

**For discussion on the March 3, 2011 teleconference of the Ozone Review Panel for the
Reconsideration of the 2008 National Ambient Air Quality Standard (NAAQS).
This is a deliberative draft letter. It does not represent consensus CASAC advice or EPA policy.
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1
2 Dear Administrator Jackson:

3
4 This letter is written to provide comments of the Clean Air Scientific Advisory Committee
5 (CASAC) in response to the charge questions submitted in the January 26, 2011 memorandum
6 from the Office of Air Quality Planning and Standards (OAQPS). The questions are related to
7 the current reconsideration of the 2008 proposed National Ambient Air Quality Standard
8 (NAAQS) for Ozone.

9
10 As you know, CASAC has an extensive record of providing independent peer review on the
11 Agency's technical documents on the Ozone NAAQS. From 2005 to 2008, CASAC reviewed
12 two drafts of the staff paper (now called the Policy Assessment), two drafts of the criteria
13 document (now called the Integrated Science Assessment), two drafts of the risk assessment and
14 two drafts of the exposure assessment. As stated in our letters of October 24, 2006, March 26,
15 2007 and April 7, 2008 to former Administrator Stephen L. Johnson, CASAC unanimously
16 recommended selection of an 8-hour average ozone NAAQS within the range proposed by EPA
17 (0.060 to 0.070 ppm). In response to the Agency's promulgation of the National Ambient Air
18 Quality Standards (NAAQS) for Ozone, published on March 12, 2008, revising the 8-hour
19 "primary" ozone standard, designed to protect public health, to a level of 0.075 ppm, CASAC
20 offered comments in a letter to former Administrator Johnson on April 7, 2008. CASAC did not
21 endorse the new primary ozone standard (0.075 ppm) as being sufficiently protective of public
22 health.

23
24 In response to EPA's reconsideration of the 2008 Ozone NAAQS and proposal published on
25 January 19, 2010, CASAC reaffirmed its support for the selection of an 8-hour average ozone
26 NAAQS within the 0.060 – 0.070 ppm range. In our letter of February 19, 2010, we reiterated
27 our support for this range and referred to the supporting evidence as presented in *Air Quality*
28 *Criteria for Ozone and Related Photochemical Oxidants* (March 2006) and *Review of the*
29 *National Ambient Air Quality Standards for Ozone: Policy Assessment of Scientific and*
30 *Technical Information* (OAQPS Staff Paper, July 2007).

31
32 While we are concerned that EPA's most recent request for additional CASAC advice is
33 redundant with our past reviews, we nonetheless are submitting this letter and the attached
34 consensus advice in the hopes that EPA will take action with this scientific input. In general we
35 found that [TO BE FILLED IN AFTER DISCUSSION].

36
37 Moreover, at EPA's request, our deliberations were constrained to the evidence assembled in the
38 prior review cycle, i.e. a science record that closed in 2006. This imposed an artificial boundary
39 on our discussions. While written comments from individual panelists include more recent
40 studies, our consensus responses to the charge questions are based on the literature considered in
41 the last cycle.

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Draft Responses to Charge Questions

1. **What is your advice on the overall strengths and limitations of the evidence from controlled human exposure and epidemiological studies and the results of the exposure and risk assessments, in the context of EPA's selection of a standard level within the proposed range that would be requisite to protect public health with an adequate margin of safety, including the need to protect susceptible populations, such as children and people with asthma?**

A major strength of the evidence from the controlled human exposures to ozone is the high quality of the established investigators engaged in the research at distinguished institutions who did their best to measure pulmonary function changes and changes in lung inflammation based on biomarkers in bronchoalveolar-lavage fluids. In general, there were more data on the acute effects of short-term exposures to a respiratory irritant here than for any other regulated and unregulated air pollutants, and the results were quite consistent over a wide range of ozone concentrations and exposure durations. While the CASAC Panel did not consider the findings of recent publications (post-2005) in reaching this judgment, it was aware that the results of these more recent studies were consistent with those of the earlier studies that formed the basis for our judgments on the effects produced by controlled human exposures. In interpreting these findings, we note that most of the studies that have influenced our judgments on the proposed range were studies that involved exercise as a necessary factor for revealing adverse responses to ozone. Of course, many Americans exercise out-of-doors, so that's relevant to their responses to ozone, since higher levels of ventilation, and especially switching from nose to mouth breathing, have a substantial effect on responses that are known to be associated with ozone inhalation. It is also important to note that controlled exposure studies usually do not include sensitive and vulnerable populations (SVP) as subjects, which makes it more difficult to extrapolate results to the SVP that the NAAQS is intended to protect, resulting in a bias that underestimates the effects on members of SVP subgroups of a given ambient air concentration.

Another strength of the available evidence is the considerable amount of epidemiologic data, which provides the advantage of being based on responses in generally much larger numbers and more diverse subjects, and typically less invasive procedures for measuring responses. In chamber studies, exposures are limited to ozone alone. While ambient ozone measurements used in epidemiological studies are reasonably specific to ozone, they are actually an indicator of the presence of other strong photochemical oxidants in the ambient air, and thus the health effects in natural settings may be larger than if the exposure were only to ozone. Since the health-related functional and inflammatory changes in seen in panel studies are also seen in the controlled chamber exposure studies with ozone, and are not known to occur with exposures to co-pollutants in ambient air at realistic concentrations, their influence is likely to exacerbate the effects of the ozone.

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1 Thus, reducing ozone concentrations is likely to reduce the effects of the mixture as a
2 whole.

3
4 While ambient ozone measurements used in epidemiological studies are reasonably
5 specific to ozone, they are actually an indicator of the presence of other strong
6 photochemical oxidants in the ambient air, and thus the health effects in natural settings
7 may be larger than if the exposure were only to ozone. Another potential difference
8 between controlled exposure and epidemiological studies is the reaction products from
9 ozone once it gets indoors. These reaction products include a wide range of gas-phase
10 respiratory irritants and ultra-fine particles. Epidemiology would take these other
11 oxidants into account to some greater or lesser extent with respect to the covariance of
12 the other ambient oxidants with ozone. It should also be noted that central monitors,
13 particularly those placed in downwind locations in urban areas to avoid significant
14 titration effects of nitric oxide in motor vehicle emissions that scavenges ozone and
15 thereby lowers ozone concentrations within traffic corridors, may not be an adequate
16 measure of population exposure to ozone across larger urban areas.

17
18 Taken together, the evidence from controlled human and epidemiological studies strongly
19 supports the selection of a new primary ozone standard that is well below the 1997
20 standard of 0.08 ppm over an 8-hour averaging time. There is scientific certainty that
21 6.6-hour exposures to concentrations ≥ 0.08 ppm with intermittent exercise, cause
22 clinically relevant decrements of lung function in young, healthy volunteers. The results
23 of multiple epidemiological studies also show that children and adults with asthma are at
24 increased risk of acute exacerbations of this disease on or shortly after days when ozone
25 concentrations are elevated above background but remain below 0.08 ppm. Given the
26 need to protect public health with an adequate margin of safety, and of the results of
27 EPA's exposure and risk assessments, setting a new NAAQS in the range of 0.060 to
28 0.070 is appropriate.

29
30 In summary, the strengths of the evidence from controlled human exposure and
31 epidemiological studies enumerated in the Criteria Document and its update were
32 substantial, and more than adequate to support the recommended range for the NAAQS
33 of 0.060 to 0.070 ppm. The limitations of the evidence from controlled human exposure
34 and epidemiological studies were well and appropriately stated in the Staff Paper.

- 35
36 **2. Recognizing that controlled human exposure studies at 0.080 ppm O₃ and above**
37 **have provided evidence of other health effects, including inflammation and**
38 **increased airway responsiveness which may occur through different physiological**
39 **mechanisms than the reduction in FEV₁, how should the results of these studies**
40 **inform our understanding the health effects to healthy adults at exposures levels**
41 **from 0.060 to 0.070 ppm?**
42

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1 Results from earlier studies at 0.08 ppm O₃ and above were reviewed in earlier Criteria
2 Documents and were primarily summarized in less detail in the current ISA. One issue
3 that should be incorporated in our thinking is that in order to extrapolate from higher to
4 lower concentrations one must consider the dosimetry of O₃. Several articles have
5 pointed out that pulmonary function [1] and other responses[2] are functions of
6 relationships between exposure concentration, ventilation rate and exposure time, among
7 other variables. The responses seen at levels below 0.08 ppm in the Adams and other
8 studies are consistent with those that one can predict using dosimetric and effective dose
9 calculations. It is also important to recognize that most of the controlled studies relevant
10 to O₃ health effects were conducted with healthy, non-smoking young adults. Chamber
11 studies of asthmatic and non-asthmatic subjects exposed to O₃ at relatively high
12 concentrations showed that the changes in FEV1 and MMEF were significantly greater in
13 the asthmatic than in the non-asthmatic subjects[3]. For ethical reasons, controlled
14 exposure studies involve effects that are relatively mild and reversible, including changes
15 in pulmonary function and increased evidence of inflammatory changes. One
16 characteristic response to low O₃ exposure levels is mucosal neutrophilic inflammation
17 probably mediated by phospholipid-derived products and by epithelial cell-derived
18 chemokines and cytokines [4]. This response may be poorly correlated with lung
19 function changes perhaps because the time course of development for these responses is
20 different from that for changes in FEV1 or because the mechanism of ozone-induced
21 decrements in lung function may not be related to airway inflammation. In fact some
22 individuals may exhibit inflammation without significant changes in pulmonary function.
23 However the data showing elevated levels of inflammatory cytokines, infiltration of
24 inflammatory cells (macrophages and neutrophils) and evidence of oxidative changes
25 provide important components of the biological plausibility and advance our
26 understanding of the mechanisms by which O₃ affects health and may provide
27 mechanistic support for the observed epidemiological associations with regard to
28 exacerbations of asthma at concentrations below 0.080 ppm. It should be noted that
29 inflammatory effects are likely to be more serious for individuals with chronic lung
30 diseases. This is consistent with the exposure chamber study findings that individuals
31 with chronic obstructive pulmonary disease had significantly greater losses of pulmonary
32 function (19% from their baseline) than did healthy controls when exposed to O₃ during
33 light exercise [5]. While these studies are often performed at exposure concentrations
34 higher than typical ambient conditions, they serve to identify disease-relevant
35 mechanisms and also to underscore the inherent variability of even healthy populations
36 with respect to their responses to O₃. It is important that we consider this person to
37 person variability in sensitivity to O₃ as we examine whether the current or proposed
38 ambient concentration ranges provide an adequate margin of safety for sensitive
39 individuals in the population.
40

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1 McDonnell, W.F., et al., *Prediction of ozone-induced FEV1 changes. Effects of*
2 *concentration, duration, and ventilation.* Am J Respir Crit Care Med, 1997. **156**(3 Pt 1):
3 p. 715-22.

4 Mudway, I.S. and F.J. Kelly, *An investigation of inhaled ozone dose and the magnitude of*
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7 Kreit, J.W., et al., *Ozone-induced changes in pulmonary function and bronchial*
8 *responsiveness in asthmatics.* J Appl Physiol, 1989. **66**(1): p. 217-22.

9 Bromberg, P.A. and H.S. Koren, *Ozone-induced human respiratory dysfunction and*
10 *disease.* Toxicol Lett, 1995. **82-83**: p. 307-16.

11 Gong, H., Jr., et al., *Responses of older men with and without chronic obstructive*
12 *pulmonary disease to prolonged ozone exposure.* Arch Environ Health, 1997. **52**(1): p.
13 18-25.

14
15
16 **3. How should the results of the controlled human exposure studies at 0.060 ppm O₃,**
17 **showing effects on FEV₁ and respiratory symptoms, in the context of the larger**
18 **body of evidence from controlled human exposure studies, mentioned above, inform**
19 **our understanding of the health effects to healthy adults at exposure levels from**
20 **0.060 to 0.070 ppm?**

21
22 The results of only one controlled human exposure study of the effect of ozone at
23 concentrations <0.080 ppm are available for the committee to consider (Adams, 2006).
24 This study was well-designed and conducted with appropriate methods. The authors
25 reported a statistically significant group mean decrement in FEV1 of 4.7% after 6.6-hour
26 exposure to 0.080 ppm as compared to the response to filtered air (a 1.35% increase in
27 FEV1). They also reported group mean decrement in FEV1 of 1.5% after 6.6-hour
28 exposure to 0.060 ppm ozone that was not significantly different from the response to
29 filtered air. However, eight of the 30 subjects in the Adams et al. study experienced
30 decrements in FEV1 >5% and two had decrements >10%, a decrease in lung function
31 determined to be clinically relevant by the American Thoracic Society. The results of the
32 Adams et al. study fit well with those from multiple other studies of the effect of ozone
33 on lung function at concentrations ≥0.080 ppm, which have consistently shown that some
34 individuals are more sensitive to this effect of ozone than others.

35
36 As discussed at length in the Criteria Document and Staff Paper, there is no evidence of a
37 threshold level for ozone with regard to decrements in lung function. The magnitude of
38 the effect diminishes with decreasing ozone concentration, but does not reach the
39 functional level associated with exposure to ozone-free filtered air. Furthermore, there is
40 a great degree of variability of response magnitude among the healthy individuals
41 studied, with some having clinically relevant responses, even at 0.060 ppm, and more of
42 them with such responses at higher concentrations.

1
2 **4. With respect to the information from controlled human exposure studies at 0.060**
3 **ppm O₃, what is the scientific importance of the small, group mean FEV₁**
4 **decrements relative to the findings that 7 to 20% of the subjects experienced FEV₁**
5 **decrements \geq 10%? Please consider this question from both a public health and a**
6 **clinical perspective.**
7

8 The inset plot of the Adams data (Adams 2006), derived from Figure 8-2 of Volume I of
9 “Air Quality Criteria for Ozone and Related Photochemical Oxidants, 2006”, shows an
10 approximate normal distribution in the O₃-induced changes in FEV₁ with exposure to
11 0.060 ppm. Although the mean decrement is less than 3% and would not be considered
12 clinically important, the shift to the right in this distribution pushes a fraction of subjects
13 (7%) into the region that becomes clinically important (>10% decrement). The
14 consistency of effects across O₃ exposure levels within the Adams study, as well as the
15 consistency with effects observed by an earlier independent study (McDonnell et al.
16 1991), indicate that the observed deficits in FEV₁ at 0.060 ppm from the Adams study
17 are not likely to be spurious. In other words, it is likely that prolonged exposure to 0.060
18 ppm O₃ causes a general shift in the distribution of FEV₁ towards lower values.
19

20 All of the Adams study subjects were healthy volunteers. From a public health
21 standpoint, these results suggest that a large number of individuals in the general
22 population (that are otherwise healthy) are likely to experience FEV₁ deficits greater than
23 10% with prolonged exposure to 0.060 ppm O₃.
24

25 A 10% decrement in FEV₁ is often associated with respiratory symptoms, especially in
26 individuals with pre-existing pulmonary or cardiac disease. For example, people with
27 chronic obstructive pulmonary disease have decreased ventilatory reserve (i.e., decreased
28 baseline FEV₁) such that a \geq 10% decrement could be associated with moderate to severe
29 respiratory symptoms. The exposure and risk assessment conducted for the last review of
30 the ozone NAAQS clearly document that a substantial proportion of the U.S. population
31 is exposed to levels of ozone at the various alternative standards considered. This means
32 that even if a NAAQS of 0.060 ppm were to be adopted, some sensitive individuals could
33 still be exposed to concentrations that could cause them to have a clinically relevant
34 decrement in lung function.
35

36 The experimental study results in healthy subjects essentially preclude, because of the
37 ethics of carrying out clinical studies in diseased individuals, extension of these studies to
38 what are likely to be more sensitive groups. Thus, without having specific studies among
39 asthmatics and children at these levels of exposure, it is prudent, in spite of the
40 uncertainty, that EPA select an exposure level below the current standard (closer to the
41 0.060 ppm level) to “protect public health with an adequate margin of safety, including
42 the need to protect susceptible populations.”

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2 Adams WC. 2006. *Comparison of chamber 6.6-h exposures to 0.04-0.08 PPM ozone via*
3 *square-wave and triangular profiles on pulmonary responses.* Inhal Toxicol 18(2): 127-
4 136.

5
6 McDonnell WF, Kehrl HR, Abdul-Salaam S, Ives PJ, Folinsbee LJ, Devlin RB, et al.
7 1991. *Respiratory response of humans exposed to low levels of ozone for 6.6 hours.* Arch
8 Environ Health 46(3): 145-150.

9
10 **5. The evidence, including that summarized above, indicates that susceptible**
11 **populations may have greater responses than healthy people. In light of this**
12 **evidence, how can we appropriately use the results of controlled human exposure**
13 **studies conducted on healthy adults, as well as the epidemiological studies of**
14 **susceptible groups, to inform a judgment on the effects of ozone exposure on**
15 **susceptible populations?**

16
17 In many ways, the lowest exposure level of 0.06 ppm showing some symptom changes
18 and statistically significant lung function changes in healthy subjects in an EPA analysis
19 conducted for the last O₃ NAAQS review represented a greatest lower bound on the
20 ozone concentration of public health concern. In all of the controlled human exposure
21 studies at 0.08-ppm ozone and below, a reasonable percentage of healthy subjects have
22 lung function changes much higher than the average response (e.g., FEV1 changes > 10
23 %). While FEV1 changes > 10% may still allow healthy individuals to go about their
24 normal daily activities, individuals with compromised lungs, such as asthmatics, incur
25 significant health impacts with such lung function changes. As CASAC has noted in the
26 past to the Agency, evidence is accumulating that persons with asthma, the elderly, and
27 particularly children, are more sensitive and experience larger decrements in lung
28 function due to O₃ exposure than do healthy volunteers.

29
30 This, coupled with the fact that a number of epidemiology studies discussed in the last
31 review were showing O₃-related effects on various health endpoints (e.g., emergency
32 department visits and increased hospital admissions for respiratory illness) at relatively
33 low exposure levels leads one to conclude that O₃ may cause effects even below 0.06
34 ppm. Since strengthening such a conclusion would need additional data from studies
35 conducted post 2006, the CASAC concluded at the last review that the lower range of
36 consideration for revision of the NAAQS should be 0.060 ppm O₃. By doing so, the
37 CASAC felt that margin of safety considerations would better be met than at 0.070 ppm
38 O₃. Moreover, since the relative strength of the science is weaker as one lowers the O₃
39 concentration under consideration, a range of 0.060 to 0.070 ppm O₃ allows the
40 Administrator to place her judgment on the weight that any uncertainties and limitations
41 in the science play in selecting an exposure level protective of public health.
42

1
2 **6. To what extent does your confidence that the effects observed in epidemiological**
3 **studies are attributable specifically to O₃ lessen or otherwise change, if at all, at the**
4 **lower levels in the proposed range as compared to the higher levels?**
5

6 While epidemiological studies are inherently more uncertain as exposures and risk
7 estimates decrease (due to the greater potential for biases to dominate small effect
8 estimates), specific evidence in the literature does not suggest that our confidence about
9 the estimated effects of ozone on health outcomes differs over the proposed range of
10 0.060-0.070 ppm. For instance, mortality effects for ozone have been found
11 concentrations well below the proposed range, both in single communities where the
12 community mean ambient concentrations are well below the proposed range (e.g. Vedal
13 et al 2003) and in a multi-city study where high ozone days have been excluded. In
14 the latter case Bell et al (2006) analyzed the NMMAPS database to directly consider the
15 evidence for a threshold and showed that the effect estimates for the excess risk of
16 mortality attributed to ozone did not change as high ozone exposure days were excluded.
17 This analysis progressively excluded days with 24-hour average ozone well below the
18 lowest level of the proposed range. Similarly, health care utilization for asthma has been
19 shown to decrease when ozone concentrations decreased. For example, when traffic
20 density was decreased during the Summer Olympic Games in Atlanta in 1996, there was
21 significantly decreased use of pediatric care for asthma that correlated best with a
22 reduction in peak ozone concentrations (Friedman et al., 2001). In this study, the relative
23 risk of asthma events increased stepwise at cumulative ozone concentrations 0.060 to
24 0.089 ppm and 0.090 ppm or more compared with ozone concentrations of less than
25 0.060 ppm. The reduction of the adverse effects on asthma in this study was dependent
26 on reduction of ozone exposures to levels below 0.060 ppm.
27

28 Our confidence that the effects from epidemiological studies are attributable to ozone is
29 also bolstered by the recognition that the endpoints of concern don't change at the lower
30 levels of the proposed range. While it is difficult to tease out the effects of a single
31 pollutant in epidemiological studies, the evidence regarding ozone-related health effects
32 from epidemiological studies is consistent with the evidence from controlled exposure
33 studies. Finally, whether or not the effects attributed to ozone in epidemiological studies
34 are specific to ozone, it is likely that reductions in population exposures to ozone will
35 result in fewer adverse health effects. Our confidence in this statement does not change
36 at the lower levels of the proposed range.
37

38 **7. EPA's exposure assessment quantified the number of all children and asthmatic**
39 **children likely to be exposed to specific benchmark levels of ozone, including in**
40 **particular 0.060 and 0.070 ppm. Considering the patterns of change in the estimates**
41 **of exposures of concern at and above the 0.060 and 0.070 ppm benchmark levels,**
42 **and the uncertainties and limitations in the estimates, what is the relative**

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importance from a public health perspective of the estimated reductions in exposures of concern, as well as the exposures remaining, for alternative standards across the proposed range?

The first issue is the estimated change in exposures for alternative standards across the proposed range of 0.060 to 0.070 ppm. Table 1 in the Proposed Rules (p. 2978 in the Federal Register January 19, 2010) presents modeled number and percentage of children with exposure (defined as at least one 8-hr average exposure per year with moderate or greater level of exercise) at each of three ozone benchmark levels of concern (0.080, 0.070 and 0.060 ppm) for ozone standards ranging from the old standard of 0.084 to a lowest standard of 0.064 ppm, for the 12 urban areas in aggregate. Since no estimates are presented down to the lower end of the proposed range, i.e., 0.060 ppm, we cannot directly answer the question for the entire proposed range of the standard, based on these model estimates. However, at least for levels of concern of 0.070 or greater, because the number and percent exposed is either zero or exceedingly small when meeting a standard of 0.064, depending on the year, it can be inferred that even fewer are exposed were a standard of 0.060 to be met. For a level of concern of 0.060, for the year with the lowest concentrations (2004), no exposures are estimated to occur when meeting the standard of 0.064, whereas for the year with the higher concentrations (2002), it is estimated that around 5% of children will be exposed, implying that even fewer will be exposed were a standard of 0.060 to be met. Some individual city estimates of exposure were lower while others were higher than these aggregate estimates. Based on earlier uncertainty and sensitivity analyses carried out by EPA, and relative to uncertainty in health effect estimates, uncertainty in these exposure estimates is acceptable.

The second issue relates to the public health significance of reductions in exposure for the range of standards from 0.070 to 0.060. Some of the public health significance is addressed by the risk assessment for selected endpoints (see responses to charge question #8). For endpoints for which it was not possible to carry out a quantitative risk assessment, we must infer public health significance in light of the toxicologic, human clinical and epidemiological findings. Toxicologic data (i.e., animal experimental data) are largely not helpful in this regard. In the absence of demonstrable effects in human clinical studies (in normals or those with mild disease) on other than lung function decrements for exposure concentrations less than 0.080 ppm, we are left inferring effects at lower concentrations and in the more severely diseased. Findings from epidemiological studies are less certain, but indicate effects at substantially lower concentrations than were used in the experimental studies. The benchmark levels in Table 1 correspond to greater degrees of uncertainty going from 0.080 down to 0.060. Part of this uncertainty relates to the precious little human clinical data at exposure concentrations below 0.080, and what exists is essentially limited to effects on lung function. Another part of the uncertainty relates to the reliance on epidemiological (non-experimental) findings at the lower concentrations. Therefore, while (in Table 1) the predicted number exposed increases for every level of the standard as the benchmark

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1 level of concern is reduced, the public health impact of this increase in number exposed
2 becomes less certain. One could argue that since there is no clear threshold for ozone
3 effects, increases in the number exposed translates directly into increases in health
4 effects. This ignores not just increasing uncertainty, but also the fact that “exposure” at
5 the decreasing benchmark levels results in an increasingly smaller percentage of people
6 affected at the decreasing levels of exposure. These latter percentages are difficult to
7 estimate for endpoints other than, perhaps, acute lung function changes. So, the public
8 health significance is difficult to gauge for these other endpoints.

9
10 What then can be said about the public health significance of exposures at the different
11 levels of concern across the different standards? It is prudent to assume that for at least
12 some segments of the population, adverse effects (in addition to acute lung function
13 effects) occur at levels below 0.080, and, making use of epidemiologic observations, that
14 there is no obvious threshold for these effects with effects occurring even at the
15 benchmark level of 0.060. At some concentration the number of individuals affected
16 must be exceedingly small, although, because the number of days with lower benchmark
17 levels is greater than with higher levels, a feature not captured by the exposure estimates
18 in Table 1, the opportunities for exposure throughout the year are greater at the lower
19 benchmark levels. This explains the observation from the risk assessment that the
20 majority of adverse effects are due to exposures occurring at relatively lower
21 concentrations.

- 22
23 **8. EPA’s quantitative risk assessment estimated the numbers of occurrences of various**
24 **ozone-related health effects associated with just meeting alternative standard levels**
25 **down to a standard level of 0.064 ppm. Considering the patterns of change in the**
26 **estimates of health effects in the risk assessment at the alternative standard levels,**
27 **and the uncertainties and limitations in the estimates, what is the relative**
28 **importance from a public health perspective of the estimated reductions in risk, as**
29 **well as the risk remaining, for alternative standards across the proposed range?**
30 **Please consider this question in light of the scientific evidence as a whole.**

31
32 Although the evidence from epidemiological studies of ozone-related mortality published
33 prior to 2006 was not considered sufficiently robust by CASAC to serve as the basis for a
34 new NAAQS, nevertheless, based upon EPA estimates of effects on morbidity and
35 mortality in the risk assessment components of the 2007 Staff Paper, in the previous
36 deliberations of this panel we concluded “Beneficial effects in terms of reduction of
37 adverse health effects were calculated to occur at the lowest concentration considered
38 (*i.e.*, 0.064 ppm). (Henderson, 10/24/06, p.4).”

39
40 The three tables available from the 2007 Staff Paper and reproduced in Federal Register
41 as part of this Proposed Rules material (Vol. 75, No. 11/Tuesday, January 19, 2010)
42 provide estimates of exposures to numbers of All and Asthmatic School Age Children in

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1 12 urban areas by various proposed air quality standard levels. Unfortunately, it is not
2 clear that 2002 is the “worse case” or 2004 is the “best case”. Nevertheless, with regard
3 to protecting the public health the range of all children aged 5-18 between 0.074-0.064
4 ppm is between 4.5 million and 950, 000 in the worse case vs 350,000 and 10,000 in the
5 best case, with proportionately lower numbers for asthmatic children. Clearly truth must
6 lay somewhere in between. Since no estimates are presented down to the lower end of
7 the proposed range, i.e., 0.060 ppm, we cannot directly answer the question for the entire
8 proposed range of the standard, based on these model estimates. However, even these
9 numbers represent a substantial fraction of at risk children, and reducing the estimates to
10 0.060 ppm would reduce the numbers further, they would still be substantial.

11
12 As discussed at length in the Criteria Document and Staff Paper, there is no evidence of a
13 threshold, i.e., the magnitude of the effects measured in clinical studies diminishes with
14 decreasing ozone concentration, but does not reach the functional level associated with
15 exposure to ozone-free clean air. Furthermore there is a great degree of variability of
16 response magnitude among the individuals studied, with some having clinically-relevant
17 responses, even at 0.060 ppm, and more of them with such responses at higher
18 concentrations. Importantly, these clinical studies were carried out in normal healthy
19 adults, and even in these groups from 7-20%, albeit small numbers in each group, had
20 clinically relevant changes in pulmonary function or symptoms that potentially could act
21 as triggers or precursors in more sensitive subjects that would lead to adverse health
22 effects in a substantial numbers of subjects with these conditions.

23
24 Thus the public health implications are that using all of the available data the prudent
25 decision that will protect a substantial fraction, albeit not all sensitive subjects, with an
26 adequate margin of safety as mandated by law would be to select a standard that reduces
27 the at risk population to a minimally acceptable number, with a reasonable degree of
28 certainty. Our original unanimous conclusion as expressed in Henderson’s Chairperson
29 letter to the Administrator in 2008 indicated that CASAC took account of these
30 uncertainties associated with assessing the risks to low levels of ozone and concluded that
31 in a range of .060 to .070 ppm exposures; one could have confidence in the observed
32 effects. We are still in agreement with that conclusion.