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on
EPA's Second Draft Risk and Exposure Assessment (REA) to Support the Review of the NO_2 Primary National Ambient Air Quality Standard EPA-452/P-08-004a August 2008

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The American Lung Association offers these preliminary comments on EPA's Draft Risk and Exposure Assessment for Nitrogen Dioxide.

We are concerned about the National Ambient Air Quality Standards (NAAQS) for nitrogen dioxide (NO_2) because there is strong evidence from all three branches of investigation -- epidemiologic, controlled human exposure, and animal toxicology studies -- of adverse respiratory effects in asthmatics.

The current standard for NO_2 -- an annual average standard -- was set in 1971 and has not been revised since then. In the past 35 plus years there has been a great deal of evidence pointing to the need for a short-term standard.

According to the Integrated Science Assessment (ISA), new evidence confirms earlier findings that short-term NO_2 exposures are associated with increased airway responsiveness, often in conjunction with respiratory symptoms, particularly in children and asthmatics. Studies of respiratory symptoms, emergency department visits and hospital admissions report increased risks associated with NO_2 even in areas where daily concentrations never go above the level of the current annual average standard (53 ppb).

In 2005, the World Health Organization reaffirmed its recommendation for both an annual average and a 1-hour standard for NO_2.[1] In 2007, after an extensive review, the California Air Resources Board established a new annual average NO_2 standard of 30 ppb and lowered the 1-hour limit to 180 ppb, not to be exceeded.

While everyone likes to see more analysis, the bottom line under the Clean Air Act is that EPA must revise the NO_2 standard without regard to the air quality data, exposure assessment and risk assessment. Whatever the output of these analyses, EPA can not

[1] The WHO guidelines for NO_2 are 21 ppb annual average standard and 104.5 ppb 1-hour standard.

report to the people of this nation and the world that the current standard for nitrogen dioxide represents a safe level of air pollution.

With that, we would like to offer a few comments on specific chapters of the draft REA.

Chapter 4: Health Effects

Since the last review, over 50 peer-reviewed epidemiological studies have been published examining the effect of short-term nitrogen dioxide concentrations on the rate of emergency and hospital admissions for respiratory diseases. We concur with the draft document's conclusion in Chapter 4 that the positive associations with nitrogen dioxide are consistent for children and older adults when looking at all respiratory outcomes (asthma, bronchitis, emphysema, pneumonia, upper and lower respiratory infections) and among children and subjects of all ages for asthma admissions. The results are robust to the effects of co-pollutants, and are coherent with findings from toxicological and controlled human exposure studies. There is also strong new evidence of respiratory symptoms, particularly in children, from the epidemiological studies.

Furthermore, there is clear evidence from the controlled human exposure studies that NO_2 enhances the responsiveness of the airways to allergens. This airway hyperresponsiveness -- a narrowing of the airways in response to various stimuli -- is a hallmark of asthma. A meta-analysis using individual level data from 19 clinical studies reports that 66 percent of subjects experience an increase in airway responsiveness following 1-hour exposures to 100 ppb NO_2 , the lowest level studied. It cannot be overemphasized that these studies typically include only mildly asthmatic adults. Thus safety factors must be incorporated to account for interindividual variability and potential effects on infants, children, and those with moderate or severe asthma or other respiratory disease. Typically, in other standard-setting arenas, EPA determines the lowest observed adverse effect level (LOAEL) from the experimental studies and applies several safety factors of ten each to account for various uncertainties, thus setting the standard at $1/10^{th}$, $1/100^{th}$, or 1/1000 of the LOAEL.

Additionally, an important development in environmental health research in recent years has been the growing use of studies based on geographic information systems to assess the effects of air pollution. In particular, since EPA's last review of the NO_2 standard, a large number of studies have been published relating traffic air pollution to a variety of health endpoints. These studies show that people that live near roads with heavy traffic are at increased risk of adverse health effects from roadway pollution.

We are concerned that a large body of studies of the effects of traffic pollution exposure measured as distance to roadway have not been included and evaluated as part of this review. The traffic studies, which evaluate residency in proximity to major roadways, have particular relevance to the question of the effects of long-term exposures.

Chapter 4 identifies potential health effect benchmark values of 100, 200, 250, and 300 ppb derived from the controlled human exposure studies. We believe the upper values

are far too high to be considered further. Not only are the majority of subjects are found to be responsive at 100 ppb, but even those studies have focused largely on mild asthmatics. To be blunt, the upper benchmarks of 250 and 300 ppb should be dropped.

In addition, we believe it is extremely confusing to define benchmarks of concern that differ from the potential alternative standards analyzed in the risk assessment. It will not be obvious to policy makers that the health effects benchmarks are based on the clinical studies only, and don't consider epidemiology studies showing effects at lower concentrations.

Chapter 5: Identification of Potential Alternative Standards for Analysis

Chapter 5 includes a discussion of potential alternative standards -- including a discussion of a potential indicator pollutant, averaging time, form, and level -- to provide some inputs for analysis in the quantitative risk assessment.

We strongly agree with EPA's judgment in Chapter 5 that it is appropriate to consider a new short-term standard, and that a 1-hour averaging time seems suitable in light of the effects observed in chamber and laboratory studies.

From the discussion, it appears that EPA may be dismissing the need for the annual average standard. This would be entirely premature. At minimum, the annual average standard is important to lowering the full distribution of exposures, not just the peak 1-hour concentrations. Furthermore, the ISA does not thoroughly discuss the distance to roadway studies that measure the effects of long-term exposures to traffic pollution. In its recent review of the NO_2 standard, California decided to establish a new annual average standard based on the traffic studies, as well as the potential effects of NO_2 on serious health endpoints suggested by the traditional epidemiology studies, and the toxicology studies showing alterations in lung structure in young animals due to long-term exposures. California, unlike the ISA, recognized that roadway studies measure the effects of long-term exposures to traffic pollution. Among the criteria pollutants, NO_2 and PM are likely to be the best markers of traffic-related pollution. It is too early in the process to dismiss the importance of an annual average standard.

The American Lung Association has a longstanding objection to percentile forms of the standard. It is inappropriate to dismiss 1 or 2 percent or more of the highest monitor readings from the compliance determination when the goal of the short-term standard is to avoid peak concentrations.

Both the 98th and 99th percentile forms of the standard are inappropriate considering that the goal of a short-term standard is to limit peak exposures. For instance, the 98th percentile form would dismiss 175 of the highest hourly readings from the compliance determination. The single exceedance or "not to be exceeded" form of the standard is far preferable.

With respect to the levels of the standard, it appears that EPA has selected both the upper end and the lower end of the range at levels clearly associated with adverse effects in the human clinical and epidemiological studies, including the Delfino et al. 2002 study that demonstrated increases in asthma symptoms at 50 ppb. Such an approach is inappropriate because it precludes the provision of a margin of safety to protect sensitive populations. The Clean Air Act requires inclusion of a margin of safety in any final standard. Furthermore, as discussed below, consideration of the epidemiological studies of respiratory symptoms, respiratory emergency department visits and hospital admissions would lead to selection of a far lower bottom end of the range.

Chapter 7: Ambient Air Quality Assessment and Health Risk Characterization

Since the last review, the number of NO_2 monitors nationwide has declined by 37 percent, down from 440 (in 1998) to 289 monitors in 2007.[2] Thus our ability to characterize ambient concentrations has diminished in the face of dramatic new evidence of short-term effects at contemporary concentrations. This chapter should include a discussion of the strengths and weaknesses of the current monitoring network with respect to the siting criteria and the ability to detect maximum NO_2 concentrations from stationary and mobile sources. With only 289 monitors to detect NO_2 concentrations over a land area of over 3.5 million square miles, there must be significant uncertainties about the spatial and temporal extent of maximum concentrations.

Given the paucity of monitoring data, we do not understand why areas with incomplete data were excluded. Information on the peak hourly values at these sites may be of interest, even though readings are not available for all the hours. In the analysis of hourly concentrations, it is really the peak rather than the average concentrations that are most relevant.

To state the obvious, assessments of current concentrations are not informative with respect to potential future emissions increases.

Chapter 8: Exposure Assessment and Health Risk Characterization

We will reserve our discussion pending release of this chapter, except to note that exposure assessments are based on numerous assumptions and fraught with uncertainty. Far too often they serve to minimize the impact on populations at risk. Exposure assessments are not an appropriate basis for standard setting under the Clean Air Act.

The ISA concludes correctly that evidence shows positive associations of short-term NO_2 concentrations below the current NAAQS level with increased numbers of ED visits and

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2 http://iaspub.epa.gov/airsdata/adaqs.count?geotype=us&geocode=USA&geoinfo=us%7EUSA%7EUnited+States&pol=NO2&year=1998&fld=siteid&fld=address&fld=city&fld=county&fld=stabbr&fld=regn&rpp=25

hospital admissions for respiratory causes, especially asthma. Standards must be set to protect against these and other respiratory effects, regardless of the number of estimated exposures.

Chapter 9: Characterization of Health Risks Using Data From Epidemiological Studies

EPA has chosen an extraordinarily narrow approach to the risk assessment, focusing only on emergency department visits in Atlanta. The danger of such a limited approach is that focuses attention on the quantified risks, which are only a small subset of the health risks, to the exclusion of the vast majority of risks, which are unquantified. Moreover, by looking at just one city, EPA is taking too conservative an approach, failing to extrapolate risk estimates beyond the cities included in the original studies.

Of the range of standards analyzed, the draft risk assessment reports potential benefits in Atlanta only at the 50 ppb standard level. According to the ISA, a number of studies of ED visits and hospital admissions for respiratory causes reported positive associations where mean 24-hour concentrations were in the range of 3 to 50 ppb. (ISA p. 5-11.) This result suggests that both the upper and lower ends of the range of alternative standards are too high, since risks are evident only at the lower end of the analyzed range.

We note that a number of factors in the analysis, such as the limited availability of baseline emergency visit data, lead to underestimates in reported risks.

Recent multi-city epidemiological studies have also reported associations between ambient NO_2 concentrations and respiratory symptoms at relatively low concentrations. Positive associations were observed in cities where the median range was 18 to 26 ppb for a 24-hour average (Schildcrout et al., 2006) and where the mean NO_2 level was 32 ppb for a 4-hour average (Mortimer et al., 2002). EPA should consider broadening the risk assessment to examine respiratory symptoms in a range of cities.