State of California
AIR RESOURCES BOARD

Final Statement of Reasons for Rulemaking, Including Summary of Comments and Agency Responses

PUBLIC HEARING TO CONSIDER AMENDMENTS TO THE AMBIENT AIR QUALITY STANDARD FOR NITROGEN DIOXIDE

Considered On: February 22, 2007
Agenda Item No: 07-2-1

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I. INTRODUCTION

“The Initial Statement of Reasons for the Proposed Rulemaking—Review of the California Ambient Air Quality Standard for Nitrogen Dioxide" (ISOR; also referred to as “the staff report”) was released January 5, 2007 and made available to the public for at least 45 days prior to the public hearing. The staff report, which is incorporated by reference herein, provides a description of the rationale and necessity for the action proposed. The purpose of the regulation is to update California’s ambient air quality standard for nitrogen dioxide (NO_2) so that it accurately reflects the current body of peer-reviewed literature on related adverse health effects and provides adequate health protection for the citizenry of California—including that of infants and children, as well as other sensitive sub-populations. The action consisted of amendments to sections 70100, 70100.1 and 70200, title 17, California Code of Regulations (CCR) concerning ambient air quality standards for NO_2, and the ARB document titled "Air Monitoring Quality Assurance Manual Volume IV”, which is incorporated by reference in section 70100.1.

On February 22, 2007, the Air Resources Board (ARB or Board) held a public hearing at which it received written and oral comments on the proposed regulation. At that time, the Board considered the revised language to the ISOR/staff report that staff recommended to address issues raised during the preceding 45 days of the public comment period. At the conclusion of the public hearing, the Board unanimously adopted Resolution 07-2-1 and the regulation as originally proposed.

As adopted by the Board, the regulation modifies the standard for NO_2. The old 1-hour standard was 0.25 parts per million (ppm). The newly approved 1-hour standard is 0.18 ppm, not to be exceeded. The Board also adopted an annual average standard for NO_2 at 0.030 ppm, not to be exceeded. In addition, the Board retained the existing monitoring method for these standards.

Finally, the Board determined to incorporate by reference (17 California Code of Regulations, Section 70101) all Federally approved methods (i.e., samplers) for NO_2 as "California Approved Samplers". This will result in no change in air monitoring equipment practices, but will align State monitoring requirements with Federal requirements.

The reference methods incorporated by reference into this regulation are currently readily available to the public through United States Environmental Protection Agency. These reference methods are also voluminous in size. Given there ready availability and size, it would be unduly expensive and otherwise impracticable to publish these reference methods in the regulation itself. The updated informative digest provides specific notice of ARB's intention to incorporate all federally approved chemiluminescence methods for NO2 and the regulation text identifies the document to be incorporated by title and date of issuance.

Environmental and Economic Impacts: As described in the staff report, the proposed ambient air quality standards will in and of themselves have no environmental or economic impacts. Standards simply define clean air. Once adopted, local air pollution control or air quality management districts are responsible for the adoption of rules and regulations to control emissions from stationary sources to assure their achievement and maintenance. The ARB is responsible for adoption of emission standards for mobile sources and consumer products. A number of different implementation measures are possible, and each could have its own environmental or economic impact. These impacts must be evaluated when the control measure is proposed. Any environmental or economic impacts associated with the imposition of future measures will be considered if and when specific measures are proposed.

Mandate on Local Agencies or School Districts: The Board has determined that this regulatory action will not result in a mandate to any local agency or school district, the costs of which are reimbursable by the State pursuant to part 7 (commencing with section 17500), division 4, title 2 of the Government Code.

Consideration of Alternatives: Pursuant to Government Code section 11346.7(b)(4), the Board has determined that no justifiable, scientifically-based alternative considered by the agency would be more effective in carrying out the purposes for which the regulatory action was proposed, or may be as effective and less burdensome to affected private persons than the action taken by the Board. In theory, a lower proposed standard would be more health protective; however, it would not be supported by the current body of scientific literature and
therefore is not sufficiently justified.

Corrections to the staff report (Initial Statement of Reasons for Proposed Rulemaking) and Technical Support Documents: The Reports are jointly titled "Review of the California Ambient Air Quality Standard for Nitrogen Dioxide," and the corrections have been detailed in the attached Errata Sheet (Appendix A).

II. SUMMARY OF COMMENTS AND AGENCY RESPONSES

A. Introduction

The Board received three individual letters from commenters during the 45-day public comment period prior to the February 22, 2007 hearing. The Board also heard testimony from one witness at the February 22, 2007 public hearing. Table 1 is a summary of public comments. Comments were grouped together if they were similar. We have responded to each comment in the order presented in Table 1.

B. Summary of Comments Received During the 45-Day Comment Period (January 5, 2007 to February 22, 2007) and Oral Testimony at the Public Hearing held on February 22, 2007.

Table 1. Summary List of Comments

Issue	Comment
1.	The margin of safety appears arbitrary and the concentration is based on the levels where effects may be observed, not in consideration of the frequency of occurrence of those concentrations. (Raised by commenter 1)
2.	The ARB should consider setting the 1-hour standard of 0.18 ppm with a more robust statistic such as 95th or 98th percentile concentration value (in place of “not to be exceeded”). Replace "not to be exceeded” with the peak indicator value. (Raised by commenter 1)
3.	The reference to premature mortality and cardiovascular disease should be removed from the proposed amendments due to possible co-pollutant health effects, inconsistent results, and publication bias of positive results. (Raised by commenter 1)
4.	The lung growth studies do not provide a basis for an annual standard since there is a threshold for inflammatory effects in the normal population at concentrations above any recent ambient exposures. Further, ozone, a stronger irritant and oxidant gas than NO_2, has not been associated with changes in lung function growth, and therefore NO_2 is unlikely the causal factor. (Raised by commenter 1)
5.	The ARB does not have a basis to establish an annual standard since there is a lack of health effects in normal subjects in controlled human studies

exposed to current ambient levels of NO_2. It is therefore extremely unlikely that NO_2 is causing premature mortality. Further, because of publication bias and model uncertainty, the ARB cannot use point estimates from the time series data for setting the annual standard. (Raised by commenter 1)

6. Formation of NO_2 in the atmosphere from nitric oxide (NO) takes hours, not minutes, as indicated in Chapter 2. (Raised by commenter 1)

7. The chemiluminescent method used in analyzers lacks sensitivity for NO and is non-specific to NO_2, since the method can convert other related nitrogen species (eg. PAN, nitric acid) to NO_2. Therefore, there is the potential for positive bias in reporting NO_2 concentrations. Staff should report sensitivity and specificity of monitors currently used in California. (Raised by commenters 1, 2)

8. Discussion of the relevance and interpretation of exposure measurements need to include consideration of the emissions occurring at the time of the study. For example, the emission inventory included in Chapter 2 of the staff report and Chapter 4 of the Technical Support Document indicates that NOx emissions from on–road vehicles were reduced over 25% between 1990 and 2000 and are forecast to be reduced by another 72% between 2000 to 2020. (Raised by commenter 1)

9. Several studies on indoor and in-vehicle air quality show or predict less exposure than the staff report indicated. (Raised by commenter 1)

10. Information on the distribution of ambient levels of NO_2 should be added to the staff report to aid the reader in evaluating the biologic plausibility of the health effects. The commenter suggests that ambient concentration data from Table 5.4 and Table 5.10 be added to the staff report. (Raised by commenter 1)

11. A more accurate picture of the indoor/outdoor NO_2 ratios in locations without NO_2 sources should be presented. The results of the NO_2 measurements in the recently completed Fresno Asthmatic Children's Environment Study (FACES) are also relevant. While the mean concentration at the Fresno central site was 0.020 ppm, the mean of 332 2-week passive sampler measurements in homes of asthmatic children was 0.013 ppm and the mean in the homes without gas stoves was 0.009 ppm. The implication here is that the indoor values and central site values do not coincide. (Raised by commenter 1)

12. Whether exposures actually exacerbate asthma to a clinically significant degree is unknown, so the overall public health significance of the effects that are being used to support a lowering of the 1 hour standard is not clear. In particular the health implications of the Follinsbee study results are unclear.

(Raised by commenter 1)

13. The current or proposed 1-hour standard should provide enough health protection without the need for an annual standard. (Raised by commenter 1)

14. The statement that results of the epidemiological studies are consistent with health effects observed during controlled chamber studies and toxicological studies when NO_2 alone is tested, is overly broad and not defensible. (Raised by commenters 1, 2)

15. The reductions in annual average concentrations (below the federal annual average standard) that have occurred in California over the past decades have occurred during a period in which the State did not have an annual average standard. Therefore, the annual standard is not needed. (Raised by commenter 1)

16. There is concern over publication bias since numerous weak but positive associations with NO_2 have been published. Based on the ozone mortality associations and meta analyses commissioned by the U.S. EPA, there is a major discrepancy between the estimated association of ozone mortality from the National Mortality and Morbidity Air Pollution Study (NMMAPS) that evaluated the 90 largest U.S. cities and the meta-analyses. (Raised by commenter 1)

17. The only conclusion that can be drawn from the analyses of epidemiological studies is that while there are many positive epidemiological associations with NO_2 in the literature, individual city studies for these associations are not reliable due to model differences. The commenter cites a study by Koop and Tole that question the reliability of the models used in epidemiologic studies. (Raised by commenter 1)

18. The results from NMMAPS are statistically insignificant in multi-pollutant models. (Raised by commenter 1)

19. The use of central station monitoring data, meteorological data and available health statistics yields many weak positive associations. The interpretation of a subset of positive findings as causal becomes problematic. (Raised by commenter 1)

20. ARB staff acknowledges that it is difficult to distinguish the effects of NO_2 from other traffic-related pollutants, but asserts that it is prudent to regulate NO_2 since other traffic-related pollutants are not regulated. This is not logical. Reducing NO_2 may or may not reduce other traffic generated pollutants, depending on the technology chosen. (Raised by commenter 1)

21. The staff should carefully evaluate the extent to which the animal studies support the biological plausibility of the adverse health effect of NO_2. The dose needed to induce observable effects in animals needs to be carefully considered as part of these analyses. (Raised by commenter 1)

22. The epidemiology results suggest that something other than NO_2 is causing the effects. For example, the Gauderman (2005) study does not implicate NO_2 per se, but rather a number of pollutants. (Raised by commenter 1)

23. The commenter is in strong support of the proposed standards. (Raised by commenter 3,4)

List of Commenters

Table 2 below contains the names and affiliations of persons who commented on the proposed staff report. The column labeled "Issue(s) #" corresponds to the comment number set forth in Table 1, and is used to link the comment to the source for the comment-and-response section that follows in this document. A representative comment or a paraphrase of the comment(s) is used for each issue requiring a response. The form (written or oral) in which the comment was received by ARB is also listed in Table 2.

Table 2. Commenters on the Nitrogen Dioxide ISOR

#	Comment Author	Issue(s) #	Written/Oral
1	Giedrius Ambrozaitis, Alliance of Automotive Manufacturers	1-22	Written
2	Robert Harley, Professor UC Berkeley	7,14	Written
3	Behrouz Farsi, member of the public	23	Written
4	Bonnie Holmes-Gen American Lung Association	In Favor	Oral

C. Responses by Issue

1. The margin of safety appears arbitrary and the concentration is based on where effects may be observed, not in considering of the frequency of occurrence of those concentrations. (Raised by commenter 1)

Under California law, the standard is established to protect the public from health impacts of NO_2 *and is not based on current concentrations or attainment status.*

The clinical studies in asthmatics found fairly consistent evidence of enhanced allergic response to inhaled allergen after NO_2 *exposures at 0.26 ppm for 15 to 30 minutes. Additionally, there was evidence of increased airway reactivity in asthmatics at 0.2 to 0.3 ppm for 30 minutes to 2 hours, although there was more variability in these results, possibly due to differences in protocols and differences between subjects. Asthma is a chronic inflammatory disease, and these two endpoints, allergic inflammation and airway reactivity, are hallmarks of asthma. Thus, mild to moderate asthmatics with respiratory infections and more severe asthmatics may have an increase in symptoms after exposures to* NO_2 *in this range.*

To provide an adequate margin of safety, we chose a level of 0.18 ppm (1 hour average). The lowest level studied where no clear effect has been demonstrated is 0.1 ppm. The level chosen as the standard, 0.18 ppm, is half-way between 0.26 ppm (where effects have been consistently demonstrated) and 0.1 ppm. A margin of safety is needed to account for the variable effects that heterogeneous human populations exposed to NO_2 *may experience and the possible deficiencies or limitations in the health and exposure data. For example, young children and other sensitive populations (e.g. more severe asthmatics and asthmatics with recent respiratory infections) have not been studied in this setting. It is plausible that they may be at risk of effects at lower concentrations. Also, because studies found effects for 30-minute exposures at about 0.25 ppm, we needed a lower 1-hour standard.*

2. Consider setting the 1-hour standard of 0.18 ppm with a more robust statistic such as 95th or 98th percentile of the NO_2 concentration value (in place of “not to be exceeded”). Replace "not to be exceeded” with the peak indicator value. (Raised by commenter 1)

Under California law, primary ambient air quality standards are health-based; thus attainability, and the number of likely standard exceedences, are not criteria for determining the levels of ambient air quality standards. Attainment of the standards, as well as adoption and implementation of control measures, is separate from the standard setting process.

As described in the Technical Support Document, after each calendar year, ARB determines the attainment status of areas in the State using the most recent three years of available data for a given pollutant. A statistical procedure utilizes this data to calculate a "design value" which largely determines attainment status when compared to the level of the relevant standard. For California's short-term standards (averaging time of 24 hours or less) the design value is a calculated value and is also called the Expected Peak Day Concentration or EPDC. This design value represents the concentration expected to be exceeded once per year on average if the rates of emissions in the future continued as they were for the years used in making the designations. Accordingly, the design value or EPDC estimates the 364/365th or 99.73rd percentile of an ongoing conceptual distribution of daily pollutant concentrations. A percentile is the level below which the percent of the observations are found. For example, the 65th percentile indicates that 65% of the measurements are smaller than that level. Daily pollutant levels above the design value are excluded from consideration when making area designations.

The EPDC is constructed to be a robust design value that is not unduly affected by unusual short-term events, such as a diesel truck idling near an NO_2 monitor. The use of three years of data helps moderate the influence of year-to-year differences on meteorological conditions.

The standard is established with a margin of safety to protect the public from health impacts of NO_2 and is based on human controlled chamber studies finding clear effects in the range of 0.26 ppm. Allowing some exceedances above 0.18 ppm would be less health protective.

3. The reference to premature mortality and cardiovascular disease should be removed from the proposed amendments due to co-pollutant health effects, inconsistent results, and publication bias of positive results. (Raised by commenter 1)

Until very recently, most epidemiological studies reporting independent effects of NO_2 on premature mortality and cardiovascular disease were primarily focused on the health effects of PM and/or ozone. Therefore, the decision to publish these studies was not influenced by the strength of the NO_2 associations with health outcomes. All relevant studies (those showing positive or negative associations between NO_2 exposure and health) are considered. Publication bias refers to the belief that studies that do not show associations between NO_2 exposure and adverse health effects are not submitted for publication, thus biasing the body of published literature toward positive findings. Publication bias is unlikely to be an issue with the epidemiologic literature reviewed in the staff report since the primary focus for the mortality and cardiovascular effects studies were concerned with

particulate matter. Therefore, all results with co-pollutants measured, including NO_2, would be analyzed for their associations with these health effects. In summary, the information is consistent enough to be included in our report.

Although respiratory effects were highlighted as being most robust, the results of epidemiologic studies on mortality and cardiovascular disease were also of concern, given the severity of the effects. Page A35 of the January 5, 2007 Technical Support Document states that "Although the findings from studies of respiratory disease are the most robust, several other health outcomes have been associated with outdoor NO_2 exposure. These studies provide further support for the annual average recommendation." Therefore, it would not be appropriate to remove these outcomes from the amendments. The recent analysis of the effects of NO_2 on mortality in 30 European cities within the Air Pollution and Health: a European Approach project (APHEA) found positive associations in the majority of cities studied (Samoli et al. 2006).

In two-pollutant models there was no evidence of confounding by black smoke, PM10, SO_2 or ozone on total or cardiovascular mortality. Studies of hospitalization for cardiovascular disease have shown a positive effect of NO_2 even after controlling for co-pollutants (Metzger et al. 2004; Wellenius et al. 2005; Simpson et al. 2005).

4. The lung growth studies do not provide a basis for an annual standard since there is a threshold for inflammatory effects in the normal population at concentrations above any recent ambient exposures. Further, ozone, a stronger irritant and oxidant gas than NO_2, has not been associated with changes in lung function growth, and therefore NO_2 is unlikely the causal factor. (Raised by commenter 1)

Human exposure studies found evidence of inflammation in healthy individuals with short-term exposures at levels primarily present above ambient levels (~1 ppm). The inflammatory effects of NO_2 on children have not been studied, and there are few studies on asthmatics. For example, one study in asthmatics found evidence of inflammation (signs of neutrophil activation in blood) 30 minutes after exposure at 0.26 ppm along with an increase in airway reactivity at 5 hours after exposure (Strand et al. 1996). Human exposure studies are not designed to study chronic, long-term exposures; however, both toxicological and epidemiological studies provide evidence that chronic, long-term exposures to NO_2 have adverse effects on lung development.

Additionally, the annual standard is not based on the lung growth studies alone. Time-series, cross-sectional and longitudinal studies suggest that health effects including increased respiratory symptoms and medication use

in asthmatics, emergency room visits for asthma in children, hospitalization for respiratory and cardiovascular disease, and premature mortality are seen with chronic exposures of around 0.030 ppm. The investigators of the Children's Health Study (Gauderman et al. 2004) found associations between deficits in lung function growth and mixtures of the oxidant pollutants (NO_2, PM, and acid vapor). We are not asserting that NO_2 is the only causal factor in this epidemiological study but NO_2 may be a contributing factor. Animal toxicology studies support the hypothesis that chronic exposures to NO_2 can lead to changes in lung architecture.

Regarding the comment on ozone, episodic ozone exposure (0.5 ppm) has recently been shown to alter the developing lung in young monkeys. Page 8-42 of the January 5, 2007 Technical Support Document states that "Cyclic exposure studies in infant monkeys to another oxidant gas, ozone, have been shown to alter postnatal maturation of the lung. Changes include loss in the number of strictly conducting airways, reduction of distal airway size, altered smooth muscle bundle orientation, and hyperinnervation and irregular epithelial nerve distribution in intrapulmonary airways" (Fanucchi et al. 2006; Kajekar et al. 2006). One likely result of these ozone-induced pulmonary changes in the monkeys is a marked increase in baseline airway resistance (Schelegle et al. 2003).

Further, the interaction of house dust mite antigen and episodic ozone exposure during lung development in monkeys has been shown to synergistically enhance allergic-reactive airway disease (Evans et al. 2003; Schelegle et al. 2003; Larson et al. 2004; Kajekar et al. 2006). So it is reasonable to suspect that ozone levels below 0.5 ppm may also result in deleterious lung maturation changes under similar exposure conditions with this animal model.

Episodic ozone exposure represents a scenario closer to typical human exposure. These types of exposure studies in young animals undergoing lung development have not been conducted with NO_2, so it is unknown whether NO_2 can induce similar types of altered development with a similar episodic exposure scenario. However, intermittent exposure to 0.25 ppm NO_2 in mice and 0.5 ppm NO_2 in ferrets during lung development have resulted in persistent, if not permanent, changes in bronchiolar and alveolar lung tissue (Sherwin and Richters 1995a; Sherwin and Richters 1995b; Rasmussen and McClure 1992; Rasmussen 1994). Considering that dosimetry studies by Miller et al. (1982) indicate humans are more sensitive to NO_2 pulmonary injury than rodents, the potential exists that high episodic NO_2 exposures to humans may result in lung maturation alterations.

In summary, inflammatory effects in the asthmatic population, especially when exposed to airborne allergens have not been adequately studied with respect to chronic exposures. However, both toxicological and

epidemiological studies provide evidence that chronic, long-term exposures to NO_2 have adverse effects on lung development. Also, ozone has recently been shown to alter the developing lung in young monkeys, so it is plausible that NO_2 could also be responsible for this damage.

5. **The ARB does not have a basis to establish an annual standard since there is a lack of effects in normal subjects in controlled human studies exposed to current ambient levels of NO_2. It is therefore extremely unlikely that NO_2 is causing premature mortality. Further, because of publication bias and model uncertainty, the ARB cannot use point estimates from the time series data for setting the annual standard. (Raised by commenter 1)**

   Controlled human studies generally focus on short-term (minutes to hours) exposures and are not designed for longer-term exposure and subsequent health effects. Point estimates (estimates of effect) from time-series studies of mortality were not used in establishing the annual standard. Rather, we used the NO_2 averages in cities where health effects (as discussed in comments # 3 and # 4) were seen. The issue of publication bias has been addressed in our response to comment # 3.

6. **Formation of NO_2 in the atmosphere from nitric oxide (NO) takes hours, not minutes, as indicated in Chapter 2. (Raised by commenter 1)**

   In the staff report, we noted that NO_2 is formed indirectly from emissions of NO that are subsequently converted photochemically to NO_2, but we did not indicate the time course of these reactions. However, in the Technical Support Document, Chapter 5, Sec 5.4.6, we stated that "NO_2 forms from nitrogen oxide in the presence of sunlight on a scale of minutes." While the reaction between NO and ozone to form NO_2 takes place quickly, we agree with the commenter that the majority of the conversion of NO to NO_2 occurs over the course of hours. The reaction with sunlight is a complex series of chemical reactions that take place in multiple minutes and hours. This is fully described in Sections 2.2 and 2.3 in the Technical Support Document.

7. **The chemiluminescent method used in analyzers lacks sensitivity for NO, is non-specific to NO_2 and can convert other related nitrogen species (for example, PAN, nitric acid) to NO_2. Therefore, there is the potential for positive bias in reporting NO_2 concentrations. Staff should report the sensitivity and specificity of monitors currently used in California. (Raised by commenters 1, 2)**

Most, if not all, chemical analyses are susceptible to some kind of interference(s) by other pollutants. While it is important to understand the potential for analytical interference, additional scientific factors were also considered when proposing to retain chemiluminescence as the official method.

Chemiluminescence is a robust, proven technology, consistent with the federal method in use throughout the country. Title 40 of the Federal Code of Regulations, Part 50, Appendix F designates chemiluminescence as the U.S. EPA federal reference method for measuring NO_2. Additionally, chemiluminescence analyzers must meet performance specifications as published by the U.S. EPA and are commercially available and cost effective for state and local air quality management agencies. Any potential high bias is not an issue due to lack of violations, and the ability to remove oxidized species with nylon filters (as done in the South Coast Air Quality Management District). Lastly, data used to develop the health endpoints of NO_2 exposure (epidemiology and chamber studies) were based on levels of NO_2 determined by chemiluminescence methods. Therefore, there is scientific consistency of use of this method for determining exposure in the studies.

<u>Specificity</u>
The conversion of interfering compounds in instruments using NO surface conversion is acknowledged by current literature and the U.S. EPA. During special studies, levels of interfering compounds (for example, nitric acid [HNO_3] and peroxyacetyl nitrate [PAN] have been reported at monitoring sites in the South Coast Air Basin. However, levels of these compounds are relatively low (in the range of approximately 0.005 to 0.019 ppm) compared to the levels of NO_2 observed during peak 1-hour events.

Further, HNO_3 is very reactive with the surfaces of the sampling probe and analyzer so the actual levels of interfering compounds reaching the analyzer's detector are likely very much lower than NO_2 levels detected. Indeed, NO_y analytical methods ($NO_Y = NO_X + HNO_3$ + other nitrate species) require that all HNO_3 be converted to NO at the very opening of the sample inlet (i.e. right at the roof top) to minimize the adsorption of HNO_3 to sampling surfaces).

<u>Sensitivity</u>
The manufacturer's specifications for two widely used NO_X analyzers (Teledyne API model 200A and the Thermo Electron model 42) state limit of detections of 0.4 and 0.5 ppb NO, respectively.

For 2004, the most recent year of finalized audit data, ARB staff conducted performance audits for 78 NO_X monitors. The performance audit data were analyzed by ARB staff to determine the network precision. Only the low audit level data point was examined for the purpose of analyzing network precision

because the low audit level is closest to the level of the proposed annual standard (0.030 ppm). The average bias of all 78 audits was 0.14%, with a standard deviation of 4.9%. To express the standard deviation in ppm we multiply it by the concentration of interest, 0.030 ppm, to obtain ±0.0015 ppm, rounded to ±0.002 ppm. By convention this means that NO_X measurements are uncertain in the third decimal place, to the degree of plus or minus 0.002 ppm. Thus, the analyzers have the sensitivity and specificity to measure NO_2 at the levels near the proposed standard.

"Real world" audit data and published limits of detection both demonstrate that the chemiluminescence method is adequately sensitive for determining compliance with the proposed ambient air quality standards for NO_2.

8. Discussion of the relevance and interpretation of exposure measurements need to include consideration of the emissions occurring at the time of the study. For example, the emission inventory included in Chapter 2 of the staff report and Chapter 4 of the Technical Support Document indicates that NO_X emissions from on–road vehicles were reduced over 25% between 1990 and 2000 and are forecast to be reduced by another 72% between 2000 to 2020. Basically, decreases in emissions means that exposures will also decrease. (Raised by commenter 1)

Although emissions of NO_X from specific source categories are important to consider for evaluation of the development and effectiveness of controls and trends over time, actual ambient air concentrations are used for determining levels of potential health effects. The ambient air quality standard for NO_2 is based on outdoor airborne concentrations. Emission values for motor vehicles are usually measured at a controlled facility, such as a chassis dynamometer and provide estimates of emissions for the State. Emission values based on a chassis dynamometer are run through standard and reproducible driving cycles that are meant to represent on-road driving accelerations and stops. Although exposure is related to emissions, under California law primary ambient air quality standards are based on health and are not based on current concentrations or attainment status.

9. Several studies on indoor and in-vehicle air quality show or predict less exposure than the staff report indicated. (Raised by commenter 1)

This comment is well taken. "Ambient air" refers to the air outside of buildings. Ambient air quality standards represent the maximum concentration of a pollutant for a given averaging time that is a safe outdoor exposure. People spend a significant portion of their time indoors, however, and central-site monitors do not, in general, accurately reflect indoor or personal exposure.

Nonetheless, ambient air quality standards are required by law to relate to outdoor exposures.

In the staff report, p. 20, first two sentences, we have corrected the range of NO_2 concentrations for in-vehicle measurements. The publication by Westerdahl et al. (2005) reported in-vehicle NO_2 levels on specific road segments in the Los Angeles area. In the 3 to 4 day study, concentrations ranged from 0.023 (±0.016) ppm to 0.068 (±0.050) ppm. This correction was indicated in the Errata sheet provided at the Board Hearing and attached in the FSOR package.

10. Information on the distribution of ambient levels of NO_2 should be added to the staff report to aid the reader in evaluating the biologic plausibility of the health effects. Commenter suggests that ambient concentration data from Table 5.4 and Table 5.10 be added to the staff report. (Raised by commenter 1)

The distribution of ambient NO_2 concentrations is detailed in the Technical Support Document, Sec 5.4. The frequency distribution of maximum daily 1-hour concentrations and the population–weighted exposures for all air basins are presented. These were not placed in the staff report due to space limitations and for purposes of being concise.

11. A more accurate picture of the indoor/outdoor NO_2 ratios in spaces without NO_2 sources should be presented. The results of the NO_2 measurements in the recently completed Fresno Asthmatic Children's Environment Study (FACES) are also relevant. While the mean concentration at the Fresno central site was 0.020 ppm, the mean of 332 2-week passive sampler measurements in homes of asthmatic children was 0.013 ppm and the mean in the homes without gas stoves was 0.009 ppm. The implication here is that the indoor values and central site values do not coincide. (Raised by commenter 1)

The commenter provides a summary of the FACES comparing measurements at central outdoor ambient sites to measurements indoors at homes. However, what is not indicated in this comment is that the central site data are based on 24-hour average data, continuously and actively sampled, while the indoor home data is based on 2 weeks of passive sampling. Therefore, two separate sampling methods and averaging times are used for the commenter's comparison. A much more accurate comparison would have been to sample, in parallel, the indoor and outdoor air using the 2-week passive sampler, for example. This however, was not done for the study. Therefore, the conclusion that the comparison of FACES data provides a more accurate measurement of indoor/outdoor ratios is unfounded. Although

there is not complete agreement between outdoor central site monitors and indoor levels of NO_2, a number of epidemiologic studies have found independent associations between outdoor NO_2, as measured at the central site, and hospitalizations and emergency room visits for asthma in children, as detailed in the Technical Support Document. The clinical and toxicological studies also support an adverse effect of NO_2 on respiratory health. Finally, as we reported in the Technical Support Document, when air conditioning is not present, there is some correlation between outdoor and indoor NO_2.

12. Whether exposures actually exacerbate asthma to a clinically significant degree is unknown, so the overall public health significance of the effects that are being used to support a lowering of the 1-hour standard is not clear. In particular the health implications of the Follinsbee study results are unclear. (Raised by commenter 1)

Clinical studies are typically conducted in subjects with mild asthma and exclude those with current or recent respiratory infections which would increase airway reactivity. As noted in the response to question #1, the authors of the clinical studies found evidence of an enhanced allergic response to inhaled allergen after NO_2 exposures at 0.26 ppm for 15 to 30 minutes and evidence of increased airway reactivity in asthmatics at 0.2 to 0.3 ppm for 30 minutes to 2 hours. These two endpoints are hallmarks of asthma, and these endpoints are likely be more pronounced in mild to moderate asthmatics with recent respiratory infections. Further, those with more severe asthma may have an increase in clinical symptoms after exposures to NO_2 in this range.

The report by Folinsbee (1992) showed pooled analysis of studies with NO_2 exposures in a qualitative manner. We did not use these results to support the selection of the 1-hour standard because of the limitations (which were stated in the Technical Support Document) that made quantitation using the pooled method difficult. Nevertheless, the findings of the pooled analyses are supportive and indicate some concern for NO_2 exposures even below 0.18 ppm.

13. The current or proposed 1-hour standard should provide enough health protection without the need of an annual average standard. (Raised by commenter 1)

Human controlled exposure studies demonstrated increased airway reactivity and enhanced allergic response in asthmatics exposed to 0.26 ppm NO_2. Thus, a 1-hour standard of 0.25 ppm NO_2 is clearly not protective. There have been essentially no studies on the enhanced immune response at lower levels to help establish a threshold. The proposed 1-hour standard of 0.18

ppm included a margin of safety as noted above. However, the epidemiologic studies that use 24-hour or longer averaging times provide some evidence for the associations of NO_2 exposure and very serious health outcomes based on longer term exposures. There are a number of epidemiological studies that provide data supporting the need for a long-term average standard. And since exposure durations greater than 1-hour may be possible, a standard for an annual average exposure is justified in order to capture exposures over a longer period of time.

14. The statement that results of the epidemiological studies are consistent with health effects observed during controlled chamber studies and toxicological studies when NO_2 alone is tested, is overly broad and not defensible. (Raised by commenters 1, 2)

Controlled chamber studies have shown effects of NO_2 on mild asthmatics, and these effects are consistent with findings of increased hospitalization for asthma in children and increased symptom reporting in panel studies of asthmatics. Toxicological studies in animals support the human exposure findings in that the primary site of lung damage due to inhalation of NO_2 is the bronchiolar-alveolar duct region. As in humans, the developing lung is a sensitive target of NO_2 toxicity. Exposures of young ferrets and mice have resulted in bronchiolar/alveolar tissue changes, including proliferation of epithelial cells and altered cellularity, increased tissue thickness in the gas exchange area of the lung, and alteration of structural proteins (elastin) in lung tissue. Additionally, consistent indicators of asthma have been produced in animal models. These indicators include enhancement of delayed-type dyspneic symptoms, increased serum IgE levels, increased pulmonary eosinophilia and epithelial injury, and increased bronchial hyperresponsiveness. Therefore, the health effect results being consistent with human chamber and animal toxicological studies are defensible.

15. The reductions in annual average concentrations (below the federal annual average standard) that have occurred in California over the past decades have occurred during a period in which the State did not have an annual average standard. Therefore the annual standard is not needed. (Raised by commenter 1)

Our standards are based on the best health information available. Previous progress on reducing pollution concentrations does not impact this decision. We cannot rely on the 1-hour standard alone to ensure a lower annual average. There is a great deal of variation by air basin in the ratios of the maximum 1-hour concentrations for the year to the yearly average concentration. Therefore, a 1-hour standard may not protect all air basins from exceeding the annual average recommended. For example, the 99th

percentile and single highest value of 1-hour average NO_2 is roughly 4 to 6 times that of the annual average. So a 1-hour standard of 0.18 would be associated with annual averages of between 0.030 and 0.045 ppm. Levels within this range are above the level staff believes to be health protective. In short, an annual standard of 0.030 ppm is necessary for protecting public health over a long exposure period.

16. **There is concern over publication bias since numerous weak but positive associations with NO_2 have been published. Based on the ozone mortality associations and meta analyses commissioned by the U.S. EPA, there is a major discrepancy between the estimated association of ozone mortality from the National Mortality and Morbidity Air Pollution Study (NMMAPS) that evaluated the 90 largest U.S. cities and the meta-analyses. (Raised by commenter 1)**

    Until very recently most epidemiological studies reporting results for NO_2 focused on PM and/or ozone. Therefore, the publication of these studies was not based upon the strength of the NO_2 associations with health outcomes. In fact, all seven studies which reported robust associations between NO_2 and hospital admissions or emergency room visits for asthma (Lee et al. 2006; Peel et al. 2005; Galan et al. 2003; Atkinson et al. 1999; Hajat et al. 1999; Anderson et al. 1998; Sunyer et al. 1997) examined several other air pollutants, including ozone, PM, CO, NO_2 and SO_2. Thus, NO_2 was not the particular focus of investigation in any of these studies. It is true that the NMMAPS analysis of ozone produced a smaller, but positive and statistically significant, effect of ozone than the three U.S. EPA commissioned meta-analyses of ozone. However, this may be due to a more conservative modeling strategy used for the NMMAPS project including use of the same model for every city in the study, even though seasonality is quite different. In addition, studies that have evaluated the potential for publication bias have only reported small drops in the effect estimates. We are not relying on the effect estimates for standard setting. Rather, as discussed in the response to comment # 5, we used the NO_2 averages in cities where effects were seen. In short, an annual standard is necessary for protecting public health over a long exposure period.

17. **The only conclusion that can be drawn from the analyses of epidemiological studies is that while there are many positive epidemiological associations with NO_2 in the literature, individual city studies for these associations are not a reliable basis for adopting an ambient standard due to model differences. The commenter cites a**

study by Koop and Tole that question the reliability of the models used in epidemiologic studies. (Raised by commenter 1)

Re-analyses by HEI (2003) of several time-series studies of air pollution and health effects have found that the results are relatively insensitive to model selection and issues such as model convergence criteria (as in the generalized additive models). In the work of Koop and Tole (2004), the findings are based on one city and included many factors in the models which are not believed to be directly related to health. Rather, these factors influence pollution concentrations, which then impact health. In summary, HEI has indicated that several time-series studies of air pollution and health effects are insensitive to the model used; therefore, the associations of NO_2 with health effects are valid.

18. **The results from NMMAPS are statistically insignificant in multi-pollutant models. (Raised by commenter 1)**

The annual average standard was not based on results from NMMAPS. Although statistically insignificant, the results in multi-pollutant models remained positive for NO_2. Statistical significance alone should not be used as a basis for determining whether an effect is due to NO_2, since the effect is based largely on the power of the study. Adding co-pollutants to the model will decrease the power, especially if there is large co-linearity. The important issue is whether adding co-pollutants decreases the effect estimate. In the NMMAPS study the NO_2 effect remained the same or increased slightly. In addition, many other studies besides NMMAPS show important effects of NO_2 on health, as summarized in Chapter 7 of the Technical Support Document.

19. **The use of central station monitoring data, meteorological data, and available health statistics yield many weak positive associations. The interpretation of a subset of positive findings as causal of a given effect is problematic. (Raised by commenter 1)**

The use of central station monitoring can actually bias the results towards the null. For example, investigators have addressed measurement error in air pollution studies using simulations and concluded that it was likely that using ambient concentrations instead of personal exposure concentrations could underestimate the magnitude of the health effect. We are not inferring causality. Rather, we maintain that several studies establish positive associations and further affirm our understanding of the health effects of NO_2

20. **ARB staff acknowledges that it is difficult to distinguish the effects of NO_2 from other traffic-related pollutants, but assert that it is prudent to**

regulate NO_2 since other traffic-related pollutants are not regulated. This is not logical. Reducing NO_2 may or may not reduce other traffic generated pollutants, depending on the technology chosen. (Raised by commenter 1)

The statement on pages 7-18 through 7-19 of the Technical Support Document indicates that we do not have ambient air quality standards for traffic-related such as black carbon, ultrafine PM (0.1 µm or less), and PAHs – not that we don't regulate traffic-related pollutants. NO_2 is part of the mix of traffic-related pollutants, but our review of the evidence strongly suggests an independent effect as well. The time-series studies evaluating the relationship between NO_2 and both hospital admissions and emergency department visits for asthma or respiratory disease in children and adults are fairly consistent and robust (Peel et al. 2005; Simpson et al. 2005; Galan et al. 2003; Atkinson et al. 1999; Hajat et al. 1999; Anderson et al. 1998; Sunyer et al. 1997; Lee et al. 2006). The associations between NO_2 and these health outcomes often remained significant in models that included both NO_2 and other pollutants, such as ozone, PM, CO, and SO_2, even when health effects from one or more of the latter pollutants were also statistically significant. In addition, the epidemiologic evidence for respiratory effects is supported by the short-term toxicological and clinical studies for which exposure mismeasurement is not an issue. Therefore, it is likely that reductions in NO_2 will bring improvements in public health protection to justify an ambient air quality standard. The comment regarding the reduction of co-pollutants is not pertinent to this rulemaking because under California law, the adoption and implementation of control measures based on chosen technologies is separate from the standard setting process.

21. The staff should carefully evaluate the extent to which the animal studies support the biological plausibility of the effect of NO_2. The dose needed to induce observable effects in animals needs to be carefully considered as part of these analyses. (Raised by commenter 1)

Staff carefully evaluated the animal toxicology studies and their support of the biological plausibility of adverse health effects from NO_2 exposure in a number of ways. First, prolonged repeated exposure of young animals during lung development show changes in lung structure ($\geq$0.25 ppm) Second, in animal models of allergic asthma, exposure to high concentrations of NO_2 ($\geq$ 5 ppm) produces consistent increased markers of allergic inflammation. Third, animal studies suggest that there is oxidant damage, a result that is consistent with findings of human studies. Although these exposures appear

to be higher than the levels to which humans are exposed, dosimetry models indicate that the amount of NO_2 reaching the deep lungs of rodents who inhale 1 ppm NO_2 is about equivalent to humans inhaling 0.25 ppm NO_2. Thus an animal exposed at 0.25 ppm would be equivalent to human exposure at ~ 0.06 ppm which is a level near the current federal standard: and is comparable to ambient concentrations experienced in California in the 1980s.

22. The epidemiology results suggest that something other than NO_2 is causing the effects. For example, the Gauderman (2005) study does not implicate NO_2 per se, but rather a number of pollutants (for example, PM). (Raised by commenter 1)

As noted in item 4, the Children's Health Study (Gauderman et al. 2004) found associations between deficits in lung function growth and mixtures of the oxidant pollutants (NO_2, PM, and acid vapor). We are not asserting that NO_2 is the only causal factor in this epidemiological study but that NO_2 may be a contributing factor. Animal toxicology studies support the conclusion that chronic exposures to NO_2 can lead to changes in lung architecture.

APPENDIX A

ERRATA

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State of California
AIR RESOURCES BOARD

ERRATA

Review of the California Ambient Air Quality Standard for Nitrogen Dioxide
Staff Report and Technical Support Documents, released January 5, 2007

PLEASE BE ADVISED that errors in the staff report (Initial Statement of Reasons for Proposed Rulemaking) and Technical Support Documents, jointly titled "Review of the California Ambient Air Quality Standard for Nitrogen Dioxide" have been corrected below. These documents were released on January 5, 2007, and are available at the following sites.
The staff report is available at the following ARB Internet site:
http://www.arb.ca.gov/regact/no207/isor.pdf.
The Technical Support Document is available at the following ARB Internet site:
http://www.arb.ca.gov/regact/no207/techsupdoc.pdf.

The corrections are shown in strikethrough, underline format: text to be deleted is shown as ~~strikethrough~~, and text to be inserted is underlined. Any questions regarding these corrections should be directed to Linda Smith, Manager, Health and Ecosystems Exposure Assessment Section at (916) 327-8225.

Date: February 22, 2007

1) Staff Report & Technical Support Documents, second cover page, "Acknowledgements":
In addition, staff also wish to thank and acknowledge the following individuals from the Air Resources Board: Sara Adams, Rebecca Boyer, Ken Bowers, Richard Corey, Robert Effa, Michael FitzGibbon, Peggy Jenkins, Larry Larsen, Karen Magliano, Steve Mara, Eileen McCauley, Lori Miyasato, Matt Quok, Mike Robert, Mena Shah, Ken Stroud, Hien Tran, William Vance, Tony VanCuren, and Bob Weller.

2) Staff report, p. 19, second paragraph:
~~Indoor/outdoor NO_2 ratios vary greatly. They range from less than 1 for homes without an indoor source to values greater than 3 for homes with indoor sources (Lee et al. 2002, Petreas et al. 1988).~~

3) Staff report, p. 19, fourth paragraph, second sentence:
This is of concern because these levels are well above the ambient air quality standard. Furthermore, these indoor measurements have been made with passive monitors that utilize a long averaging time, and do not adequately reflect peak exposure levels that occur throughout the day.

4) Staff report, p. 20, first two sentences:
Westerdahl et al. (2005) reported in-vehicle NO_2 levels on specific road segments in the Los Angeles area. In the 3-4 day study, the concentrations ranged from 0.023 (±0.016) to ~~0.039 (± 0.012)~~ 0.068 (±0.050) ppm on the road.

5) Technical Support Document, p. 5-68, alphabetical list of References:
ARB ~~2005.~~ 2006. 2005 Air Quality Data CD

6). Technical Support Document, p.10-4, second paragraph:
The spectral distribution of these phenomena is shown in Fig. ~~11-6.~~ 10-6.

7) Technical Support Document, p. 8-76, alphabetical list of References:
Drumm, K., Buhl, R., Kienast, K. 1999. Additional NO_2 exposure induces a decrease in cytokine specific mRNA expression and cytokine release of particle and fibre exposed human alveolar macrophages. Eur J Med Res 4:59-66.

State of California
AIR RESOURCES BOARD

CORRECTIONS to ERRATA

Under 1) “Acknowledgements” in the ERRATA page, Sara Adams is from the Office of Environmental Health Hazard Assessment and is incorrectly listed under the Air Resources Board.