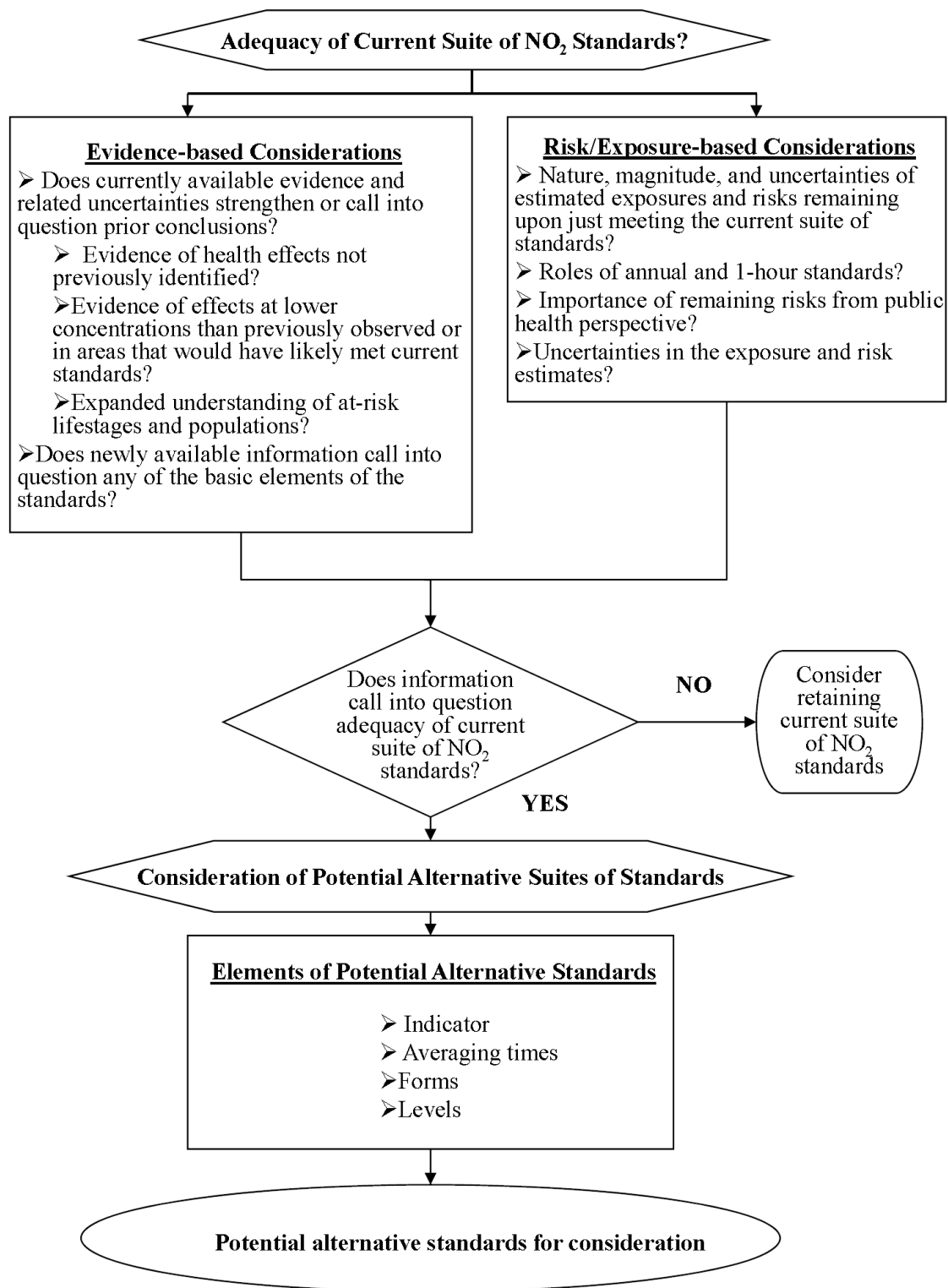
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<sup>38</sup> Evidence-based considerations include those related to the health effects evidence assessed and characterized in the ISA. Exposure/risk-based considerations draw from the results of the quantitative analyses.



1 Administrator to establish primary standards that, in the Administrator's judgment, are requisite  
2 to protect public health with an adequate margin of safety. In so doing, the Administrator seeks  
3 to establish standards that are neither more nor less stringent than necessary for this purpose. The  
4 CAA does not require that primary standards be set at a zero-risk level, but rather at a level that  
5 avoids unacceptable risks to public health. The four basic elements of the NAAQS (i.e.,  
6 indicator, averaging time, form, and level) will be considered collectively in evaluating the  
7 health protection afforded by the current or any alternative standards considered.

8 We note that the final decision on the adequacy of the current standards and, if  
9 appropriate, potential alternative standards, is largely a public health policy judgment to be made  
10 by the Administrator. The Administrator's final decision must draw upon scientific information  
11 and analyses about health effects, population exposure and risks, as well as judgments about how  
12 to consider the range and magnitude of uncertainties that are inherent in the scientific evidence  
13 and analyses. As in the previous review as well as other recent NAAQS reviews, the EPA will  
14 consider the implications of placing more or less weight or emphasis on different aspects of the  
15 scientific evidence and exposure/risk-based information to inform the public health policy  
16 judgments that the Administrator will make in reaching final decisions on whether to retain or  
17 revise the current standards in this review.



**Figure 3-1. Overview of General Approach for Review of Primary NO<sub>2</sub> Standards**

1       The initial overarching question in reviewing the adequacy of the current suite of primary  
2 NO<sub>2</sub> NAAQS is whether the available body of scientific evidence, assessed in the ISA and used  
3 as a basis for developing or interpreting any risk/exposure analyses, supports or calls into  
4 question the scientific conclusions reached in the last review regarding health effects related to  
5 exposures to oxides of nitrogen. The evaluation of the available scientific evidence and  
6 risk/exposure information with regard to adequacy of the current standards will focus on key  
7 policy-relevant issues by addressing a series of questions including the following:

- 8       • To what extent has new information altered the scientific support for the occurrence of  
9 health effects as a result of short- and/or long-term exposure to oxides of nitrogen in the  
10 ambient air?
  - 11       ○ What evidence is available from recent studies focused on specific chemical  
12 components within the broader group of oxides of nitrogen (e.g., NO<sub>2</sub>, NO, NO<sub>x</sub>) to  
13 inform our understanding of the nature of exposures that are linked to various health  
14 outcomes?
  - 15       ○ To what extent is key scientific evidence becoming available to improve our  
16 understanding of the health effects associated with various time periods of exposures,  
17 including peak (e.g., 1-hour) and chronic exposures (e.g., more than one month to  
18 years)?
  - 19       ○ At what pollutant concentrations do these health effects occur?
  - 20       ○ Is there evidence of effects at exposure concentrations lower than previously  
21 observed or in areas that would likely have met the current primary NO<sub>2</sub> standards?
  - 22       ○ To what extent is new information available to improve the characterization of the  
23 magnitude and/or potential adversity of NO<sub>2</sub>-induced respiratory effects reported in  
24 controlled human exposure studies?
  - 25       ○ To what extent is new information available to improve our understanding of the  
26 range of ambient concentrations over which we continue to have confidence in the  
27 health effects observed in the epidemiological studies?
  - 28       ○ To what extent are health effects associated with exposures to oxides of nitrogen,  
29 including NO<sub>2</sub>, as opposed to one or more co-occurring pollutants (e.g., PM<sub>2.5</sub>, ozone,  
30 SO<sub>2</sub>)?
  - 31       ○ Has new information altered our understanding of human lifestages and populations  
32 that are particularly at increased risk for experiencing health effects associated with  
33 exposure to oxides of nitrogen?
  - 34       ○ Is there new information to shed light on the nature the of exposure-response  
35 relationship in different at-risk lifestages and/or populations?
  - 36       ○ Is there new or emerging evidence on health effects beyond respiratory effects in  
37 asthmatics or effects in high exposure populations (e.g., people living, working, or  
38 going to school in near-road environments) that suggest potential additional at-risk  
39 lifestages and populations should be given increased focus in this review?

- To what extent is new information available to improve our understanding of the NO<sub>2</sub> concentration gradients around important sources, such as major roads and combustion sources, and to relate those gradients to broader ambient monitoring concentrations?
- To what extent does risk or exposure information suggest that exposures of concern are likely to occur with recent ambient NO<sub>2</sub> concentrations or with concentrations that just meet the current primary NO<sub>2</sub> standards?
  - Are the estimated risks/exposures considered in this review of sufficient magnitude such that the health effects might reasonably be judged to be important from a public health perspective?
  - What are the important uncertainties associated with any risk/exposure estimates?
- To what extent have important uncertainties identified in the last review been reduced and/or have new uncertainties emerged?
- To what extent does newly available information reinforce or call into question any of the basic elements of the current primary NO<sub>2</sub> standards?

If the evidence suggests that revision of the current standards might be appropriate, the EPA will address a second overarching question related to what alternative standards are appropriate for consideration. Specifically, we will evaluate how the scientific information and assessments inform decisions regarding the basic elements of the primary NO<sub>2</sub> NAAQS: indicator, averaging time, level, and form. These elements will be considered collectively in evaluating the health protection afforded by the current or any alternative standards considered. With regard to consideration of alternative standards, specific policy-relevant questions that will be addressed include the following:

- To what extent does any new information provide support for consideration of a different *indicator* for oxides of nitrogen in addition to or in place of NO<sub>2</sub>?
- To what extent does the health effects evidence evaluated in the ISA, air quality analyses, and, if available, new REA provide support for considering any different *averaging times*?
- To what extent do air quality analyses and other information provide support for consideration of alternative standard *forms*?
- What range of alternative standard *levels* should be considered based on the scientific evidence evaluated in the ISA, air quality analyses and, if available, new REA<sup>39</sup>?
- What are the important uncertainties and limitations in the available evidence and assessments and how might those uncertainties and limitations be taken into

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<sup>39</sup> As outlined in Table 2-1 and discussed in Chapter 6 below, the REA Planning Document will consider the extent to which newly available scientific evidence and tools/methodologies warrant the conduct of new quantitative risk and exposure assessments. To the extent completely new assessments are not developed for this review, assessments from the last review may be interpreted in light of the newly available information in addressing the key policy questions for the review.

1 consideration in identifying alternative standard *indicators, averaging times, forms*  
2 *and/or levels?*

## 4 SCIENCE ASSESSMENT

The ISA comprises the science assessment phase of the NAAQS review process. As outlined in section 1.4 above, the purpose of the current review is to inform the review of the primary NO<sub>2</sub> standards only.<sup>40</sup> Hence, the ISA will focus on updating the air quality criteria associated with health effects evidence only.<sup>41</sup>

### 4.1 SCOPE OF THE ISA

The ISA provides an updated critical evaluation and synthesis of the current scientific literature pertaining to known and anticipated effects on public health associated with the presence of oxides of nitrogen in the ambient air, including the nature of any remaining or newly identified uncertainties and limitations associated with the health evidence. Discussions in the ISA will primarily focus on scientific evaluations that can inform the key policy questions described in section 3.2 above. Although emphasis will be placed on the discussion of the health effects information, other scientific information will also be presented and evaluated in order to provide a better understanding of the following issues: (1) the sources of oxides of nitrogen to ambient air; (2) measurement of and recent ambient concentrations of oxides of nitrogen including NO<sub>2</sub>, including subsequent fate and transport in the environment; and (3) important considerations related to characterizing potential population exposures to oxides of nitrogen. The process for evaluating and synthesizing scientific literature and addressing key policy questions is detailed in the Preamble to the ISA.

The ISA is not intended to provide a detailed literature review but rather, will draw from the existing body of evidence to synthesize the current state of knowledge on the most relevant issues pertinent to the review of the primary NO<sub>2</sub> NAAQS. The ISA serves to revise the scientific assessment available at the time of the last review. Thus, the ISA will build on the conclusions of the last review of the air quality criteria for oxides of nitrogen as presented in the 2008 ISA and focus on peer-reviewed literature published since that document<sup>42</sup> as well as on any new interpretations of previously available literature. Key findings, conclusions, and uncertainties from the 2008 ISA will be briefly summarized at the beginning of the ISA and of

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<sup>40</sup> As outlined in section 1.4 above, evidence related to potential welfare (e.g., ecosystem) effects of oxides of nitrogen will be considered separately in the science assessment conducted as part of the review of the secondary NAAQS for NO<sub>2</sub> and SO<sub>2</sub>.

<sup>41</sup> In this review of the primary NAAQS for NO<sub>2</sub>, a draft plan for development of the ISA was prepared by NCEA prior to development of this draft IRP. The draft plan for development of the ISA was made available for public comment and was the subject of a consultation with CASAC (78 FR 26026; 78 FR 27234). Comments received during that consultation have been considered in preparation of chapter 4 in this draft IRP. Further comments received on this draft IRP will be considered in preparing the final IRP and the second draft ISA.

<sup>42</sup> For the current ISA, searches were conducted for studies published beginning in January 2008.

individual sections. Important older studies may be discussed in detail to reinforce key concepts and conclusions and/or if they are open to reinterpretation in light of newer data. Older studies also may be the primary focus in some subject areas or scientific disciplines where research efforts have subsided, and these older studies remain the definitive works available in the literature. Emphasis will be placed on studies that examine health effects relevant to humans and concentrations of oxides of nitrogen that represent the range of human exposures across ambient microenvironments. Other studies, generally at higher exposure concentrations, may be included if they contain unique data, such as previously unreported effects, evidence of the potential biological mechanism(s) for an observed effect, or information on concentration-response relationships.

## **4.2 ORGANIZATION OF THE ISA**

The organization of the ISA for the health criteria of oxides of nitrogen will be consistent with that used in the recent assessments for other criteria pollutants (e.g., ISA for Ozone and Related Photochemical Oxidants, U.S. EPA, 2013c). The ISA will begin with a discussion of major legal and historical aspects of prior NAAQS reviews as well as procedures for the assessment of scientific information. An integrative synthesis chapter will summarize the key information for each topic area, the causal determinations for relationships between exposure to oxides of nitrogen and health effects, information describing the extent to which health effects can be attributable specifically to oxides of nitrogen, and other uncertainties related to the interpretation of scientific information. The integrative synthesis chapter also will discuss policy-relevant issues such as the exposure averaging times and lags associated with health effects, the concentration-response relationships including whether or not the evidence supports identification of a discernible threshold below which effects are not likely to occur, and the public health significance of effects associated with exposure to oxides of nitrogen. Subsequent chapters are organized by subject area (see draft outline of the ISA in Appendix A) and contain the detailed evaluation of results from recent studies integrated with previous findings (see section 4.4 for specific issues to be addressed). Sections for each major health effect category (e.g., respiratory effects) conclude with a causal determination about the relationship with relevant exposures to oxides of nitrogen. The ISA will conclude with a chapter that examines exposure and health outcome data to draw conclusions about potential at-risk lifestyles and populations.

The ISA may be supplemented with other materials if additional documentation is required to support information contained within the ISA. These supplementary materials may include more detailed and comprehensive coverage of relevant publications and may accompany the ISA or be available in electronic form as output from the Health and Environmental Research

1 Online (HERO) database developed by EPA (<http://hero.epa.gov/>). Supplementary information  
2 that is available in the HERO database will be presented as electronic links in the ISA.

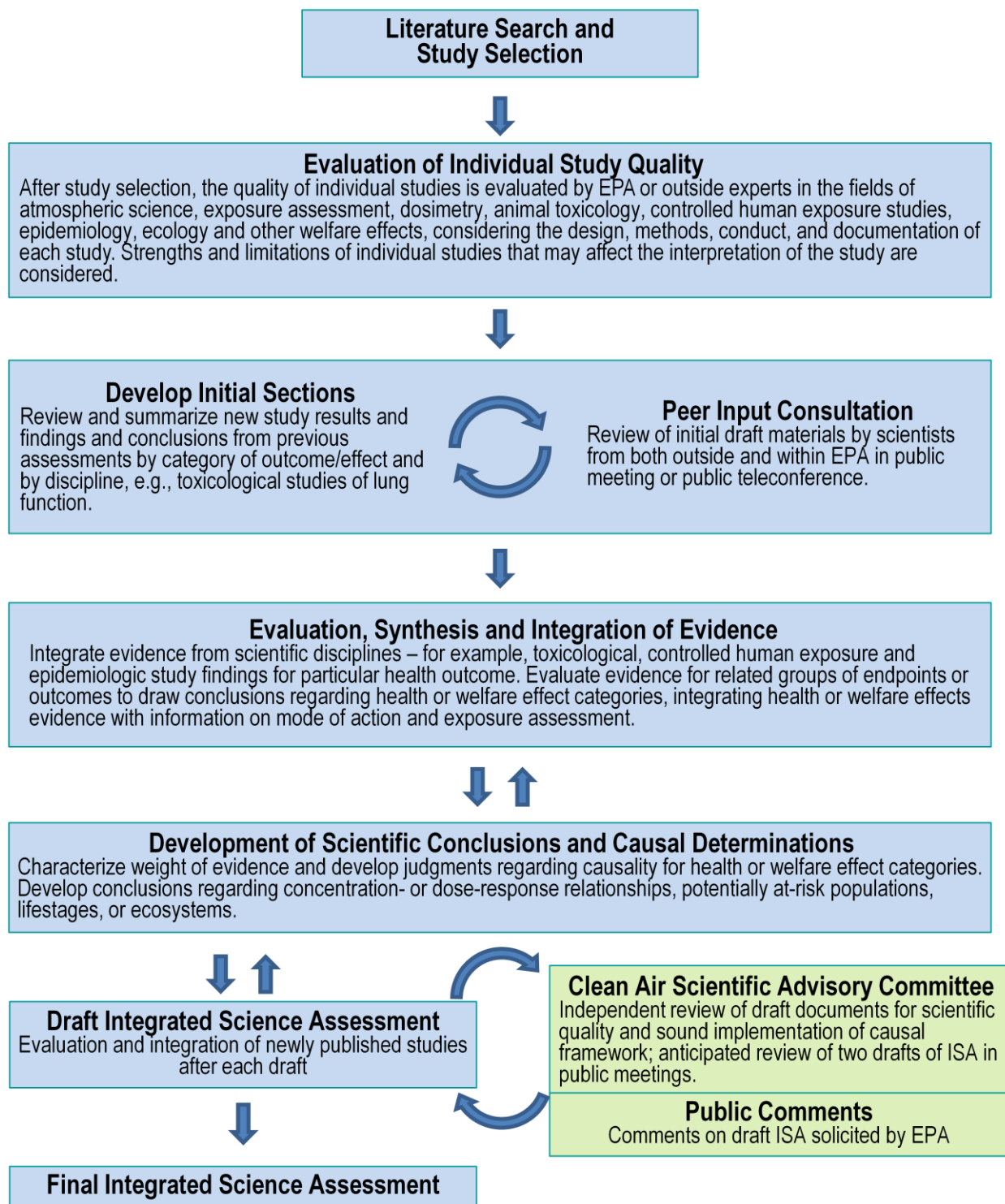
### 3 **4.3 ASSESSMENT APPROACH**

#### 4 **4.3.1 Introduction**

5 The NCEA-RTP is responsible for preparing the ISA. In each NAAQS review,  
6 development of the science assessment begins with a “Call for Information” published in the  
7 *Federal Register*. This notice announces EPA’s initiation of activities in the preparation of the  
8 ISA for the specific NAAQS review and invites the public to assist through the submission of  
9 research studies in the identified subject areas. This and subsequent key components of the  
10 process currently followed for the development of an ISA (i.e., the development process) are  
11 presented in Figure 4-1 and are described in greater detail in the Preamble to the ISA. Section 1.2  
12 above briefly describes how the ISA fits into the larger NAAQS review process.  
13 Important aspects of the development of the ISA are described in the sections below, including  
14 the approach for searching the literature and identifying relevant publications and informing  
15 specific policy-relevant questions that are intended to guide the assessment. These  
16 responsibilities are undertaken by expert authors of the ISA chapters which include EPA staff  
17 with extensive knowledge in their respective fields and extramural scientists solicited by EPA for  
18 their expertise in specific fields. The process for scientific and public review of drafts of the ISA  
19 is described in section 4.5 below.



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Source: Modified from Figure II of the Preamble to the ISA (U.S. EPA, 2013b).

**Figure 4-1. General process for development of Integrated Science Assessments.**

### 4.3.2 Literature Search and Selection of Relevant Studies

The NCEA-RTP uses a structured approach to identify relevant studies for consideration and inclusion in the ISA. A *Federal Register* notice is published to announce the initiation of a review and request information, including relevant literature, from the public. In addition, publications are identified by the EPA through a recursive multi-tiered literature search process that includes extensive manual and computer-aided citation mining of computer databases on specific topics in a variety of disciplines using as keywords terms such as oxides of nitrogen, NO<sub>x</sub>, NO<sub>2</sub>, NO, nitric acid, peroxyacetyl nitrate, and total reactive nitrogen. The search strategies are designed *a priori* and iteratively modified to optimize identification of pertinent published papers. Papers are identified for inclusion in several additional ways: specialized searches on specific topics; relational searches that identify recent publications that have cited references from previous assessments; identification of relevant literature by expert scientists; recommendations from the public and CASAC during the call for information and external review process; and review of citations in previous assessments. These search methods are used to identify recent research published or accepted for publication since the 2008 ISA for Oxides of Nitrogen, i.e., starting in January 2008 through approximately two months before the release of the second external review draft of the ISA (target of July/August 2014, see Table 2-1). Studies published after that date may also be included in the ISA if they provide new information that impacts one or more key scientific issues. Studies published after the ISA cut-off date also may be considered in subsequent phases of the NAAQS review, after assessing whether they provide new information that impacts key scientific issues.

Once identified through the multipronged search strategy, studies are reviewed for relevance. Relevant publications are epidemiological, toxicological, and controlled human exposure studies that examine health effects in relation to exposure to oxides of nitrogen as well as studies on sources, emissions, atmospheric chemistry, human exposure, dosimetry, and modes of action of oxides of nitrogen. Relevant publications include studies and reports that have undergone scientific peer review and have been published or accepted for publication. Some publications are excluded as not being relevant based on screening of the title. Publications considered for inclusion in the ISA after reading the title are documented in the HERO database.

From the group of considered references, studies and reports are selected for inclusion in the ISA based on review of the abstract and full text. The selection process is based on the extent to which the study is potentially informative and policy-relevant. Potentially policy-relevant and informative studies include those that provide a basis for or describe the relationship between the criteria pollutant and effects, in particular, those studies that offer innovation in method or design and studies that reduce uncertainty on critical issues. Uncertainty can be addressed, for example,

by analyses of potential confounding or effect modification by copollutants or other factors, analyses of concentration-response or dose-response relationships, or analyses related to time between exposure and response. In keeping with the purpose to accurately reflect the latest scientific knowledge, the ISA generally will emphasize studies published since the 2008 ISA. However, evidence from previous studies will be included to integrate with results from recent studies, and in some cases, characterize the key policy-relevant information in a particular subject area or scientific discipline. Analyses conducted by the EPA using publicly available data, for example, air quality and emissions data, also are considered for inclusion in the ISA. The combination of approaches described above is intended to produce the comprehensive collection of pertinent studies needed to address the key scientific issues that form the basis of the ISA. References are cited in the ISA by a hyperlink to the HERO database and also are compiled into reference lists.

### **4.3.3 Evaluation of Individual Study Quality**

After selecting studies for inclusion, individual study quality is evaluated by considering the design, methods, conduct, and documentation of each study but not considering whether the study results are positive, negative, or null. This uniform approach aims to consider the strengths, limitations, and possible roles of chance, confounding, and other biases that may affect the interpretation of the results from individual studies. In assessing the scientific quality of studies, the following parameters are considered:

- How clearly were the study design, study groups, methods, data, and results presented to allow for study evaluation?
- To what extent are the air quality data, exposure, or dose metrics of adequate quality to serve as credible exposure indicators?
- Were the study populations, subjects, or animal models adequately selected, and are they sufficiently well defined to allow for meaningful comparisons between study or exposure groups?
- Are the statistical analyses appropriate, properly performed, and properly interpreted? Do the analytical methods provide adequate sensitivity and precision to support study conclusions?
- Are likely covariates (i.e., potential confounding factors, modifying factors) adequately controlled for or taken into account in the study design or statistical analyses?
- Are the health endpoint measurements meaningful, valid, and reliable?

Additional considerations specific to particular scientific disciplines are discussed below.

Atmospheric Science and Exposure Assessment

1 Atmospheric science and exposure assessment studies focus on measurement of,  
2 chemistry, fate, and transport of, and exposure to ambient air pollution using quality-assured  
3 field, experimental, and/or modeling techniques. The most informative measurement-based  
4 studies will include detailed descriptive statistics for high-quality measurements made at varying  
5 spatial and temporal scales. These studies will also include a clear and comprehensive  
6 description of measurement techniques and quality control procedures used. Quality control  
7 metrics (e.g., method detection limits) and quantitative relationships between and within  
8 pollutant measurements (e.g., regression model coefficients, intercepts, and fit statistics) should  
9 be provided when appropriate. Measurements including contrasting conditions for various time  
10 periods (e.g., weekday/weekend, season), populations, geographic regions, land use types (e.g.,  
11 urban/rural), and proximity to various source sectors are particularly useful. The most  
12 informative modeling-based studies will incorporate appropriate chemistry, transport, dispersion,  
13 and/or exposure modeling techniques with a clear and comprehensive description of model  
14 science, evaluation procedures, and metrics.

15 Exposure measurement error, which refers to the uncertainty associated with the exposure  
16 metrics used to represent exposure of an individual or population, can be an important  
17 contributor to uncertainty in air pollution epidemiological study results. Exposure measurement  
18 error can influence epidemiological associations observed between ambient pollutant  
19 concentrations and health outcomes by biasing effect estimates toward or away from the null and  
20 widening confidence intervals around those estimates (Zeger et al., 2000). Factors that could  
21 influence exposure estimates include, but are not limited to, non-ambient sources of exposure,  
22 topography of the natural and built environment, meteorology, air quality measurement  
23 instrument errors, model uncertainties, time-activity patterns, and the infiltration of outdoor  
24 pollutants into indoor environments. Additional information present in high-quality exposure  
25 studies includes location and activity information from diaries, questionnaires, global positioning  
26 system data, or other means, as well as information on commuting patterns.

## 27 Epidemiology

28 In evaluating quality of epidemiological studies, the EPA additionally considers whether a  
29 given study: (1) presents quantitative information on associations of health effects with short- or  
30 long-term exposures that represent ambient concentrations of oxides of nitrogen across various  
31 microenvironments; (2) examines health effects of specific oxides of nitrogen; (3) assesses  
32 oxides of nitrogen as a component of a complex mixture of air pollutants by considering  
33 concentrations of copollutants, correlations of oxides of nitrogen with these copollutants,  
34 potential copollutant interactions (e.g., synergistic effects of oxides of nitrogen with other  
35 pollutants), potential copollutant confounding (e.g., bias of associations observed between oxides

of nitrogen and health endpoints by the effects of copollutants), and other methods to assess the independent effect of oxides of nitrogen; (4) evaluates health endpoints not previously extensively researched; (5) evaluates lifestages or populations that potentially are at increased risk of health effects related to oxides of nitrogen; (6) examines other potential confounding factors or effect modifiers (e.g., socioeconomic status [SES]); and/or (7) examines important methodological issues (e.g., lag or time period between exposure and effects, model specifications, thresholds, mortality displacement) related to the health effects of exposure to oxides of nitrogen. Among epidemiological studies characterized as high quality by these parameters, emphasis will be given to multicity studies that employ standard methodological analyses for evaluating effects of oxides of nitrogen across cities, provide overall estimates for effects by pooling information across cities, and examine consistency of results across cities. To address specific issues relevant to standard setting in the U.S., such as regional heterogeneity in effects, emphasis will be placed on studies that involve exposures and population characteristics that are relevant to current U.S. populations (e.g., studies conducted in the U.S. or Canada).

#### Controlled Human Exposure and Animal Toxicology

Controlled human exposure and animal toxicological studies experimentally evaluate the health effects of administered exposures in human volunteers and animal models under highly controlled laboratory conditions. Controlled human exposure studies are also referred to as human clinical studies. These experiments allow investigators to expose subjects or animal models to known concentrations of oxides of nitrogen under carefully regulated environmental conditions and/or activity levels. In addition to the general quality considerations discussed previously, evaluation of controlled human exposure and animal toxicological studies includes assessing the design and methodology of each study with focus on: (1) characterization of the intake dose, dosing regimen (e.g., duration), and exposure route; (2) characterization of the pollutant(s) (i.e., oxides of nitrogen species); (3) sample size and statistical power to detect differences; and (4) control of other variables that could influence the occurrence of effects. The evaluation of study design generally includes consideration of factors that minimize bias in results such as randomization, blinding and allocation concealment of study subjects, investigators, and research staff, and unexplained loss of animals or withdrawal/exclusion of subjects. Additionally, studies must include appropriate control groups and exposures to allow for accurate interpretation of results relative to exposure. Emphasis is placed on studies that address concentration-dependent responses or time-course of responses. Also, with the recognition that controlled human exposure studies typically are conducted in young adults and healthy individuals, emphasis will be placed on studies that investigate potentially at-risk lifestages or populations (e.g., with pre-existing disease). In addition, consideration will be given

1 to studies that investigate exposure to oxides of nitrogen separately and in combination with  
2 other pollutants such as ozone, PM, and sulfur dioxide.

3 Controlled human exposure or animal toxicological studies involving exposures that  
4 approximate expected human exposures in terms of concentration, duration, and route of  
5 exposure are of particular interest. Relevant pollutant exposures are considered to be those  
6 generally within two orders of magnitude of ambient concentrations measured across various  
7 microenvironments. Studies using higher concentration exposures or doses will be considered to  
8 the extent that they provide information relevant to understanding mode of action or  
9 mechanisms, interspecies variation, or at-risk human lifestages and populations. *In vitro* studies  
10 may be included if they provide mechanistic insight or support results demonstrated *in vivo*.

#### 11 **4.3.4 Integration of Evidence and Determination of Causality**

12 As described in the Preamble to the ISA, the EPA uses a consistent and transparent basis  
13 for the integration of scientific evidence and evaluation of the causal nature of air  
14 pollution-related health effects in the ISA. The evidence evaluated from previous and recent  
15 studies is integrated across scientific disciplines and related health effects to form causal  
16 determinations. Evaluation of human health effects is informed by controlled human exposure,  
17 epidemiological, and toxicological studies. Other information including mechanistic evidence,  
18 toxicokinetics, and exposure assessment may be highlighted if it is relevant to the evaluation of  
19 health effects and if it is of sufficient importance to affect the overall evaluation. The relative  
20 importance of different sources of evidence to the conclusions varies by pollutant or assessment,  
21 as does the availability of different sources of evidence for causality determination. In judgments  
22 of causality, scientists will also evaluate uncertainty in the scientific evidence, considering issues  
23 such as generalizing results from a small number of controlled human exposure subjects to the  
24 larger population; quantitative extrapolations of observed pollutant-induced pathophysiological  
25 alterations from laboratory animals to humans; confounding by co-exposure to other ambient  
26 pollutants, meteorological factors, or other factors; the potential for effects to be due to exposure  
27 to air pollution mixtures; and the influence of exposure measurement error on epidemiological  
28 study findings.

29 The EPA uses a framework to provide a consistent and transparent basis for classifying  
30 the weight of available evidence according to a five-level hierarchy: (1) causal relationship; (2)  
31 likely to be a causal relationship; (3) suggestive of a causal relationship; (4) inadequate to infer a  
32 causal relationship; and (5) not likely to be a causal relationship (U.S. EPA, 2013c, Table II). In  
33 the framework, key considerations in drawing conclusions about causality include consistency of  
34 findings for an endpoint across studies, coherence of the evidence across disciplines and across  
35 related endpoints, and biological plausibility, including key events that inform modes of action.

Causal determinations are developed for major outcome categories (e.g., respiratory effects) or more specific groups of related endpoints and for the range of exposure concentrations of oxides of nitrogen that are representative of those across various ambient microenvironments. Findings based on higher exposure concentrations may be considered if they inform biological plausibility and potential modes of action. Causal determinations are based on the confidence in the body of evidence, considering study design and quality and strengths and weaknesses in the overall collection of studies across disciplines. In discussing the causal determination, the EPA characterizes the evidence on which the judgment is based, including weight of evidence for individual endpoints within the outcome category or group of related endpoints.

#### **4.3.5 Quality Management**

NCEA participates in the Agency-wide Quality Management System, which requires the development of a Quality Management Plan (QMP). Implementation of the NCEA QMP ensures that all data generated or used by NCEA scientists are “of the type and quality needed and expected for their intended use” and that all information disseminated by NCEA adheres to a high standard for quality including objectivity, utility, and integrity. Quality assurance (QA) measures detailed in the QMP are being employed for the current primary NO<sub>2</sub> NAAQS review, including the development of the ISA for the health criteria of oxides of nitrogen. The NCEA QA staff is responsible for the review and approval of quality-related documentation. NCEA scientists are responsible for the evaluation of all inputs to the ISA, including primary (new) and secondary (existing) data, to ensure their quality is appropriate for their intended purpose. NCEA adheres to Data Quality Objectives, which identify the most appropriate inputs to the science assessment and provide QA instruction for researchers citing secondary information. The approaches utilized to search the literature and criteria for study selection and evaluation were detailed in the two preceding subsections. Generally, NCEA scientists rely on scientific information found in peer-reviewed journal articles, books, and government reports. The ISA also can include information that is integrated or reduced from multiple sources to create new figures, tables, or summation, which is subject to rigorous quality assurance measures to ensure their accuracy.

#### **4.4 SPECIFIC ISSUES TO BE ADDRESSED IN THE ISA**

The ISA for oxides of nitrogen will contain information relevant to considering whether it is appropriate to retain or revise the current primary NO<sub>2</sub> standards. Decisions on the specific content of the ISA will be guided by policy-relevant questions that frame the entire review of the primary NO<sub>2</sub> NAAQS as outlined in section 3.2 above. These policy-relevant questions are related to two overarching issues. The first issue is whether new evidence reinforces or calls into question the evidence presented and evaluated in the last primary NO<sub>2</sub> NAAQS review with

respect to factors such as the concentrations of oxides of nitrogen associated with health effects and plausibility of health effects caused by exposure to oxides of nitrogen. The second issue is whether uncertainties from the last review have been reduced and/or whether new uncertainties have emerged. The ISA also will address a set of more specific policy-relevant questions related to the available scientific evidence that stem from these issues. These questions were derived from the last primary NO<sub>2</sub> NAAQS review, as well as from discussions of the scientific evidence that occurred at the February/March 2012 kickoff workshop for the current review (77 FR 7149, February 10, 2012); a CASAC consultation on the draft plan for development of the ISA (U.S. EPA, 2013a; 78 FR 27234, May 9, 2013); and a public workshop that included review of initial draft materials for the ISA (78 FR 27374, May 10, 2013). The specific questions to be addressed in the ISA are listed below by topic area. In the ISA, these topic areas will be discussed in separate chapters or sections.

### **Atmospheric Science and Ambient Concentrations**

The ISA will present and evaluate data related to ambient concentrations of oxides of nitrogen; sources leading to the presence of oxides of nitrogen in the atmosphere; and chemical reactions that determine the formation, degradation, and lifetime of oxides of nitrogen in the atmosphere. Key conclusions from the 2008 ISA were that motor vehicles and power plants are the major U.S. sources of NO<sub>x</sub> emissions and that ambient concentrations of NO<sub>2</sub> display heterogeneity across spatial and temporal scales, are higher near roadways, and are correlated with ambient concentrations of several other traffic-related pollutants (U.S. EPA, 2008a, section 5.2.1). The formation and reactions of NO<sub>2</sub> are strongly influenced by volatile organic compounds and O<sub>3</sub>. The relationships among these pollutants are critical to the understanding of ambient NO<sub>2</sub> concentrations. In the current review, with regard to air quality and atmospheric chemistry, specific policy-relevant questions that will be addressed include:

- What new information is available to inform our understanding of the atmospheric chemistry of oxides of nitrogen? How does new information characterize the role of atmospheric chemistry in determining relationships among oxides of nitrogen species? What new information is available with respect to nitroaromatics and nitropyrenes, which have shown toxic effects and thus, may be important in assessing health effects from multipollutant exposures? How does the near-source environment (e.g., near major highways or large combustion sources) influence chemistry of oxides of nitrogen?
- What new information exists regarding characterization of sources of ambient oxides of nitrogen in both urban and rural environments? What are the relevant spatial and temporal scales for considering ambient emissions of oxides of nitrogen? What new information is available regarding existing and emerging sources of energy and impacts on emissions of oxides of nitrogen?
- To what extent have new methods been developed to improve measurements of oxides of nitrogen, particularly those that measure NO<sub>2</sub> directly? How have these new methods



1 reduced interference problems in measuring oxides of nitrogen? What limitations still  
2 remain?

- 3 • Based on recent air quality and emissions data, what do we know about recent emissions  
4 and resulting ambient concentrations of oxides of nitrogen? How have emissions and  
5 concentrations of NO<sub>x</sub> and of NO<sub>2</sub> changed since the 2008 ISA? To what extent can new  
6 data sources (e.g., satellites) or air quality analyses be used to improve the  
7 characterization of ambient concentrations of oxides of nitrogen?
- 8 • What spatial and temporal patterns can be seen in ambient NO<sub>2</sub> and NO<sub>x</sub> concentrations?  
9 In particular, what spatial and temporal patterns can be seen on a micro-scale near  
10 sources including major roadways and combustion sources such as power plants and  
11 biomass burning? What do ambient air quality characterizations (including examinations  
12 of the influence of meteorological parameters) indicate regarding spatial patterns on  
13 neighborhood, urban, regional, and national scales?
- 14 • Based on air quality and emissions data for oxides of nitrogen and atmospheric chemistry  
15 models, what are likely background concentrations of oxides of nitrogen in the absence of  
16 anthropogenic emissions?
- 17 • What new information is available to characterize the influence of meteorological  
18 parameters on micro- to neighborhood-scale concentrations of oxides of nitrogen?

## 19 **Human Exposure**

20 The ISA will evaluate the factors that influence exposure to ambient oxides of nitrogen  
21 and the measurement error and other uncertainties associated with extrapolation of ambient  
22 concentrations to personal exposures to oxides of nitrogen of ambient origin, particularly in the  
23 context of interpreting results from epidemiological studies. The evaluation will build upon the  
24 discussion in the 2008 ISA, which concluded that measurement error associated with using  
25 ambient NO<sub>2</sub> concentrations obtained from central site monitors as measures of exposure in  
26 epidemiological studies tended to bias the magnitude of associations between ambient NO<sub>2</sub> and  
27 health effects toward the null (U.S. EPA, 2008a, section 5.2.2). Uncertainties related to exposure  
28 measurement error differ by the exposure period of interest as most epidemiological studies of  
29 short-term exposure (e.g., population-level studies using time-series analyses, field/panel studies)  
30 rely on temporal variation in exposure while epidemiological studies of long-term exposure (e.g.,  
31 longitudinal cohort studies) rely on spatial variability of exposure. In the current review, with  
32 regard to exposure, specific policy-relevant questions that will be addressed include:

- 33 • How have modeling techniques such as sub-grid scale modeling within chemical  
34 transport models, air quality dispersion models, and land use regression models been  
35 advanced in recent years? What new information is available regarding modeled  
36 estimates of spatially-resolved (at the micro-, middle-, and neighborhood scales) ambient  
37 NO<sub>2</sub> and NO<sub>x</sub> concentrations used for exposure assessment?
- 38 • How have ambient models been merged with stochastic population exposure models  
39 recently to improve estimates of exposure? What advancements have been made

1 regarding validation of stochastic population exposure models and their ability to  
2 estimate source attribution for exposures to NO<sub>2</sub> or NO<sub>x</sub>?

- 3 • What are the relationships between oxides of nitrogen measured at stationary monitoring  
4 sites and personal exposure? What evidence is available regarding these relationships in  
5 environments near roads or other sources?
- 6 • What new information exists about the relationship between NO, NO<sub>2</sub>, and NO<sub>x</sub>  
7 concentrations and indicators of near-source pollution including distance to sources (e.g.,  
8 major roadways) and source activity levels (e.g, traffic counts)?
- 9 • What studies are available to examine the relationship between near-road oxides of  
10 nitrogen, on-road oxides of nitrogen, and in-vehicle exposures to oxides of nitrogen?  
11 Given the concern over short-term exposures at or less than one hour in duration, are the  
12 directly emitted NO<sub>2</sub>/NO<sub>x</sub> ratios sufficiently high such that on-road NO<sub>2</sub> exposure is a  
13 significant component of total NO<sub>2</sub> exposure?
- 14 • To what extent is information available characterizing how well the current near-road  
15 NO<sub>2</sub> monitoring sites represent exposures to populations living near major roads?
- 16 • What new information exists regarding indoor exposures to oxides of nitrogen, including  
17 those generated indoors and those that infiltrate from outdoors? What new information is  
18 available regarding how oxides of nitrogen are generated indoors?
- 19 • What new information exists regarding characterization of error in exposure assessment  
20 of oxides of nitrogen and how it influences personal-ambient exposure relationships?
- 21 • What information is available regarding differences in exposure patterns for oxides of  
22 nitrogen and personal-ambient exposure relationships among various lifestages and  
23 populations?
- 24 • What are the implications for epidemiology for assessing health effects of exposures to  
25 oxides of nitrogen when there are instrumentation errors, such as measurements of  
26 ambient concentrations being subject to interferences from other nitrogen compounds?
- 27 • What new information exists regarding oxides of nitrogen measurements in a  
28 multipollutant context? To what extent do NO<sub>2</sub> measurements serve as surrogates of  
29 exposure to other gaseous pollutants (e.g., carbon monoxide, nitrous acid), particle phase  
30 pollutants (e.g., ultrafine particles, black carbon, organic carbon, transition metals)  
31 generated by traffic or other combustion sources, or a mixture of traffic-related  
32 pollutants?
- 33 • What new information is available regarding the interaction of oxides of nitrogen with  
34 organic compounds emitted from home cleaning and deodorizing products to form  
35 organic nitrates indoors that may influence human exposure to NO<sub>2</sub>?

## 36 **Dosimetry and Modes of Action**

37 The ISA will evaluate literature focusing on dosimetry and modes of action that may  
38 underlie the health outcomes associated with exposure to NO<sub>2</sub> and/or NO. These topic areas will  
39 be evaluated using both human and animal data. The 2008 ISA concluded that ambient-relevant  
40 concentrations of inhaled NO<sub>2</sub> are consumed by constituents of the epithelial lining fluid of the

1 respiratory tract, including antioxidants, to form secondary reaction products (U.S. EPA, 2008a,  
2 section 2.6). These secondary reaction products initiate a cascade of events that are thought to be  
3 responsible for health effects observed in association with NO<sub>2</sub> exposure. Additionally, findings  
4 of NO<sub>2</sub>-induced changes in airway responsiveness, airway inflammation, and lung host defenses  
5 were described as key mechanistic support for NO<sub>2</sub>-related respiratory effects such as respiratory  
6 symptoms and ED visits. In the current review, specific policy-relevant questions related to  
7 dosimetry and modes of action that will be addressed include:

- 8 • What new information is available to inform our understanding of the potential biological  
9 mechanisms underlying responses to NO<sub>2</sub> and/or NO exposures at or near  
10 environmentally-relevant concentrations, with a focus on response pathway(s) and  
11 exposure-dose-response relationships?
- 12 • What information is available to characterize intra- and inter-individual variability in  
13 biological responses following exposure to NO<sub>2</sub> and/or NO?
- 14 • What are the effects of host factors such as lifestage, sex, pre-existing disease, genetic  
15 background, and physical activity on the uptake of NO<sub>2</sub> and/or NO and cellular and tissue  
16 responses as well as biological mechanisms that may underlie health effects associated  
17 with exposure to oxides of nitrogen?
- 18 • What information is available to discern the relative contributions to internal NO<sub>2</sub> and/or  
19 NO of: (1) ambient exposures to NO<sub>2</sub> and/or NO; (2) dietary consumption of nitrite and  
20 nitrate which undergo transformation to NO; and (3) endogenous formation of NO<sub>2</sub>  
21 and/or NO?
- 22 • What NO<sub>2</sub> and/or NO reaction products, including oxides of nitrogen metabolites, can be  
23 found in the cells, tissues, or fluids of the respiratory tract and in the systemic circulation  
24 that may serve as markers of NO<sub>2</sub> and/or NO exposure and effect?
- 25 • What biological processes, from the molecular to whole organ level, can be qualitatively  
26 compared across species?
- 27 • To what extent can the inhalation dosimetry of NO<sub>2</sub> and/or NO be extrapolated between  
28 species, qualitatively or quantitatively?
- 29 • Do interactions between inhaled NO<sub>2</sub> and/or NO and other inhaled pollutants influence  
30 the mechanisms underlying the toxic potential of NO<sub>2</sub> and/or NO?

## 31 **Health Effects**

32 In the 2008 ISA, the health effects evidence for oxides of nitrogen was largely indexed by  
33 studies of NO<sub>2</sub> with the bulk of the evidence provided by short-term exposure studies evaluating  
34 respiratory effects. The EPA will build on this assessment and evaluate the newly available  
35 literature related to respiratory, cardiovascular, reproductive, and developmental health effects,  
36 mortality, and cancer associated with exposure to oxides of nitrogen. Depending on data  
37 availability, other health effects also may be evaluated, for example, those related to the central  
38 nervous system or gastrointestinal system. Health effects that occur following both short- and

1 long-term exposures as examined in epidemiological, controlled human exposure, and animal  
2 toxicological studies will be evaluated. Efforts will be directed at identifying the concentrations  
3 at which effects are observed, including those in potential at-risk lifestages and populations, and  
4 assessing the role of oxides of nitrogen within the broader mixture of ambient pollutants. The  
5 discussion of health effects also will be integrated with relevant information on dosimetry and  
6 modes of action. In the current review, with regard to consideration of health effects associated  
7 with short-and long-term exposure to oxides of nitrogen, specific policy-relevant questions that  
8 will be addressed include the following:

9 *Short-Term Exposure*

- 10 • What do controlled human exposure, animal toxicological, and epidemiological studies  
11 indicate regarding the relationship between short-term exposures to oxides of nitrogen  
12 and health effects of concern (e.g., respiratory effects, cardiovascular effects, premature  
13 mortality)?
- 14 • How does evidence for health effects associated with oxides of nitrogen compare among  
15 healthy individuals, those with pre-existing disease states (e.g., people with asthma or  
16 cardiovascular disease), particular lifestages, or groups characterized by other factors that  
17 potentially modify risk (e.g., genetic, nutritional)?
- 18 • At what ambient concentrations of oxides of nitrogen are associations with the various  
19 health effects observed in epidemiological studies most well characterized?
- 20 • To what extent does the scientific evidence support the occurrence of health effects  
21 associated with short-term (i.e., minutes up to 1 month) exposure to oxides of nitrogen at  
22 ambient concentrations that are lower than those previously demonstrated? If so, what  
23 uncertainties are related to these associations and are the health effects in question  
24 important from a public health perspective?
- 25 • How do results of recent studies or new interpretations of previous findings expand our  
26 understanding of the relationship between short-term exposure to oxides of nitrogen and  
27 airway hyperresponsiveness or other lung function changes, inflammation, host defense  
28 against infection disease, and respiratory symptoms?
- 29 • What are the effects of oxides of nitrogen exposure on cardiovascular health in humans  
30 (e.g., inflammation, heart rate variability, arrhythmias, vasomotor function, risk of  
31 myocardial infarction)?
- 32 • How do results from recent population-level time-series studies expand our  
33 understanding of relationships between exposure to oxides of nitrogen and mortality (all  
34 nonaccidental-cause, respiratory, cardiovascular), hospital admissions, or emergency  
35 department visits?
- 36 • To what extent does short-term exposure to oxides of nitrogen contribute to health effects  
37 beyond the respiratory and cardiovascular systems?
- 38 • What is the extent of coherence of findings for changes in lung function, airway  
39 hyperresponsiveness, heart rate variability, and vasomotor function and effects such as

hospital admissions, emergency department visits, and mortality? What other biomarkers of early effect may be used in the assessment of health effects?

- What evidence is available regarding the shape of concentration-response relationships between short-term exposure to oxides of nitrogen and various health endpoints?
  - Is there evidence to support the identification of a discernible threshold below which health effects will not occur?
- What evidence is available regarding the nature of health effects from interactions between oxides of nitrogen and other ambient air pollutants in comparison to health effects following exposure to oxides of nitrogen alone?
  - To what extent are the observed epidemiological health effect associations attributable to ambient oxides of nitrogen, another ambient pollutant, or to the pollutant mixtures that oxides of nitrogen may be representing? What information is available specifically from studies conducted near roads or other sources? To what extent do findings from experimental studies provide biological plausibility for the effects observed in epidemiologic studies?
- To what extent does information across scientific disciplines on the pattern of exposure to oxides of nitrogen (e.g., peak, repeated peak, average) provide understanding of the time course for changes in health effects? What information is available on time-activity patterns of study subjects such as time spent outdoors or activity levels that can aid in the understanding of nature of exposure or dosimetry of ambient oxides of nitrogen that are associated with health effects?
- To what extent do data across scientific disciplines provide information on health effects related to specific oxides of nitrogen (e.g., NO<sub>2</sub>, NO) or averaging times of exposure to oxides of nitrogen that are relevant to the 1-hour standard? What data exist comparing associations of health effects among various short-term metrics of exposure to oxides of nitrogen (e.g., 1-hour versus 24-hour)?

#### *Long-Term Exposure*

- How do results of recent studies expand our understanding of the relationships between long-term exposure to oxides of nitrogen and chronic respiratory effects manifested as morphological changes, a reduction in baseline lung function, or a reduction in lung function growth?
- To what extent does long-term exposure to oxides of nitrogen promote exacerbation and development of asthma or other chronic lung diseases, cardiovascular diseases, and other conditions?
- What is the relationship between long-term exposure to oxides of nitrogen and all-cause mortality and cardiovascular and respiratory mortality?
- To what extent does long-term exposure to oxides of nitrogen contribute to other health effects or changes in molecular and cellular processes, e.g., cognitive, behavioral, reproductive, developmental, cancer or epigenetic effects?
- How does evidence for health effects associated with oxides of nitrogen compare among healthy individuals, those with pre-existing disease states (e.g., people with asthma or

cardiovascular disease), particular lifestages, or other factors that potentially modify risk (e.g., genetic, nutritional)?

- At what ambient concentrations of oxides of nitrogen are associations observed in epidemiological studies most well characterized?
- To what extent does the scientific evidence support the occurrence of health effects from long-term (i.e., more than 1 month to years) exposure to oxides of nitrogen at ambient concentrations that are lower than those previously demonstrated? If so, what uncertainties are related to these associations and are the health effects in question important from a public health perspective?
- What evidence is available regarding the shape of concentration-response relationships between long-term exposure to oxides of nitrogen and health effects?
  - Is there evidence to support the identification of a discernible threshold below which health effects will not occur?
- What evidence is available regarding the nature of health effects from interactions between long-term exposure to oxides of nitrogen and other ambient air pollutants in comparison to health effects following exposure to oxides of nitrogen alone?
  - To what extent are the observed epidemiological health effect associations attributable to ambient oxides of nitrogen, another ambient pollutant, or to the pollutant mixtures that oxides of nitrogen may be representing? What information is available specifically from studies conducted in populations living near roads or other sources? To what extent do findings from experimental studies provide biological plausibility for the effects observed in epidemiological studies?
- What information is available regarding the effect of long-term, low-concentration exposure to oxides of nitrogen on an individual's sensitivity to short-term but higher concentration exposures?
- What evidence is available regarding health effects related to long-term exposure windows other than annual or lifetime average (e.g., preconception, pregnancy average, pregnancy trimester average)? What data are available comparing associations of health effects among various long-term oxides of nitrogen exposure metrics (e.g., annual, seasonal, pregnancy average)?

## **Causality**

In the 2008 ISA, the EPA concluded that the findings of epidemiological, controlled human exposure, and animal toxicological studies collectively provided evidence “sufficient to infer a likely causal relationship” between short-term NO<sub>2</sub> exposures and respiratory effects (U.S. EPA, 2008a, sections 3.1.7 and 5.3.2.1). In looking at a broader range of health effects associated with short- or long-term exposures to oxides of nitrogen, the 2008 ISA concluded there was evidence “suggestive but not sufficient to infer a causal relationship” between short-term NO<sub>2</sub> exposures and premature mortality and between long-term NO<sub>2</sub> exposures and respiratory effects (U.S. EPA, 2008a, sections 5.3.2.3 and 5.3.2.4). Furthermore, the 2008 ISA

1 concluded that the scientific evidence was “inadequate to infer the presence or absence of a  
2 causal relationship” between short-term NO<sub>2</sub> exposures and cardiovascular effects as well as  
3 between long-term NO<sub>2</sub> exposures and cardiovascular effects, reproductive and developmental  
4 effects, premature mortality, and cancer (U.S. EPA, 2008a, sections 5.3.2.2, 5.3.2.5, and 5.3.2.6).

5 The causal determinations, based on the causal framework and integration of available  
6 evidence (see sections 4.3.3 and 4.3.4 above), are presented with a summary of the available  
7 evidence at the end of the sections for each health effect outcome category and in the integrative  
8 synthesis chapter at the beginning of the ISA. In the current review, specific policy-relevant  
9 questions related to the causality determinations that will be addressed include:

- 10 • Does the evidence base from recent studies contain new information to support or re-  
11 evaluate the causal determinations made for relationships between NO<sub>2</sub> exposure and  
12 various health effects in the 2008 ISA?
- 13 • What information is available to support a rationale for forming causal determinations for  
14 other oxides of nitrogen (e.g., NO, NO<sub>x</sub>)?
- 15 • What information is available regarding the health impacts of a decrease in ambient  
16 concentrations of oxides of nitrogen?

## 17 **Uncertainties/Limitations**

18 The causal determinations described above for the relationships between NO<sub>2</sub> exposure  
19 and health effects were informed by uncertainties and limitations in the evidence including the  
20 possibility that pollutants other than oxides of nitrogen in broad ambient mixture were  
21 responsible for health effects observed in association with NO<sub>2</sub> and/or limited information from  
22 experimental studies to provide biological plausibility. In each of the health effects sections and  
23 the integrative synthesis chapter, the ISA will evaluate uncertainties and limitations in the  
24 scientific data, particularly in relation to observed epidemiological findings and their coherence  
25 with human exposure and toxicological studies in terms of observed effects and biological  
26 pathways. These uncertainties also will inform causal determinations. In the current review,  
27 specific policy-relevant questions related to the evaluation of uncertainties/limitations that will  
28 be addressed include:

- 29 • To what extent are the observed health effect associations attributable specifically to  
30 ambient oxides of nitrogen versus other pollutants contained in the broader air pollution  
31 mixture? For example, the ISA will consider the possibility that ambient concentrations  
32 of NO<sub>2</sub> serve not only as an indicator for oxides of nitrogen but as a surrogate for  
33 exposure to other vehicle exhaust gaseous and particulate pollutants.
- 34 ○ What information about the independent health effects of exposure to oxides of  
35 nitrogen can be synthesized from the various lines of available evidence, for example,  
36 copollutant models, associations with other traffic-related pollutants, analysis of  
37 indoor NO<sub>2</sub>, comparisons of results from locations with varying pollutant mixtures,  
38 studies of traffic proximity or intensity, and experimental studies?

- How does confounding by co-exposure to other ambient pollutants (e.g., ozone, particulate matter, sulfur dioxide, carbon monoxide) or meteorological factors influence relationships observed between health effects and both short- and long-term exposures to oxides of nitrogen? To what extent do other factors serve as potential confounding factors in epidemiological studies (e.g., demographic and lifestyle attributes, other exposures such as noise)?
- What information is available to assess the influence of exposure measurement error on uncertainty in epidemiological study results?
  - How can the influence of exposure measurement error be assessed through the examination of various study designs, study populations and locations, exposure assessment methods, and analytical models?
  - What information is available regarding the time-activity patterns of study subjects including time spent outdoors, spatial distribution of study subjects and ambient monitors, exposure assessment methods, potential interference in the measurement of NO<sub>2</sub> from other oxides of nitrogen in low traffic, downwind locations?

## **At-risk Lifestages and Populations**

The 2008 ISA discussed persons with pre-existing respiratory disease (e.g., people with asthma), children, and older adults as populations and lifestages potentially at greater risk of NO<sub>2</sub>-related health effects (U.S. EPA, 2008a, section 5.3.2.8). Since completion of the 2008 ISA, the EPA has developed a framework to provide a consistent and transparent basis for classifying the weight of evidence about at-risk lifestages or populations according to one of four levels: adequate evidence, suggestive evidence, inadequate evidence, and evidence of no effect (U.S. EPA, 2013c, Table 8-1). In this framework, key considerations in drawing such conclusions include consistency of findings for a factor within a discipline and coherence of the evidence across disciplines. The ISA will evaluate an array of factors that may characterize potential at-risk lifestages or populations: intrinsic factors (biological factors such as age or genetic variants), acquired factors (e.g., pre-existing disease), extrinsic factors (nonbiological factors such as diet, lower socioeconomic status), and/or factors affecting dose or exposure (sex, age, outdoor activity or work, lower socioeconomic status, physical activity). The ISA will not distinguish among risk due to intrinsic, extrinsic, or other types of factors. The various factors listed above (e.g., age) may influence risk through various mechanisms, including increasing exposure, dose, or increasing biological effect for a given dose, and some factors may contribute to risk via multiple mechanisms. In the current review, with regard to at-risk lifestages and populations, specific policy-relevant questions that will be addressed include:

- Based on evidence integrated across studies and disciplines that examine factors that may increase exposure to oxides of nitrogen and/or risk of health effects related to exposure to oxides of nitrogen, what conclusions can be drawn about the presence of at-risk lifestages (e.g., the developing fetus, children, older adults) or populations?



- Which disciplines contribute information about particular at-risk lifestyles and populations, and to what extent does limited or lack of information from specific disciplines produce uncertainty in conclusions about at-risk lifestyles and populations?
- How does new information compare with that evaluated in the 2008 ISA regarding people with pre-existing respiratory disease, genetic variants, or low SES as potential at-risk populations and children or older adults as potential at-risk lifestyles?
- What information is available that provides insight as to whether a potential at-risk lifestyle or population has higher exposure or dose of oxides of nitrogen and/or has a greater biological response to a given exposure?
- What is the extent of the coherence of evidence regarding potential at-risk lifestyles or populations for both short- and long-term exposures to oxides of nitrogen?
- What quantitative information is available to characterize the magnitude of greater biological response or risk of health effects associated with exposure to oxides of nitrogen in a particular at-risk lifestyle or population?

## **Public Health Impact**

The integrative synthesis chapter at the beginning of the ISA will present concepts that integrate evidence on health effects and consequent public health significance to aid in the assessment of the public health implications of exposure to short- and long-term exposure to oxides of nitrogen. The discussion will include evaluation of the adversity of the health effects potentially associated with exposure to oxides of nitrogen. Development of these concepts may include, as appropriate, an estimation of the sizes of potential at-risk lifestyles and populations and discussion of the public health significance of the magnitudes of change in health outcomes characterized to result from ambient air exposure to oxides of nitrogen. Further, to the extent that evidence is available, the integrative synthesis chapter of the ISA will discuss what evidence is available regarding interrelationships among risk factors (e.g., young age and lower SES, old age and pre-existing cardiovascular disease) in a particular lifestyle or population that may add to the understanding of the public health impact of exposure to oxides of nitrogen.

## **4.5 SCIENTIFIC AND PUBLIC REVIEW OF THE ISA**

Drafts of the ISA will be made available for review by the CASAC and the public as indicated in Figures 2-1 and 4-1 above. Availability of draft documents will be announced in the *Federal Register*. The CASAC will review the draft ISA documents and discuss its comments in public meetings that will be announced in the *Federal Register*. The EPA will take into account comments, advice, and recommendations received from the CASAC and from the public in revising the draft ISA documents. The EPA has established a public docket for the development

1 of the ISA.<sup>43</sup> After appropriate revision based on comments received from the CASAC and the  
2 public, the final document will be made available on an EPA website. A notice announcing the  
3 availability of the final ISA will be published in the *Federal Register*.

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<sup>43</sup>The ISA docket can be accessed at [www.regulations.gov](http://www.regulations.gov) using Docket ID number EPA-HQ-ORD-2013-0232.

## 5 QUANTITATIVE RISK AND EXPOSURE ASSESSMENT

Within the context of NAAQS reviews, a quantitative risk and exposure assessment (REA) is designed to estimate human exposure and health risks associated with existing and potential alternative standards. The appropriate scope of any REA will be informed by the availability of scientific information from the ISA as well as air quality information and information on data and models that may help to address important uncertainties or provide additional insights beyond those provided by previous REAs. As a result, the first step in the REA planning process is an assessment of the appropriate scope of the REA, which includes a determination of whether a distinct REA document is needed. As part of this planning process, we evaluate the 2008 REA in the context of the extent to which important uncertainties may be addressed by new information available since the previous review and the extent to which new information may change results of the 2008 REA in important ways or may allow for additional analyses that can address important gaps in our understanding of the exposures and risks associated with NO<sub>2</sub>.

This phase of the NAAQS review begins with the preparation of a REA Planning Document and considers the extent to which newly available scientific evidence and tools/methodologies provide support for conducting quantitative risk and exposure assessments. To the extent warranted, the scope and methods for components of exposure/risk assessments will be described. As outlined in Table 2-1 above, the EPA plans to issue this REA Planning Document in September 2014. This document will be the subject of a CASAC consultation and will be made available to the public for review and comment. CASAC advice and public comments on this draft IRP will be considered in developing the REA Planning Document. If warranted, one or more drafts of an REA will then be prepared and released for CASAC review and public comment prior to completion of a final REA.

The information newly available in this review will be considered in light of the comprehensive, complex and resource-intensive quantitative assessments of human exposure and health risks documented in the 2008 REA as discussed in section 6.1 below. As discussed in section 6.2 below, the REA Planning Document will consider the available scientific evidence, tools, and methodologies in light of areas of uncertainty identified in the 2008 REA and the potential for new analyses to provide notably different exposure and risk estimates, with lower associated uncertainty. The timeline for collection of ambient NO<sub>2</sub> measurement data within near-road environments under the recently revised monitoring requirements is recognized as an important consideration for the REA Planning Document. CASAC advice and comments from

the public on this draft IRP, as well as the availability of resources, will inform development of the REA Planning Document.

## **5.1 OVERVIEW OF RISK AND EXPOSURE ASSESSMENT FROM PRIOR REVIEW**

In the last review, as summarized in section 3.1 above, the EPA designed and developed three approaches to estimating exposures and health risks associated with a number of ambient air quality scenarios (i.e., recent air quality unadjusted, air quality adjusted to simulate just meeting the then-existing annual standard (i.e., annual average of 53 ppb), and air quality adjusted to simulate just meeting several potential alternative daily maximum 1-hour standards). Briefly, in the first approach ambient NO<sub>2</sub> concentrations (measured and modeled) were compared to 1-hour health effect benchmark levels derived from the controlled human exposure literature. In the second approach, modeled estimates of human exposures in an urban study area were compared to these same health effect benchmark levels. In the third approach, concentration-response relationships from an epidemiological study were used to estimate health impacts associated with ambient NO<sub>2</sub> concentrations in an urban study area. An overview of these approaches used and results generated in characterizing health risks is provided below.

### **5.1.1 Ambient Air Quality Characterization**

In the first approach, we compared 1-hour ambient NO<sub>2</sub> concentrations (1995 to 2006) with short-term health effect benchmark concentrations of 100, 150, 200, 250, and 300 ppb NO<sub>2</sub><sup>44</sup> in order to identify the number of days a particular benchmark concentration was exceeded per monitor per year. All U.S. monitoring sites where NO<sub>2</sub> data have been collected were included in this analysis and, as such, the results generated were considered a broad characterization of national air quality and potential human exposures that might be associated with these concentrations.<sup>45</sup> The available NO<sub>2</sub> air quality for 18 MSA/CMSA named study areas<sup>46</sup> and two aggregate study areas were separated into two six-year groups; one contained

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<sup>44</sup> The 1-hour NO<sub>2</sub> health effect benchmark levels were based on NO<sub>2</sub> exposure concentrations associated with increased airway responsiveness in asthmatics and determined from 1 to 2 hour duration controlled human exposure studies. These benchmark values were used for the evaluation of both the NO<sub>2</sub> air quality concentrations and estimated NO<sub>2</sub> exposures.

<sup>45</sup> After applying a 75% data completeness criterion the final analytical data base included 627 monitors collecting ambient concentrations for 4,177 site-years of data (a valid monitoring day had ≥18 hourly measurements; monitors included in the analysis had ≥75% valid monitoring days in a year).

<sup>46</sup> An initial pool of monitors was subset from the total set of monitors based on their belonging to specific CMSA/MSAs. Then we selected study areas having annual mean NO<sub>2</sub> concentrations occurring at a minimum of one monitor at or above 25.7 ppb (i.e., the 90<sup>th</sup> percentile concentrations across all study areas and site-years) and/or had at least one reported 1-hour NO<sub>2</sub> level greater than or equal to 200 ppb (i.e., the lowest level of the potential health effect benchmarks indicated by the ISA at the time these study areas were identified for investigation in the 2008 REA). All remaining not included in this collection of named study areas were aggregated into either one of two groups: all other CMSA/MSA or all other non-CMSA/MSA.

1 data from years 1995-2000, representing an historical data set; the other contained the  
2 monitoring years 2001-2006, representing recent ambient monitoring (U.S. EPA, 2008b, section  
3 7.2.2).

4 Each of these monitoring year-groups and study areas were evaluated considering the  
5 ambient NO<sub>2</sub> concentrations as they were reported and representing the conditions at that time  
6 (termed in that assessment “*as is*”). This served as the first air quality scenario. Further, within  
7 each year-group and study area we categorized the monitors using their sited distance from a  
8 major road: at or within 20 meters ( $\leq 20$  m), between 20 and 100 meters ( $> 20$  m to  $< 100$  m),  
9 and at least 100 meters from a major road ( $\geq 100$  m).<sup>47</sup> These ambient monitor data were  
10 categorized in this manner to account for the potential influence of vehicle emissions on NO<sub>2</sub>  
11 concentrations measured at the monitors within close proximity to roadways (U.S. EPA, 2008b,  
12 section 7.2.3). There was potential for different concentration levels measured at each of these  
13 locations (i.e., near-road monitors versus those sited away from roadways) and thus potentially  
14 different exposure concentrations experienced by those persons spending time in these locations.  
15 Then, for each ambient monitor, we summed the number of days per year that monitor recorded  
16 a daily maximum 1-hour concentration at or above the health effect benchmark levels and  
17 summarized this metric for each study area, year-group, and roadway-distance group, using  
18 descriptive statistics (e.g., means, maximums) (U.S. EPA, 2008b, section 7.2.5).

19 A second air quality scenario used the *as is* ambient monitoring data obtained from  
20 monitors sited  $\geq 100$  m from a major road combined with an on-road concentration adjustment  
21 factor to estimate *on-road NO<sub>2</sub> concentrations* for each of the year-groups and study areas. This  
22 scenario was developed by recognizing that motor vehicles are important emission sources of  
23 NO<sub>x</sub> and NO<sub>2</sub> and that people spend time inside vehicles while travelling on roadways. At that  
24 time, a strong relationship had been reported between NO<sub>2</sub> concentrations measured on roadways  
25 and NO<sub>2</sub> concentrations measured at increasing distance from the road, generally in the form of a  
26 first-order exponential decay (e.g., Cape et al., 2004). We derived an empirical distribution of  
27 on-road adjustment factors using data from published studies that reported on- and near-road  
28 NO<sub>2</sub> concentrations and NO<sub>2</sub> concentrations occurring at greater distances of a major road ( $\geq 100$   
29 m).<sup>48</sup> Then, we probabilistically applied these on-road adjustment factors to NO<sub>2</sub> concentrations  
30 reported at monitors sited  $\geq 100$  meters from a major road (and generally assumed to be at a  
31 background non-roadway influenced concentration) to approximate on-road NO<sub>2</sub> concentrations

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<sup>47</sup> Major road distances to each monitor were generally determined using a Tele-Atlas roads database in a GIS application. Major road types were defined as: 1=primary limited access or interstate, 2=primary US and State highways, 3=Secondary State and County, 4=freeway ramp, 5=other ramps. Note only the monitors falling within the 18 identified study areas had estimated distances to major roads, all other monitors (either characterized as ‘other CMSA/MSA’ or ‘all other non-CMSA/MSA’) were assumed to be  $\geq 100$  m from a major road.

<sup>48</sup> See Table 7-10 of the 2008 REA for the specific values of distributions that were used and Appendix A, section 8 for the studies used and the derivation methodology (U.S. EPA, 2008b).

1 for each study area and monitor-year. As described above for the area-wide ambient monitor  
2 data, we counted the number of days per year an estimated daily maximum 1-hour on-road  
3 concentration exceeded the benchmark levels and summarized these data using simple  
4 descriptive statistics (U.S. EPA, 2008b, section 7.2.4).

5 Additional summaries of benchmark exceedances were generated for the above two air  
6 quality scenarios (i.e., using the complete set of ambient monitoring concentrations at each of the  
7 three roadway distance categories and the simulated on-road NO<sub>2</sub> concentrations), though they  
8 differed in that the ambient concentrations were first adjusted to just meet the then-existing  
9 annual standard or alternative daily maximum 1-hour standards. Because the annual average  
10 2001 to 2006 ambient concentrations<sup>49</sup> were below the level of the existing annual standard (i.e.,  
11 < 53 ppb) as well as most of the potential daily maximum 1-hour standards being evaluated,  
12 ambient concentrations were primarily adjusted *upwards* to reflect these additional air quality  
13 scenarios. A simple proportional adjustment approach was selected to simulate concentrations to  
14 meet a particular standard level, an approach supported by within-monitor comparisons of low  
15 and high NO<sub>2</sub> concentration years that largely demonstrated characteristics of a proportional  
16 relationship.<sup>50</sup> We note also that the *as is* air quality could be characterized in all study areas as  
17 falling within the evaluated alternative standard levels of 50 and 100 ppb (either a 98<sup>th</sup> or 99<sup>th</sup>  
18 percentile daily maximum 1-hour concentration); thus simulating these particular air quality  
19 scenarios required the smallest proportional adjustment. Simulations of just meeting an  
20 alternative standard level of 50 ppb required a *downward* adjustment (U.S. EPA, 2008b, section  
21 6.3.1). That said, the number of benchmark exceedances for *as is* air quality scenarios in each  
22 study area also fell within the range of that estimated considering the 50 and 100 ppb daily  
23 maximum 1-hour alternative standard scenarios.

#### 24 5.1.1.1 Key Observations

- 25 • **Ambient monitoring NO<sub>2</sub> concentrations:** When considering any of the air quality  
26 scenarios, NO<sub>2</sub> concentrations and estimated number of benchmark exceedances are  
27 typically higher for monitors that are within 20 meters (m) of a major roadway than when  
28 monitors are sited farther from a major roadway (i.e., between 20 m and 100 m or ≥100  
29 m from a major road) (U.S. EPA, 2008b, section 7.3.1). As expected, fewer health effect  
30 benchmark exceedances were estimated to occur at highest health effect benchmark

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<sup>49</sup> Only the 2001 to 2006 ambient concentrations were used to evaluate the existing and alternative standard levels, the historical air quality data set with measurements from 1995 to 2000 was not used in this part of the assessment.

<sup>50</sup> Linear regressions were performed using the daily maximum 1-hour concentration distributions of each a low and high concentration year measured at the same ambient monitor and evaluated for model linearity and presence of statistically significant regression intercepts. Statistically significant linear regression slopes and model R<sup>2</sup> values strongly supported features of linearity. On a few occasions however, the presence of statistically significant regression intercepts and deviation from linearity at upper percentile concentrations tends to obfuscate a conclusion of proportionality existing at all monitors (Rizzo, 2008; U.S. EPA, 2008b, section 7.4.5).

levels (e.g., 300 ppb) when compared with the lowest health effect benchmark level (100 ppb). While results were generated for health effect benchmark levels ranging from 100 to 300 ppb in 50 ppb increments, the discussion in the 2008 REA focused only on the health effect benchmark levels of 100, 200, and 300 ppb.

- **100 ppb health effect benchmark level:** When air quality is adjusted to simulate just meeting the then-existing annual (i.e., 53 ppb, annual average), most study areas were estimated to have, on average, 50 days or more per year with daily maximum 1-hour ambient NO<sub>2</sub> concentrations ≥ 100 ppb, while about 1/3 were estimated to have 100 days or more per year with daily maximum 1-hour ambient NO<sub>2</sub> concentrations ≥ 100 ppb. When air quality is adjusted to simulate just meeting alternative daily maximum 1-hour standard levels of 50 and 100 ppb (98<sup>th</sup> or 99<sup>th</sup> percentile in a year), far fewer days per year were estimated to have, on average, daily maximum 1-hour ambient concentrations ≥ 100 ppb (i.e., <10 days per year, on average) than compared with just meeting higher alternative daily maximum 1-hour standard levels of 150 and 200 ppb (generally tens to hundreds of days per year with daily maximum 1-hour ambient NO<sub>2</sub> concentrations ≥ 100 ppb) (U.S. EPA, 2008b, section 7.5).
- **200 ppb health effect benchmark level:** When air quality was adjusted to simulate just meeting the then-existing annual standard, only two study areas were estimated, on average, to have 10 or more days per year with daily maximum 1-hour ambient NO<sub>2</sub> concentrations ≥ 200 ppb. When air quality was adjusted to simulate just meeting alternative daily maximum 1-hour standard levels of 50 and 100 ppb (98<sup>th</sup> or 99<sup>th</sup> percentile in a year), only four study areas were estimated, on average, to have at least one day per year with daily maximum 1-hour ambient NO<sub>2</sub> concentrations ≥ 200 ppb.
- **300 ppb health effect benchmark level:** When air quality was adjusted to simulate just meeting the then-existing annual standard, only five study areas were estimated, on average, to experience any days with daily maximum 1-hour ambient NO<sub>2</sub> concentrations at central site monitors ≥ 300 ppb, and none of those study areas were estimated to experience more than 2 such days per year, on average. When air quality was adjusted to simulate just meeting alternative daily maximum 1-hour standard levels of 50 and 100 ppb (98<sup>th</sup> or 99<sup>th</sup> percentile in a year), only three study areas were estimated, on average, to have at least one day per year with daily maximum 1-hour ambient NO<sub>2</sub> concentrations ≥ 300 ppb.
- **Simulated on-road NO<sub>2</sub> concentrations:** Simulated on-road annual average NO<sub>2</sub> concentrations, estimated using an on-road adjustment factor, were on average, 80 percent higher than the respective ambient concentrations measured at distances ≥100 m from a road; thus, there were a greater number of days per year where estimated daily maximum 1-hour concentrations on roads exceeded the health effect benchmark levels.
  - **100 ppb health effect benchmark level:** In the majority of study areas, exceedances of the 100 ppb health effect benchmark level were estimated to occur on roadways for most days of the year when air quality was adjusted to simulate just meeting the then-existing standard. Most study areas were estimated, on average, to have between 100 and 300 days per year with daily maximum 1-hour on-road NO<sub>2</sub> concentrations ≥ 100 ppb. The mean number of days per year where estimated on-road concentrations

were  $\geq 100$  ppb was always greater than that estimated using concentrations at ambient monitoring locations (e.g., up to 18 days per year for a standard level of 50 ppb, 257 for a standard level of 100 ppb, 343 for a standard level of 150 ppb, and 351 for a standard level of 200 ppb, based on the 98<sup>th</sup> percentile of daily maximum 1-hour concentrations, averaged over three years).

- **200 and 300 ppb health effect benchmark levels:** Even considering the higher health effect benchmark levels, most study areas were estimated, on average, to exceed these benchmark levels on roadways when air quality was adjusted to simulate just meeting the then-existing annual standard. Most study areas were estimated, on average, to have between 25 and 100 days per year with daily maximum 1-hour on-road NO<sub>2</sub> concentrations  $\geq 200$  ppb. All study areas evaluated, except one, were estimated to have on-road NO<sub>2</sub> concentrations  $\geq 300$  ppb. Four of these study areas were estimated, on average, to experience an average of greater than 20 days per year with on-road NO<sub>2</sub> concentrations  $\geq 300$  ppb.

#### 5.1.1.2 Key Uncertainties

An advantage of this approach to estimating potential health risk is its relative simplicity; however, there were a number of important uncertainties identified (US EPA, 2008b, section 7.4). One of the most important uncertainties overall regards the spatial representation of the ambient monitors, hence part of the reasoning to revise ambient monitoring networks at the conclusion of the last NO<sub>2</sub> NAAQS review to include monitoring near roadways. To overcome this lack of near-roadway measurement data in the 2008 REA and as briefly described above we developed a simple statistical model using measurement data reported in a limited number of peer-reviewed studies to estimate our on-road NO<sub>2</sub> concentrations. In doing so, this statistical model was characterized as having moderate or greater uncertainty in estimating on-road NO<sub>2</sub> concentrations, both in potentially under- and over-estimating the number of exceedances of health effect benchmark levels. In addition, the proportional adjustment applied to ambient air quality measurements to simulate just meeting the existing and alternative standards was characterized as another important uncertainty, particularly when adjusting concentrations upwards to meet or approach concentrations reflecting the existing annual standard. Further, the selection of health effect benchmark levels used to characterize risk was based on controlled human exposure studies that used mild asthmatics. In the absence of information regarding the potential health response of persons characterized as having moderate or severe asthma, we characterized the health effect benchmark level selection as an important uncertainty.

#### 5.1.2 Human Exposure Assessment

In the second approach, we used an inhalation exposure model to generate more realistic estimates of personal NO<sub>2</sub> exposure concentrations and compared those estimates of personal exposure to the health effect benchmark levels. The EPA's Air Pollutants Exposure model (APEX) probabilistically estimated individual exposures considering the time people spend in



1 different microenvironments and the variable NO<sub>2</sub> concentrations that occur within these  
2 microenvironments across time, space, and microenvironment type, including estimation of on-  
3 and near-roadway exposure concentrations (U.S. EPA, 2008b, section 8.2). The EPA's air  
4 dispersion model (AERMOD) was used to estimate hourly NO<sub>2</sub> concentrations occurring at a  
5 census tract level and at roadway receptors, considering emissions from stationary, area-wide,  
6 and on-road mobile sources (U.S. EPA 2008b, section 8.4). This approach to assessing  
7 exposures at that time was more resource intensive than using ambient measurements as a  
8 surrogate for exposure as discussed in section 6.1.1 above; therefore, only one specific study area  
9 was selected for analysis (four counties comprising the core Atlanta, GA metropolitan statistical  
10 area, or MSA). Although the geographic scope of this analysis is restricted, the approach  
11 provides realistic estimates of NO<sub>2</sub> exposures, particularly those exposures associated with  
12 important emission sources of NO<sub>x</sub> and NO<sub>2</sub>, and serves to complement the results of the broad  
13 NO<sub>2</sub> air quality characterization.

14 For the characterization of risks in the exposure modeling analysis, staff used the same  
15 range of short-term potential health effect benchmark levels described above in the air quality  
16 characterization summarized in section 6.1.1 (i.e., 1-hour NO<sub>2</sub> concentrations of 100, 150, 200,  
17 250, and 300 ppb) and considered the same air quality scenarios (recent "as is" ambient  
18 concentrations and ambient concentrations adjusted to just meet the existing and potential  
19 alternative standards, though using only years 2001-2003).<sup>51</sup> Asthmatic school-age children (5  
20 to 17 years of age) and all asthmatics (0 to 99 years of age) were considered the most important  
21 exposure study groups in this assessment based on their having potentially increased health risk  
22 to NO<sub>2</sub> exposure concentrations (U.S. EPA, 2008a, section 4.3). Exposure estimates for  
23 asthmatic school-age children were segregated from that estimated for the broader asthmatic  
24 population group because of their potential to have greater participation rate and time engaged in  
25 outdoor activities, thus possibly increasing their NO<sub>2</sub> exposures. When personal exposures for  
26 either exposure study group were simulated, the output of the analysis was an estimate of the  
27 number of individuals at risk for experiencing daily maximum 1-hour levels of NO<sub>2</sub>  
28 concentrations of ambient origin that exceeded particular health effect benchmark levels. An  
29 advantage of using potential health effect benchmark levels based on evidence from controlled  
30 human exposure studies to characterize health risks in this exposure modeling approach was that  
31 the effects observed in these studies clearly resulted from NO<sub>2</sub> exposure. This was in contrast to  
32 using health effects associated with ambient NO<sub>2</sub> concentrations in epidemiological studies (as

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<sup>51</sup> This three-year period was selected to bound the most recent year of NO<sub>x</sub> emissions data available (i.e., 2002) and used to model ambient concentrations at the time of our exposure assessment was conducted (U.S. EPA, 2008b)

discussed in the third approach described in section 5.1.3 below), which can also be associated with pollutants that co-occur with NO<sub>2</sub> in the ambient air.

### 5.1.2.1 Key Observations

- Estimated daily maximum 1-hour exposures at or above potential health effect benchmark levels using APEX were largely a function of roadway-related exposure concentrations (greater than 99 percent). Of these exposures, approximately 70 percent resulted from in-vehicle exposures, with the remainder associated with outdoor near-road exposures. Overall, when simulating air quality that just meets the then-existing annual standard, virtually all asthmatics in Atlanta were estimated to experience six or more daily maximum 1-hour exposures per year to NO<sub>2</sub> concentrations above the highest health effect benchmark level evaluated (i.e., >300 ppb), indicating the extremely limited ability of the then-existing annual standard at that time to protect against daily maximum 1-hour exposures at or above any of the selected health effect benchmark levels (U.S. EPA, 2008b, section 8.10).
  - **100 ppb health effect benchmark level:** For all air quality scenarios considered, more than 90 percent of all asthmatics in Atlanta were estimated to be exposed to concentration > 100 ppb at least one time per year. Of the daily maximum 1-hour alternative standard levels evaluated, 50 ppb was the only standard level estimated to reduce repeat daily maximum 1-hour NO<sub>2</sub> exposures above 100 ppb compared to recent air quality concentrations.
  - **200 ppb health effect benchmark level:** Of all the air quality scenarios considered, only the 98<sup>th</sup> and 99<sup>th</sup> percentile daily maximum 1-hour alternative standards set at 50 ppb were estimated to reduce the percent of asthmatics exposed at least one time per year to concentrations > 200 ppb (by approximately 40 to 50 percent) relative to recent air quality concentrations.
  - **300 ppb health effect benchmark level:** Of all the air quality scenarios considered, only alternative standard levels set at 50 ppb or 100 ppb were estimated to reduce the percent of asthmatics exposed at least one time per year to concentrations > 300 ppb (by approximately 80 percent and 15 percent, respectively) relative to recent air quality concentrations.

### 5.1.2.2 Key Uncertainties

The same important uncertainties exist for the exposure modeling results as described in section 6.1.1.2 above for the air quality characterization where similar approaches were used (i.e., proportional air quality adjustment approach and selection of health effect benchmark levels). One important uncertainty identified as specific to the exposure assessment was the AERMOD estimated concentrations used to represent the air quality surface across the Atlanta study area (U.S. EPA, 2008b, section 8.12). An evaluation with limited ambient monitor measurement data suggested a potential bias in overestimating ambient concentrations, potentially associated with uncertainty in mobile source emissions and/or diurnal profiles used as input (among other sources of uncertainty) (U.S. EPA, 2008b, section 8.4.8). Given the few

monitors available and overall confidence in the AERMOD system and other input data, it was difficult to reasonably justify adjusting all estimated concentrations across the entire 4-county modeling domain based on the differing concentrations observed at the few monitor locations, thus they were used without adjusting for this observed difference. An additional uncertainty, though not specifically identified as an exposure uncertainty in the prior assessment, was the similar factors approach used to adjust 1-hour AERMOD ambient concentrations to estimate on- and near-roadways concentrations. While AERMOD estimated 1-hour NO<sub>2</sub> concentrations occurring on roadway link-based receptors, these on-road concentrations could not be used directly as an input to APEX based on its existing configuration. Thus an on-road adjustment factor was developed from the AERMOD estimated on-road and census tract level concentrations (U.S. EPA, 2008b, section 8.7.2.5). These new on-road adjustment factor distributions used by APEX, along with the number of estimated on-road peak concentrations, were compared with those used for the air quality characterization (U.S. EPA, 2008b, section 8.4.8.3). The two similar, though independently developed, concentration adjustment approaches were found to be comparable across a wide range of estimated values, though they diverge at the upper percentiles of the distribution.<sup>52</sup> And finally, in a limited set of targeted exposure analyses, exposures were also modeled considering indoor source emissions (U.S. EPA, 2008b, section 8.7.2.1).<sup>53</sup> The characterization of indoor source emissions of NO<sub>2</sub> and estimated air exchange rates used to simulate indoor microenvironments were considered an important uncertainty.

### 5.1.3 Epidemiological-based Human Health Risk Assessment

In the third approach, respiratory-related hospital emergency department (ED) visits were estimated as a function of short-term ambient NO<sub>2</sub> concentrations measured at a fixed-site monitor representing ambient air quality for an urban area (U.S. EPA, 2008b, chapter 9). This health endpoint was selected because the 2008 ISA reported several epidemiological studies with observed positive associations between ambient NO<sub>2</sub> concentrations and ED visits and hospitalizations for all respiratory diseases and asthma (U.S. EPA, 2008a, section 3.1.6). In this

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<sup>52</sup> See Figure 8-8 and Table 8-7 of the 2008 REA (U.S. EPA, 2008b, pp175 to 176). While the divergence between the two on-road concentration estimations was noteworthy, particularly at the upper percentiles of the distribution, important differences in the data used to develop the two approaches were likely a highly influential contributing factor. For example, the on-road adjustment factor used in the exposure modeling approach used 1-hour concentrations, while the on-road adjustment factor used in air quality characterization approach was developed from measurement data time averaged over 7 to 14 days. It is likely that the latter approach smoothes the distribution of possible concentration ratios by using the long-term time-averaged concentrations, though we believe it is reasonable to still highlight this issue here as an important uncertainty in the exposure assessment conducted for the last review.

<sup>53</sup> While potentially important in understanding health effects and the total exposure/health risk from NO<sub>2</sub>, exposures resultant from indoor sources of NO<sub>2</sub> have limited relevance in understanding health risk associated with ambient concentrations.

1 type of risk estimation approach, concentration-response functions were based on findings from  
2 NO<sub>2</sub> epidemiological studies that relied on fixed-site, population-oriented, ambient monitors as a  
3 surrogate for actual ambient NO<sub>2</sub> exposures and were used to estimate the impact of daily  
4 maximum 1-hour ambient NO<sub>2</sub> concentrations, as measured at a single fixed-site monitor, on ED  
5 visits (U.S. EPA, 2008b, section 9.3). By focusing on a different health endpoint from the first  
6 two approaches described above, this epidemiological-based approach provided additional  
7 perspective on the potential public health impacts resultant from NO<sub>2</sub> exposures.

8 Because of the limited number of epidemiological studies reporting concentration-  
9 response (C-R) functions and the limited availability of other data needed for a quantitative risk  
10 assessment (e.g., baseline incidence rates), this type of health risk assessment was only  
11 conducted in one study area (Atlanta, GA) using C-R functions extracted from one study  
12 (Tolbert et al., 2007). The same general air quality scenarios described in section 5.1.1 above  
13 were evaluated (i.e., ambient concentrations *as is* and those adjusted to just meeting the then-  
14 existing annual and potential alternative daily maximum 1-hour standard levels), using ambient  
15 air quality data from 2005 to 2007, the most recent ambient monitoring data available at the time  
16 the assessment was conducted and similar to the years of air quality used in the epidemiological  
17 study in determining C-R functions (1993 through 2004) (Tolbert et al., 2007).

#### 18 **5.1.3.1 Key Observations**

- 19 • Health risks associated with just meeting the existing annual standard: Central estimates  
20 of annual NO<sub>2</sub>-related respiratory ED visits associated with air quality adjusted upward to  
21 simulate just meeting the then-existing annual standard (based on 2006 to 2007 air  
22 quality data) range from 8.1 to 9.0 percent of total incidence (or 9,800 to 10,900 NO<sub>2</sub>-  
23 related incidences per year) based on single-pollutant models and from 1.7 to 7.7 percent  
24 (or 3,100 to 9,400 NO<sub>2</sub>-related incidences per year) based on co-pollutant models.
- 25 • Health risks associated with just meeting alternative daily maximum 1-hour standards:  
26 Central estimates of annual NO<sub>2</sub>-related respiratory ED visits associated with air quality  
27 adjusted to simulate just meeting a 100 ppb, 1-h daily maximum, 98<sup>th</sup> percentile standard  
28 (based on 2005 to 2007 air quality data) ranged from 3.9 to 4.3 percent of total incidence  
29 based on single-pollutant models and from 0.8 to 3.7 percent based on co-pollutant  
30 models. Central estimates of annual NO<sub>2</sub>-related respiratory ED visits associated with air  
31 quality adjusted to simulate just meeting a 50 ppb, 1-h daily maximum, 98<sup>th</sup> percentile  
32 standard (based on 2005 to 2007 air quality data) ranged from 2.0 to 2.2 percent based  
33 on single-pollutant models and from 0.4 to 1.9 percent based on co-pollutant models.

#### 34 **5.1.3.2 Key Uncertainties**

35 A few of the same important uncertainties exist for the health risk modeling results as  
36 described in sections 5.1.1.2 and 5.1.2.2 above for the air quality characterization and exposure  
37 modeling assessments where similar approaches were used (i.e., uncertainties related to the  
38 proportional air quality adjustment approach and the spatial representativeness of air quality

1 data, in general). In addition, two uncertainties unique to the epidemiological-based health risk  
2 assessment approach recognized as important included 1) the risk model specification (i.e.,  
3 overall form for concentration-response functions and the presence or not of a threshold) and 2)  
4 the adequacy of the ambient NO<sub>2</sub> monitors serving as a surrogate for population exposure (U.S.  
5 EPA, 2008b, section 9.6).

## 6 **5.2 CONSIDERATION OF QUANTITATIVE ASSESSMENTS FOR THIS** 7 **REVIEW**

8 This discussion is focused particularly on considering the extent to which newly available  
9 scientific evidence and tools/methodologies are available to inform our understanding of the key  
10 areas of uncertainty identified in the 2008 REA as discussed in sections 5.1.1.2, 5.1.2.2 and  
11 5.1.3.2 above. As outlined in Table 2-1 above, the EPA plans to release an REA Planning  
12 Document for consultation with CASAC and for public comments in September 2014 that will  
13 consider the extent to which new quantitative risk and exposure assessments would be  
14 appropriate to conduct in the current review. CASAC review and public comments on this draft  
15 IRP will be considered in developing the REA Planning Document.

16 Some key areas being considered by staff, including types of data, methodologies and  
17 tools, are identified and summarized below. Building upon each of the three approaches used to  
18 estimate exposure or health risk in the previous review, we summarize the potential areas where  
19 additional information, if available, would provide reasonable substance to address key  
20 uncertainties identified in the previous review. We then discuss the potential utility and impacts  
21 of this new information to improve upon the assessments performed in the prior review.

### 22 **5.2.1 Air Quality Characterization**

23 Table 5-1 summarizes the potentially important uncertainties where additional  
24 information, if available, would provide reasonable substance to the discussion of improving the  
25 air quality characterization performed in the prior review (U.S. EPA, 2008b, section 7.4). The  
26 major uncertainties identified in section 5.1 above based on the 2008 REA were related to 1)  
27 ambient monitoring representativeness, 2) the approach used to estimate on-road NO<sub>2</sub>  
28 concentrations, 3) the approach used to estimate the existing and alternative air quality standard  
29 scenarios, and 4) the selection of health effect benchmark levels.

### 30 **5.2.2 Human Exposure Assessment**

31 In addition to some of the uncertainties identified and described above in section 5.2.1,  
32 three additional uncertainties were identified as specific to the exposure assessment conducted  
33 for the 2008 REA. The major uncertainties identified in section 5.1.2.2 above that warrant  
34 additional discussion here include 1) the use of unadjusted AERMOD estimated ambient NO<sub>2</sub>

1 concentrations as input to APEX, 2) the factors approach used to estimate in-vehicle and near-  
2 road NO<sub>2</sub> concentrations, and 3) the limited input data used to estimate the contribution of a  
3 single source emission (indoor gas stoves) to a simulated person's total NO<sub>2</sub> exposure (Table 5-  
4 2).

1 **Table 5-1. Information (data, methods, models, etc.) identified as potentially important and/or newly available to inform the**  
2 **air quality characterization for the current review.**

Major Uncertainty or Limitation	Uncertainty/Limitation Remaining from 2008 REA		Consideration of Potential Utility and Impact of Information Newly Available in This Review Could Have on Assessment
	Sub-group	Description	
Ambient Monitor Spatial and Temporal Representativeness	Near-Road Ambient Monitoring Data	There is a general lack of existing ambient monitoring data near-roads in most U.S. urban areas. This, combined with the potential for short-term high NO <sub>2</sub> concentrations occurring in these locations creates a significant uncertainty regarding how often on- and near-road NO <sub>2</sub> concentrations may exceed exposure levels of concern. This uncertainty served as a driver for revising ambient monitor siting.	The near-road monitoring network is to be developed in three phases: the first set of 52 monitors to begin measuring near-road NO <sub>2</sub> concentrations starting January 1, 2014, followed by the addition of 22 monitors by January 1, 2015, and phase III adding 52 monitoring sites (see section 5.2 of this IRP). Given this schedule, it is possible that there will be a lag in the availability of the newest near-road ambient monitor concentration data due to quality assurance reviews, potentially delaying the utilization of this new and important data in this NO <sub>2</sub> review.
	Long-term Exposures	The annual average standard of 53 ppb was retained in the last review due to some evidence suggesting NO <sub>2</sub> concentrations had a causal relationship with respiratory-related health effects. Newly identified for this review would be the consideration of how long-term, though spatially variable, ambient NO <sub>2</sub> concentrations could adversely affect health.	Model and data fusion techniques could improve the estimation of the spatial and temporal distribution of NO <sub>2</sub> concentrations across urban areas (not simply area-wide and on-road distinctions), generally accounting for increased emission sources and other influential factors within a defined spatial sector. There could be utility in estimating screening level long-term NO <sub>2</sub> concentrations if there were a newly defined long-term health effect benchmark level of interest.
Approach Used to Estimate On-Road NO <sub>2</sub> Concentrations	Exponential Relationship Used to Characterize Concentration Decline with Increasing Distance from Roads	Based on a literature review of studies that measured both near- and away from road NO <sub>2</sub> concentrations conducted by OAQPS staff at the time of the last review and our analysis of the NO <sub>2</sub> concentration decline with distance from a roadway, an exponential relationship was used to derive our on-road adjustment factors. Variability in the form of the relationship could result in the derivation of different factors and potentially influencing estimated on-road NO <sub>2</sub> concentration levels, though of course is dependent on the form and parameters describing the relationship.	We could use air quality models, e.g., AERMOD dispersion model, to characterize near-source gradients (major roadways and combustion sources). In addition, we could evaluate alternative relationships (e.g., linear, biphasic, etc.), better characterize the distributions of on-road adjustment factors, and consider other factors used to define ambient monitors if there are studies newly available (modeling and/or measurement) that indicate alternative relationships exist outside of the range already considered in the 2008 REA.
	Distribution of	Two distributions of NO <sub>2</sub> on-road adjustment factors were	

Major Uncertainty or Limitation	Uncertainty/Limitation Remaining from 2008 REA		Consideration of Potential Utility and Impact of Information Newly Available in This Review Could Have on Assessment
	Sub-group	Description	
	On-road Adjustment Factors	derived and used in their empirical form, one for summer months ranging from 1.5 to 3.7 (median 1.9), the other non-summer months ranging from 1.2 to 2.5 (median 1.75).	
	Effect of Using Longer-term (weekly) Data versus Hourly Data to Estimate On-road Adjustment Factors	Data used to derive on-road adjustment factors were all from data collected over 1-week or longer term measurements. It is possible that there is variability in the derived relationship over different time-averaging periods and concentration levels. Thus there is uncertainty in application of the time-averaged derived distribution to accurately estimate variability in hourly NO <sub>2</sub> concentrations.	
	Definition of monitors minimally influenced by roadway emissions to use in the calculation of on-road concentrations	We used any ambient monitor that was > 100 meters from a major road to estimate on-road concentrations. At that time, this distance alone was considered a reasonable criterion given the literature reviewed and patterns noted in the then-existing ambient monitoring data. As stated in the prior REA section 7.4.6, it is possible that some of the ambient monitors used to estimate on-road concentrations could have been influenced by emissions from a non-road NO <sub>x</sub> source.	
Approach Used to Simulate Just Meeting Potential Air Quality Standard Scenarios	N/A	Six study areas (Los Angeles, Atlanta, New York, Philadelphia, Denver, and Chicago) were used to evaluate existence of a proportional relationship between high concentration and low concentration years. The proportional adjustment factors derived from the area design monitor was similarly applied to adjust all ambient monitors within a given study area. Deviation from proportionality (where exists) at any monitor could result in either over or under-estimation of concentrations.	New, adjusted ambient air quality data sets could be developed if there are studies newly available that indicate alternative approaches to adjusting air quality exist that would generate demonstrably different data sets outside of those already considered in the 2008 REA. This could include additional analysis of ambient monitor data trends and air quality model based approaches.
Selection of Health Effect Benchmark Levels	N/A	A generally common and important uncertainty in controlled human exposure studies is the limited number of study subjects as well as limits to the type of pre-existing health conditions subjects may have, particularly if the health condition affords the subject with heightened effects	New estimates of benchmark exceedances could be developed if there are studies newly available that indicate alternative benchmark levels exist outside of the range already considered in the 2008 REA. This would also apply where any new health endpoints are



Major Uncertainty or Limitation	Uncertainty/Limitation Remaining from 2008 REA		Consideration of Potential Utility and Impact of Information Newly Available in This Review Could Have on Assessment
	Sub-group	Description	
		sensitivity to the pollutant exposure. Further, there is a lack of exposure data from study groups at potentially sensitive lifestages (e.g., pregnant women, children).	identified beyond those associated with respiratory effects due to short-term exposures. Further, additional analysis of existing human exposure study data sets and an improved characterization of adversity could be possible using newly identified approaches or information.

1 **Table 5-2. Information (data, methods, models, etc.) identified as potentially important and/or newly available to inform the**  
2 **exposure assessment for the current review.**

Major Uncertainty or Limitation	Uncertainty/Limitation Remaining from 2008 REA	Consideration of Potential Utility and Impact of Information Newly Available in This Review Could Have on Assessment
	Description	
Use of Unadjusted AERMOD Estimated Concentrations as Input to APEX	AERMOD was used to reasonably represent spatial variability in ambient NO <sub>2</sub> concentrations across an urban area where using limited monitor data alone cannot. Even though comparisons made with limited ambient monitoring data suggest AERMOD estimated ambient concentrations may have been systematically over-estimated, concentrations were not adjusted for this potential upward bias.	We could further evaluate existing data generated for the 2008 REA (both the modeled exposures and ambient concentrations) to approximate the potential impact of developing a newly modeled alternative ambient concentration data set. In addition, we could use AERMOD, with recent improvements by EPA, to improve the quality and characterization of the ambient concentration data set for input to APEX.
Approach Used to Estimate In-Vehicle and Near-Road Microenvironmental (ME) Concentrations in APEX	In-vehicle and near-road NO <sub>2</sub> concentrations were estimated using a similar concentration adjustment approach described above for the air quality characterization, only differing in that the relationship between on-road and away-from-road receptor concentrations were estimated using AERMOD and that penetration/decay inside motor vehicles was accounted for by APEX. While the distribution of adjustment factors was stratified by time-of-day (11PM-6AM, 6AM-7PM, 7PM-11PM) and seasons (summer and not-summer) (U.S. EPA, 2008b, Table B-42), it is possible that use of a factors approach and randomly sampling from distributions occasionally leads to a mismatching of on-road adjustment factors and the away from road census block concentrations, leading to either over or under estimated on-road NO <sub>2</sub> concentrations. In addition, near-road NO <sub>2</sub> concentrations were considered at the same level as the estimated on-road concentrations without additional adjustment for their occurring at a given distance from the road.	APEX has been recently modified to allow for a time series of on-road concentrations, and can be stratified by a geographic identifier, as an input to estimating in-vehicle exposure concentrations. Thus, APEX is capable of utilizing the AERMOD on-road concentrations themselves rather than using a factors-based approach. In the absence of having a time-series of on-road concentrations for potential study areas of interest, it is possible that new factors or concentration distributions could be developed and used to estimate near-road microenvironmental concentrations, where newly published data are identified.
Limited Input Data Used to Estimate Contribution of Indoor Source Emissions of NO <sub>2</sub> to Total Exposures	For a few APEX simulations, we estimated exposures associated with ambient concentrations along with those associated with a single indoor emission source (gas stoves). The estimation was based on limited input data readily available to represent variability in the source emissions, population prevalence of gas stoves, frequency of source use per cooking event and times of occurrence, and indoor removal rates.	The role and relevance of understanding the contribution of indoor source emissions to exposures when setting ambient air quality standards could be further evaluated.

### 5.2.3 Controlled Exposure-based Human Health Risk Assessment

One question to be raised for this review is whether or not there are newly identified controlled human exposure studies on top of what was previously considered in the 2008 REA that substantially expand our understanding of respiratory-related (or other) adverse health effects. If new studies are identified and adequate data are available to develop exposure concentration response relationships, these functions could be combined with NO<sub>2</sub> exposure concentrations (e.g., output from a population-based exposure model) and thus, warrant conducting a quantitative risk assessment based on the controlled human exposure evidence. In addition, having new human exposure study data would not necessarily preclude a comparison of earlier approaches (e.g., meta-analyses) used to develop the health effect benchmarks with any newly identified or alternative approaches identified in this review.

### 5.2.4 Epidemiological-based Human Health Risk Assessment

In addition to a few relevant uncertainties identified above in section 5.2.1 above, two additional uncertainties were identified as unique to the epidemiological-based health risk conducted for the 2008 REA. The major uncertainties identified in section 5.1.3.2 above that warrant additional discussion here include 1) the selection of the C-R function and 2) the ability of the ambient NO<sub>2</sub> monitors to serve as a surrogate for population exposure. The risk assessment conducted in the last review focused on one health endpoint (i.e., respiratory-related ED visits) in one urban study area (Atlanta). An important issue in this review is whether or not additional information is available to consider conducting a quantitative risk assessment that would include additional health effect endpoints and/or additional urban study areas. The EPA's decisions regarding the conduct of and associated scope of an REA for this review can be informed by the ISA causality determinations,<sup>54</sup> in addition to the availability of appropriate data for quantitative analyses (e.g., availability of C-R functions, baseline incidence data, etc.). General criteria to be evaluated in identifying potential candidate studies to inform a quantitative risk assessment include the following:

- the study was a published, peer-reviewed study that had been evaluated in the ISA for the pollutant of interest and judged adequate by the EPA staff for purposes of inclusion in the risk assessment based on that evaluation;
- it directly measured, rather than estimated, the pollutant of interest on a reasonable proportion of the days in the study;
- it preferably included both single- and co-pollutant models.

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<sup>54</sup> The strength of the ISA causal determinations serves as a preliminary screen in identifying health endpoints to consider in conducting our health assessments; historically we have considered those health endpoints having either 'causal' or 'likely to be causal' determinations.

Table 5-3 summarizes the potentially important uncertainties where additional information, if available, would provide reasonable substance to the discussion of improving the epidemiological-based human health risk assessment performed in the prior review.

**Table 5-3. Information (data, methods, models, etc.) identified as potentially important and/or newly available to inform the epidemiological-based risk assessment for the current review.**

Major Uncertainty or Limitation	Uncertainty/Limitation Remaining From 2008 REA	Consideration of Potential Utility and Impact that Information Newly Available in this Review Could Have on Assessment
	Description	
Form of Concentration - Response Functions	In the epidemiological-based health risk assessment, a single short-term NO <sub>2</sub> epidemiological study was used to estimate respiratory-related health risk (ED visits) in Atlanta (Tolbert et al., 2007). A log-linear form assuming no threshold was selected, and both single and co-pollutant models were employed. An additional study by Ito et al. (2007) conducted in New York City was also identified but due to time and resource constraints, was not included in the 2008 REA.	It is possible that new epidemiological-based health risk assessments in additional study areas could be performed using new or alternative C-R functions and potentially assuming alternative model specifications if such published studies are available.
Adequacy of the Ambient NO <sub>2</sub> Monitors to Serve as a Surrogate for Population Exposure	For the epidemiological-based health risk assessment developed from data reported in Tolbert et al. (2007), concentrations from a single ambient monitor were used to represent area-wide exposures.	While this is a common approach used in these types of assessments, it is possible that the effect of using a single monitor could be further evaluated where new studies have employed additional or alternative monitors in estimating health risk.

### 5.3 SCIENTIFIC AND PUBLIC REVIEW

The REA Planning Document will be distributed to the CASAC for their consideration and provided to the public for review and comment. The document will be the subject of a consultation with the CASAC at a public meeting or teleconference that will be announced in the *Federal Register*.

If, upon consideration of CASAC recommendations and public comments, the EPA concludes that development of a new REA, or updating or expanding the last assessment, is warranted, staff will take into account comments received from CASAC and the public in designing and conducting the assessment. In such a case, staff would prepare at least one draft of the assessment for CASAC review and public comment. Review would be conducted by CASAC and discussed at a public meeting that would be announced in the *Federal Register*. Based on past practice by CASAC, the EPA expects that key advice and recommendations for revision of the document would be summarized in a letter to the EPA Administrator. In revising the draft REA document, the EPA would take into account any such recommendations, and also consider comments received from the public, at the meeting itself and any written comments received. A final document would then be made available on an EPA website, with its public availability announced in the *Federal Register*.

If upon consideration of CASAC and public comments on the REA planning document, the EPA concludes that development of a new REA is not warranted, a REA will not be developed and the Policy Assessment for this review will draw from the REA developed in the last review in light of analyses or assessments made in the REA planning document with regard to the current evidence pertaining to exposure and risk, as well as the evidence presented in the ISA and other documents prepared for the review. Review steps for the PA are described in section 7.1 below.

## 6 AMBIENT AIR MONITORING

In the course of NAAQS reviews, aspects of the methods for sampling and analysis of the NAAQS pollutant, and the current network of monitors, including their physical locations and monitoring objectives, are reviewed. The methods for sampling and analysis of each NAAQS pollutant are generally reviewed in conjunction with consideration of the indicator element for each NAAQS. Consideration of the ambient air monitoring network generally informs the interpretation of current data on ambient air concentrations, and helps identify if the monitoring network is adequate to determine compliance with the existing or, as appropriate, a potentially revised NAAQS. This chapter describes plans for considering these aspects of the ambient air monitoring program for oxides of nitrogen which includes the indicator NO<sub>2</sub>.

### 6.1 CONSIDERATION OF SAMPLING AND ANALYSIS METHODS

Generally, in order to be used for regulatory purposes, ambient NO<sub>2</sub> concentration data must be obtained using Federal Reference Methods (FRMs) or Federal Equivalent Methods (FEMs) which are designated by the Agency in accordance with 40 CFR part 53.<sup>55</sup> As described earlier, NO<sub>2</sub> is the indicator for the oxides of nitrogen NAAQS, and has been routinely measured by chemiluminescent FRMs since the early 1980s.<sup>56</sup> However, in 2012 a photolytic chemiluminescent method became commercially available and was approved by the Agency as an FEM (Federal Register: Vol 77, page 32632, 06/01/2012; <https://www.federalregister.gov/articles/2012/06/01/2012-13350/ambient-air-monitoring-reference-and-equivalent-methods-designation-of-three-new-equivalent-methods>). This new FEM is expected to be used to some degree into the ambient NO<sub>2</sub> monitoring network, but not displace a majority of traditional chemiluminescence FRMs. Both the chemiluminescent FRM and the photolytic chemiluminescent FEM are indirect measurement techniques for NO<sub>2</sub>. In the chemiluminescent FRM, the analyzer can only detect NO in the sample stream and therefore utilizes a two-step process in determining the amount of NO<sub>2</sub> in ambient air. First, the analyzer determines the amount of NO in the sample air. Second, the analyzer re-routes air flow so that the sample air stream passes over a heated molybdenum oxide catalytic converter reducing all oxidized nitrogen species in the sample to NO, before again measuring the amount of NO in the sample stream. The analyzer then subtracts the measured, actual ambient NO from the amount measured in the second step, allowing for the determination of NO, NO<sub>2</sub>, and NO<sub>x</sub> (where NO<sub>x</sub>

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<sup>55</sup> A list of designated FRMs and FEMs is available on EPA's website: <http://www.epa.gov/ttn/amtic/criteria.html>.

<sup>56</sup> See 40 CFR part 50, Appendix F.

= NO + NO<sub>2</sub>). Similarly, the photolytic-chemiluminescence FEM follows the same two step process as the FRM except that the reduction of NO<sub>2</sub> to NO is carried out in a photolytic converter with a known converter efficiency rate. Data produced by FRM and FEM analyzers include NO, NO<sub>2</sub>, and NO<sub>x</sub>, which are all routinely logged by state and local agencies whom typically report the hourly average values to EPA's Air Quality System (AQS).

The Agency is aware of a number of recent technological advances for direct measurements of NO<sub>2</sub> which are now or will soon become commercially available as FEMs, e.g., cavity attenuated phase shift spectrometry and cavity ring-down spectroscopy. The first of these new methods was approved in November of 2013

(<http://www.epa.gov/ttnamti1/files/ambient/criteria/reference-equivalent-methods-list.pdf>.)

These new direct measurement techniques are anticipated to be specific to NO<sub>2</sub>. This would create a notable, anticipated difference with the traditional chemiluminescent FRMs in that these direct measurement methods will only provide NO<sub>2</sub> data, and will not provide NO or NO<sub>x</sub> data.

Sampling and analysis issues to be considered during the current review include the following:

- To what extent are additional direct NO<sub>2</sub> measurements available for consideration as an FEM?
- If new, direct NO<sub>2</sub> measurement methods become available and integrated into the ambient network, what would be the anticipated impact to subsequent air quality data analyses by potentially losing NO and NO<sub>x</sub> measurements?

## **6.2 CONSIDERATION OF AIR MONITORING NETWORK REQUIREMENTS**

The majority of data used to determine compliance with the NO<sub>2</sub> NAAQS are obtained from monitors operated by state, local, and tribal air monitoring agencies. These monitors are either required due to federal regulation contained in 40 CFR Part 58, Appendix D, State Implementation Plans, industrial permits, or other state or local based requirements or voluntary actions. The monitoring networks support three major objectives: (1) to provide air pollution data to the general public in a timely manner; (2) to support compliance with NAAQS and emissions strategy development; and (3) to support air pollution research studies.

A review of the available NO<sub>2</sub> monitoring network and data was performed as part of the primary NO<sub>2</sub> NAAQS review completed in 2010. In conjunction with revising the primary standards in that review, the Agency promulgated minimum monitoring requirements to support the implementation of a new primary 1-hour NO<sub>2</sub> standard. The minimum requirements consisted of: (1) near-road monitors which would be placed in locations of expected maximum 1-hour NO<sub>2</sub> concentrations near heavily trafficked roads in urban areas and (2) monitors located to characterize areas with the highest expected NO<sub>2</sub> concentrations at the neighborhood and

1 larger spatial scales (also referred to as “area-wide” monitors) (75 FR 6505 to 6506, February 9,  
2 2010), and (3) a specific set of monitors to maintain in areas with susceptible and vulnerable  
3 communities exposed to NO<sub>2</sub> concentrations that have the potential to approach or exceed the  
4 standards (75 FR 6509). The near-road NO<sub>2</sub> monitoring requirements were novel at the time of  
5 promulgation and stemmed from findings that roadway associated exposures account for a  
6 majority of exposures to peak NO<sub>2</sub> concentrations (75 FR 6514). The area-wide and the  
7 susceptible and vulnerable communities monitoring requirements each minimally required  
8 approximately 52 and 40 monitors, respectively, and were consistent with traditional monitoring  
9 approaches, meaning the existing network did not require significant modification in order to  
10 satisfy these two requirements. Sites satisfying these two monitoring network requirements were  
11 identified and documented, or became fully operational, on or before January 1, 2013.

12 Conversely, the near-road NO<sub>2</sub> monitoring network did not exist at the time of promulgation, and  
13 the Agency acknowledged that it would have to be designed, funded, and installed in its entirety.

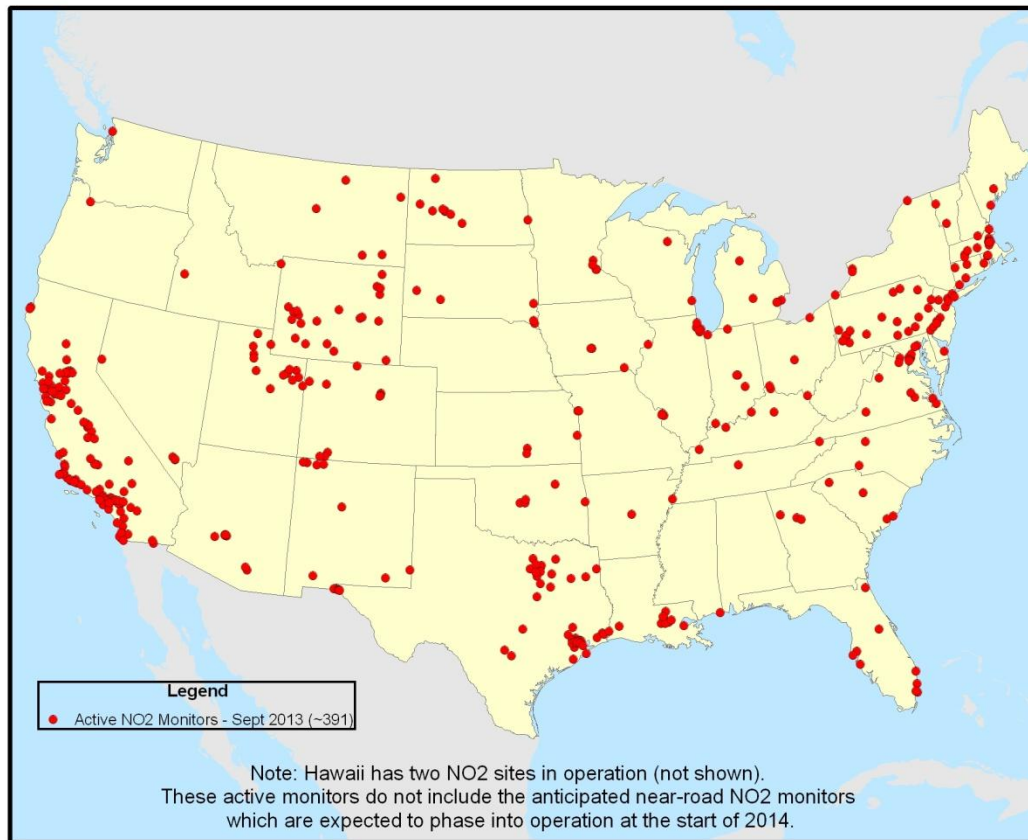
14 One near-road NO<sub>2</sub> monitor is required in each Core Based Statistical Area (CBSA)  
15 having 500,000 or more persons, per 40 CFR part 58, Appendix D, section 4.3.2. A second near-  
16 road NO<sub>2</sub> monitor is required in those CBSAs having either (a) 2,500,000 persons or more, or (b)  
17 any CBSA having 500,000 or more persons that also has one or more road segments carrying  
18 250,000 or greater Annual Average Daily Traffic (AADT) counts. At each of the near-road NO<sub>2</sub>  
19 sites, the monitors are subject to all requirements in 40 CFR part 58 and its appendices, which  
20 include specific siting criteria such as having the monitor probe placed “...as near as practicable  
21 to the outside nearest edge of the traffic lanes of the target segment; but shall not be located at a  
22 distance greater than 50 meters, in the horizontal, from the outside nearest edge of the traffic  
23 lanes of the target road segment” and having the monitor probe placed between 2 and 7 meters  
24 above the ground.

25 The near-road NO<sub>2</sub> monitors are required to be installed in three phases (78 FR 16184,  
26 March 14, 2013). The first phase required one monitor in any CBSA of 1,000,000 or more  
27 persons to be operational by January 1, 2014. We anticipated that 52 near-road sites would be  
28 added in Phase I. The second phase is for any second monitor required in a CBSA (those having  
29 2,500,000 or more persons or those CBSAs having 500,000 or more persons that also has one  
30 more road segments carrying 250,000 or greater AADT counts) to be operational by January 1,  
31 2015. We anticipate 22 near-road sites will be added in Phase II. The third phase is for those  
32 monitors in CBSAs having between 500,000 and 1,000,000 persons, which are to be operational  
33 by January 1, 2017. We anticipate 52 near-road sites will be added in Phase III.

34 By the end of 2013, the ambient NO<sub>2</sub> monitoring network was estimated to have 391 NO<sub>2</sub>  
35 monitors in operation nationwide. This estimate does not reflect the impending additions of the  
36 three-phased implementation of the near-road NO<sub>2</sub> monitors. We anticipate 126 near-road sites



1 will be operational on or before January 1, 2017, potentially resulting in more than 500 NO<sub>2</sub>  
2 monitors nationwide when the NO<sub>2</sub> network is fully operational.



3 **Figure 6-1. NO<sub>2</sub> Monitoring Network: Active monitors as of September 2013.**

4  
5 In the last review, there was limited near-road ambient NO<sub>2</sub> monitoring data. Analyses  
6 conducted as part of the 2008 REA (U.S. EPA, 2008b,) along with public comment on the  
7 proposed rule were considered in reaching final decisions on how many and where near-road  
8 NO<sub>2</sub> monitors would be required. In particular, the 2008 REA considered estimates of on- or  
9 near-roadway exceedances in 17 urban areas associated with CBSA populations ranging from  
10 approximately 540,000 to 19,000,000 persons. Those analyses indicated that the areas under  
11 explicit consideration were estimated to experience NO<sub>2</sub> concentrations on- or near-roads that  
12 exceeded health benchmark levels. In this review, the EPA will have the benefit of monitored  
13 near-road data for consideration in analyzing potential exposures and exceedances. Although the  
14 new near-road NO<sub>2</sub> monitoring network is not yet fully installed, data from newly operational  
15 monitors, plus data from more recent research efforts, may provide a clearer picture of what NO<sub>2</sub>  
16 concentrations are in the near-road environment, with the continued understanding that factors

1 including traffic counts, fleet mix, congestion patterns, roadway design, terrain, and meteorology  
2 all play a major role in measured roadside NO<sub>2</sub> concentrations.

3       Considering the availability of new near-road NO<sub>2</sub> monitoring data, the EPA may be in a  
4 position to re-evaluate the analyses underlying the minimum monitoring requirements  
5 promulgated in the 2010 revisions in this review.

## 7 POLICY ASSESSMENT AND RULEMAKING

As outlined in section 1.2 above, the fourth and final stage of the NAAQS review is the preparation of a Policy Assessment (PA) and rulemaking notices. These two steps are described, respectively, in sections 7.1 and 7.2 below.

### 7.1 POLICY ASSESSMENT

The PA provides a transparent OAQPS staff analysis and staff conclusions regarding the adequacy of the current standards and potential alternatives that are appropriate to consider prior to the issuance of proposed and final rules. The PA integrates and interprets the information from the ISA and, if available, REA(s) to frame policy options for consideration by the Administrator. The PA is also intended to facilitate CASAC's advice to the Agency and recommendations to the Administrator on the adequacy of the existing standards or revisions that may be appropriate to consider, as provided for in the CAA. Staff conclusions in the PA are based on the information contained in the ISA, and, as available, the REA, and any additional staff evaluations and assessments discussed in the PA. In so doing, the discussion in the PA is framed by consideration of a series of policy-relevant questions drawn from those outlined in section 3.2 above, including the fundamental questions associated with the adequacy of the current standards and, as appropriate, consideration of alternative standards in terms of the specific elements of the standards: indicator, averaging time, level, and form.

The PA for the current review will identify conceptual evidence-based and risk/exposure-based approaches for reaching public health policy judgments. It will discuss the implications of the science and quantitative assessments for the adequacy of the current primary standards and for any alternative standards under consideration. The PA will also describe a broad range of policy options for standard setting, identifying the range for which the staff identifies support within the available information. In so doing, the PA will describe the underlying interpretations of the scientific evidence and risk/exposure information that might support such alternative policy options that could be considered by the Administrator in making decisions for the primary NO<sub>2</sub> standards. Additionally, the PA will identify key uncertainties and limitations in the underlying scientific information and in our assessments. The PA will also highlight areas for future health-related research, model development, and data collection.

In identifying a range of primary standard options for the Administrator to consider, it is recognized that the final decision will be largely a public health policy judgment. A final decision must draw upon scientific information and analyses about health effects and risks, as well as judgments about how to deal with the range of uncertainties that are inherent in the scientific evidence and analyses. Staff's approach to informing these judgments recognizes that

1 the available health effects evidence generally reflects a continuum consisting of ambient  
2 concentrations at which scientists generally agree that health effects are likely to occur, through  
3 lower concentrations at which the likelihood and magnitude of the response become increasingly  
4 uncertain. This approach is consistent with the requirements of the NAAQS provisions of the  
5 CAA and with how the EPA and the courts have historically interpreted the Act. These  
6 provisions require the Administrator to establish primary standards that are requisite to protect  
7 public health and are neither more nor less stringent than necessary for this purpose. As  
8 discussed in section 1.1 above, the provisions do not require that primary standards be set at a  
9 zero-risk level, but rather at a level that avoids unacceptable risks to public health, including the  
10 health of at-risk populations.<sup>57</sup>

11 Staff will prepare at least one draft of the PA document for CASAC review and public  
12 comment. The draft PA document will be distributed to the CASAC Oxides of Nitrogen Primary  
13 NAAQS Review Panel for their consideration and provided to the public for review and  
14 comment. Review by the CASAC Panel will be discussed at public meetings that will be  
15 announced in the *Federal Register*. Based on past practice by CASAC, the EPA expects that  
16 CASAC will summarize key advice and recommendations for revision of the document in a  
17 letter to the EPA Administrator. In revising the draft PA document, OAQPS will take into  
18 account any such recommendations and also consider comments received, from CASAC and  
19 from the public, at the meeting itself, and any written comments received. The final document  
20 will be made available on an EPA website, with its public availability announced in the *Federal*  
21 *Register*.

## 22 **7.2 RULEMAKING**

23 Following issuance of the final PA and the EPA management consideration of staff  
24 analyses and conclusions presented therein, and taking into consideration CASAC advice and  
25 recommendations, the Agency will develop a notice of proposed rulemaking. The proposed  
26 rulemaking notice conveys the Administrator's proposed conclusions regarding the adequacy of  
27 the current standards and any revision that may be appropriate. The EPA will submit a draft  
28 notice of proposed rulemaking to the Office of Management and Budget (OMB) for interagency  
29 review, to provide OMB and other federal agencies the opportunity for review and comment.  
30 After the completion of interagency review, the EPA will publish the notice of proposed

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<sup>57</sup> The at-risk population groups identified in a NAAQS review may include low income or minority groups. Where low income/minority groups are among the at-risk populations, the rulemaking decision will be based on providing protection for these and other at-risk populations and lifestages (e.g., children, older adults, persons with pre-existing heart and lung disease). To the extent that low income/minority groups are not among the at-risk populations identified in the ISA, a decision based on providing protection of the at-risk lifestages and populations would be expected to provide protection for the low income/minority groups.

1 rulemaking in the *Federal Register*. Monitoring rule changes associated with review of the  
2 primary NO<sub>2</sub> standards, and drawing from considerations outlined in Chapter 6 above, will be  
3 developed and proposed, as appropriate, in conjunction with this NAAQS rulemaking.

4 At the time of publication of the notice of proposed rulemaking, all materials on which  
5 the proposal is based are made available in the public docket for the rulemaking.<sup>58</sup> Publication  
6 of the proposal notice is followed by a public comment period, generally lasting 60 to 90 days,  
7 during which the public is invited to submit comments on the proposal to the rulemaking docket.  
8 Taking into account comments received on the proposed rule, the Agency will then develop a  
9 notice of final rulemaking, which again undergoes OMB-coordinated interagency review prior to  
10 issuance by the EPA of the final rule. At the time of final rulemaking, the Agency responds to all  
11 significant comments on the proposed rule.<sup>59</sup> Publication of the final rule in the *Federal Register*  
12 completes the rulemaking process.

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<sup>58</sup> The rulemaking docket for the current primary NO<sub>2</sub> NAAQS review is identified as EPA-HQ-OAR-2013-0146. This docket has incorporated the ISA docket (EPA-HQ-ORD-2013-0232) by reference. Both dockets are publicly accessible at [www.regulations.gov](http://www.regulations.gov).

<sup>59</sup> For example, Agency responses to all substantive comments on the 2009 notice of proposed rulemaking in the last review were provided in the preamble to the final rule and in a document titled *Responses to Significant Comments on the 2009 Proposed Rule on the Primary National Ambient Air Quality Standards for Nitrogen Dioxide* (July 15, 2009; 74 FR 34404) (U.S. EPA, 2010).

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# APPENDIX A

## DRAFT OUTLINE FOR INTEGRATED SCIENCE ASSESSMENT FOR OXIDES OF NITROGEN – HEALTH CRITERIA

1		
2	<b>Preamble</b>	Process of ISA Development
3	(will be available online)	Literature Search
4		Study Selection
5		Evaluation of Individual Study Quality
6		Evaluation, Synthesis, and Integration across Disciplines and
7		Development of Scientific Conclusions and Causal
8		Determinations
9		EPA Framework for Causal Determinations
10		Public Health Impact
11		Approach to Classifying At-risk Factors
12		Concepts in Evaluating Adversity of Health Effects
13		
14	<b>Preface</b>	Legislative Requirements for the Primary NAAQS Review
15		History of the Review of the Air Quality Criteria for the Oxides
16		of Nitrogen and NAAQS for Nitrogen Dioxide
17		
18	<b>Executive Summary</b>	
19		
20	<b>Chapter 1</b>	<b>Integrative Summary</b>
21		
22	1.1	ISA Development and Scope
23	1.2	Organization of the ISA
24	1.3	Sources of Oxides of Nitrogen to Human Exposure
25	1.4	Health Effects of Oxides of Nitrogen
26		Dosimetry and Modes of Action
27		Causal Determinations and Key Evidence for Evaluated
28		Health Effects
29	1.5	Evaluation of the Independent Effects of Nitrogen Dioxide
30		Potential confounding by time-varying and individual- or
31		population-level characteristics
32		Potential confounding by copollutant exposures –
33		multivariate models, indoor NO <sub>2</sub> ,
34	traffic proximity	
35		and intensity
36	1.6	Policy-Relevant Considerations
37		NO <sub>2</sub> Exposure Metrics
38		Lag Structure of NO <sub>2</sub> -related Morbidity and Mortality
39		Associations
40		Concentration-Response Relationships and Thresholds
41		Public Health Significance – Adversity of Effects, At-risk
42		Lifestages and Populations
43	1.7	Conclusions



1		
2	<b>Chapter 2</b>	<b>Atmospheric Chemistry and Exposure to Nitrogen Oxides</b>
3	2.1	Introduction
4	2.2	Atmospheric Chemistry and Fate
5	2.3	Sources
6	2.4	Measurement Methods
7	2.5	Ambient Concentrations of Oxides of Nitrogen
8	2.6	Exposure Assessment
9	2.7	Summary and Conclusions
10		
11	<b>Chapter 3</b>	<b>Dosimetry and Modes of Action of Inhaled Nitrogen Oxides</b>
12	3.1	Introduction
13	3.2	Dosimetry of Inhaled Oxides of Nitrogen
14		Dosimetry of Nitrogen Dioxide
15		Dosimetry of Nitric Oxide
16		Metabolism, Distribution, and Elimination of
17		Products Derived from Inhaled Oxides of Nitrogen
18		Summary
19	3.3	Modes of Action for Inhaled Oxides of Nitrogen
20		Introduction
21		Nitrogen Dioxide
22		Nitric Oxide
23		Metabolites of Nitric Oxide and Nitrogen
24		Dioxide
25		Summary
26	3.4	Summary
27		
28	<b>Chapter 4</b>	<b>Integrated Health Effects of Short-term Exposure to Oxides</b>
29		<b>of Nitrogen<sup>60</sup></b>
30	4.1	Introduction
31	4.2	Respiratory Effects
32	4.3	Cardiovascular Effects
33	4.4	Total Mortality
34		
35	<b>Chapter 5</b>	<b>Integrated Health Effects of Long-term Exposure to Oxides</b>
36		<b>of Nitrogen<sup>35</sup></b>
37	5.1	Introduction
38	5.2	Respiratory Effects
39	5.3	Cardiovascular Effects
40	5.4	Reproductive and Developmental Effects
41		Fertility, Reproduction, and Pregnancy
42		Birth Outcomes
43		Postnatal Development

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<sup>60</sup>Sections for each of the major health effect outcome categories will include a review of the available evidence and conclude with the causal determination and summary of contributing evidence.

1	5.5	Total Mortality
2	5.6	Cancer
3		
4	<b>Chapter 6</b>	<b>Lifestages and Populations Potentially at Increased Risk for</b>
5		<b>Health Effects Related to Exposure to Oxides of Nitrogen</b>
6	6.1	Introduction
7	6.2	Genetic Factors
8	6.3	Pre-existing Disease/Conditions
9	6.4	Sociodemographic Factors (lifestage, socioeconomic status,
10		race/ethnicity, sex)
11	6.5	Behavioral and Other Factors (diet, obesity, smoking, residential
12		location)
13	6.6	Summary

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