ALLIANCE OF AUTOMOBILE MANUFACTURERS

Comments on EPA's Proposed Revisions to the National Ambient Air Quality Standards for Ozone

Docket No. EPA-HQ-OAR-2008-0699

Submitted March 17, 2015

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Introduction

The Alliance of Automobile Manufacturers ("Alliance") respectfully make this submission in response to the invitation of the Environmental Protection Agency ("EPA") in its December 17, 2014 public notice[1] seeking comment on its proposed rule to change the National Ambient Air Quality Standards (NAAQS) for ozone (O3).

The Alliance is a trade association of twelve car and light truck manufacturers comprised of BMW Group, Fiat Chrysler Automobiles, Ford Motor Company, General Motors Company, Jaguar Land Rover, Mazda, Mercedes-Benz USA, Mitsubishi Motors, Porsche Cars, Toyota, Volkswagen Group and Volvo Cars. Alliance members account for over 77% of the cars and light trucks sold in the U.S. Auto manufacturing is a cornerstone of the U.S. economy, supporting eight million private-sector jobs, $500 billion in annual compensation, over $50 billion in annual exports and $70 billion in personal income-tax revenues.

The products manufactured by Alliance members are subject to EPA's emission standards for precursors to anthropogenic ozone and would be affected by the proposed changes to the ozone NAAQS.

These comments are divided into two parts. Part 1 addresses EPA's proposal to change the ozone NAAQS and explains the reductions that have occurred to the ozone precursor emissions inventory from the light duty car and light truck fleets. These reductions have become so great that in the future by 2030 they will lead to automobiles and light trucks having a negligible contribution to the ozone problem. The comments also address the issue of setting standards that would be in many areas nearly indistinguishable from background levels. The tremendous reductions in emissions from an entire American industry sector, coupled with the proposed level of the standard being set at almost background levels, and the lack of a clear health benefit signal to further lower the standard, lead to the need for a new approach to NAAQS setting.

Part 2 of these comments contains a detailed technical discussion of the reports, studies and analyses on which EPA's proposal is based. The comments address alternative interpretations of EPA's assumptions regarding health related associations from human and clinical studies.

The Alliance believes that, as a consequence of these and other considerations, the Administrator should use her discretion in making her policy decision informed by science and retain the current level of the ozone NAAQS standard as protective of public health and welfare.

The Alliance also supports the comments submitted by the Truck and Engine Manufacturers Association and by the National Association of Manufacturers.

[1] 79 Federal Register 75234, December 17, 2014.

Executive Summary

A unique set of circumstances surround the current review of the ozone NAAQS, circumstances which have never before occurred during a NAAQS rulemaking. These include the tremendous reduction in ozone precursor emissions that will occur under existing regulations; the fact that, due to the complex chemistry surrounding ozone formation, reducing precursors even further will have the effect of actually increasing ozone levels in certain urban areas; and the proximity of the existing and proposed ozone standard to background levels that are due to natural causes and due to ozone being transported into the U.S. from overseas countries and regions. These unique circumstances, combined with scientific uncertainty surrounding proposed changes to the ozone standard, dictate that EPA retain the current standard, allowing time for the ozone reduction requirements that are already on the books to take effect.

The following paragraphs, and the attached comments, further explain the circumstances outlined above and detail why the public would be better served if EPA were to retain the current ozone NAAQS and continue to focus on implementation of the existing standards:

1. **The contribution of ozone precursors from automotive sector will soon fall to negligible levels.**

   From the pre-control passenger cars of the 1960s to the light-duty passenger cars and trucks produced today, exhaust emissions have been reduced 99.3% for hydrocarbons (HC), 98.8% for nitrogen oxides (NOx), and 99.1% for the sum of the two. With the phased-in implementation of Tier 3 emission standards starting in 2017 model year (MY), the sum of the two pollutants will have been reduced 99.4% by 2017 MY and 99.8% by 2025 MY. Using EPA's Motor Vehicle Emission Simulator (MOVES) model, it was estimated that the contribution of on-road U.S. light-duty passenger cars and trucks to U.S. ozone (O3) formation was 6.1% in 2011 and will decline to 1.2% by 2030. This means that additional controls on the light-duty fleet (beyond Tier 3) will have no measureable impact on U.S. ozone concentrations.

2. **EPA's Analysis shows that further reduction of ozone precursors could actually increase ozone.**

   Counterintuitively, in certain areas further reducing ozone precursor levels of NOx will actually increase levels of ozone. Because of the complex non-linear nature of ozone formation, massive reductions in NOx actually increase ozone exposures in many populated urban locations. It is a widely known fact that maximum ozone concentrations generally occur in areas that are downwind of the central cities. This is because it takes time for the ozone precursors, VOCs and NOx, to react in the presence of sunlight to form ozone, and because freshly emitted NO will initially scavenge O3 suppressing the concentrations in the center city.

Consequently, a NOx-focused control strategy that reduces O3 at the downwind Design Value sites in the less densely populated suburbs could result in increasing the O3 in the high population density center city. Based on EPA's own analyses presented in the Health Risk and Exposure Assessment (HREA), this phenomena has been occurring over the past decade, as NOx emissions have declined nationwide by almost 50%, and is projected to continue to occur in EPA's two future modeling scenarios, with additional cuts in NOx emissions of 50% and 90%. Based on EPA's own calculations, by forcing additional NOx emission reductions to meet the alternative O3 standards, the purported O3-related mortality will actually increase in Los Angeles, Houston and Detroit. This will also likely be the case in many other central city areas.

3. **A standard set the same as natural, uncontrollable background levels leaves available control measures powerless to reduce ozone.**

   EPA's estimates of background O3 are incorrectly low. As a result, a NAAQS in the range of 60 - 70 ppb will be frequently exceeded or approached by background concentrations, especially in the mountainous Western states. It appears that EPA's models are underestimating the contributions from stratospheric intrusions and international transport. In addition, the method EPA used to estimate background is still biased low because it is not designed to determine how much of the modeled O3 is due to background; rather, it attributes maximum culpability to controllable anthropogenic precursors. Finally, the regulatory mechanisms that EPA posits can deal with high incidents of background are inadequate to provide regulatory relief to the states, especially for those states that will experience frequent violations from background. It is clear that there will be frequent exceedances of a new, lower standard in many parts of the U.S. just from background O3 concentrations.

4. **The weight of evidence from the available health effects studies supports retaining the present standard.**

   For additional reasons explained in the technical issues section (Part 2 of these comments), the weight of evidence from the available health effects studies supports retaining the present standard. The technical review of EPA’s cited studies and analyses related to causality, threshold level determination and other technical issues, presents an alternative interpretation of the human clinical and observational studies and shows that a revision of the current 8-hour ozone NAAQS is not justified.

Part 1

I. Light-Duty Vehicles Are Becoming Negligible Contributors to Ozone Formation

Since the 1960s when it was first recognized that O_3, the principle constituent of concern in photochemical smog, was formed in the atmosphere from the interactions of hydrocarbons (HC) and nitrogen oxides (NO_x) in the presence of sunlight, the motor vehicle industry has made steady and significant progress in reducing the emissions of these O_3 precursors from vehicles. Table 1 shows how the exhaust emissions have declined from light-duty vehicles since the pre-control days of the 1960s to the present and also shows that the emissions will continue to decline in new vehicles through 2025 as the Tier 3 regulations are implemented.

Table 1: U.S. Light-Duty Vehicle Emission Standards[2,3]

Model Year	Federal Tailpipe Standard[a] (g/mi)			Emission Reduction		
	HC	NOx	HC+ NOx	HC	NOx	HC+ NOx
Pre-Control	10.6	4.1	14.7	0.0%	0.0%	0.0%
1968	6.3	4.1	10.4	40.6%	0.0%	29.3%
1970	4.1	4.1	8.2	61.3%	0.0%	44.2%
1972	3.0	4.1	7.1	71.7%	0.0%	51.7%
1973	3.0	3.0	6.0	71.7%	26.8%	59.2%
1975	1.5	3.1	4.6	85.8%	24.4%	68.7%
1977	1.5	2.0	3.5	85.8%	51.2%	76.2%
1980	0.41	2.0	2.41	96.1%	51.2%	83.6%
1981	0.41	1.0	1.41	96.1%	75.6%	90.4%
1994[b]	0.25	0.4	0.65	97.6%	90.2%	95.6%
2001	0.075	0.2	0.275	99.3%	95.1%	98.1%
2004[b]	0.075	0.05	0.125	99.3%	98.8%	99.1%
2017[c]			0.086			99.4%
2025[d]			0.03			99.8%

[a] Based on (or adjusted to the equivalent of) the 1975 Federal Test Procedure.
[b] First year of multi-year phase in.
[c] First year of Tier 3 phase-in.
[d] Last year of Tier 3 phase-in.

Table 1 presents the emission factors for both HC and NO_x and shows the percent reductions from pre-controlled vehicles that have been achieved. Vehicles currently being produced are meeting the phased-in 2004 Tier 2 emission standards which represent HC and NO_x reductions

[2] Ehlmann J and Wolff G, (2005) Automobile emissions: the road toward zero, *Environmental Manager*, 11(1), 33-36.
[3] U.S. EPA, *Control of Air Pollution from Motor Vehicles:Tier 3 Motor Vehicle Emission and Fuel Standards Final Rule Regulatory Impact Analysis,* EPA-420-R-14-005, March 2014.

of 99.3% and 98.8%, respectively. Prior to Tier 3, which begins phase-in in 2017, EPA regulated the emissions of HC and NO_x separately. In the Tier 3 rules, EPA regulates the sum of the HC and NO_x emissions recognizing that both pollutants contribute to the formation of O_3. By 2025, the sum of the emissions of HC and NO_x will have declined 99.8%. The diminishing trends in vehicle emissions are illustrated in Figure 1.

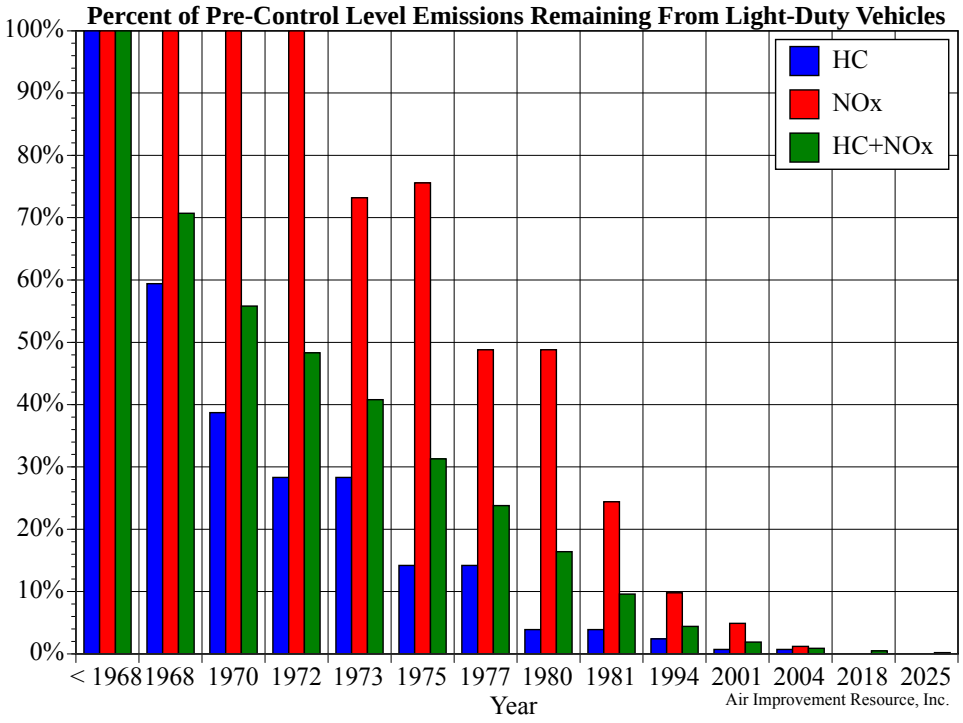

Figure 1: Percentage of emissions relative to pre-controlled vehicles.

To place these emission reductions in proper context, they need to be compared to the trends of other sources of ozone precursors. This information is summarized in Table 2 which shows how the total on-road vehicle emissions (i.e. emissions from cars, light trucks, and medium- and heavy-duty trucks) decreased over time compared to the decrease in total US anthropogenic emissions. From 1970 to present (2011 is the closest inventory available from the O_3 Regulatory Impact Analysis[4]) onroad NO_x emissions decreased 55.7% while VOC or HC decreased 83.8%. These numbers compare to the reductions from all anthropogenic U.S. of 48.2% for NO_x and 48.1% for VOC. Consequently, the emissions from vehicles have been disproportionately reduced relative to other man-made sources. By 2030, the onroad reductions will be 89.1% for NO_x and 95.9% for VOC compared to total emission reductions of 66.3% for NO_x and 63.2% for VOC.

Because the emissions from onroad vehicles have been reduced more than the total emissions from all anthropogenic sources, the contribution of vehicle emissions to O_3 production has also declined relative to all other sources. This is illustrated in Table 3. This table shows the percentage of emissions from onroad vehicles compared to total U.S. VOC and NO_x emissions

[4] U.S. EPA. *Regulatory Impact Analysis of the Proposed Revisions to the National Ambient Air Quality Standards for Ground-Level Ozone,* EPA-452/P-14-006, November 2014.

from 1970 to present (2011) and projects the trend to 2030 based on EPA emission forecasts. The sum of the percentage of VOC and NO_x emissions from onroad vehicles is measure of the total contribution of vehicles to the anthropogenic O_3 formed in the U.S.

Table 2: Anthropogenic U.S. Emissions (1000 Tons/Year) and Reductions[5]

	VOC				NOx				VOC+NOx			
	Onroad		Total		Onroad		Total		Onroad		Total	
Year	Emis.	Red.	Emis.	Red.	Emis.	Red.	Emis.	Red.	Emis.	Red.	Emis.	Red.
1970	16,910	0.0%	33,742	0.0%	12,624	0.0%	26,883	0.0%	29,534	0.0%	60,625	0.0%
1980	13,869	18.0%	30,083	10.8%	11,493	9.0%	27,079	0.0%	25,362	14.1%	57,162	5.7%
1990	9,388	44.5%	23,125	31.5%	9,592	24.1%	25,167	7.0%	18,980	35.7%	48,292	20.3%
2000	5,325	68.5%	16,898	49.9%	8,394	33.6%	22,335	17.5%	13,719	53.5%	39,233	35.3%
2005	3,268	80.7%	16,986	49.7%	8,235	34.8%	20,148	25.5%	11,503	61.1%	37,134	38.7%
2007	3,223	80.9%	17,320	48.7%	7,563	40.1%	17,821	34.1%	10,786	63.5%	35,141	42.0%
2011	2,738	83.8%	17,496	48.1%	5,592	55.7%	13,994	48.2%	8,330	71.8%	31,490	48.1%
2017	1,353	92.0%	13,225	60.8%	2,967	76.5%	11,402	57.7%	4,320	85.4%	24,627	59.4%
2025	1,060	93.7%	15,130	55.2%	1,492	88.2%	8,512	68.3%	2,552	91.4%	23,642	61.0%
2030	700	95.9%	12,420	63.2%	1,372	89.1%	9,063	66.3%	2,072	93.0%	21,483	64.6%

That percentage has decreased from 48.7% in 1970 to 26.5% in 2011 and is projected to further decline to 9.6% by 2030. However, since U.S. background O_3 (USB = the sum from all sources except that produced from anthropogenic U.S. emissions) on average in the U.S. is between 59 - 66%[6], a better estimate of the contribution of a source to total observed O_3 is given by the numbers in the last column in Table 3. This column shows the onroad contribution to total U.S. emissions including biogenic NO_x and VOC. Thus the contribution from onroad vehicles to observed O_3 has decreased from 28.9% in 1970 to 11.4% in 2011 and is projected to decline to 3.3% by 2030. This is also graphically illustrated in Figure 2.

Table 3: Onroad Vehicle Contribution to Ozone Precursors

	Anthropogenic			Anthropogenic + Biogenic
Year	VOC	NOx	VOC+NOx	VOC+NOx
1970	50.1%	47.0%	48.7%	28.9%
1980	46.1%	42.4%	44.4%	25.7%
1990	40.6%	38.1%	39.3%	21.1%
2000	31.5%	37.6%	35.0%	17.0%
2005	19.2%	40.9%	31.0%	14.6%
2007	18.6%	42.4%	30.7%	14.0%
2011	15.7%	40.0%	26.5%	11.4%
2017	10.2%	26.0%	17.5%	6.5%
2025	7.0%	17.5%	10.8%	3.9%
2030	5.6%	15.1%	9.6%	3.3%

[5] 1970 to 2000 from http://www.epa.gov/ttn/chief/trends/index.html, 2005, 2017 and 2030 from http://www.epa.gov/otaq/documents/tier3/454r13002.pdf, 2007 from http://www.epa.gov/ttn/naaqs/standards/pm/data/201212aqm.pdf, and 2011 and 2025 from U.S. EPA. *Regulatory Impact Analysis of the Proposed Revisions to the National Ambient Air Quality Standards for Ground-Level Ozone,* EPA-452/P-14-006, November 2014.

[6] U.S. EPA. *Health Risk and Exposure Assessment for Ozone Second External Review Draft Chapter 4 Appendices,* EPA-452/P-14-004b, February 2014.

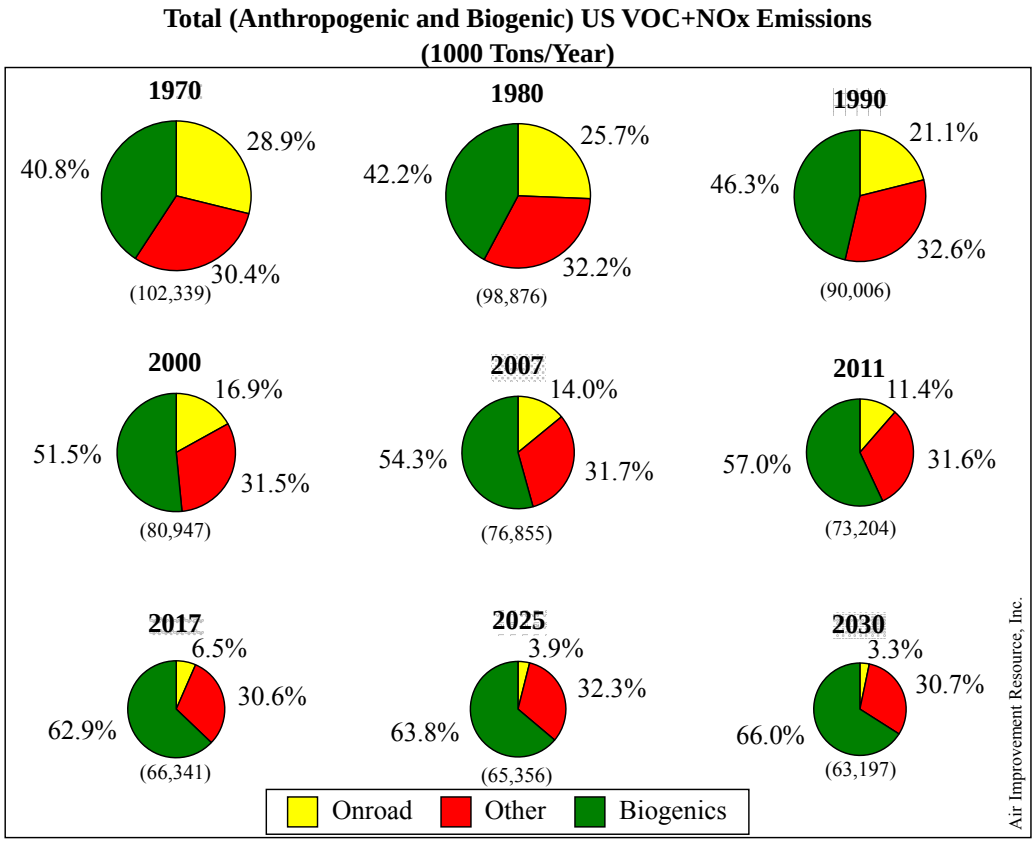

Figure 2: Contribution of onroad to total HC and NO_x emissions.

These onroad estimates can be subjected to a reality test using information from the Health Risk and Exposure Assessment appendices.[7] The USB percentages cited above were obtained from modeling runs performed by EPA for the year 2007. Using two different modeling platforms, they estimated USB to be 59 - 66% of the observed O_3 in the U.S. That means the part due to anthropogenic emissions is 34 - 41%. From Table 3, EPA estimated that in 2007 onroad VOC plus NO_x emissions represented 30.7% of the total VOC plus NO_x anthropogenic emissions. Thus the percentage of total O_3 due to onroad emissions would be 34 - 41% times 30.7% which equals 10.4 - 12.6%. This compares to the 14.0% estimate in Table 3 for 2007 using just the emission ratio. We suspect that the lower estimates are probably closer to reality because USB includes other contributions to background O_3 besides the biogenic contributions. USB also includes a stratospheric contribution (this is likely underestimated) and intercontinental transport. If that is the case, then all of the estimates of the onroad contributions to ozone in the last column of Table 3 can be considered overestimates as well.

An additional consideration is that the estimates made above for onroad contributions include light-duty cars and trucks as well as medium- and heavy-duty vehicles emissions. Using EPA's MOVES-2014[8] model, AIR, Inc. calculated the percentage of VOC and NO_x emissions that were or will be emitted from just the light-duty vehicles. Table 4 shows that the contribution from

[7] Ibid, p. 2A-16.
[8] U..S. EPA. 2013. MOVES (Motor Vehicle Emission Simulator). http://www.epa.gov/otaq/models/moves/.

light-duty vehicles will have declined from just 6.7% in 2007 to 1.6% in 2025 and 1.2% in 2030. Consequently, additional controls beyond the Tier 3 standards on the light-duty fleet will not have a measureable impact on U.S. ozone concentrations.

Table 4: Percent Contribution of Light Duty Vehicles to Ozone	
Year	Percent
2007	6.7
2011	6.1
2017	3.1
2025	1.6
2030	1.2

II. NOx-Disbenefits Comments

EPA's Modeling Shows That a NO_x-Focused Control Strategy Results in the Widespread Occurrence of Higher O_3 in Central Cities

It is a widely known fact that maximum ozone concentrations generally occur in areas that are downwind of the central cities. This is because it takes time for the precursors, VOCs and NO_x, to react in the presence of sunlight to form ozone and because freshly emitted NO will initially scavenge O_3 suppressing the concentrations in the center city. This is acknowledged in the proposed rule which states:

> In some areas, such as urban centers where NO_x emissions typically are high, NO_x leads to the net destruction of O_3, decreasing O_3 concentrations in the immediate vicinity.

and,

> However, while NO_x can initially destroy O_3 near emission sources, these same NO_x emissions eventually react to form O_3 downwind of those sources. Photochemical model simulations suggest that reductions in NO_x emissions will slightly increase O_3 concentrations near NO_x sources on days with lower O_3 concentrations, while at the same time decreasing the highest O_3 concentrations in outlying areas.[9]

Consequently, a NO_x-focused control strategy that reduces O_3 at the downwind Design Value sites in the less densely populated suburbs could potentially result in increasing the O_3 in the higher density central city. Based on EPA's own analyses presented in the Health Risk and Exposure Assessment (HREA),[10] this phenomena has been occurring over the past decade when

[9] Proposed Rule, supra note 1, at 75270.
[10] U.S. Environmental Protection Agency. (2014). *Health Risk and Exposure Assessment for Ozone*. Office of Air Quality Planning and Standards, Research Triangle Park, NC. EPA–452/P-14–004a. Available at: http://

NO_x emissions have declined nationwide by almost 50% and is projected to continue to occur in EPA's two modeling scenarios with 50% and 90% additional cuts in NO_x emissions.

In Section 8.2.3.1 of the HREA, EPA documents that peak O_3 concentrations at monitors located in low population density areas (< 400 people/km^2) where most of the Design Value Monitors are located are generally decreasing as well as the mid-level concentrations (25th to 75th percentiles). On the other hand, at the highest population density sites (> 1000 people/km^2), the mid-level concentration trends are increasing at most of the sites. This is shown in Figure 8-31 in the HREA and reproduced here as Figure 3. EPA states: "[t]hese results reflect increasing mid-range O_3 concentrations mainly confined to urban centers during periods of NO_x reductions."[11]

In Section 8.2.3.2 of the HREA, EPA presents modeling results in which they reduce NOx emissions another 50 and 90%, respectively. Results for the 15 cities included in their analysis are presented in Figures 8-42 and 8-43 of the HREA and are reproduced here as Figures 4 and 5.

Figure 4 shows that in 14 of the 15 cities studied the mean O_3 increases in the central city with a 50% NO_x reduction. For Detroit, Los Angeles and New York, this increase affects about 70% of the population. At a 90% reduction, only 4 of the cities still experience locations where the means increase.

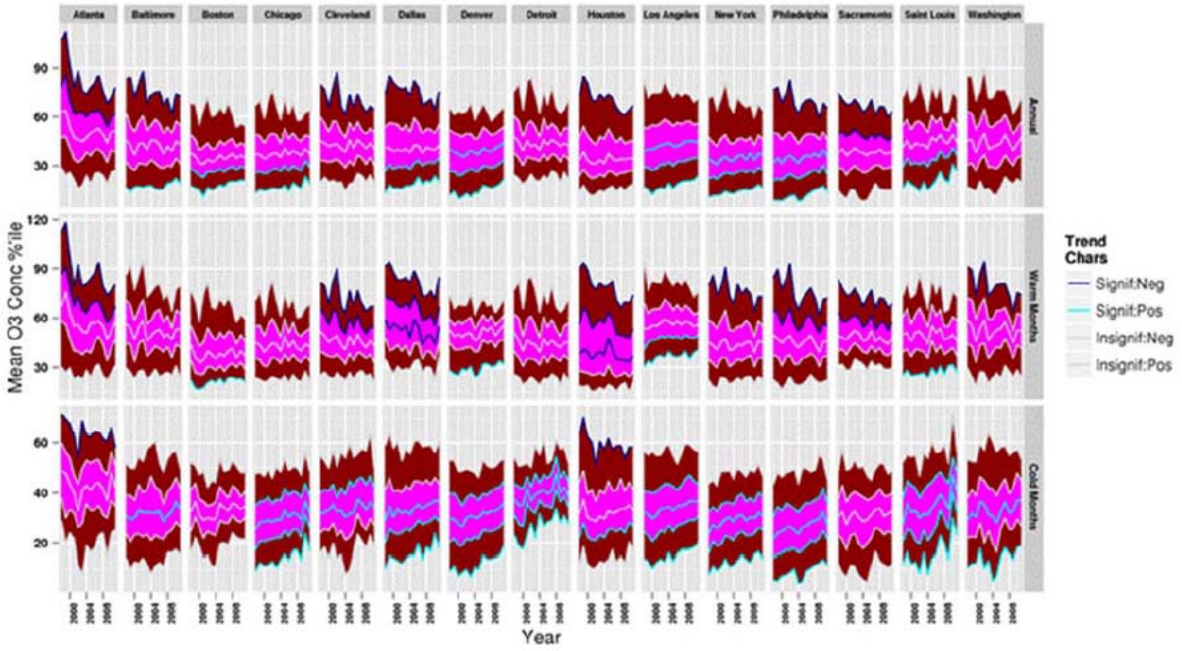

Figure 3: Distributions of O_3 concentrations for high population density monitors by different subsets of months over a 13-year period. From top to bottom in each ribbon plot, the blue and white lines indicate the spatial mean of the 95th, 75th, 50th, 25th, and 5th percentiles for each monitor for every year from 1998-2011.

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www.epa.gov/ttn/naaqs/standardozone/s_o3_index.html.

[11] Ibid., p. 8-48.

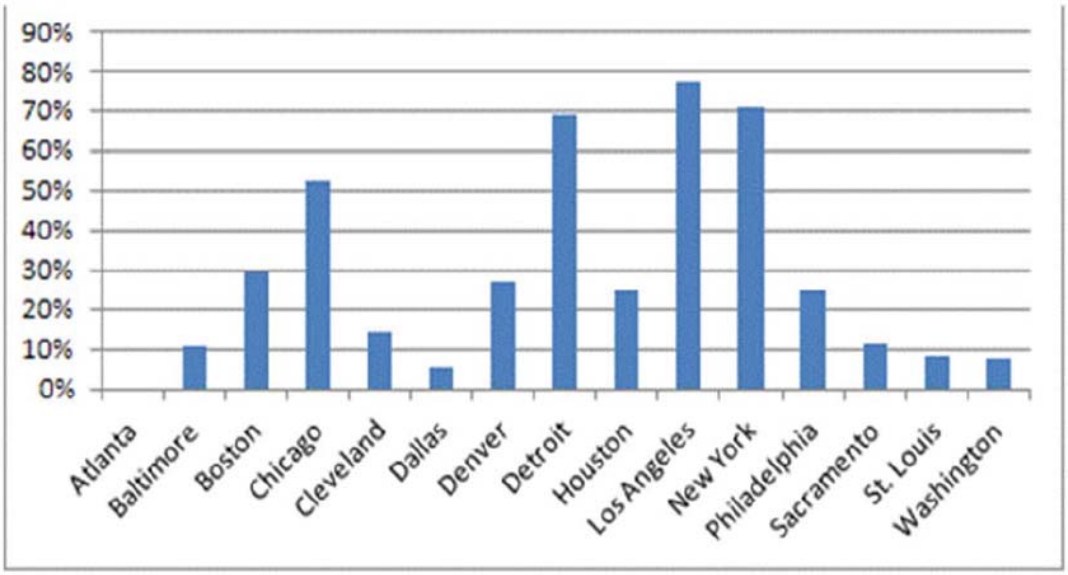

Figure 4: Population (as % of total area population) living in locations of increasing April-October seasonal mean O_3 in the 50% NO_x reduction CMAQ simulation.

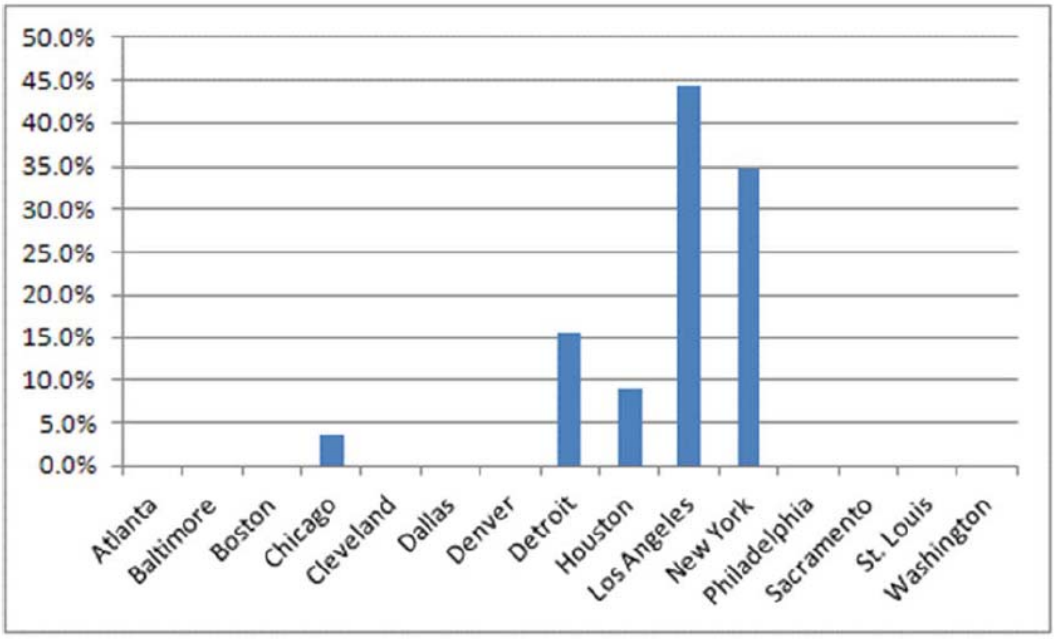

Figure 5: Population (as % of total area population) living in locations of increasing April-October seasonal mean O_3 in the 90% NO_x reduction CMAQ simulation.

These results have two ramifications. First, decreasing the NO_x emissions increased the mean O_3 which means the total annual exposure to O_3 will increase for a portion of the population. This is an important point because, as will be shown below, most of EPA estimated mortality does not occur on the highest O_3 days, but on the days with near mean O_3 concentrations because they

occur much more frequently. Second, even though the situation improves with a 90% reduction, NO_x reductions would be gradually phased-in. Consequently, an area that requires a 90% reduction would still have to reach an interim target of 50% and therefore would see increasing mean O_3 concentrations before they would begin to decline.

EPA's current and future mortality estimates from short-term O_3 exposure are presented in Appendix 7B[12] of the HREA. The top graph in Figure 7B-3 contains EPA's short-term mortality estimates from exposure to 2009 O_3 levels in 15 cities as a function of the daily 8-hour maximum O_3 concentration. This figure is reproduced as Figure 6 below. As indicated in the Figure, most of the mortality occurs in all cities, not on the highest O_3 days, but on days when the concentrations are generally in the range of 35 to 55 ppb, which is in the range of the seasonal mean 8-hour concentrations. For comparison, the estimated modeled seasonal means are shown in the top row in Table 5.[13]

Recent conditions

Study area	Daily 8hr Max Ozone Level (ppb)																Total
	0-5	5-10	10-15	15-20	20-25	25-30	30-35	35-40	40-45	45-50	50-55	55-60	60-65	65-70	70-75	>75	
Atlanta, GA	0	0	1	3	6	16	13	20	36	32	26	23	18	8	1	0	204
Baltimore, MD	0	0	1	1	6	12	20	20	20	29	40	33	15	7	5	0	210
Boston, MA	0	0	0	0	6	19	21	32	29	31	25	6	2	3	5	2	182
Cleveland, OH	0	0	0	4	8	17	20	31	50	33	35	24	7	15	2	0	246
Denver, CO	0	0	0	0	0	1	1	2	7	11	13	13	6	1	1	0	56
Detroit, MI	0	0	1	7	5	21	36	53	89	116	30	40	36	0	17	5	456
Houston, TX	0	1	7	18	34	68	80	85	60	55	53	41	21	14	6	7	549
Los Angeles, CA	0	1	4	12	23	40	68	51	63	109	98	75	67	41	12	10	672
New York, NY	0	0	5	93	165	248	322	373	466	367	370	240	153	116	25	0	2,944
Philadelphia, PA	0	0	4	10	22	56	88	67	116	110	114	124	68	30	7	0	817
Sacramento, CA	0	0	2	3	7	12	17	15	22	21	19	13	10	15	9	3	166
St. Louis, MO	0	0	1	5	4	15	21	47	38	55	60	39	17	9	0	0	311

Figure 6: Short-term ozone-attributable mortality (2009) (heat map tables – absolute ozone-attributable incidence).

All days, CAMx	ATL	BAL	BOS	CLE	DEN	DET	HOU	LA	NYC	PHI	SAC	STL
Model MDA8 seasonal mean	59.3	54.4	43.0	48.9	47.3	39.1	48.5	51.1	45.4	48.7	46.4	49.8
Model MDA8 seasonal mean from emissions other than U.S. anthropogenic sources	25.3	25.9	26.2	25.7	31.3	23.3	27.0	29.1	24.5	24.2	29.7	24.3
Fractional contribution from background	0.43	0.48	0.61	0.53	0.66	0.60	0.56	0.57	0.54	0.50	0.64	0.49

Table 5: Seasonal mean 8-hour daily maximum O_3 (ppb), seasonal mean apportionment-based USB contribution (ppb), and fractional apportionment-based USB contribution to total O_3 (all site-days) in the 12 REA urban case study areas.

EPA also makes projections for future O_3-related short-term mortality when the areas come into attainment with the various alternative standards in Figure 7B-3 and these have been reproduced below in Figure 7. To achieve the various O_3 standards, EPA reduces the NO_x emissions in each

[12] U.S. EPA, (2014) *Health Risk and Exposure Assessment for Ozone Final Report Chapters 7-9 Appendices*, EPA-452/R-14-004c, August 2014.

[13] U. S. Environmental Protection Agency, (2014) *Policy Assessment for the Review of the Ozone National Ambient Air Quality Standards,* EPA–452/R–14–006, August 2014, p. 225

city so the Design Value site reaches the standard. But as explained above, this has the unintended consequence of increasing the ozone in the more densely populated central city. As a result, EPA's mortality estimates decrease in the highest bins of ozone concentrations in Figure 7, but rise in some of the mid-concentration bins because more people are now being exposed to these ranges of concentrations. In some of the cities, this results in a net increase in mortality as lower standards are achieved. This is illustrated for four of the cities in Figure 8.

Current Standard (75)

Study area	Daily 8hr Max Ozone Level (ppb)																Total
	0-5	5-10	10-15	15-20	20-25	25-30	30-35	35-40	40-45	45-50	50-55	55-60	60-65	65-70	70-75	>75	
Atlanta, GA	0	0	1	2	7	13	15	28	41	37	24	25	8	1	0	0	201
Baltimore, MD	0	0	0	0	2	7	21	36	33	47	33	23	6	0	0	0	207
Boston, MA	0	0	0	0	7	14	26	33	29	31	27	4	2	3	5	2	183
Cleveland, OH	0	0	0	0	3	16	28	42	46	50	35	17	7	4	0	0	249
Denver, CO	0	0	0	0	0	1	2	3	6	12	15	13	4	1	0	0	56
Detroit, MI	0	0	1	7	5	21	36	53	89	116	30	40	36	0	17	5	456
Houston, TX	0	0	0	5	24	43	105	107	96	77	72	31	23	6	3	3	595
Los Angeles, CA	0	0	0	0	0	0	1	10	168	196	297	91	5	0	0	0	770
New York, NY	0	0	0	7	41	246	489	407	724	538	314	201	64	0	0	0	3,031
Philadelphia, PA	0	0	0	2	12	38	118	93	162	130	151	67	50	0	0	0	822
Sacramento, CA	0	0	0	0	1	10	28	30	32	24	18	14	3	0	0	0	162
St. Louis, MO	0	0	1	5	5	14	22	44	42	63	53	43	11	7	0	0	310

Alternative Standard 70

Study area	Daily 8hr Max Ozone Level (ppb)																Total
	0-5	5-10	10-15	15-20	20-25	25-30	30-35	35-40	40-45	45-50	50-55	55-60	60-65	65-70	70-75	>75	
Atlanta, GA	0	0	0	1	8	14	18	38	48	27	24	16	1	0	0	0	194
Baltimore, MD	0	0	0	0	2	7	20	40	42	46	37	10	0	0	0	0	203
Boston, MA	0	0	0	0	1	17	23	37	34	33	25	3	0	5	5	0	184
Cleveland, OH	0	0	0	0	1	16	35	47	53	49	31	5	5	0	0	0	242
Denver, CO	0	0	0	0	0	0	2	2	7	11	20	11	2	1	0	0	56
Detroit, MI	0	0	0	0	9	10	33	58	82	137	66	50	7	15	4	0	472
Houston, TX	0	0	0	2	21	41	104	124	99	97	70	22	10	3	3	0	596
Los Angeles, CA	0	0	0	0	0	0	1	24	198	301	185	36	0	0	0	0	745
New York, NY	0	0	0	0	42	203	548	609	847	434	256	0	0	0	0	0	2,940
Philadelphia, PA	0	0	0	0	13	33	109	127	152	180	127	62	5	0	0	0	808
Sacramento, CA	0	0	0	0	1	7	34	35	35	21	22	6	0	0	0	0	159
St. Louis, MO	0	0	0	3	8	12	28	51	58	58	52	25	8	0	0	0	304

Alternative Standard 65

Study area	Daily 8hr Max Ozone Level (ppb)																Total
	0-5	5-10	10-15	15-20	20-25	25-30	30-35	35-40	40-45	45-50	50-55	55-60	60-65	65-70	70-75	>75	
Atlanta, GA	0	0	0	1	7	10	27	44	53	21	23	1	0	0	0	0	187
Baltimore, MD	0	0	0	0	1	6	22	44	56	38	29	2	0	0	0	0	198
Boston, MA	0	0	0	0	1	17	27	37	40	33	14	1	5	5	0	0	181
Cleveland, OH	0	0	0	0	1	15	50	51	57	43	10	5	0	0	0	0	231
Denver, CO	0	0	0	0	0	0	1	3	7	16	21	5	1	0	0	0	55
Detroit, MI	0	0	0	0	8	8	31	68	115	135	52	26	14	4	0	0	461
Houston, TX	0	0	0	0	10	38	118	142	115	109	41	12	5	3	0	0	592
Los Angeles, CA	0	0	0	0	0	0	1	55	241	319	96	5	0	0	0	0	717
New York, NY	0	0	0	0	43	540	827	1,080	58	0	0	0	0	0	0	0	2,547
Philadelphia, PA	0	0	0	0	11	31	102	171	193	172	85	25	0	0	0	0	791
Sacramento, CA	0	0	0	0	0	6	36	43	34	19	18	1	0	0	0	0	156
St. Louis, MO	0	0	0	1	10	10	33	61	70	52	46	12	0	0	0	0	294

Figure 7: Modeled short-term ozone-attributable mortality when achieving alternative levels of the standard (heat map tables – absolute ozone-attributable incidence).

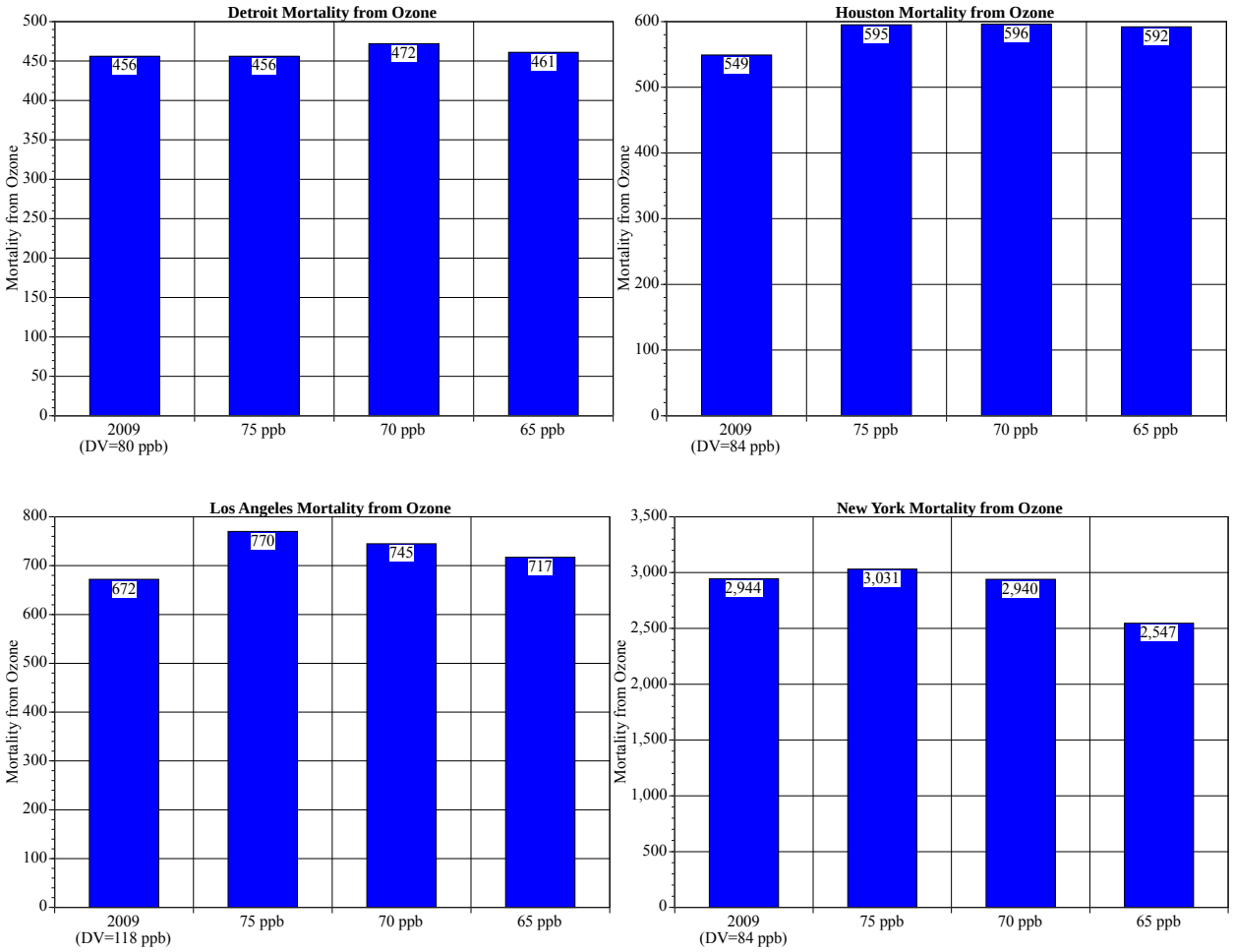

Figure 8: Total annual mortality from short-term O_3 exposure in Detroit, Houston, Los Angeles and New York in 2009 and when meeting alternative standards.

In Detroit, Houston and Los Angeles, EPA's total O_3-related mortality estimates are the lowest for the 2009 air quality levels in which none of these cities meets even the present 75 ppb NAAQS. By forcing additional NO_x reductions to meet the alternative standards, EPA's mortality estimates *go up* in all 3 cities! In New York, EPA mortality estimates increase as it meets the 75 ppb standard and then decrease slightly at lower standards.

The fact that EPA's own modeling of future control scenario designed to meet alternative ozone standards results in increasing ozone exposure in some densely populated central cities is another reason to retain the current NAAQS of 75 ppb, and revisit the scientific basis for the SIPs that are being developed to meet that standard. Clearly this should be done at the local level to insure that all local plans utilize the state-of-the-art photochemical grid models to develop optimal control strategies and avoid NOx disbenefits.

III. Consideration of Background Ozone Flawed

A. Background Has Been Underestimated

The presence of ozone in the atmosphere is a very complex phenomenon since it is both a natural constituent of the atmosphere and a pollutant. As the federal ozone standard has been reviewed since first established in 1971, the way uncontrollable background has been considered has changed over time. In the current review, the proposal acknowledges that the seasonal mean background is a substantial fraction of the current standard and that there can be episodic events where ozone exceeds the current standard. However, the proposal notes:[14]

> These events are relatively infrequent and the EPA has policies that allow for the exclusion of air quality monitoring data from design value calculations when they are substantially affected by certain background influences.

In discussing how background will be dealt with in implementation, the proposed rule notes:[15]

> …there can be events where O_3 levels approach or exceed the concentration levels being proposed in this notice (i.e., 60–70 ppb) in large part due to background sources. These cases of high USB levels on high O_3 days typically result from stratospheric intrusions of O_3, wildfire O_3 plumes, or long-range transport of O_3 from sources outside the U.S. In most locations in the U.S., these events are relatively infrequent and the CAA contains provisions that can be used to help deal with certain events, including providing varying degrees of regulatory relief for air agencies and potential regulated entities.

It is now clear that the policy relevant background EPA used in the prior review substantially underestimated the background of ozone from natural and non-U. S. sources. This underestimation of background O_3 led CASAC in the previous review to recommend a low range for the primary standard from 0.060 to 0.070 ppm that seemed well above background. The current proposal acknowledges that the seasonal mean background is substantially higher than previously estimated and that peak background can reach between 0.060 to 0.075 ppm. The proposal argues, however, that EPA's exceptional events policy and other means of regulatory relief can be used to identify and set aside such events. However, routine measurements and EPA models cannot clearly identify such events. Thus, a standard set in the range of 0.060 to 0.070 ppm would be exceeded by background a portion of the time.

Prior comments[16] by AIR have documented how the USB estimates generated in the current review are biased low. This arises because the modeling approach was not designed to

[14] Proposed Rule, supra note 1, at 75242.
[15] Ibid., at 75382.
[16] Wolff GT, Heuss JM, and Kahlbaum DF, Review and Critique of the U. S Environmental Protection Agency Second External Review Drafts of the "Health Risk and Exposure Assessment for Ozone" and the "Policy Assessment for the Review of the Ozone National Ambient Air Quality Standards," Air Improvement Resource, Inc.

determine how much of the modeled ozone has resulted from background sources, but rather to attribute maximum culpability to controllable anthropogenic precursors. Given the bias toward underestimation, the background is higher than EPA now assumes and the alternative standards under consideration are even more likely to be exceeded by background. In addition, there are several new studies that document contributions to peak background from stratospheric intrusions, wildfires, and/or long-range transport that will make attaining a lower standard even more problematic than the Agency acknowledges.

Because a primary ozone standard between 60 and 75 ppb has been under consideration since the prior review, there have been new studies published that address various factors that can inform that decision as it relates to background ozone. These studies have evaluated ground level ozone across the U. S., evaluated trends in ozone and precursor levels, estimated mean and peak background using models and measurements, and provided information on particular sources of ozone in different situations. In the following, we summarize the most pertinent of these studies.

B. Ozone Throughout the Intermountain West Exceeds Some or All of the Alternative Standards Under Consideration

Even though the Intermountain West is the area of the U. S. with the lowest population and precursor emissions density, the area has ozone levels that the Agency acknowledges can approach or exceed 60 to 75 ppb. Fine et al. (2014)[17] reported on ozone levels at six rural sites in Nevada. The monitor at Great Basin National Park was the only site where the maximum daily 8-hour concentration exceeded the current NAAQS, although 8-hour maximum values exceeded 60 ppb at all the rural sites over a period from March to September.

Peak ozone levels at four other National Parks in the West show similar 4th highest 8-hour

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report prepared for The Alliance of Automobile Manufacturers, March 2014; Heuss JM, Wolff GT, and Kahlbaum, DF, Review and Critique of the U. S Environmental Protection Agency First External Review Drafts of the "Health Risk and Exposure Assessment for Ozone" and the "Policy Assessment for the Review of the Ozone National Ambient Air Quality Standards," Air Improvement Resource, Inc. report prepared for The Alliance of Automobile Manufacturers, October 2012; Heuss JM and Wolff GT, Review and Critique of the U. S. Environmental Protection Agency's First External Review Draft of the "Integrated Science Assessment for Ozone and Related Photochemical Oxidants," Air Improvement Resource, Inc. Report, Prepared for The Alliance of Automobile Manufacturers, May 2011; Heuss JM, Wolff GT, and Kahlbaum DF, Review and Critique of the U. S. Environmental Protection Agency's Second External Review Draft of the "Integrated Science Assessment for Ozone and Related Photochemical Oxidants," Air Improvement Resource, Inc. Report, Prepared for The Alliance of Automobile Manufacturers, November 2011; Heuss JM and Wolff GT, Review and Critique of the U. S. Environmental Protection Agency's Third External Review Draft of the "Integrated Science Assessment for Ozone and Related Photochemical Oxidants," Air Improvement Resource, Inc. Report, Prepared for The Alliance of Automobile Manufacturers, August 2012; Wolff GT, Comments on Policy Relevant Background Ozone As Discussed in EPA's Draft Integrated Science Assessment for Ozone and Related Photochemical Oxidants. Prepared for the Utility Air Regulatory Group, May 5, 2011; Wolff GT, Heuss JM and Kahlbaum, DF, Comments on Background Ozone Related to the Review of the Secondary Ozone NAAQS As Discussed in the Second Draft of EPA's Policy Assessment and Welfare REA. Prepared for the Utility Air Regulatory Group and the Alliance of Automobile Manufacturers, March 24, 2014.

[17] Fine R, Miller MB, Burley J, Jaffe DA, Pierce RB, Lin M, and Gustin MS, (2014) Variability and sources of surface ozone at rural sites in Nevada, USA: Results from two years of the Nevada Rural Ozone Initiative, 2014, *Science of the Total Environment*, dx.doi.org/10.1016/j.scitotenv.2014.12.027.

maximum averages between 60 and 75 ppb over the last ten years. This is shown in Figure 9.[18]

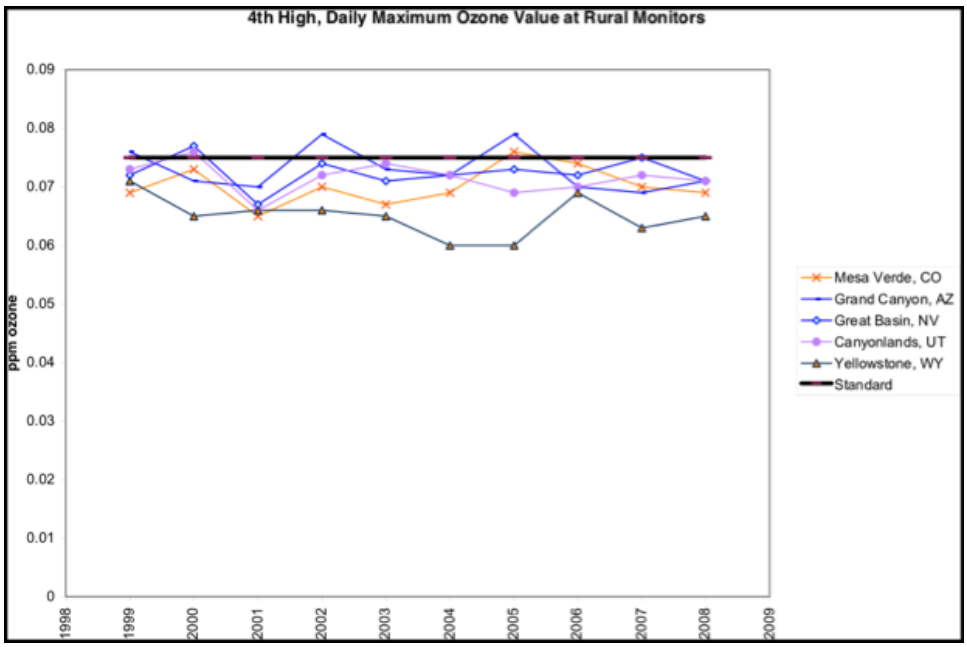

Figure 9: Fourth highest daily maximum ozone values at western rural monitors.

Musselman and Korfnacher (2014)[19] report on ozone measurements at 23 sites in remote mountain areas of the Southern Rockies in Western Colorado, Northeast Utah, and Southern Wyoming. Although a few sites were accessible year round, many were only accessible by mid-June. The authors report that more than 60% (14 of 23) of the remote sites had ozone concentrations from 2007 to 2011 where the 4th highest 8-h average was 75 ppb and would contribute to exceedance of the current primary NAAQS; and more than 78% (18 of 23) had values that would contribute to exceedance of the alternative primary NAAQS of 70 ppb.

All seven sites with complete datasets and 69% of all sites (16 of 23) had at least one year with a three-month 12-h W126 value greater than 13 ppm-h contributing to exceedance of the possible new secondary standard. The three-month 12-h W126 values were as high as 25 ppm-h; Five of the seven sites with complete datasets had three month 12-h W126 values of >21ppm-h.

Thus, there are high ozone values in rural and remote locations throughout the Intermountain West, despite the low population and emissions density in this area of the U. S.

C. Ozone Trends in the Rural West Have Not Responded to Emission Reductions

As man-made emissions have been reduced throughout the U. S., the levels of ozone at rural and remote sites in the Intermountain West have not decreased. While the number of monitoring sites with long-term trends is limited, there is strong evidence that rural and remote ozone levels

[18] Data downloaded from Utah Department of Environmental Quality website, February 2015.
[19] Musselman RC and Korfmacher JL, (2014) Ozone in remote areas of the Southern Rocky Mountains, *Atmospheric Environment*, 82, 383-390.

in the West have not responded to emission reductions. This is in dramatic contrast to the trends in and immediately downwind of the major Western cities and the trends in the Eastern U. S.

For example, the ozone trend at the Great Basin National Park site reported by Fine et al. (2014) showed actual increases in the 95th percentile maximum daily 8-hour ozone in May and several winter months and no significant trend in the other months over the 20-year period, 1994 through 2013. The increase is ascribed to long-range transport of Asian pollution influencing the air entering the West Coast of the U. S.

The analysis of trends by Cooper et al. (2012)[20] is particularly insightful. Cooper et al. evaluated long-term (1990–2010) rural ozone trends using all available data in the West (12 sites) and East (41 sites). Rather than focus solely on average ozone values or air quality standard violations, they considered the full range of ozone values, reporting trends for the 5th, 50th and 95th percentiles, for daytime hours (11:00 to 16:00 local time) when the atmospheric boundary layer is well mixed.

Cooper et al. report that domestic ozone precursor emissions decreased sharply during 1990–2010, by roughly half each for NOx, CO, and VOC precursors.. Accordingly 83%, 66% and 20% of summertime Eastern U.S. rural sites experienced statistically significant ozone decreases in the 95th, 50th and 5th percentiles, respectively. During spring 43% of the Eastern sites had statistically significant ozone decreases for the 95th percentile with no sites showing a significant increase. At the 50th percentile there is little overall change in the Eastern U.S.

In contrast, only two rural sites in the polluted region of Central California had statistically significant ozone decreases in the 95th percentile in the summer. During spring no Western site had a significant decrease, while 50% had a significant median increase. Cooper et al. discuss this dichotomy in U.S. rural ozone trends in terms of changing anthropogenic and biomass burning emissions and possible changes in temperature. They conclude that increasing baseline ozone flowing into the Western U.S. is counteracting ozone reductions due to domestic emission reductions.

Cooper et al. show with tropospheric column NO_2 measurements that NO_2 has been decreasing steadily in both the Eastern and Western U. S., and that NO_2 is much higher in the East, in agreement with emission inventory information. Despite much lower NO_2 levels in the rural West, Cooper et al. show that the spring daytime 95th percentile ozone levels at the Eastern and Western rural sites both average 66 ppb in more recent data (2006-2010). The 50th percentile is somewhat higher in the West (53 vs. 47 ppb), while the 5th percentile is definitely higher in the West (40 vs. 28 ppb). Thus, despite much lower NO_2 levels in the rural West, peak daytime ozone is the same as at rural sites in the East. In addition, since the average level of 95th percentile ozone in the rural West in spring is 66 ppb, and has not decreased over the 21 year period of the study, during which time man-made emissions of the major precursors were roughly halved, it is clear that peak ozone in the rural West is (1) not responsive to man-made precursor controls in the U. S., and (2) is high enough to cause exceedances of the various

[20] Cooper OR, Gao RS, Tarasick D, Leblanc T, and Sweeney C. (2012), Long-term ozone trends at rural ozone monitoring sites across the United States, 1990–2010*, J. Geophys. Res*., 117, D22307, doi:10.1029/2012JD018261.

alternative primary standards under consideration by the Agency.

Cooper et al. also provide information on the changing levels of ozone in the free troposphere above midlatitude North America. They report that for 1995–2011 the median ozone rate of increase is 0.41ppb/yr. They note that because free tropospheric ozone can be transported to the surface of the U.S., it is likely that a trend in free tropospheric ozone could influence ozone trends at the surface. This is more likely in the West because of the elevated terrain.

It is well established that ozone in the free troposphere (>2 km a.s.l) is similar on the East and West coasts of the U.S. in springtime due to the rapid eastward transport during this season and that free tropospheric ozone is much greater than at the surface. In fact, Cooper et al report that the median free troposphere ozone in April and May above the West is about 60 ppb and the 95th percentile is now about 90 ppb. The presence of a reservoir of increasing ozone in the free troposphere is an impediment to achieving a stricter ozone standard and is posited by Cooper et al. as a probable explanation for the lack of progress in reducing peak ozone in the rural West.

Another contributor to zone in the rural West is transport of man-made ozone and precursors from urban areas. Cooper et al. discuss this source as it relates to sites near Denver. They show that NO_2 has been reduced dramatically at Denver urban sites as expected from the nation's emission control programs. The large source area in Southern California is another possible source of ozone transported to rural Western sites. However, the ozone and precursor levels in and immediately downwind of the South Coast Air Basin of California have decreased substantially over the period that Fine et al. and Cooper et al. studied ozone trends. For example, the peak 8-hour ozone levels in the South Coast Air Basin have decreased from 186 ppb in 1990 to 112 ppb in 2010 and maximum annual average NO_2 levels have decreased from 0.055 ppm to 0.026 ppm over the same time period, so the contribution from transport of ozone and precursors from Southern California (as well as other Western urban areas) has been steadily decreasing, not increasing.

Huang et al. (2013)[21] evaluated the impact of Southern California pollution on Western States using data from a May 2010 multi-institution field campaign and showed that the impact of transport from California was greatest in Arizona and New Mexico, with median contributions of ~3, ~2, ~5 ppb when the total surface max-daily 8-hour ozone exceeded thresholds of 60, 65, and 70 ppb, respectively. In Utah, Colorado, Wyoming, Idaho, and Montana, the median contributions were the order of 1 ppb at high ambient ozone concentrations. They also report that different scales of transport (e.g., trans-Pacific, stratospheric intrusions, and interstate) can be dynamically and chemically coupled and simultaneously affect ozone in the mountain states when the meteorological conditions are favorable. Although some individual episodes had higher South Coast contributions, transport from Southern California cannot explain the vast bulk of incidences of ozone greater than 60 ppb in the Intermountain West.

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[21] Huang M, Bowman KW, Carmichael GR, Pierce RB, Worden HM, Luo M, Cooper OR, Pollack IB, Ryerson TB, and Brown SS, (2013) Impact of Southern California anthropogenic emissions on ozone pollution in the mountain states: Model analysis and observational evidence from space, *J. Geophys. Res. Atmospheres,* 18, 12,784–12,803, 2013.

D. Estimates of Background from Models Have Increased Substantially Since the Previous Review

In the previous review, EPA relied on one global model to estimate mean seasonal background. The Alliance pointed out numerous problems with the approach, including issues with the definition of background, the formulation of the model, and the lack of consideration of peak background.[22] In the intervening years, additional modeling studies have been conducted, the definition of background has been changed to be more in line with Alliance comments, and more refined model estimates are now available. However, more recent Alliance comments[23] have documented how the USB estimates generated in the current review are biased low. This arises because the modeling approach was not designed to determine how much of the modeled ozone has resulted from background sources, but rather to attribute maximum culpability to controllable anthropogenic precursors.

During the development of the ISA, the estimates of mean background rose due to refinements in the modeling and, in addition, there has been consideration of peak background. Although the proposed rule indicates that the "proportional influence of background sources tends to be lower on high O_3 days," there is increasing evidence that this is not the case. For example, Zhang et al. (2011)[24] used a refined global model and conclude that background is higher than average when ozone exceeds 60 ppb, particularly in the Intermountain West. Zhang et al. also acknowledge that the model cannot reproduce background-relevant events associated with wildfires or stratospheric intrusions. The Zhang et al. analysis continued the trend for higher resolution global models to estimate modest upward shifts in mean background ozone.

Emery et al. (2012)[25] shifted the paradigm to estimating background with a regional model (CAMx) run at 12 km resolution, with boundary conditions coming from a global model. Emery et al. compared their results to the results from the global model used previously to estimate US background. They report that, in general, the regional model performed better in replicating observations at remote monitoring sites, and performance remained better at higher concentrations. In addition, the regional model predicted somewhat higher summer mean background, which reached well over 60 ppb in the West due to event-oriented phenomena such as stratospheric intrusion and wildfires. The regional model also showed a higher correlation between modeled background and total observed ozone than the global model. Emery et al. indicate that a case study during April 2006 suggests that stratospheric exchange of ozone is underestimated in both models on an event basis. The authors concluded that wildfires, lightning NOx and stratospheric intrusions contribute a significant level of uncertainty in estimating

[22] Comments of the Alliance of Automobile Manufacturers on EPA's Proposal to Revise National Ambient Air Quality Standards for Ozone,72 Fed. Reg. 37,818 (July 11, 2007), October 9, 2007, Docket NO. EPA-HQ-OAR-2005-0172.

[23] Comments to Third External Review Draft of the "Integrated Science Assessment for Ozone and Related Photochemical Oxidants" Docket ID No. EPA-HQ-ORD-2011-0050, submitted by the Alliance of Automobile Manufacturers, August 20, 2012.

[24] Zhang L, et al. (2011).Improved estimate of the policy-relevant background ozone in the United States using the GEOS-Chem global model with 1/2° × 2/3° horizontal resolution over North America, *Atmospheric Environment,* 45, 6769-6776.

[25] Emery C, et al., (2011) Regional and global modeling estimates of policy relevant background ozone over the United States, *Atmospheric Environment* , doi:10.1016/j.atmosenv.2011.11.012

background.

E. There is Growing Evidence for Sources and Mechanisms that Can Increase Peak Background Ozone and that Are Not Modeled Appropriately

In comments on the third draft ISA, Downey et al. provided the Agency evidence contradicting the Agency view that stratospheric intrusions that reach the surface are rare, noting:[26]

> Observational evidence, however, suggests that stratospheric intrusions, folds, streamers and downwelling of ozone rich upper tropospheric air significantly contributes to surface ozone exceedance events. Models continue to underestimate the contribution of this effect to surface ozone concentrations. The recent CalNex field campaign (2010) in California observed 8 stratospheric intrusions in 6 weeks (May 9 to June 26, 2010) in California (*Oltmans et al.* 2010), and these events led to surface level MDA8 ozone > 75 ppb at least one surface site (*Langford et al.* 2010). Additionally, the downward mixing of free tropospheric air enriched with Asian emissions of ozone precursors led to Paradise, CA exceeding an MDA8 of 75 ppb (*Langford et al.* 2010). *Hocking et al.* (2007, 608032) concluded that stratospheric intrusions can be relatively frequent and that intrusions can significantly impact ambient ozone concentrations. *Langford et al.* (2009) also observes that stratospheric-tropospheric-transport (STT) leads to exceedances of the NAAQS, which has also been observed by *Lefohn et al.* (2010, submitted), and it is clear that global CTM's do not reproduce the frequency or magnitude of stratospheric intrusions and upper tropospheric downwelling events.

In addition, to the references Downey et al. provided, there is additional confirming evidence.

Zhang et al. (2014)[27] evaluated the sources of ozone in the Intermountain West with a global model and report that the highest ozone concentrations observed in the Intermountain West in spring are associated with stratospheric intrusions. They noted the model captures the timing of these intrusions but not their magnitude. They also evaluated the influence of California pollution, concluding that it frequently exceeds 10 ppb in parts of the Intermountain West but is generally not correlated with the highest ozone events.

Lin et al. (2012a)[28] used a combination of ozonesondes, lidar, and surface measurements over the Western U.S. from April to June 2010 to show that a new global model could capture the

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[26] Downey N, Blewitt D, and Wood D. (2011) Comments on the 'Integrated Science Assessment of Ozone and Related Photochemical Oxidants' EPA Document EPA/600/R-10/076A Released March 2011, Docket # EPA-HQ-ORD-2011-0050, May 5, 2011, at page 18.

[27] Zhang L, Jacob DJ, Yue X, Downey NV, Wood DA, and Blewitt D, (2014) Sources contributing to background surface ozone in the US Intermountain West, *Atmos. Chem. Phys*., 14, 5295–5309.

[28] Lin M, Fiore AM, Cooper OR, Horowitz LW, Langford AO, Levy H, Johnson BJ, Naik V, Oltmans SJ, Senff CJ, (2012) Springtime high surface ozone events over the western United States: Quantifying the role of stratospheric intrusions. *J. Geophys. Res.-Atmos.* 2012, 117(D21), D00V22.

observed layered features and sharp ozone gradients of deep stratospheric intrusions. They identified thirteen intrusions that enhanced daily maximum 8-h average ozone to 70–86 ppb at surface sites. They report that stratospheric intrusions can episodically increase surface ozone by 20–40 ppb including on days when observed ozone exceeds the current NAAQS. The stratospheric intrusions elevated background ozone concentrations (estimated by turning off North American anthropogenic emissions in the model) to values of 60–75 ppb. At high-elevation Western U.S. sites, Lin et al. estimate the 25th–75th percentile of the stratospheric contribution is 15–25 ppb when observed max daily ozone is 60–70 ppb, and increases to 17–40 ppb for the 70–85 ppb range. Their estimates, which are up to 2–3 times greater than previously reported, indicate a major role for stratospheric intrusions in contributing to springtime high-O_3 events over the high-altitude Western U.S. In contrast to the Agency view, Lin et al. conclude that the background ozone concentration and its stratospheric component peak at the high-end of the observed ozone O_3 distribution over the U.S. Mountain West. They indicate that their findings pose a challenge for staying below the ozone NAAQS threshold, particularly if a value in the 60–70 ppb range were to be adopted.

Lin et al. (2012b)[29] used the same model and observational data to evaluate the role of transport of Asian pollution on Western U. S. ozone. They report that Asian emissions can contribute from 8 to 15 ppb ozone on days when the observed ozone exceeds 60 ppb. Effects were seen in the densely-populated Los Angeles Basin as well as in more rural and remote areas of the West. They also note that there can be mixing and interweaving of Asian pollution and stratospheric air during transport.

Yates et al. (2013)[30] analyzed two stratospheric intrusion events that occurred over California in the Spring of 2012 and influenced ozone over large areas of the West, including a site in Wyoming. They note that the Western United States, due to its location at the end of the North Pacific mid-latitude storm track, has been identified as a preferred location for deep stratospheric intrusions. The intrusions typically form filamentary structures that appear as laminae that can be detected in ozone profiles by ozonesondes, by in-situ aircraft measurements, or by lidar.

In addition, Lefohn et al. (2012)[31] used trajectory calculations to evaluate the coincidence between enhanced ozone concentrations and stratospheric ozone intrusions. The coincidence was frequent at high-elevation sites in the Intermountain West, as well as at the high-elevation sites in the East. These sites exhibited a preference for coincidences during the springtime and in some cases, the summer, fall, and late winter. Besides the high-elevation monitoring sites, Lefohn et al. report that low-elevation monitoring sites across the entire US experience enhanced ozone concentrations coincident with stratospheric events.

NOx produced by lightning is another source of elevated background ozone that was not

[29] Lin M, et al. (2012), Transport of Asian ozone pollution into surface air over the western United States in spring, *J. Geophys. Res*., 117, D00V07, doi:10.1029/2011JD016961.
[30] Yates EL, Iraci LT, Roby MC, Pierce RB, Johnson MS, Reddy PJ, Tadi*ƒ*á JM, Loewenstein M, Gore W, (2013) Airborne observations and modeling of springtime stratosphere-to-troposphere transport over California. *Atmos. Chem. Phys. Discuss*., 13(4), 10157-10192.
[31] Lefohn AS, Wernli H, Shadwick D, Oltmans SJ, and Shapiro M, (2012) Quantifying the importance of stratospheric-tropospheric transport on surface ozone concentrations at high- and low-elevation monitoring sites in the United States, *Atmospheric. Environ*., 22, 646–656.

properly modeled by the Agency in the prior review. Cooper et al. (2006)[32] presented evidence that the upper troposphere above midlatitude Eastern North America contained 15 ppb more tropospheric residual ozone than the more polluted layer between the surface and 2 km above sea level. Lowest ozone values in the upper troposphere were found above two upwind sites in California. The upper troposphere above midlatitude Eastern North America contained 16 ppb more tropospheric residual ozone than the upper troposphere above three upwind sites, with the greatest enhancement above Houston, Texas, at 24 ppb. Cooper et al. demonstrated that the upper tropospheric ozone maximum above eastern North America is largely the result of in situ ozone production from lightning NOx. Cooper et al. (2007)[33] reinforced this conclusion with additional analyses.

Hudman et al. (2007)[34] evaluated upper troposphere data obtained by aircraft with a global model and found that they had to increase the NOx emission rate from lightning by a factor of seven compared to the standard GEOS-CHEM model that EPA has relied upon to estimate background ozone.

F. The Regulatory Mechanisms that EPA Posits Can Deal with High Background Ozone are Expensive, Cumbersome, Time-consuming, and Ineffectual

The proposed rule lists three potential sources of regulatory relief:[35]

> Relief from designation as a nonattainment area (through exclusion of data affected by exceptional events).
>
> Relief from the more stringent requirements of higher nonattainment area classifications (through treatment as a rural transport area; through exclusion of data affected by exceptional events; or through international transport provisions).
>
> Relief from adopting more than reasonable controls to demonstrate attainment (through international transport provisions).

The Agency indicates that none of these relief mechanisms are completely burden-free, meaning they all require some level of assessment or demonstration by a state and/or EPA to legally invoke. In addition, the exceptional event exclusion is the only mechanism that does not require some local controls. Thus, the rural transport and international transport provisions offer only partial relief.

The exceptional events policy is not well-suited to deal with the background ozone issue.

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[32] Cooper OR, et al. (2006), Large upper tropospheric ozone enhancements above midlatitude North America during summer: In situ evidence from the IONS and MOZAIC ozone measurement network, *J. Geophys. Res*., 111, D24S05, doi:10.1029/2006JD007306.
[33] Cooper OR, et al. (2007), Evidence for a recurring eastern North America upper tropospheric ozone maximum during summer, *J. Geophys. Res*., 112, D23304, doi:10.1029/2007JD008710.
[34] Hudman RC, et al. (2007), Surface and lightning sources of nitrogen oxides over the United States: Magnitudes, chemical evolution, and outflow, *J. Geophys. Res*., 112, D12S05, doi:10.1029/2006JD007912.
[35] Proposed Rule, supra note 1, at 75382-75383.

Uncontrollable background varies on an event level due to multiple factors including: upper tropospheric/lower stratospheric downwelling (UT/LS), biomass burning, lightning and long-range transport of pollution plumes. No regulatory mechanism exists for excluding high ozone events caused by downwelling of upper tropospheric air, ozone production by lightning, or a combination of multiple background influences that cause exceedance of the standard.

The current regulations[36] require that "There would have been no exceedance or violations but for the event" which indicates there is only one source involved. Furthermore, the definition of an Exceptional Event[37] states that it "Is an event caused by human activity that is unlikely to recur at a particular location or a natural event," meaning that events that continue to occur from transport of anthropogenic emissions or other processes could not be excluded. The Agency indicates that not all background ozone can be excluded as an exceptional event, noting, for example:[38]

> However, exceedances due to natural emissions that occur every day and contribute to policy relevant background, such as biogenic emissions, do not meet the definition of an exceptional event and are thus not eligible for exclusion under the EER.
>
> Routine anthropogenic emissions outside of the U.S. contribute to policy relevant background, but are not exceptional events.

Thus, the existing exceptional events policy is not suited to the use the Agency envisions in the proposed rule. The proposal indicates that there would be a future rulemaking to address such issues. However, States need to know now how they and their data will be treated in the attainment designation process in order to properly comment on the proposed rule. Based on the experience to date, the exceptional events procedures are costly, time-consuming, and overly burdensome to the States. There is nothing in the proposed rule to indicate that the situation will change if the standard is revised.

The Executive Director of the Utah Department of Environmental Quality provided testimony to Congress[39] noting that the exclusion application process is complex, time-consuming, and resource intensive. Yet applications by Utah have been routinely denied by EPA staff.

In the case of particulate matter, EPA has provided tools to use to analyze for exceptional events, however, it is a very difficult and time-consuming process to get data excluded from attainment status determinations. In the case of ozone, there are no approved protocols or tools to perform comparable analyses. As noted above, routine ozone monitoring and current EPA models cannot clearly identify the processes that may lead to exceedances from uncontrollable background. The kinds of detailed measurements and models that are needed to unravel and understand the

[36] 40 CFR 50.14(c)(3)(iv).
[37] 40 CFR 50.1(j).
[38] 77 Fed. Reg. 39959, July 6, 2012, in the answer to Question 16a of Attachment1, Draft Exceptional Events Rule Frequently Asked Questions.
[39] A. Smith testimony before the Subcommittee on Environment of the of the Committee on Science, Space, and Technology, June 12, 2013.

various sources of ozone at a ground level site are not readily available. Putting them in place would require a massive increase in the cost of monitoring. Even if such a major expansion took place, the evaluation of each incidence would turn into an extensive research project. The States do not have the resources or trained personnel to carry out such an effort.

If a revised ozone standard is established, there will be many ozone events exceeding the standard at rural Western sites. For example, in the spring and summer of 2006 there were over 600 ozone events greater than 60 ppb for only 12 CASTNET sites, an average of 50 days per site. Each could involve a local agency analysis and a case-by-case approval. The level of effort and time involved for both local agencies and EPA would create a logistical nightmare and be unworkable. Even a 70 ppb standard would be unworkable.

If a high background event is caused by multiple sources, including long range transport and natural ozone production, the requirement to demonstrate that there would have been no exceedance or violation but for the event would be a high threshold and unworkable.

For all these reasons, the Agency should not rely on the existing mechanisms of regulatory relief to deal with the incidences of background ozone that approach or exceed the alternative standards under consideration.

G. Summary of Background Issues

In the previous review, EPA significantly underestimated the background O_3 in the U.S. which lead CASAC to conclude that the range of the NAAQS (60-70 ppb) that they supported in the previous review was higher than background. In the present review, EPA concedes that the modeling assumptions used in the previous review did, in fact, underestimate the background. As a result, they have made incremental but continuous improvements in their modeling assumptions about background and have produced more credible estimates of background.

However, new monitoring and modeling studies show that the background estimates are still too low and that a NAAQS in the range of 60 - 70 ppb will be exceeded or approached by background concentrations, especially in the mountainous Western states, frequently. It appears that EPA's models are still underestimating the contributions from statospheric intrusions and international transport. In addition, the method they use to estimate background is still biased low because it is not designed to determine how much of the modeled O_3 is due to background, but rather attribute maximum culpability to controllable anthropogenic precursors.

Finally, the regulatory mechanisms that EPA posits can deal with high incidents of background are inadequate to provide regulatory relief to the states, especially for those states that will experience frequent violations from background.

IV. The Current Standard Protects the Public Health with an Adequate Margin of Safety

In discussing the adequacy of the current standard, the proposed rule considers the results of the human clinical studies, the results of observational studies, the results of the risk assessment, and

the views of CASAC. As documented in Part 2 of these comments, the current 0.075 ppm 8-hour standard effectively limits human exposure to the first respiratory effects of ozone as documented in human clinical studies. The HREA risk estimates for FEV1 decrements demonstrate that the current standard renders exposures that result in the first mild effects as rare and sufficiently limits repeat exposures. Isolated instances of mild, transient decrements have not been considered adverse in prior reviews. The protective nature of the current standard can be documented by using the fraction of person-days metric that the Agency calculates but omits from presentation in the PA and proposal. Although stricter standards would provide additional protection, the changes in fraction or percent of person-days are *de minimis* and, thus, there is no additional public health protection. There is no bright line that separates the current standard or any of the alternatives as being necessary to protect public health.

When the fact that the HREA risk estimates significantly overestimate the number of exposures to high ventilation rates is considered, the protective nature of the current standard is even more apparent. The HREA estimated the risk of FEV1 decrements using two methods. The HREA shows in Appendix 6C that the results with the exposure-response method are essentially the same as calculated in the prior review. Part 2 of these comments demonstrate that the MSS model, as applied in the HREA, overestimates FEV1 decrements by assuming that there is no measurement error in the clinical data, in contradiction of the MSS author's acknowledgement that the data is noisy. Even with the overestimation, the HREA demonstrates that the current standard protects almost everyone almost all the time from even the first mild respiratory effects.

With regard to the observational studies, the proposal notes five studies that purport to show ozone effects in locations that meet the current standard. As demonstrated in Section V.B.2, there are inconsistencies in the five studies that raise questions about interpreting these associations as effects caused by ozone as claimed in the Proposed Rule. In addition, APHENA shows that the relationships observed in Canada are different and inconsistent with the relationships observed in U.S. and European cities and brings into question the appropriateness of using any Canadian observational data to decide the level of an ambient air quality standard in the U.S.

Throughout the proposal the Administrator gives less weight to the observational results than the human clinical results, noting:[40]

> The determination to attach less weight to the epidemiologic-based estimates reflects the uncertainties associated with mortality and morbidity risk estimates, including the heterogeneity in effect estimates between epidemiologic study areas, the potential for epidemiologic-based exposure measurement error, and uncertainty in the interpretation of the shape of concentration-response functions at lower O_3 concentrations.

This is entirely appropriate. In fact, because of the issues raised in Section V.B, particularly the lack of consistency and coherence in the full pattern of the epidemiological associations for ozone, and especially the biologically implausible wide range of associations in the observational data, there is enormous uncertainty as to whether the serious morbidity and mortality effects posited by EPA are real. In addition, the Agency has not acknowledged or discussed the

[40] Proposed Rule, supra note 1, at 75276.

discrepancy between (1) the threshold nature of the mild and transient respiratory effects in clinical studies, and (2) the EPA assumption that there is no threshold for ozone causing premature mortality and hospital admissions.

Because of the issues with the observational studies, the epidemiological risk assessment should not be given any weight in setting the primary standard. Therefore, retention of the current standard should be considered as a viable alternative in the current review. Due to the current standard being close to the background of ozone, retention of the current standard is an appropriate choice among reasonable alternatives, which would be a rational policy decision supported by previous judicial review.

The CASAC recommendation for a standard between 60 and 70 ppb is based on the desire to eliminate any and all exposures that might cause respiratory effects, no matter how few or how minor in terms of public health. However, because the current standard effectively limits such exposures already, as the standard is revised downward, there are diminishing returns.

In contrast to the diminishing returns for public health, the photochemical modeling carried out for the Proposed Rule demonstrates that massive additional emission reductions will be necessary if the standard is revised downward. Because of the complex non-linear nature of ozone formation, the massive reductions actually increase ozone exposures in many populated urban locations. CASAC did not consider the diminishing returns in terms of public health as ozone is reduced while the cost and potential adverse effects on health of attainment efforts rises dramatically for a more stringent standard. This was an important omission in the CASAC deliberations since CASAC has a statutory requirement to advise the Administrator of any adverse public health, welfare, social, economic, or energy effects which may result from various strategies for attaining the national standards.

Part 2 – Technical Issues Comments

V. Health Effect Studies Do Not Support a Lower Standard

Health Issues

Human clinical studies do not support the necessity of a lower O3 standard. When individuals engaged in extended moderate exercise are exposed to O3 concentrations below the current standard of 0.075 ppm, only small, temporary, non-clinically significant symptoms/effects have been reported. (See Section V.A below.)

Observational (epidemiological) studies do not support the necessity of a lower O3 standard either. Because of stochastic variability (observing a false positive result by chance), model selection issues, confounding, measurement errors, publication bias, the lack of plausible biological mechanisms, and EPA's tendency to emphasize positive associations over null and negative associations, EPA's conclusions concerning causality should be dismissed. The five studies that EPA weighs heavily because they purport to show health effects in areas that are below the current standard are seriously flawed. In addition, the Proposed Rule overstates the evidence from epidemiological studies for the first effects identified in human clinical studies. (See Section V.B and Appendix 1 below.)

The Proposed Rule exaggerates the health risk and exposure to O3 in the real world. Based on the risk assessment using the clinical studies, the current primary ozone standard is highly protective of public health. Using even EPA's favored epidemiological associations and assumptions, the risk assessment shows that the risk of mortality effects is small and highly uncertain. When the full range of associations in the literature is considered, along with the lack of biological plausibility for such serious effects below the level of the current standard, the epidemiological risk assessment should not be considered in setting the primary standard. (See Sections V.C.1-3 below.)

The Proposed Rule notes that EPA was directed to consider the potential beneficial health effects of ozone in shielding the public from the effects of solar ultraviolet (UV) radiation, as well as adverse health effects. However, in this review, EPA concluded in their Integrated Science Assessment (ISA) that the evidence was inadequate to determine even if there was a causal relationship between tropospheric O3 and the effects on health and welfare related to UV-B shielding. However, in a separate evaluation of human health impacts of reducing O3-depleting substances conducted for another rulemaking, EPA did make quantitative estimates for incidences of melanoma, basal cell, and squamous cell carcinoma, and deaths from melanoma. Thus, when it comes to estimating the morbidity and mortality benefits of proposed rules, the Agency quantifies the benefits, but when it comes to UV-related disbenefits from precursor controls as in the current Proposed Rule,

the Agency claims that there is too much uncertainty to make quantitative estimates. This is an unacceptable double standard. (See Section V.C.4 below.)

A. Human Clinical Studies Do Not Support a Lower Standard

The human clinical studies of ozone are particularly important since these data provide a strong and consistent body of information on the dose-response of effects of 1- to 3- hour and 8-hour exposures to ozone. For example, the proposed rule indicates:[41]

> Controlled human exposure studies provide direct evidence of relationships between pollutant exposures and human health effects (U.S. EPA, 2013a, p.lx). Controlled human exposure studies provide data with the highest level of confidence since they provide human effects data under closely monitored conditions and can provide exposure response relationships. Such studies are particularly useful in defining the specific conditions under which pollutant exposures can result in health impacts, including the exposure concentrations, durations, and ventilation rates under which effects can occur.

Two new studies – Schelegle et al. (2009)[42] and Kim et al. (2011)[43] - add to the two prior studies – Adams (2002)[44] and Adams (2006)[45] - that were available in the last review to inform us of the effects of ozone at 120 ppb and below.

Goodman et al. (2014)[46] evaluated causality and adversity in discussing this database with regard to effects below 80 ppb and concluded:

> In summary, the small decrements in pulmonary function, as represented by slightly decreased mean FEV1 values with no or slight concomitant changes in FVC, observed at relatively low ozone concentrations, are of low severity because they do not interfere with normal activity and do not result in permanent respiratory injury or progressive respiratory dysfunction. In addition, because the decrements in FEV1 and FVC are reversible, transient and represent a reflexive nervous response, these small changes represent a lesser degree of adversity than irreversible and sustained changes in cellular composition or in lung function.

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[41] Proposed Rule, supra note 1, at 75244.
[42] Schelegle ES, Morales CA, Walby WF, Marion S, Allen RP. (2009) 6.6-Hour inhalation of ozone concentrations from 60 to 87 parts per billion in healthy humans. *Am. J. Respir. Crit. Care Med*. 180: 265–272.
[43] Kim CS, Alexis NE, Rappold AG, Kehrl H, Hazucha MJ, Lay JC, Schmitt MT, Case M, Devlin RB, Peden DB, Diaz-Sanchez D. (2011) Lung function and inflammatory responses in healthy young adults exposed to 0.06 ppm ozone for 6.6 hours. *Am. J. Respir. Crit. Care Med*. 183: 1215–1221.
[44] Adams WC. (2002). Comparison of chamber and face-mask 6.6-hour exposures to ozone on pulmonary function and symptoms responses. *Inhal. Toxicol*. 14: 745–764.
[45] Adams WC. (2006) Comparison of chamber 6.6-h exposures to 0.04-0.08 ppm ozone via square-wave and triangular profiles on pulmonary responses. *Inhal. Toxicol*. 18: 127–136.
[46] Goodman JE, Prueitt RL, Chandalia J, Sax JN. (2014) Evaluation of adverse human lung function effects in controlled ozone exposure studies. *Journal of Applied Toxicology*, 34, 516-524.

In contrast, the Policy Assessment (PA) and the proposed rule strain to make the case that the effects below the level of the current standard are adverse and important from a public health perspective. The proposed rule refers to the framework for evaluating respiratory effects and adversity developed in the 1997 review and applied in the 2007 review. The rule acknowledges that moderate functional responses are very unlikely to interfere with normal activity for active healthy people including children. It also notes:[47]

> Although some experts would judge single occurrences of moderate responses to be a nuisance, especially for healthy individuals, a more general consensus view of the adversity of such moderate responses emerges as the frequency of occurrence increases. Thus it has been judged that repeated occurrences of moderate responses, even in otherwise healthy individuals, may be considered to be adverse since they could well set the stage for more serious illness.

However, in evaluating repeated occurrences in the HREA, the Agency limits the data presented to one or more and two or more occurrences to the 70 and 80 ppb levels, rather than also presenting the data for five or more, ten or more, etc. which could be used to evaluate the likelihood of responses repeatedly during the course of the year that might lead to a more serious health condition.

In addition, the proposed rule argues that children, asthmatics or persons with respiratory disease may be more at risk than healthy young adults. However, young adults have been shown to be the most sensitive subjects for the mild respiratory responses identified in the clinical studies. Asthmatics and children have been shown to have similar lung function responses while older adults have lesser responses. In addition, children have fewer symptoms than young healthy adults.

Finally, the proposed rule discusses the effects below the current standard in relation to the American Thoracic Society (ATS) guidelines for what constitutes an adverse effect, noting that combination of lung function decrements and respiratory symptoms, which has been considered adverse in previous reviews, has been demonstrated in healthy adults following prolonged (6.6 hour) exposures, while at intermittent moderate exertion to 72 ppb. However, the ATS guidelines for adverse effects do not specify a 10 % cutpoint and caution against considering FEV1 decrements by themselves as adverse. Goodman et al. (2014) note that the group mean decrement in the 72 ppb exposure is less than 10 % and that the study was not designed to assess ozone effects in individuals. In previous reviews, isolated FEV1 decrements even with mild symptoms were not considered a concern.

The proposed rule indicates that medical experts differ in their judgments when applying the ATS guidelines to these effects that are acknowledged as the least serious category of ozone effects. The effects reported below the current standard are arguably somewhere between the mild and moderate categories of functional changes used by the Agency in prior reviews. Goodman et al. (2014) refer to these changes as being of low severity. The proposed rule also indicates that moderate functional changes (with even more symptoms that have been reported at

[47] Proposed Rule, supra note 1, at 75263.

exposures below the current standard) can be viewed as a nuisance that will not interfere with daily activities.

In addition, it is accepted that these lung function decrements are the body's reflexive reaction to the presence of an irritant gas unrelated to sensations of discomfort. The Integrated Science Assessment (ISA), PA, and proposed rule acknowledge that a key event in the mode of action of ozone is the activation of neural reflexes that lead to involuntary truncation of inspiration that results in decrements in the performance of lung function tests.

The proposed rule also raises the issue of ozone-induced pulmonary inflammation at 60 ppb (Kim et al., 2011), claiming that inflammation is evidence that injury has occurred[48] and raising the concern that repeated events of acute inflammation can have several potentially adverse outcomes. However, the extent of inflammation at 60 ppb is small. In addition, Pino et al.[49] concluded that "…neutrophils do not play a detectable role in contributing to the early epithelial damage in the lung caused by an acute exposure to ozone" based on experiments with neutrophil-depleted rats exposed to 1,000 ppb ozone.

The immune system responses discussed in the rule as the first indications of "inflammation" are physiological processes that occur in all living organisms under the stimuli of daily life. The first reported changes are small and reversible and well within the range of physiological variability. They fall into the category of biochemical markers that the ATS guidelines indicate do not necessarily imply adversity. EPA has noted that the initiation of inflammation is an important component of the defense process; however, the concern is that its persistence and/or its repeated occurrence can possibly result in adverse health effects.

A recent human clinical study sponsored by the California Air Resources Board,[50] that was designed to test for systemic effects of ozone on inflammation in order to evaluate potential cardiovascular effects from ozone, found instead that the exercise intensity used in the human clinical studies, by itself, produced an acute systemic inflammation that was of the same order of magnitude as the acute lung inflammation reported by Kim et al. (2011). Thus, the stress of vigorous exercise, by itself, produces an acute pro-inflammatory response. Therefore, the initial ozone pro-inflammatory responses below the current standard should not be considered a threat to public health.

The discussion of adequacy of the current standard needs to consider that the kind of effects identified in the most recent controlled human studies are mild, transient decrements in the performance of lung function tests generally unaccompanied by symptoms. They occur near the current standard only if the subject is exposed and exercising over an extended period of time at a rate that, when sustained for a long period, is at the very high end of real-world situations. For exposures at rest or under typical levels of exertion, the threshold for even the first mild,

[48] Ibid., at 75252.
[49] Pino MV et al. (1992) Acute ozone-induced lung injury in neutrophil-depleted rats. *Toxicology and Applied Pharmacology* 114 (2), 268–276.
[50] Balmes JR, Arjomandi M, Wong H, Donde A, and Power K, Effects of Ozone Exposure on Cardiovascular Responses in Healthy and Susceptible Humans, California Air Resources Board Contract Number 04-322, October 2011.

transient effects is well above the current standard, between 300 and 500 ppb. The proposed rule acknowledges that "Ozone exposure concentrations well above those typically found in ambient air are required to impair lung function in healthy resting adults.[51]

Another important consideration is that the first effects (small FEV1 decrements, neutrophilic inflammation, and mild respiratory symptoms) all exhibit threshold behavior. The PA and proposed rule acknowledge that antioxidants within the airway lining fluid have been shown to prevent ozone-mediated cellular and tissue effects. The ISA acknowledges "The first line of defense against oxidative stress is antioxidants-rich ELF which scavenges free radicals and limits lipid peroxidation."[52] Pryor et al. (1995)[53] indicated that antioxidants "provide a sacrificial protection system that leads to few toxic products." Therefore, only ozone exposures of sufficient duration and concentration will overwhelm the body's antioxidant defenses and begin to trigger or activate other defenses. For FEV1 decrements, the key event is the activation of neural reflexes that lead to involuntary truncation of inspiration.

In addition to FEV1 decrements, there is substantial evidence that mild inflammatory processes occur in the lung that increase with increased dosage of ozone. The subjects in the human clinical studies also report respiratory symptoms, such as cough, shortness of breath, and pain on deep inspiration, that increase with the ozone dose. As with FEV1 decrements, there is clear evidence of a threshold in the inflammatory and symptom responses.

The proposed rule refers to a meta-analysis of 21 controlled human exposure studies (Mudway and Kelly, (2004)[54]) that involved O_3 exposures from 80 to 600 ppb, exposure durations from 1 to 6.6 hours, and from light to heavy exercise. While the PA and proposed rule indicate that Mudway and Kelly reported that PMN influx in healthy subjects is linearly associated with total ozone dose, the actual paper indicates that there is a threshold in the dose-response and one rationale for the study was that "Establishing these relationships is vital in determining threshold doses of ozone below which adverse responses are negligible in the healthy population."

With regard to symptoms, the proposed rule refers to the McDonnell et al. (1999)[55] study to indicate that symptoms increase with increasing ozone concentrations, duration of exposure and activity level.[56] The data reported by McDonnell et al. also clearly show a threshold phenomenon. For example, ozone exposures of 2 hours at rest with concentrations up to 300 ppb caused no symptoms.

As Goodman et al. (2014) point out, the exercise regimen (i.e., 40 L/min for 6–8h) used

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[51] Proposed Rule, supra note 1, at 75429.
[52] U.S. Environmental Protection Agency (2013). Integrated Science Assessment of Ozone and Related Photochemical Oxidants (Final Report). U.S. Environmental Protection Agency, Washington, DC. EPA/600/R–10/076F. Available at: *http://www.epa.gov/ttn/naaqs/standards/ozone/s_o3_2008_isa.html*.
[53] Pryor WA, et al. (1995) The cascade mechanism to explain ozone toxicity: The role of lipid ozonation products *Free Radical Biology and Medicine*, 19, 935-941.
[54] Mudway IS, Kelly FJ. (2004). An investigation of inhaled ozone dose and the magnitude of airway inflammation in healthy adults. *Am J Respir Crit Care Med*. 169: 1089–1095.
[55] McDonnell WF, Stewart PW, Smith MV, Pan WK, Pan J. (1999) Ozone-induced respiratory symptoms: exposure-response models and association with lung function. *Eur Respir J ,* 14, 845 - 853.
[56] Proposed Rule, supra note 1, at 75255.

in almost all recent human controlled exposure studies conducted below 80 ppb ozone is meant to simulate work performed during a day of heavy manual labor common of outdoor workers. Shamoo et al. (1991)[57] investigated the summer activity patterns of outdoor workers in Los Angeles and reported estimated ventilation rates based on heart rate recordings. The subjects also used diaries to record their location and activity. The ventilation rate reported for fast activity (44 L/min) was comparable to the ventilation rate used in the recent clinical studies. The outdoor workers diaries showed fast activity only 1 % of the time, and only at leisure, never at work. In addition, Schelegle et al. (2009) point out that the mean overall ventilation used in their study is equal to or greater than mean ventilations that might be encountered during a day of heavy to severe manual labor among the construction workers observed by Linn and colleagues[58] and that this represents the higher end of ventilations that might be encountered in the normal population for this prolonged period. Thus, the ventilation rate used in the most recent human clinical studies is at the extreme of prolonged daily activity.

The most important issue or question with regard to these data then is how to translate the results into human risk as people go about their daily life. For example, it should be borne in mind that a subject has to be outside, undergoing strenuous activity at the time and place of high ozone for there to be an exposure that could cause an effect. Thus, the results of the recent clinical studies carried out near the level of the current standard with strenuous exercise cannot be used directly to claim public health concerns from ozone exposures below the current standard.

The proposed rule acknowledges this fact, noting:[59]

> For these types of effect, information from controlled human exposure studies, which provides an indication of the magnitude and thus adversity of effects at different ozone concentrations, combined with estimates of occurrences in the population from the HREA, provide information about their importance from a policy perspective.

B. Observational (Epidemiological) Studies Do Not Support a Lower Standard

1. EPA's Mortality and Hospital Admissions Claims Are Flawed

In contrast to the controlled studies of ozone exposure which, when replicated, demonstrate causal relationships, the observational studies only provide statistical associations of ozone with various health endpoints. There are seven major issues that bedevil the interpretation of these studies. First, there is a great deal of stochastic variability in the results as demonstrated in numerous multi-city studies. Second, there is a great deal of uncertainty due to model selection issues. Third, there is potential confounding by meteorology and other pollutants. Ozone is always present in the ambient air along with a large number of other pollutants and their concentrations are influenced by meteorological conditions. Fourth, there are measurement errors that prevail in all environmental epidemiological studies which are sufficient to produce a

[57] Shamoo D, Johnson T, Trim S, Little D, Linn W, and Hackney J. (1991) Activity patterns in a panel of outdoor workers exposed to oxidant pollution, *J. Exp. Anal. Environ. Epidemiol*., 1, 423-438.
[58] Linn W, Spicer C, and hackney J. (1993) "Activity patterns in ozone-exposed construction workers," *J. Occup. Med. Toxicol*., 2, 1-14 (1993).
[59] Proposed Rule, supra note 1, at 75264.

false low-dose linear result. Fifth, there is publication bias by which authors tend to submit papers and editors seek to publish papers that have positive rather than negative results. Sixth, there is a disconnect between the results from controlled human studies and epidemiological studies that undermine the biological plausibility of the reported statistical relationships. Finally, the seventh issue is that EPA tends to emphasize positive associations over studies with null associations.

Public comments from AIR and from other scientists have detailed these concerns and inconsistencies.[60] However, the ISA, HREA, and PA continued to gloss over the issues that have been raised in public comments and fail to fully address the uncertainty and inconsistencies that are present in the epidemiologic data. As a result, the proposed rule overstates the consistency and coherence of the observational evidence. Each one of these issues will be summarized below.

a. Stochastic Variability Produces Biologically Implausible Results.

The stochastic variability is best illustrated by examining the individual city-specific raw estimates of the mortality increase attributed to ozone exposure. An example from Smith et al. (2009)[61] is shown in Figure 10. The individual estimates range from -2% to about +3.5% change in mortality per 10 ppb increase in ozone, with about 25% of the cities experiencing a protective (negative) effect and 75% a slight increase in mortality. In other words, the data suggest that in 25% of the cities, increased ozone results in lower mortality. This is not biologically plausible.

It should be noted that very few of the risk estimates are statistically significant.

[60] Heuss JM and Wolff GT, Review and Critique of the U. S. Environmental Protection Agency's First External Review Draft of the "Integrated Science Assessment for Ozone and Related Photochemical Oxidants," Air Improvement Resource, Inc. Report, Prepared for The Alliance of Automobile Manufacturers, May 2011; Long CR et al. "Comments on U.S. EPA's Causality Determinations for Short-term and Long-term Ozone Exposures and Mortality in the Integrated Science Assessment for Ozone and Related Photochemical Oxidants, First External Review Draft," May 5, 2011. Available as Attachment B at: http://www.regulations.gov/#!documentDetail;D=EPA-HQ-ORD-2011-0050-0009; Goodman JE, Comments on the 'Integrated Science Assessment of Ozone and Related Photochemical Oxidants,' EPA Document EPA/600/R-10/076A; released March 2011." Available as Attachment 1 to Docket ID EPA-HQ-ORD-2011-0050-0007.

[61] Smith RL, Xu B, and Switzer P. (2009) Reassessing the Relationship between O_3 and Short- term Mortality in U.S. Urban Communities. *Inhalation Toxicology*, 21: 37-61.

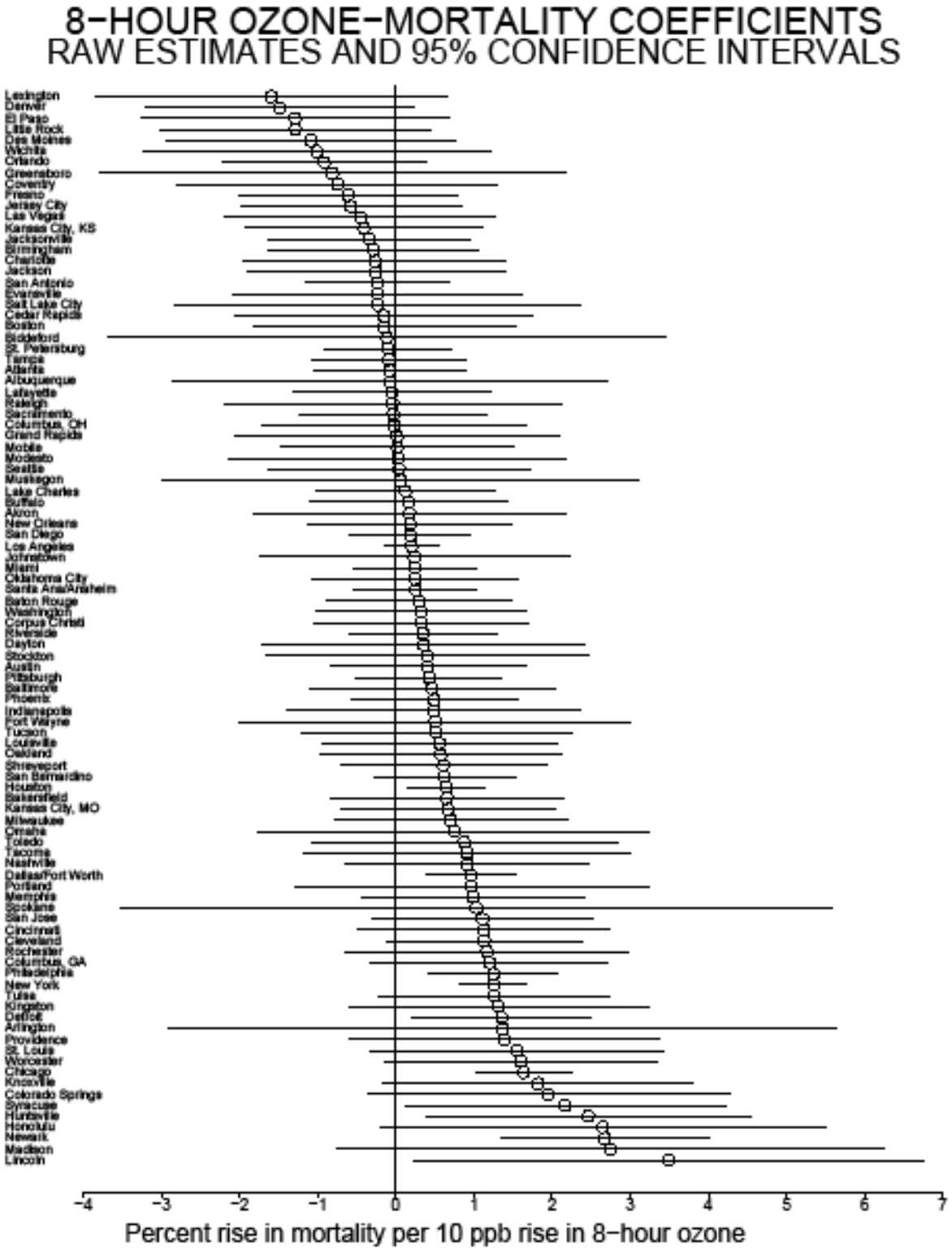

Figure 10: Change in mortality per 10 ppb change in 8-hour ozone in U.S. cities.[2]

The stochastic variability is further illustrated by comparing the individual risk estimates from two studies with cities in common. That is shown in Figure 11 for the Zanobetti and Schwartz (2008)[62] and Bell et al. (2004)[63] studies. The Bell et al. unadjusted associations are not given in the original paper but are shown in Figure 4 of Smith et al. (2009). As shown in Figure 11, there is little or no correspondence between the associations in individual cities in the two studies that EPA considers the best sources of data on this subject. Note that there are many negative associations in the data. Nine cities have a negative association in one study and a positive association in the other. Eight cities have negative associations in both studies. These results are not plausible.

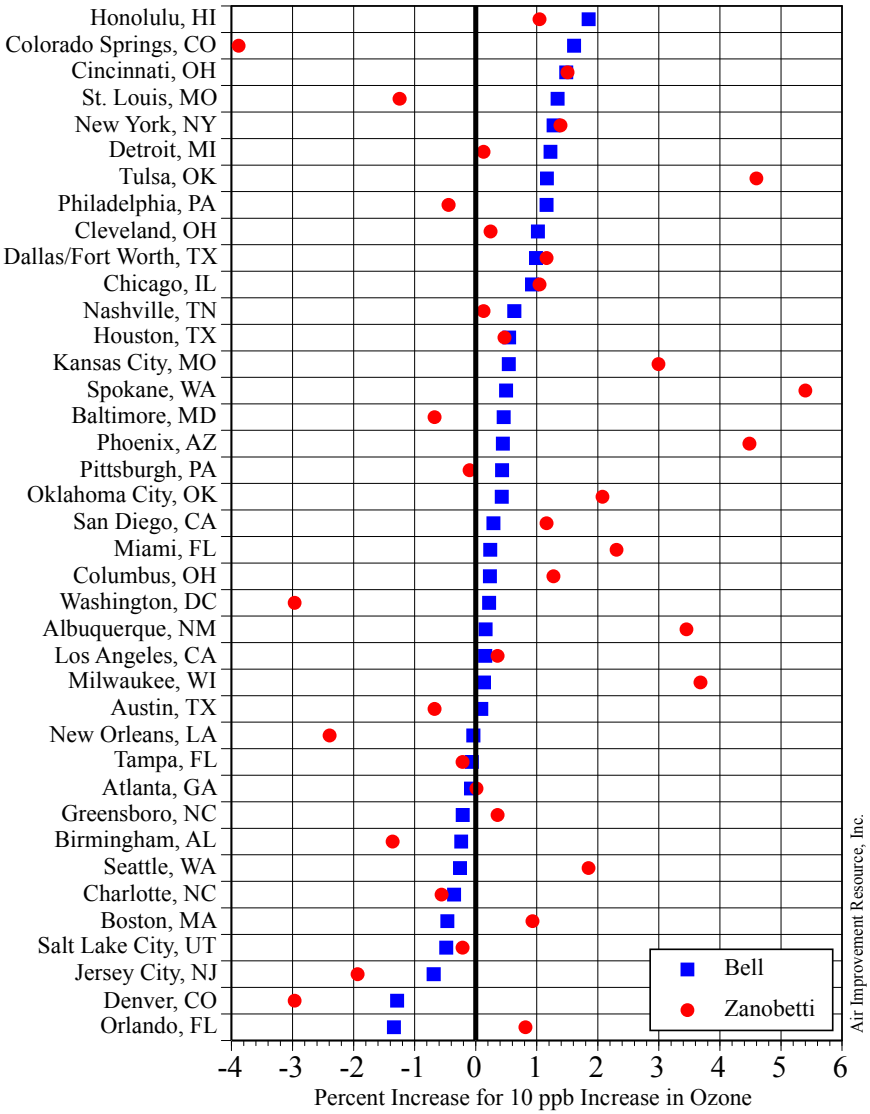

Figure 11: Comparison of unadjusted maximum likelihood estimates for mortality from Bell et al. (2004) and Zanobetti and Schwartz (2008).

[62] Zanobetti A, Schwartz J. (2008) Mortality Displacement in the Association of O_3 with Mortality: An Analysis of 48 Cities in the United States. *American Journal of Respiratory and Critical Care Medicine,* 177: 184-189.
[63] Bell ML, McDermott A, Zeger SL, Samet JM, Dominici F. (2004) O_3 and Short-term Mortality in 95 U.S. Urban Communities, 1987-2000. *JAMA,* 292: 2372-2378.

b. Great Uncertainties Due to Model Selection

In epidemiology, statistical models are used to relate a health outcome to various factors that may contribute to the occurrence of that health outcome. Selecting an appropriate statistical model for epidemiological analyses of air pollution data is an extremely important process that can affect the outcome of the study in a very significant way. It can make the difference between finding a positive association, a negative association or no association. It involves making a number of choices which include:

- How is confounding by weather to be controlled? That is, what functional form should be assumed for the effects of weather variables, such as temperature and relative humidity?
- What weather variables should be used?
- What co-pollutants should be included and what averaging time should be used?
- What temporal effects need to be controlled and to what degree?
- What lag structure should be assumed? That is, how many days after exposure to a pollutant should one expect to see an effect on health?

There is little biological knowledge to inform these choices that must be made. Unfortunately, most investigators do not make these choices systematically and many choose the model that maximizes the effect estimates. Because of the large number of possible models, the results that are reported could have occurred by chance.

The strength of an association as well as the sign of the risk depends critically on the statistical model that is employed. One of the best examples of this is a paper that EPA uses in their core analysis to develop a concentration-response (C-R) function for ozone and mortality.[64] The first sentence of the paper states: "The purpose of this paper is to reexamine the evidence of an association between ambient ozone and nonaccidental all-cause mortality, based in particular on a series of papers by Bell and co-authors that used the NMMAPS database." To accomplish this, they state: "We look extensively at alternative treatments of meteorology and co-pollutants, showing that there are confounding and effect modifier relationships that have been understated or overlooked in previous studies."

The relative risk value that EPA uses from Smith et al. to develop the C-R for non-accidental mortality was an increase of 0.32% ± 0.08 for a 10 ppb increase in MDA8 O_3. Smith et al. generated that number using a model that was identical to that used by Bell et al. to make sure they could first replicate Bell et al.'s result before conducting their sensitivity analyses. Since Bell et al. used 24-hour average O_3, Smith et al. first reproduced their result using the same model and then ran it a second time with MDA8 O_3 values to generate the relative risk value in terms of MDA8. Then Smith et al. conducted their sensitivity analyses by running many more alternative models and generated hundreds of different relative risk values that ranged from negative values to statistically significant positive values. Smith et al.'s analyses demonstrate that the 0.32% risk estimate is not robust to alternative model formulations. Smith et al. do not identify any one model as being the correct model as the point of their calculations was to show

[64] Smith et al., supra note 61.

that different model specifications produce different answers. As a result, their conclusions include:

- The basis for the national effect estimates published by Bell and others is questionable in the face of clear evidence that the [geographical] effect is not homogeneous.

- Further, we believe that the heterogeneity and sensitivity of ozone effect estimates to a variety of covariates leaves open the issue of *whether or not ozone is causally related to mortality. Consequently, the question arises whether any particular ozone-mortality effect estimate can reliably be used to predict mortality reductions that would ensue from specific ozone reductions* [emphasis added].

- There is clear evidence of a PM_{10} co-pollutant effect that has been understated or misinterpreted in previous publications.

- The nonlinear analysis shows that much of the evidence for an ozone-mortality relationship in fact comes from the low-ozone days, but human studies do not support an ozone effect at such low ozone levels. It is possible that the appearance of an association at low ozone levels may be due to the effect of co-pollutants, or an artifact caused by differences between personal and ambient exposure.

- There are other methodological issues that have not been discussed in this paper, but that could affect the results.

- In summary, it is our view that estimates of the association between ozone and mortality, based on time-series epidemiologic analyses of daily data from multiple cities, reveal important still-unexplained inconsistencies and show sensitivity to modeling choices and data selection. *These inconsistencies and sensitivities contribute to serious uncertainties when epidemiological results are used to discern the nature and magnitude of possible ozone-mortality relationships or are applied to risk assessment* [emphasis added].

In essence, EPA pulled one out of hundreds of risk estimates contained in the Smith et al. paper because it met their criteria and ignored many others. In addition, they make no mention of the conclusions that Smith et al. come to when all of the results of their analyses are considered in context.

Heterogeneity of results and the dependence of the results on model selection were also illustrated in the multi-continent APHENA study[65] that is cited in the proposed rule. APHENA

[65] Katsouyanni K and Samet J. (2009) Air Pollution and Health: A European and North American Approach, (APHENA), *HEI Report* 142, Health Effects Institute, Boston, MA.

provides a particularly large data base and set of analyses with various statistical models that can be used to evaluate important questions concerning the ozone-mortality and ozone-hospital admissions associations. As documented in Appendix 1, the combined results of the large and comprehensive APHENA study are not consistent with ozone having a causal role in mortality or morbidity below the current standard.

The strong regional differences in ozone-mortality associations that have now been identified should supersede the EPA assumption of a common national mortality health effect. In addition, the APHENA results, as discussed in detail in Appendix 1, indicate results that are mixed, inconsistent, and model-dependent.

The Proposed Rule acknowledges that there is heterogeneity in ozone-mortality associations. However, the heterogeneity is much wider than EPA acknowledges and includes many cities with negative associations.

Another demonstration of model uncertainty is given in Figure 12 which compares the NMMAPS associations for individual cities that come from the 24-hour ozone associations at lag 1 from the 2003 revised analysis of time series data[66] with the ozone associations from the same cities using 8-hour ozone and the distributed lag model from Bell et al. (2004). Lag 1 was chosen for the comparison even though lag 0 had a somewhat higher combined association in the revised analysis because lag 0, in the case of ozone, runs afoul of the temporality requirement that the cause precede the effect. Since the peak ozone occurs in the late afternoon, the bulk of the mortality on a given day occurs before the peak ozone exposure. Again the wide variation in associations for most cities is apparent in Figure 12.

Thus the outcome of an epidemiology study is highly dependent upon the model used. Since there is no *a priori* way to determine the correct method, the full range of associations needs to be considered. When this is done it will become apparent, as Koop and Tole pointed out in 2004:[67]

> Point estimates of the effect of numerous air pollutants all tend to be positive, albeit small. However, when model uncertainty is accounted for in the analysis, measures of uncertainty associated with these point estimates became very large. Indeed they became so large that the hypothesis that air pollution has no effect on mortality is not implausible. On the basis of these results, we recommend against the use of point estimates from time-series data to set regulatory standards for air pollution exposure.

[66] F. Dominici et al. 2003. "Revised Analyses of Time-Series Studies of Air Pollution and Health," *HEI Special Report*, pp. 9-24.

[67] Koop G. and Tole L. (2004) Measuring the Health Effects of Air Pollution: to What Extent Can We Really Say that People are Dying from Bad Air, *J. of Environmental Economic Management*, 47, 30-54.

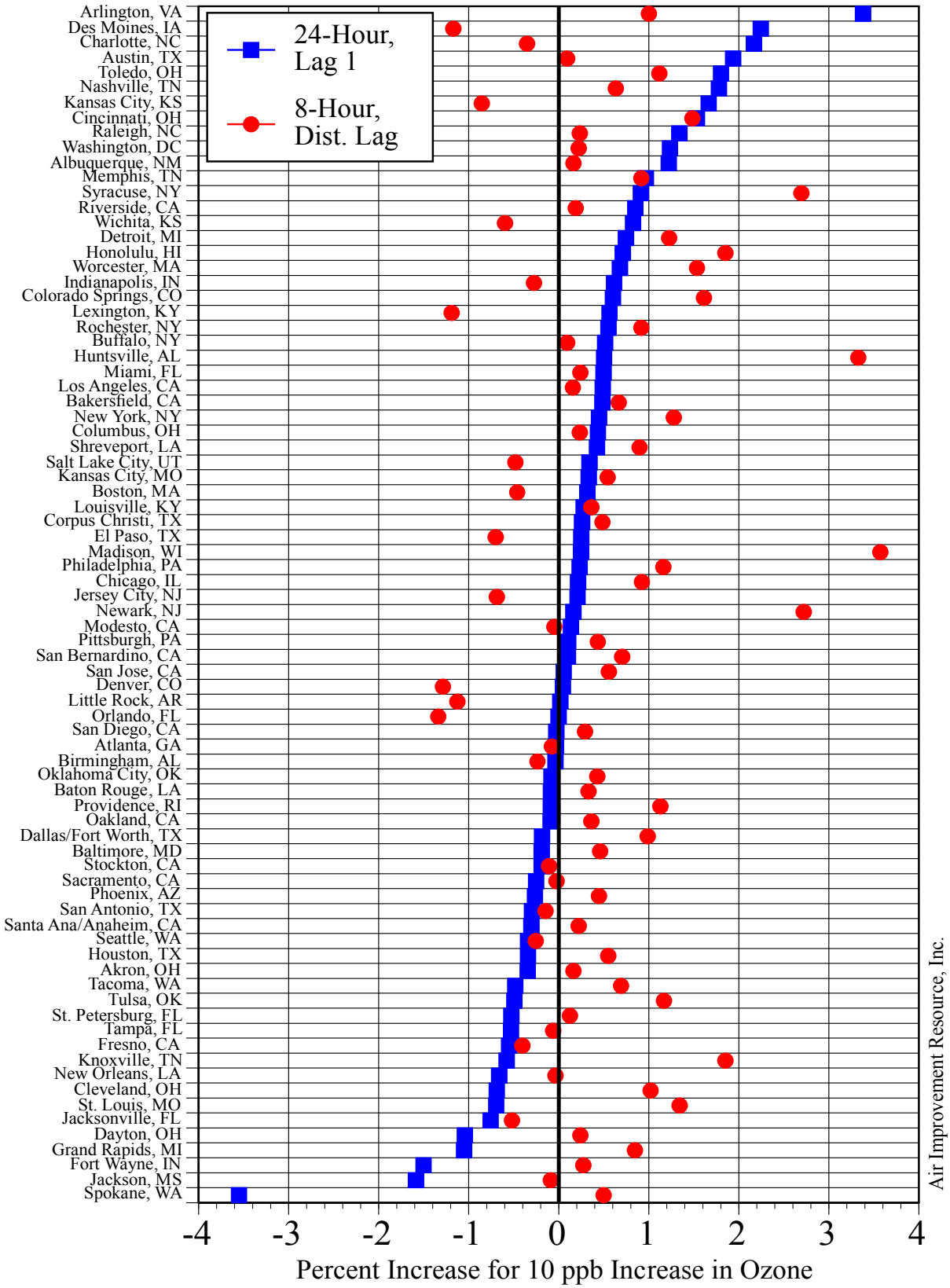

Figure 12: Maximum likelihood estimates for mortality from two NMMAPS analyses.

c. Confounding Not Adequately Controlled

A confounder is an extraneous variable that correlates with both the dependent and independent variable. Such a relationship is termed a spurious relationship. All air pollution epidemiology studies must deal with the issue of confounding. The ambient air can contain trace amounts of hundreds of chemical species both in the gas and particulate phase. Many of the pollutants have some common sources and all are influenced to some degree by the prevailing meteorology. Consequently, there is some degree of correlation present among many of the variables. Because of this, in a study of any one component of air pollution such as ozone, other components that may be associated with health impacts must be controlled. Very few studies do this for even the ones that are measured. This means that the potential for confounding by other substances in the atmosphere can never be completely controlled and their effects ruled out.

Many short-term, time-series studies of air pollution report associations between ozone and various measures of human health, such as the numbers of daily deaths and hospital admissions, in single pollutant analyses. However, when possible confounding by other pollutants is explicitly addressed, many of the studies find a reduced association or no association between ozone and measures of human health. A good example of this is NMMAPS (Dominici et al., 2003)[68] which showed that in single pollutant models each criteria pollutant, including ozone, had a statistically positive association with mortality. When models with two or more pollutants were used, the single-pollutant coefficients were attenuated and, in most cases, lost statistical significance.

Smith et al. (2009)[69] found evidence of confounding in their study that reexamined the evidence for ozone caused mortality. They conclude that the appearance of an association at low ozone concentrations "may be due to the effect of co-pollutants."

The APHENA study[70] also provides multiple examples of PM confounding the reported ozone/mortality associations in Canada, Europe and the U.S. When PM was added to the models, mortality due to all-cause, cardiovascular or respiratory effects were either attenuated or lost their statistical significance. Similar results were also shown for hospital admissions.

In all air pollution epidemiology, weather is also an obvious confounder. In addition, other temporal effects such as season, cyclic diseases, and day-of-the-week patterns must be controlled for. In a discussion of this subject, a Special Panel of HEI's Health Review Committee (Special Panel of the Health Effects Review Committee, 2003)[71] noted:

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[68] Dominici F, McDermott A, Daniels M, Zeger SL, and Samet JM. (2003) Revised analysis of the National Morbidity, Mortality, and Air Pollution Study, Part II. In: *Revised Analyses of Time-Series Studies of Air Pollution and Health,* HEI Special Report, pp. 5-24.
[69] Smith et al., supra note 31.
[70] Katsouyanni and Samet, supra note 35.
[71] Special Panel of the Health Review Committee. 2003. Commentary on Revised Analyses of selected studies. In: *Revised Analyses of Time-Series Studies of Air Pollution and Health,* HEI Special Report, pp. 255-291.

> Neither the appropriate degree of control for time in these time-series analyses, nor the appropriate specification of the effects of weather, has been determined. This awareness introduces an element of uncertainty into the time-series studies that has not been widely appreciated previously. At this time, in the absence of adequate biological understanding of the time course of PM and weather effects and their interactions, the Panel recommends exploration of the sensitivity of these studies to a wider range of alternative degrees of smoothing and to alternative specifications of weather variables in time-series models.

In other words, it is widely known that weather and temporal confounders must be controlled, but the correct method to do so is not known.

Consequently, very little weight should be given to the studies that use only single pollutant models and do not consider the possibility of confounding influences.

d. Measurement Errors Not Given Appropriate Weight

Because of all the issues with stochastic variability, publication bias, model selection uncertainty, confounding, etc., time-series epidemiology of air pollution associations is a very blunt tool. CASAC raised this issue in a June 2006 letter to the Administrator noting that "[b]ecause results of time-series studies implicate all of the criteria pollutants, findings of mortality time-series studies do not seem to allow us to confidently attribute observed effects specifically to individual pollutants."[72] Further, due mainly to measurement error issues, CASAC questioned the likelihood of ozone itself causing mortality and noted the limitation that measurement error obscures thresholds in time-series studies, adding additional concerns about the utility of the time-series mortality estimates. More recently, Rhomberg et al. (2011)[73] have shown, as others have previously shown, that measurement error can give a false linear result. Although the Rhomberg et al. study of the impact of measurement error in environmental epidemiology was cited in public comments on the second draft ISA and second draft HREA, it is still ignored by the Agency. CASAC's prior concerns and the Rhomberg et al. findings are consistent with points made by the Special Panel of the HEI Review Committee (Special Panel of the Health Review Committee, 2004)[74] that raised several cautions in interpreting the NMMAPS concentration-response results. They point out that measurement error could obscure any threshold that might exist, that city-specific concentration-response curves exhibited a variety of shapes, and that the use of Akaike Information Criterion may not be an appropriate criterion for choosing between models. The HEI Panel cautioned *that lack of evidence against a linear model should not be confused with evidence in favor of it* (emphasis added).

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[72] CASAC Letter, EPA-CASAC-06-07, June 5, 2006, at 3 and 4.

[73] Rhomberg LR, Chandalia JK, Long CM, and Goodman JE. (2011) Measurement error in environmental epidemiology and the shape of exposure-response curves, *Critical Reviews in Toxicology*, 41 (8), 651-671. (doi: 10.3109/10408444.2011.563420).

[74] Special Panel of the Health Review Committee. (2004) Commentary. In: *The National Morbidity, Mortality, and Air Pollution Study Part III: Concentration-Response Curves and Threshold for the 20 Largest US Cities,* HEI Report 94, Part III, pp. 23-30.

Consequently, EPA has not given appropriate weight to the potential bias from measurement error.

e. Impact of Publication Bias Underestimated

Publication bias is another major issue in assessing the epidemiological literature. Publication bias occurs because authors are inclined to mine the data for positive results and editors are more likely to publish a paper with positive findings. Consequently, there will be more papers in the literature that show positive epidemiology results than those that show negative results. Publication bias results in inflated risk estimates (Ioannidis, 2008).[75] Thus any meta-analysis performed on the air pollution epidemiology literature uses biased inputs and the results are thus biased. The commentary by Goodman (2005)[76] concerning meta-analyses is particularly insightful. He noted that there was greater than a factor of three difference between the results of ozone meta-analyses and the NMMAPS individual city results which are not affected by publication bias. Goodman concludes that the implications of an EPA-sponsored exercise of funding three separate meta-analyses "go far beyond the question of the ozone mortality effect." He cautions that "depending on published single-estimate, single-site analyses are an invitation to bias." He notes that "the most plausible explanation is the one suggested by the authors, that investigators tend to report, if not believe, the analysis that produces the strongest signal; and in each single-site analysis, there are innumerable model choices that affect the estimated strength of that signal." A separate review by a panel of ten air pollution health effect experts concluded "taken together, the meta-analyses provide evidence of a disturbingly large publication bias and model selection bias" (Rochester Conference Report, 2007).[77]

f. The Disconnect Between Epidemiological and Controlled Human Studies

There is a major disconnect between the results of the human clinical studies and the Agency's interpretation of the epidemiological studies. The human clinical studies clearly demonstrate that the first ozone effects are mild and transient and occur above a threshold dose due to the protective effects of antioxidants in the epithelial lining fluid. Only at concentrations above the current standard and with vigorous exercise does the dose approach effects that may be considered adverse. Yet the Agency assumes that ozone causes premature mortality and hospital admissions down to zero ozone levels. Such an assumption is not consistent with either the general principles of toxicology or the specific findings of controlled ozone exposure studies.

The proposal rationalizes the biological plausibility of ozone-caused mortality by noting:[78]

> Moreover, evidence from experimental studies indicates multiple potential pathways of respiratory effects from short-term O_3 exposures, which support the continuum of respiratory effects that could potentially result in respiratory-related mortality in adults.

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[75] Ioannidis J, (2008) Why most discovered true associations are inflated, *Epidemiology*, 14, 640-648.
[76] Goodman S. (2005) The Methodologic ozone effect. *Epidemiology,* 16, 430-435.
[77] Rochester Conference Report. (2007). *Critical Considerations in Evaluating Scientific Evidence of Health Effects of Ambient Ozone,* University of Rochester School of Medicine.
[78] Proposed Rule, supra note 1, at 75258.

Biological plausibility involves consideration of the kinds of effects and the doses that can cause them. The EPA argument addresses the kinds of effects that ozone causes but does not address dose plausibility. Since ozone indoors where people spend the vast majority of their time is typically only a small fraction of that measured outdoors, EPA's assumption that ozone causes mortality at low ambient concentrations involves assuming that personal ozone exposures of the order of 10 ppb are causing mortality, which is not at all plausible given the extensive clinical and toxicological data gathered over many decades.

Biological plausibility means that there needs to be an exposure-response relationship between the cause and effect. Goodman et al. (2013)[79] point out that EPA has overlooked this. For example they note that four studies of outdoor workers[80] show no exposure-response relationship for lung function changes and conclude that this provides evidence against a causal relationship.

g. EPA Favors Positive Associations Over Null Results

It has recently been documented by Goodman et al. (2013)[81] that EPA selectively ignores certain studies that report null results in favor of studies that find positive associations. In addition, in papers where the results of more than one statistical model are reported, EPA tends to report the results with the strongest associations. These were the conclusions drawn by Goodman et al. in their evaluation of the causal framework used by EPA to set the National Ambient Air Quality Standards.

These authors note that EPA provides a database of the studies considered for inclusion in their evaluations and they note which ones were cited in the ozone ISA and which were not. However, it is not clear why certain studies were excluded. They provide the following examples:

> For example, in the ozone ISA, EPA (2013a, p 2-2) states, ''[l]iterature searches have been conducted routinely since then to identify studies published since the last review, focusing on studies published from 2005 (closing date for the previous scientific assessment) through July 2011''. EPA included the study by Zanobetti & Schwartz (2011)[82] in the ozone ISA but omitted a study by Lipsett et al. (2011)[83] that was published online the same day (23 June 2011). EPA also omitted a study by Spencer-

[79] Goodman JE, Prueitt RL, Sax SN, Bailey LI, and Rhomberg LR, (2013) Evaluation of the causal framework used for setting the National Ambient Air Quality Standards, *Crit. Rev. Toxicol.* DOI: 10.3109/10408444.2013.837864..
[80] Brauer M, Blair J, Vedal S. (1996). Effect of ambient ozone exposure on lung function in farm workers. *Am J Respir Crit Care Med*, 154, 981–7; Chan CC, Wu TH. (2005). Effects of ambient ozone exposure on mail carriers' peak expiratory flow rates. *Environ Health Perspect*, 113, 735–8; Hoppe P, Praml G, Rabe G, et al. (1995). Environmental ozone field study on pulmonary and subjective responses of assumed risk groups. *Environ Res*, 71, 109–21; Romieu I, Meneses F, Ramirez M, et al. (1998). Antioxidant supplementation and respiratory functions among workers exposed to high levels of ozone. *Am J Respir Crit Care Med*, 158, 226–32.
[81] Goodman et al., supra note 79.
[82] Zanobetti A, Schwartz J. (2011) Ozone and survival in four cohorts with potentially predisposing diseases. *Am J Respir Crit Care Med*, 184, 836–41.
[83] Lipsett MJ, Ostro BD, Reynolds P, et al. (2011). Long-term exposure to air pollution and cardiorespiratory disease in the California teachers study cohort. Am J Respir Crit Care Med, 184, 828–35.

> Hwang et al. (2011)[84], which was published online on 21 July 2011. In addition, there were several studies of both ozone and PM that were not included in the ozone ISA but played a prominent role in EPA's PM evaluation (e.g. Jerrett et al., 2005[85]; Miller et al., 2007[86]). This indicates that not all relevant studies were captured by the literature search strategy used.

They further state that:

> there are many examples in the ozone ISA where studies with positive associations were emphasized over studies with null associations, as opposed to studies of greater quality being emphasized over those of lesser quality. This provided a false perception that most of the reliable evidence supported a positive causal association.

They then cite some additional examples:

> In the discussion of respiratory effects in adult day-hikers in the ozone ISA, positive associations with lung function decrements reported in one study (Korrick et al., 1998[87]) were emphasized over the null associations for the same endpoints reported in another study (Girardot et al., 2006[88]), and there was no discussion of the strengths and limitations of either study. In the evaluation of studies examining short-term ozone exposure and cause-specific mortality, EPA stated that there is evidence of associations with cardiovascular (CV)- and respiratory-specific mortality, yet all risk estimates for respiratory mortality and almost all for CV mortality were null in analyses of these endpoints year-round; results were mixed for both endpoints in analyses of the summer months, when ambient ozone concentrations are highest.
>
> In its summary of epidemiology data for short-term effects of ozone on pulmonary inflammation and oxidative stress in the ozone ISA, EPA stated that many recent studies reported positive associations. Yet throughout its discussion, EPA noted that the results were mixed and inconsistent. EPA did not provide an explanation for why studies with positive associations should carry more weight than those reporting null associations. Finally, in the discussion of short-term effects of ozone on

[84] Spencer-Hwang R, Knutsen SF, Soret S, et al. (2011) Ambient air pollutants and risk of fatal coronary heart disease among kidney transplant recipients. *Am J Kidney Dis*, 58, 608–16.
[85] Jerrett M, Burnett RT, Ma R, et al. (2005) Spatial analysis of air pollution and mortality in Los Angeles. *Epidemiology*, 16, 727–36.
[86] Miller KA, Siscovick DS, Sheppard L, et al. (2007) Long-term exposure to air pollution and incidence of cardiovascular events in women. *N Engl J Med*, 356, 447–58.
[87] Korrick SA, Neas LM, Dockery DW, et al. (1998) Effects of ozone and other pollutants on the pulmonary function of adult hikers. *Environ Health Perspect*, 106, 93–9.
[88] Girardot SP, Ryan PB, Smith SM, et al. (2006) Ozone and PM2.5 exposure and acute pulmonary health effects: a study of hikers in the Great Smoky Mountains National Park. *Environ Health Perspect*, 114, 1044–52.

> respiratory symptoms, EPA stated there is a ‘‘strong’’ body of evidence demonstrating associations between ozone and increased respiratory symptoms (e.g. wheezing) and asthma medication (e.g. bronchodilator) use in asthmatic children, yet almost all risk estimates were null for these outcomes. This also suggests that EPA's evaluation of the epidemiology data did not fully consider evidence from studies with null results.

In the section above on model selection it was shown how different statistical model formulations used in the APHENA study produced very different outcomes that, if viewed collectively, did not support a causal relationship. However, as Goodman et al. point out, EPA did not adequately consider all the results:

> In the Air Pollution and Health: a European and North American Approach (APHENA) study[89], which included datasets from US, Canadian, and European multi-city studies, ozone mortality estimates were sensitive to the smoothing function type applied (Katsouyanni et al., 2009). Despite extensive sensitivity analyses comparing a number of different models, Katsouyanni et al. (2009) were unable to identify a model deemed most appropriate for comparing health effect estimates across the different study locations they evaluated. They reported large differences with penalized versus natural splines, as results were negative when penalized splines were used and positive when natural splines were used. In the ozone ISA, EPA only presented the positive associations that were reported from the use of natural splines, because ‘‘alternative spline models have been previously shown to result in similar effect estimates’’. Although EPA provided a justification for why it did not present the APHENA results from both smoothing functions, this justification does not make sense when the large APHENA study (upon which EPA relied heavily in the ozone ISA for its causal determinations) indicates that there is sensitivity of risk estimates to the type of smoothing function used in the model.

In addition, Goodman et al. note that EPA ignored that the many limitations of the epidemiology might mean that ozone is not a causal factor.

> There are several instances in the ozone ISA where EPA did not discuss or give due weight to alternative views. For example, EPA noted that consideration of the limitations of epidemiology studies, such as potential confounding and exposure measurement error, must be taken into account to properly inform the interpretation of epidemiology evidence. Yet, in its final evaluation, EPA did not consider that another factor may have caused the health effects associated with ozone in certain epidemiology studies. EPA did not discuss the reasons why this view (i.e. ozone is not causal) is less likely to be true than the view that ozone is the causal factor.

[89] Katsouyanni and Samet, supra note 65.

2. Studies Purporting to Show Effects Below the Current Standard Are Flawed

The proposed rule identifies five U.S. and Canadian epidemiological studies that show associations between ozone and mortality and morbidity in areas that likely were in compliance with the current 8-hour NAAQS of 75 ppb.[90] EPA concludes that these studies give them confidence that the present NAAQS is not sufficiently protective. The five studies are Katsouyanni et al. (2009),[91] Stieb et al. (2009),[92] Dales et al. (2006),[93] Cakmak et al. (2006)[94] and Mar and Koenig (2009).[95]

The most extensive study among these was the Katsouyanni et al. study which is known as Air Pollution and Health: A European and North American Approach (APHENA) which was a multi-continental effort utilizing data from the U.S., numerous European countries and Canada. However, with regards to the above citation in this part of the proposed rule, EPA is only relying on the Canadian part of the APHENA study because many of the U.S. and European cities that were included in the analyses had ozone levels in excess of the current NAAQS. APHENA is described in detail in the Appendix to these comments. In the Appendix we describe how the results obtained in APHENA are highly dependent upon the statistical model that is used and that applies to the Canadian results as well. In addition, in the HEI commentary, the HEI Health Review Committee raise two other concerns regarding the Canadian results. The first is that despite experiencing lower concentrations of ozone in the Canadian cities than in the U.S. and European cities, the ozone effect estimates in some cases were an order of magnitude higher in Canada. The Review Committee cites "the persistent and puzzling large differences between the air pollution effect estimates in Canada and those in the United States and Europe."[96] In their concluding remarks, the Review Committee states: "(a)s a result, some of the more puzzling differences between regions therefore remained unexplained — in particular the much higher effect estimates for PM_{10} and O_3 in Canada relative to Europe and the United States."[97]

The second concern raised by the Committee is that a comparison of the mortality effects to the hospitalization effects shows the results lack coherence. They state:

> On the other hand, it is remarkable how little coherence there is for the O_3 effects. In all three study regions, O_3 was associated with increased cardiovascular mortality, but not with increased respiratory mortality. However, also in all three regions, O_3 was associated with increases in respiratory hospitalizations, but not with increases in cardiovascular

[90] Proposed Rule, supra note 1, at 75280-75281.
[91] Katsouyanni et al., supra note 65.
[92] Stieb DM, Szyszkowicz M, Rowe BH, Leech JA. (2009) Air pollution and emergency department visits for cardiac and respiratory conditions: A multi-city time-series analysis. *Environ Health Global Access Sci Source* 8: 25. *http://dx.doi.org/10.1186/1476-069X-8-25*.
[93] Dales RE, Cakmak S, Doiron MS. (2006) Gaseous air pollutants and hospitalization for respiratory disease in the neonatal period. *Environ Health Perspect* 114: 1751–1754. *http://dx.doi.org/10.1289/ehp.9044*.
[94] Cakmak S, Dales RE, Judek S. (2006) Respiratory health effects of air pollution gases: Modification by education and income. *Arch Environ Occup Health* 61:5–10. *http://dx.doi.org/10.3200/AEOH.61.1.5-10*.
[95] Mar TF, Koenig JQ. (2009) Relationship between visits to emergency departments for asthma and ozone exposure in greater Seattle, Washington. *Ann Allergy Asthma Immunol* 103: 474–479.
[96] Katsouyanni et al., supra note 65 at 109.
[97] Ibid, at 112.

> hospitalizations. These findings do not "complement one another" as the investigators suggest, but on the face of it appear somewhat paradoxical.[98]

The Committee's concluding remark:

> To the extent that such findings support a lack of coherence, plausibility of the mortality or hospitalization findings might be questioned.[99]

Because the Canadian APHENA results are model dependent, the risks are implausibly high relative to the more polluted U.S. and European cities, and they lack coherence among the various mortality and morbidity outcomes, they cannot be used to support EPA's contention that effects are occurring below the current NAAQS.

Of the other four studies EPA uses to support effects below the current NAAQS, three are also Canadian studies using data from Canada's largest cities. APHENA used hospitalization data from the 10 largest Canadian cities from 1993 to 1996. Stieb et al. use hospital ED data for cardiac and respiratory visits in the 7 largest cities from 1992 to 2002. Cakmak et al. use hospital admissions data for respiratory admissions in the 10 largest cities from 1993 to 2000, and Dales et al. use hospital admissions data for respiratory disease in the neonatal period from 1986 to 2000 in the 11 largest cities. Consequently, the first flag that is raised is that all the Canadian studies used data that overlapped to some degree with the APHENA data that produced results that were not plausible.

Stieb et al. examined the associations for four criteria pollutant gases for a variety of cardiac and respiratory endpoints and presented individual city as well as pooled results. For ozone, the results are mixed and inconsistent with very few of the associations being positive and statistically significant. While there were positive associations for cardiac-related ED visits with other pollutants, there were no significant cardiac associations with ozone. For respiratory ED visit categories, there was only one positive and significant association and two negative and significant associations out of the 54 associations evaluated for all the pollutants, three lags, and three ED visit categories. Thus, the one positive association with ozone is less than would be expected by chance alone. Even for that association, the point estimates for the 7 cities cover a wide range, with two being negative and one being null. Consequently, the results from Stieb et al. are ambiguous with respect to showing ozone effects below the current NAAQS.

Cakmak et al. examined respiratory hospitalizations and found a statistically significant increase in admissions of 3.8% per 17.4 ppb increase in O_3 concentration as well as similar positive associations for other pollutants. In contrast to Stieb et al., Cakmak et al. evaluated the lag that had the greatest association among 0 to 5 days in each city for each pollutant and combined those associations for the 10 cities to give the pooled result. However, to test for possible socio-economic confounding, they separated the admissions by education and found that the ozone effect remain positive and statistically significant only for those who did not go to school beyond 8th grade, the lowest quartile in education. Such evidence of confounding or effect modification does not support EPA's claim of evidence of effects below the current NAAQS. In addition, the

[98] Ibid, at 109.
[99] Ibid.

lack of presentation of the individual city results limits the ability to evaluate the consistency or lack of consistency across lags and across cities. In all the other multi-city studies that report individual city results, there is substantial stochastic variability that leads to a wide range of positive and negative associations in the individual cities, a finding that is not consistent with ozone causality.

Dales et al. examined respiratory admissions in neonates, which they define as newborns, 0 to 28 days old. Because of the age restriction, their sample size was quite limited. After choosing the optimum model for each city and calculating an effect estimate for each city, they pooled the results even if the individual estimates were not statistically significant. However, they report the resulting pooled estimate for O_3 as being statistically significant. They also report positive and significant associations with the other pollutants they investigated. Since they did not report the individual city-specific estimates except to say that some were not statistically significant, it is impossible to judge whether their claimed 'statistically significant pooled estimate' is appropriate.

The last paper, Mar and Koenig (2009), examined ED visits in Seattle, WA for children and adults. They presented results separately for adults and children for: six lags (0 to 5 days), two ozone monitoring sites and the ozone averaged over the two sites, and two ozone metrics, 1-hour and 8-hour maxima. Although the authors claim that "[t]his study found a robust relationship between visits to the hospital ED for pediatric asthma and ambient ozone," the results are more mixed. The only significant 8-hour associations for children occurred on day 0 (relative risk = 1.10 (1.01-1.19)) and day 3 (1.11 (1.02-1.21). However, associations on day 0 are always suspicious because ozone typically peaks in the afternoon and since daily ED visits go from midnight to midnight, many of the visits likely occurred before the exposure to ozone. Mar and Koenig acknowledge that day 0 associations are problematic. On day 0, the association for adults is actually negative, suggesting a protective influence which is not plausible. On day 3, the relative risk for children is marginally significant only when both ozone monitoring sites are averaged, but not both individual sites. For adults, the only significant positive association is on day 4 (1.08 (1.02-1.14)). In addition, the authors report that despite the findings of previous investigators and despite their own findings in neighboring Tacoma, WA, they could not find any significant associations between asthma ED visits and $PM_{2.5}$ in Seattle. Given all of the inexplicable results in this paper, it is hard to have confidence in the reality of any of the reported findings.

Based on an analysis of the five studies that EPA claims support health effect beings observed at ozone concentrations below the current ozone NAAQS, we conclude that is not the case. Either individually or collectively the inconsistencies identified in the five studies raise questions about the validity of claims made by the authors. In addition, APHENA shows that the relationships observed in Canada are different and inconsistent with the relationships observed in U.S. and European cities and brings into question the appropriateness of using any Canadian observational data to decide the level of an ambient air quality standard in the U.S.

There are two additional concerns with EPA searching for the study or studies that report the strongest associations at the lowest ambient concentrations. First, the uncertainty due to model

selection issues is not being taken into account. For example, as Koop and Tole (2004)[100] have demonstrated, the outcome of an epidemiology study is highly dependent upon the model used and there is no *a priori* way to determine the correct method. Thus, when model uncertainty is accounted for in the analysis, the uncertainty associated with the point estimates reported in the typical air pollution epidemiology study become very large, much larger than the confidence intervals normally reported.

Another example of model selection uncertainty can be found in Sacks et al. (2012).[101] Sacks et al. compared the results of applying six regression models that previously had been used in multi-city analyses using a data base of cardiovascular mortality in Philadelphia. Each model applied different temporal adjustments (smoothing function and degrees of freedom) and differed in how it controlled for weather. The author's report that the point estimates of the association of ozone with mortality varied greatly depending on the model, from + 2.2 % to – 1.7 % for a 20 ppb increase in ozone averaged over lag 0 and 1. The authors conclude that risk estimates were inconsistent for ozone in all-year and warm-season analyses. Importantly, the variation in ozone-mortality risk estimates across the models examined suggests that the uniform statistical approaches used in multicity ozone-mortality and morbidity studies to adjust for temporal and weather covariates are not reliable.

The second concern is that due to the uncertainty related to stochastic variability in the underlying data combined with model selection uncertainty, the search for the strongest association at the lowest concentration will find the outliers in the data rather than real effects.

3. The Proposed Rule Overstates the Evidence from Epidemiology for the First Effects of Ozone Identified in Human Clinical studies

In contrast to the human clinical studies that, if replicated, can establish cause and effect, the observational (or epidemiological) studies are more difficult to interpret as discussed above. In this section, we discuss the observational studies of the health endpoints identified in clinical studies - pulmonary function decrements, symptoms, and inflammation – to evaluate what they reveal about the effects of ozone on public health.

a. The Lung Function Data Are Less Consistent Than Claimed in the Proposed Rule

Although there are many small positive associations of ozone with changes in lung function in the observational literature, the data are less consistent than indicated in the Proposed Rule. The Proposed Rule claims that observational studies have consistently linked short-term increases in ozone to lung function decrements in diverse populations and life-stages.[102] However, the ISA acknowledges that the recent data is mixed, noting:

> Recent epidemiologic studies focused more on children with asthma rather than groups with increased outdoor exposures or other healthy

[100] Koop G and Tole L. (2004) Measuring the Health Effects of Air Pollution: to What Extent Can We Really Say that People are Dying from Bad Air, *J. of Environmental Economic Management*, 47, 30-54.
[101] Sacks JD, Ito K, Wilson WE, Neas LM. (2012). Impact of covariate models on the assessment of the air pollution-mortality association in a single- and multipollutant context. *Am J Epidemiol*. 176(7):622-634.
[102] Proposed Rule, supra note 1, at page 75251.

> populations. Whereas recent studies contributed less consistent evidence, the cumulative body of evidence indicates decreases in lung function in association with increases in ambient O_3 concentration in children with asthma. Collectively, studies in adults with asthma and individuals without asthma found both O_3-associated decreases and increases in lung function.[103]

The first draft ISA noted that newer data on children attending camps, outdoor workers, and other healthy populations were limited, and across these studies, ambient O_3 exposure was associated with both decreases and increases in lung function.[104] The final ISA indicates only that "recent studies contributed less consistent evidence."

The results for asthmatic children, the group claimed to have the most consistent data, are illustrated in Figure 6-7 of the ISA, where there are few statistically significant changes in FEV1. In addition, the small changes in lung function that have been reported, to the extent they may be caused by ozone, are small -- acknowledged in the ISA as < 1 to 2 % for a 30 ppb increase in 8-hour ozone -- and not medically significant given the transient, reversible nature of ozone-mediated lung function changes

The ISA presents the results for ozone/lung function associations but neglects to point out that many of the studies evaluated other pollutants and report many similar associations for those pollutants in single pollutant models. For example, the O'Connor et al. (2008) study evaluated five pollutants including ozone in a group of 861 asthmatic children in seven U. S. inner-city communities. The authors report stronger and significant positive associations of lung function parameters with three other pollutants compared to ozone in single-pollutant models. For asthma symptoms and missed school days, other pollutants also had stronger associations than ozone. Thus, the ISA and the Proposed Rule give a misleading impression of the role of ozone in the air pollution mix with regard to lung function and other respiratory effects.

b. The Data on Inflammatory Markers and Respiratory Symptoms Is Inconsistent

The Proposed Rule indicates that a number of recent epidemiologic studies report ozone-associated increases in markers of pulmonary inflammation, particularly in children.[105] However, the full range of data is less consistent than the proposal claims. There was some evidence of associations of ozone with exhaled NO in Figure 6-11 of the ISA, but little consistency for other biomarkers. Even for the exhaled NO data, which is indicated as the strongest evidence of inflammatory effects in the ISA, the data are mixed, with a mix of positive, null, and negative results. In addition, a number of these studies were conducted in Los Angeles and Mexico City where the subjects are exposed to high concentrations of both ozone and many other pollutants and report positive associations with various pollutants.

The observational studies of ozone association with the presence of inflammatory markers or

[103] ISA, supra note 52, at p. 6-28.
[104] U.S. Environmental Protection Agency (2011). Integrated Science Assessment for Ozone and Related Photochemical Oxidants: First External Review Draft, U.S. Environmental Protection Agency, Washington, DC. EPA/600/R–10/076A.
[105] Proposed Rule, supra note 1, at page 75254.

respiratory symptoms suffer from limitations due to the presence of other pollutants and multiple comparisons. The ISA also notes that the clinical relevance of most biomarker changes is not clear. Regarding inflammatory markers, the ISA indicates "The limited available evidence in children and adults with increased outdoor exposures and older adults was inconclusive."[106]

A particularly important study is described in the ISA as a well-designed panel study, Ferdinands et al. (2008). In this study, 16 adolescent long-distance runners in Atlanta, GA, were followed before and after exercise for 10 days in August 2004. Effect estimates for lags 0, 1, and 2 indicated O_3-associated decreases in airway inflammation. This study is important because the subjects, setting, and exercise level are prime for seeing ozone-induced inflammatory increases based on the clinical studies. Another study by Chimenti et al. (2009) measured some biological changes in adult male runners before and after races. However, the authors concluded that since no relationship was observed between neutrophil counts and inflammatory mediators 20 h after races, airway inflammation at this time point appears blunted in healthy runners and little affected by exposure to mild seasonal changes and airborne pollutants. Thus, in the situations with the greatest likelihood of inflammatory changes caused by ozone, there is little evidence of effects.

The lack of consistent increases in subclinical inflammatory markers is important information for the Administrator's decisions. The lack of substantive effects in heavily exercising subjects suggests that there is even less likelihood of inflammatory changes due to ozone in the rest of the population as is goes about its daily activities. The findings in Adamkiewicz et al. (2004) of no inflammatory changes associated with ozone in elderly subjects including those with asthma and COPD confirm this view.

The evidence for respiratory symptoms associated with ozone in observational studies is mixed and inconsistent. For asthmatic children, the data appears somewhat consistent, but when one recognizes that similar data have been used by EPA to claim consistent effects on asthma from other pollutants, the reliance on single-pollutant studies is problematic. There are three multi-city studies that come to different conclusions with regard to individual pollutants. In fact, CASAC noted with respect to the second draft ISA:[107]

> Newer multi-city studies of symptoms in asthmatic children, which should arguably carry the most weight, are not convincing or show no association. The conclusions regarding respiratory symptoms and medication use in asthmatic children can therefore be questioned.

Thus, the characterization of ozone having consistent effects on asthmatics cannot be supported. For children without asthma, the ISA acknowledges that the data are inconsistent, noting:[108]

> Short-term increases in ambient O_3 concentration were not consistently

[106] ISA., supra note 52, at p. 6-94.
[107] CASAC Review of the EPA's Integrated Science Assessment for Ozone and Related Photochemical Oxidants (Second External Review Draft – September 2011), March 13, 2012 J. Samet letter to Administrator Jackson, EPA-CASAC-12-004, at page 16.
[108] ISA, supra note 52, at p. 6-121.

associated with increases in respiratory symptoms in groups comprising children with and without asthma.

A particular important study was carried out by the Health Effects Institute in the Los Angeles Basin, the area of the country with the highest ambient ozone concentrations. Groups of asthmatic, wheezy, and normal 10 to 12 year old children participated in a study to evaluate the acute respiratory effects of ozone in the Spring and Summer of 1994. The protocol involved use of daily activity and symptom diaries, heart rate recordings, personal ozone monitors, and spirometry several times per day. Avol et al. (1998)[109] reported no consistent symptom, medication use, or lung function changes associated with ozone. The authors ascribe the lack of respiratory effects to the fact that the children spent less time outdoors and less time exercising at the high levels of the chamber studies even though the 1-hour ambient ozone levels were as high as 200 ppb during the Summer.

Although there are some positive associations with all the clinically-identified effects of ozone, there are also negative associations and null findings in the literature. The Proposed Rule refers only to the positive single-pollutant associations, thereby giving a false impression of the overall data. The lack of consistent evidence implicating ozone as being associated with inflammation or respiratory symptoms in observational studies is an important finding that needs to be considered as the Administrator evaluates the biological plausibility of more serious potential effects such as hospital admissions and mortality.

C. Health Risk and Exposure Assessment Exaggerates Risk

1. The Proposal Overestimates the Real-World Risk of the Effects Identified in Clinical Studies

a. Overestimates in the "Exposures of Concern"

The HREA[110] uses probabilistic modeling of ozone exposures with the Air Pollutants Exposure (APEX) model to estimate the real-world risk of FEV1 decrements. The results are given in Table 2 of the Proposed Rule.[111] In addition, the HREA estimates exceedances of what are referred to as "exposures of concern" that are provided in Table 1 of the Proposed Rule.[112] An exposure of concern is a personal ozone exposure in the model at moderate or greater exercise. This calculation, however, is not directly a measure of risk of adverse effects or risk to public health. Although the benchmarks chosen -- 8-hour exposures of >60 ppb, >70 ppb and >80 ppb -- coincide with the concentrations used in the most recent clinical studies, the calculation does not include consideration of any physiological responses. In addition, the physiological responses from single exposures to such levels have not been considered adverse in prior reviews. The proposal acknowledges that the exposures of concern cannot be translated into estimates of the number of people experiencing specific health effects.[113] The Agency presents

[109] Avol EL, Navidi WC, Rappaport EB, Peters JM. (1998) Acute effects of ambient ozone on asthmatic, wheezy, and healthy children, Health Effects Institute Research Report 82, Boston, Massachusetts.
[110] HREA, supra note 10.
[111] Proposed Rule, supra note 1, at 75275.
[112] Ibid., at 75272-75273.
[113] Ibid., at 75273.

and discusses the exposure of concern data first since the distribution of personal exposures from APEX is an essential input into the lung function calculation in Table 2.

Because of the importance of exercise, the portions of the APEX model that simulate activity and ventilation rate need special scrutiny, particularly the extremes of the ventilation rate predictions. AIR has identified three ways in which APEX substantially overestimates the number of exposures with high ventilation rates in the population and thus overestimates the real-world risk of the effects identified in the clinical studies. The factors that lead to the overestimation of risk are acknowledged in the body of the HREA, but are ignored as the results from APEX are summarized and then used in the PA and the proposed rule. In all three cases, the Agency has been aware of the concerns, either acknowledges the concern or presents data to confirm the concern in the HREA, yet has chosen not to evaluate the sensitivity of the results to these factors.

First, the APEX model predicts more elevated ventilation rate occurrences than observed in real world data. In the previous review, Langstaff acknowledged that the "values produced by the ventilation rate algorithm may exhibit an excessive degree of variability."[114] An excessive degree of variability will produce an excessive number of extreme values of ventilation rate.

The 1997 EPA analysis had also over-estimated the number of high ventilation rates in the population by using an algorithm to assign ventilation rates based on individuals who exercised regularly and were motivated to reach a high ventilation rate. As a result, the 1996 Staff Paper acknowledged that the analysis allowed more high ventilation rates (hence greater risk) than would actually occur in the populations of interest - outdoor workers, outdoor children, etc.[115]

The final HREA includes a comparison of predicted ventilation rates with mean values in the literature, but the upper tails of the distribution which impact the risk estimates were not compared.[116] This was an important oversight because the upper percentiles of ventilation rate are responsible for the exposures that cause the perceived risk. In comments on the first draft HREA, AIR presented a comparison of the APEX modeled values with the measured ventilation rates from Brochu et al. (2006),[117] in which the model had a much higher standard deviation at all ages. This suggests that the upper percentiles of ventilation rates in the model are substantially above those measured by Brochu et al. in a database of over 30,000 person-days from a cohort of over 2,200 free-living individuals between the ages of 3 and 96.

Another comparison can provide further insight into this issue. A comparison of personal O_3 exposure measurements from Detroit with an APEX simulation reported in the HREA showed that the outdoor concentrations and time outdoors tracked well between the simulation and the observations, but that there were major differences in the mean daily ozone exposures and,

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[114] J. Langstaff Technical Memorandum, (2007) *Analysis of Uncertainty in Ozone Population Exposure Modeling*, at pp.42 (EPA-HQ-OAR-2005-0172-0174).

[115] U. S. Environmental Protection Agency, (1996) *Review of the National Ambient Air Quality Standards for Ozone: Assessment of the Scientific and Technical Information*, OAQPS Staff Paper, EPA-452/R-96-007, pp. 62-72.

[116] HREA, supra note 10, at 5-64.

[117] Brochu P, Ducre-Robitaille J, Brodeur J. (2006) Physiological daily inhalation rates for free-living individuals aged 2.6 months to 96 years based on doubly labeled water measurements: comparison with time-activity-ventilation and metabolic energy conversion estimates, *Int. J. Hum. Ecol. Risk. Asses*., 12, 736-761 (2006).

importantly, the maximum daily ozone exposures, as shown in Figure 5-18 from the HREA.[118] This comparison clearly shows the influence of the excessive variability in the APEX model.

A second way the counts of benchmark exposures are biased high relates to how EPA defines moderate or greater exercise over 8 hours. The HREA follows the approach begun in 1996 of defining Equivalent Ventilation Rates (EVR, L/min-m^2 body surface area) between 13 and 27 as moderate.[119] The counts in Chapter 5 thus accumulate exposures accompanied by 8-hour EVRs of 13 or greater. In Chapter 6, the risks are calculated for individuals with daily 8-hour average EVR greater than 13 using response functions developed from chamber study data conducted at a significantly higher EVR, ~ 20. In comments on the first draft HREA, AIR, Inc. presented data that showed the EPA algorithm predicts that the 95th percentile 8-hour EVR is between 14 and 15 while the EVR used in the clinical studies of 20 is about the 99th percentile.[120] AIR included figures showing the distribution of mean EVR, maximum 2-hour EVR and maximum 8-hour EVR for both asthmatics and non-asthmatics. AIR noted that APEX accumulates headcounts for subjects that are associated with 8-hour EVRs in the low 90s of percentiles while the EVR used in the clinical studies represents the 99th percentile. Thus, the resulting benchmark headcounts overestimate the number of subjects at potential risk and the FEV1 risks calculated with the E-R method are unreasonably high.

The HREA acknowledges the mis-match, noting:[121]

> Given that the EVR serves as a cut point for selecting persons performing at moderate or greater exertion and is a lower bound value (~5th percentile), the simulated number of persons achieving this level of exercise is possibly overestimated.

Figure 6-11 in the HREA, shows that the distribution of EVRs greater or equal to 13 for the Atlanta simulation

> …is clearly shifted much lower than the distribution of EVR in the clinical studies. This could lead to an overestimation of the percent of responders by the E-R method, since higher EVRs lead to higher lung function decrements and it is applying an E-R function based on EVRs around 20 to a population with median EVRs around 14.5.[122]

The binning of EVRs for use as moderate or greater exercise is a policy choice that EPA made first in 1996. It would be straightforward to evaluate the sensitivity to that choice in APEX and thereby evaluate the extent of bias before the Final Rule. Based on Figure 6-11, the impact of this one factor is much greater than the differences between the current and alternative standards considered by the Administrator.

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[118] HREA, supra note 10, at 5-58.
[119] Ibid., at 5-16.
[120] Johnson T, Background Information on EVR Sequence Statistics, September 25, 2007, Attachment 2 to Comments of the American Petroleum Institute on National Ambient Air Quality Standards for Ozone, Proposed Rule, October 9, 2007, Docket No. EPA-HQ-OAR-2005-0172-12158-1.1.
[121] HREA, supra note 10 at 5-79.
[122] Ibid., at 6-35.

The third way the counts of benchmark exposures are biased high relates to the fact that ozone exposure is lower at "breathing" height compared to "measurement" height (3-15 meters) as acknowledged in the 2006 Ozone Criteria Document. In addition to the height differential, ozone monitors are also placed in open areas removed from sources so as to capture the highest ozone concentrations expected in an area. Since downwind sites are usually the design value sites, they will dominate the upper tail of the ozone distribution and yet may not reflect the overall outdoor exposures in the vicinity of the site. If people spend time outdoors in closer proximity to streets or in areas with more surface area (buildings, etc.) to quench ozone, their exposures will be below that measured at the monitor. The 2007 Langstaff Memorandum acknowledged the issue of vertical variation in ozone but indicated that the Agency did not plan to address it due to a lack of data. This vertical difference was corrected in the vegetation risk assessment in the previous review but not in the human risk assessment. In the vegetation risk, the metric summing concentrations of 60 ppb and higher was halved with a 10 percent vertical correction.[123] By analogy, a vertical correction in the human risk assessment would likely halve the number of human exposures of concern at ground level. The HREA acknowledges:[124]

> Differences between ground-level (0-3 meters) and building rooftop sited (25 meters) monitor concentrations can be significant. Most importantly, use of higher elevation monitors would tend to overestimate ground-level exposures (i.e., persons outdoors).

Thus, there are major overestimations of the number of occurrences of elevated ozone exposures accompanied by exertion levels similar to those used in the clinical studies. Each of the three factors cause individually an overestimation of a factor of two or more.

b. Overestimates in the Lung Function Decrements

When the distribution of ozone exposures from APEX is used as input to the calculation of FEV1 decrements, one particular assumption that the Agency makes results in a significant overestimation of FEV1 decrements caused by ozone. As discussed below, the Agency assumes that there is no measurement error involved in the FEV1 lung function test.

The HREA reports the results of two approaches to estimate FEV1 decrement risk. The first uses probabilistic exposure-response (E-R) functions similar to the risk assessment in the prior review. These functions were applied to the APEX estimated population distribution of 8-hour maximum exposures for persons at or above moderate exertion ($\geq$ 13 L/min-m^2 body surface area) to estimate the number of persons expected to experience lung function decrements. The second approach, based on the McDonnell-Stewart-Smith (MSS) FEV1 model,[125] uses the time-series of O_3 exposure and corresponding ventilation rates for each APEX simulated individual to estimate their personal time-series of FEV1 reductions, selecting the daily maximum reduction for each person.

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[123] U.S. EPA (2007), Review of the National Ambient Air Quality Standards for Ozone: Policy Assessment of Scientific and Technical Information OAQPS Staff Paper, EPA-452/R-07-003, Jan. 2007, at pp. 7-46 and 7-47.
[124] HREA, supra note 10, at p.5-74.
[125] McDonnell W, Stewart P, Smith M, Kim C, and Schelegle E. (2012) Prediction of lung function response for populations exposed to a wide range of ozone conditions. *Inhal. Toxicol.,* 24(10), 619-633.

The MSS model predicts substantially more occurrences of various decrements, about a factor of three higher than the E-R approach. As shown in Figures 6-9 and 6-10 of the HREA, the MSS model predicts FEV1 ≥ 10 % decrements at exposures as low as 10 to 20 ppb and predicts substantial decrements below 60 ppb. Also as shown in Tables 6-9 and 6-10, almost half of the profiles with instances with FEV1 ≥ 10 % never experience 8-hour EVR ≥ 13. Table 2 in the proposal reports the decrements calculated using the MSS model, and the discussion of lung function effects in the proposal relies on the data in Table 2.

The question arises as to why the MSS model predicts FEV1 decrements at low ozone concentrations and mild exercise rates even though the model includes consideration of a threshold. First, McDonnell et al. acknowledge that the data from the individual lung function measurements are noisy. The model was developed from a dataset of 8477 lung function measurements during ozone exposure. There is also a dataset of 2948 measurements made during filtered air exposures. The fit of the individual model predictions versus the observations for the 8477 individual measurements during ozone exposure is shown in Figures 2a and 3a from McDonnell et al. 2012 and reproduced here as Figure 13. The noise in the individual response data is evident in these figures with the range of the data as the predictions approach zero being roughly between a 10% improvement in FEV1 to a 10% decrement. In fact, the HREA acknowledges that the model does not have good predictive ability for individuals, with r^2 = 0.28.[126] McDonnell et al. point out:

> All within-subject variability is currently lumped into a single term E as a result of limitations of the model fitting program. It is likely that some of the within-subject variability is due to true changes in responsiveness to ozone over time while much is simply noise.

Second, in contrast to McDonnell's acknowledgement that the lung function measurements are noisy, the Agency assumes that there is zero measurement error, noting:[127]

> The MSS model estimated intra-individual variability Var(ε) has two basic components: (1) the intra-individual variability of the true response to O_3 (both within-day and between-day) and (2) measurement error. These cannot be distinguished based on the available data. We are assuming that all of this variability is due to the true response, which will (absent other uncertainties) tend to overestimate the response to O_3…. The assumption of no measurement error in Var(ε) has the potential to significantly affect the risk results.

[126] HREA, supra note 10, at p. 6-39.
[127] Ibid., at 6-43.

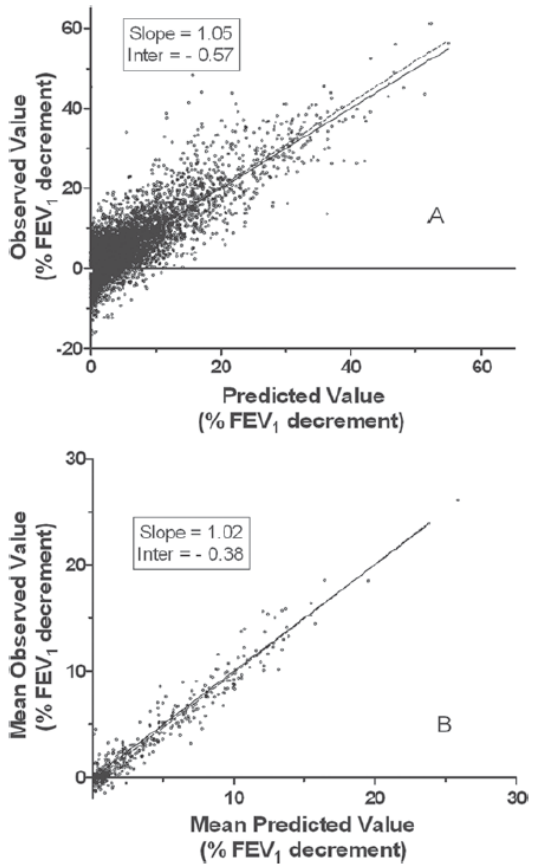

Figure 2. (A) Observed versus predicted individual FEV_1 decrements (n = 8477). (B) Mean observed versus mean predicted FEV_1 decrements. Means (across subjects) are calculated for each time point of each exposure condition of each study (n = 365 data points). Both figures use the empirical best linear unbiased predictor of U for each individual for calculation of predicted values. Solid line: identity; dashed line: regression.

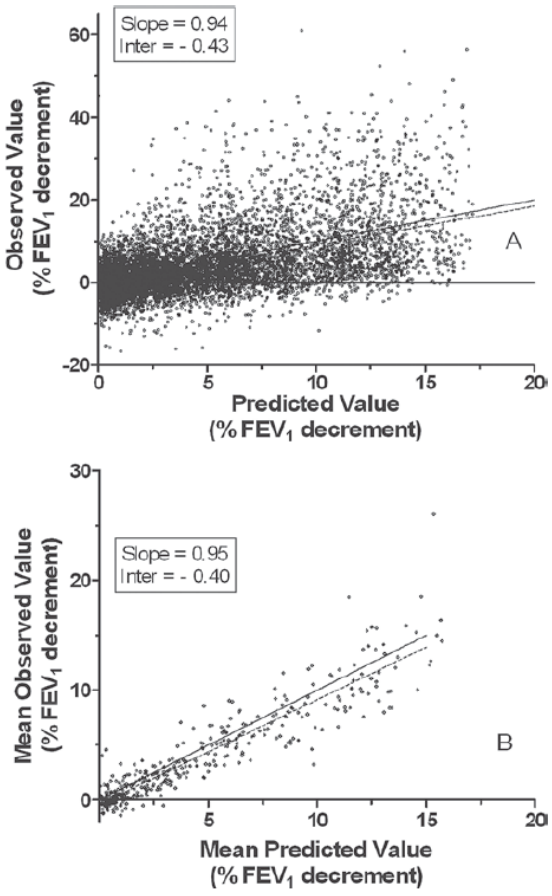

Figure 3. (A) Observed versus predicted individual FEV_1 decrements (n = 8477). (B) Mean observed versus mean predicted FEV_1 decrements. Means are calculated for each time point of each exposure condition of each study (n = 365). Both figures use the population mean of U for calculation of predicted values. Solid line: identity; dashed line: regression.

Figure 13: Figures 2 and 3 from McDonnell et al. 2012.

When the model is used to predict the portion of responses greater than 10, 15 or 20% there is substantial variability in the individual predictions as shown in Figure 4 from McDonnell and shown below as Figure 14. The substantial variability in the individual responses means that there will be predictions of both decrements and improvements in FEV1 in the model output. The largest decrements are counted in the EPA analysis so that it gives the appearance of potential risk at low exposures and ventilation rates when the group mean FEV1 changes are null or extremely small.

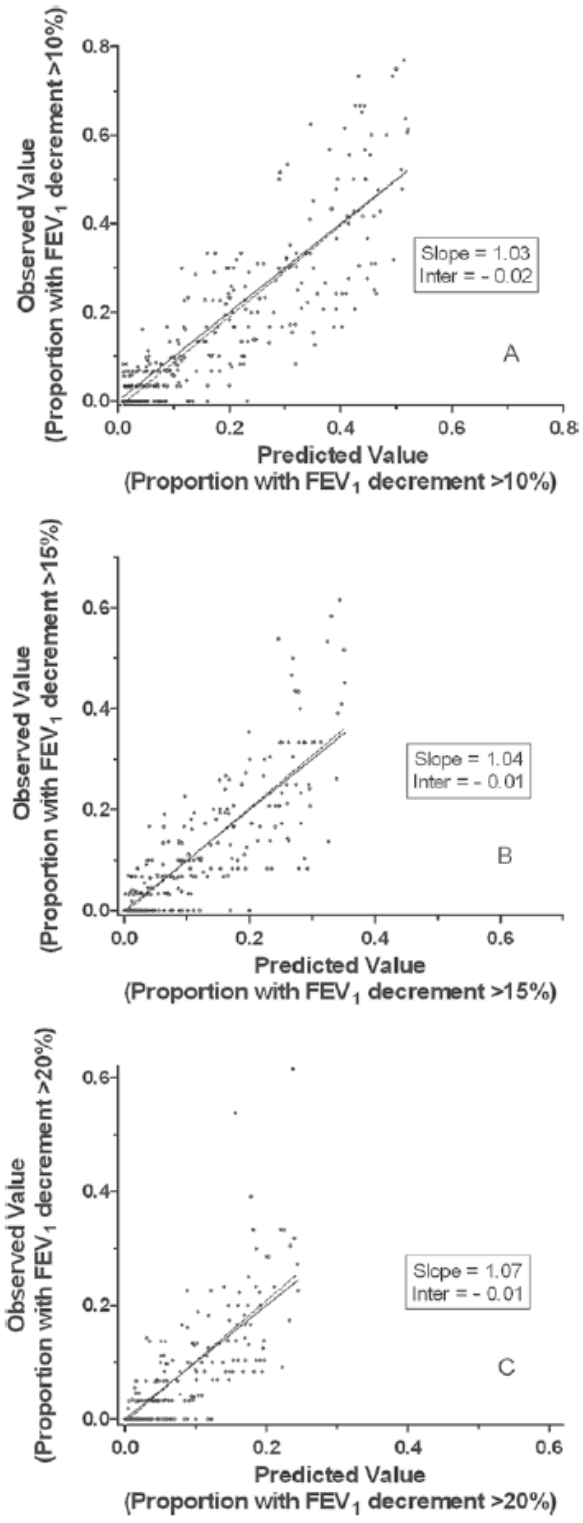

Figure 4. Observed versus predicted proportions of individuals experiencing an FEV_1 decrement greater than 10% (A), 15% (B), or 20% (C). Proportions are calculated for each time point of each exposure condition of each study (n = 365). Solid line: identity; dashed line: regression.

Figure 14: Figure 4 from McDonnell et al. 2012.

Thus, the FEV1 decrements in Table 2 of the proposal are overestimates due to the overestimation of elevated ozone exposures with exercise as well as the assumption of no measurement error in the lung function test.

c. Despite the Overestimations, the Output of EPA's Risk Assessment Shows that the Current Standard is Protective of Public Health

The way the output of the clinical risk assessment is presented and discussed in the proposal is misleading and not directly relevant to public health. The HREA notes that APEX provides two basic outputs (1) counts of people exposed one or more times to a given O_3 concentration while at a specified breathing rate, and (2) counts of person-occurrences which accumulate occurrences of specific exposure conditions over all people in the population groups of interest over an ozone season. The first of these metrics, counts of people exposed one or more times, is not as relevant to public health as the second metric, the distribution of person–occurrences over the entire group and ozone season. Single occurrences of small, transient FEV1 decrements have not been considered adverse during prior reviews, so being exposed only once a season is not particularly relevant to public health. On the other hand, the second metric can be quite informative of the portion of people and portion of time when there may be potential risk.

In order to put the results of the risk assessment into a public health perspective, the Final Rule should also evaluate the percent of person-days with various FEV1 decrements. Using the counts in Appendix 6B and the population and ozone season data in Table 5-1 of the HREA, AIR prepared Figure 15 which is similar to Figure 4-5 of the PA, except that it is the percent of school-age children person-days that is plotted.

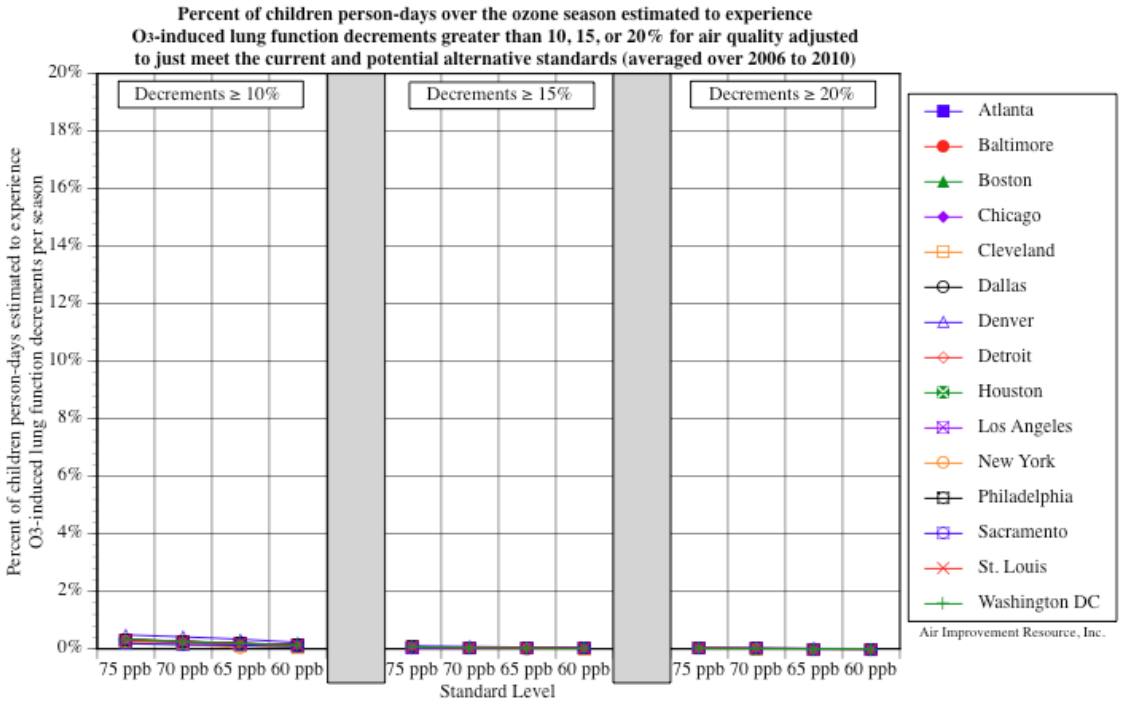

Figure 15: Percent of children experiencing decrements.

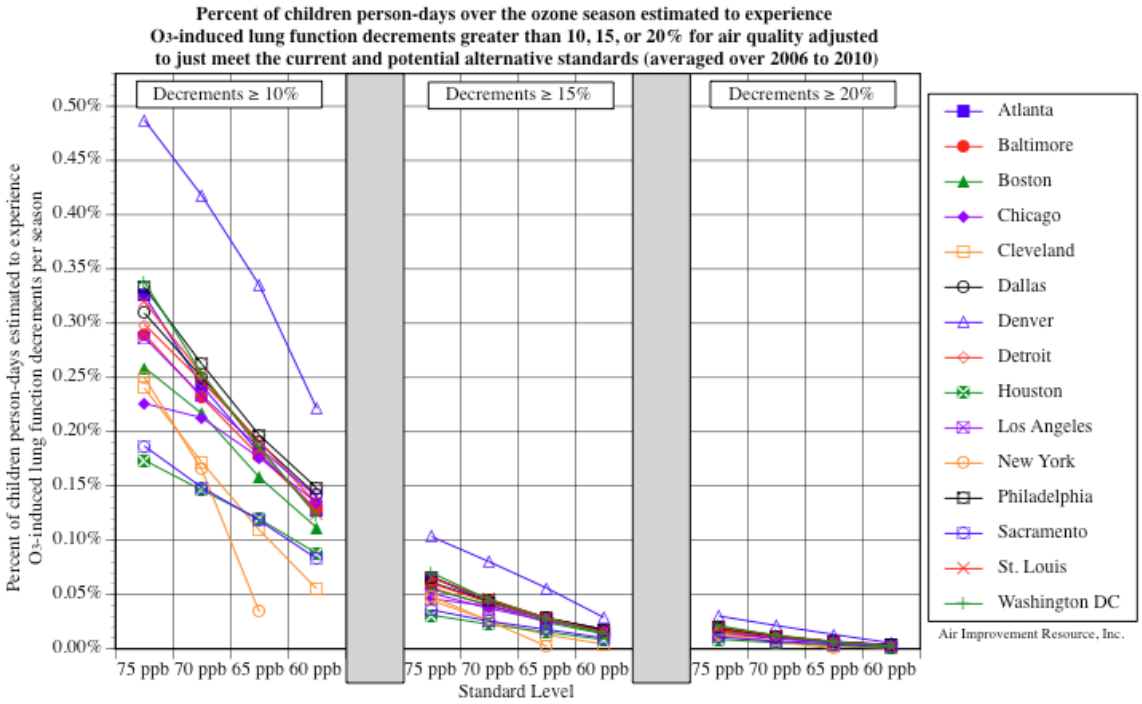

Figure 16: Same as 15 with an expanded scale.

Since the percent of person-days of occurrences is vanishingly small, the same data is presented in Figure 16 with the x-axis expanded. Clearly the current standard is extremely protective, with only a portion of a percent of the total exposures resulting in an exposure of any potential concern.

Since as discussed above the MSS FEV1 responses, which are displayed in Figures 15 and 16, were about three times as numerous as the E-R FEV1 responses. Due to the noise in the underlying FEV1 data, the MSS model predicts 10 % FEV1 decrements a small fraction of the time even at low ozone exposures and low levels of exercise. Therefore, 15 % decrements are a more appropriate endpoint to look at to overcome the noise in the underlying data from the MSS model.

Since both MSS and E-R FEV1 decrements are based on APEX exposure and ventilation rate estimates, both are also biased high because of the three factors discussed in Section V.C.1.a. Therefore, the estimates in Figures 15 and 16 should be considered an upper limit of the potential risks of FEV1 decrements for school-age children. The risks for young adults are even smaller and the risks for older adults are smaller yet. Even at the upper limit, the risk is minimal, and there is no real public health difference among the various alternatives under consideration.

Thus, based on the controlled exposure studies, the current standard is highly protective of public health. The proposal obfuscates this interpretation of the data by omitting any presentation or discussion of the percent of person-days metric and by arguing that the first mild, transient effects may be considered adverse since they, when repeated, may possibly lead to more serious effects.

However, the risk assessment evaluated multi-day exposure benchmark exceedances for air quality adjusted to just meet the existing standard, and noted that there were no people estimated to experience any multi-day exposures at or above 80 ppb for any study group in any study area, while only 0.27 % of school-age children were estimated on-average (across the 15 cities and 5 years of baseline ozone data) to experience two or more daily maximum 8-hr exposures at or above 70 ppb.[128] In addition, the number of children exposed and the number of person-days at or above the 70 ppb benchmark were very similar in value, indicating that on average the highest exposed individuals in the simulation experienced only a single day at or above the exposure of concern. Since an exposure of concern is not indicative of a health effect, isolated single-day exceedances of 70 ppb are not a threat to public health. Given that these estimates are biased high, the chances of multi-day exposures are even lower than the Agency calculates, providing additional support for the conclusion that the current standard protects the public health with an adequate margin of safety.

In addition, exposures at much higher concentrations in the many human clinical studies, including multi-day exposures and exposures that resulted in moderate or strong transient symptoms have proven to be remarkably safe for the subjects. Rom et al. (2013) point out that the human clinical studies for ozone that have involved thousands of exposures including exposures up to 600 ppb,

> …have been remarkably safe; even exposure of members of sensitive subgroups, including individuals with asthma and individuals with atherosclerosis, appears so far to have a most minimal risk of severe adverse effects requiring medical intervention.[129]

Thus, the current standard is highly protective against the first mild and transient effects of ozone identified in the human clinical studies.

2. The Proposal Overestimates the Risks Derived from Epidemiologic-Based (Observational) Studies

EPA made choices as to which associations to include in the core analyses, how to model the concentration-response functions, and how the analyses are presented in the HREA, PA, and proposed rule that dramatically overstate the magnitude and certainty of risks for mortality and morbidity due to ozone.

For example, the HREA uses selected results from the Smith et al. (2009) mortality analysis. However, the authors of that study concluded:

> …the heterogeneity and sensitivity of ozone effect estimates to a variety of covariates leaves open the issue of whether or not ozone is causally related to mortality. Consequently, the question arises whether any

[128] HREA, supra note 10, Table 5-12 and discussion at page 5-82.
[129] Rom WM, Boushey H, and Caplan A. (2013) Experimental Human Exposure to Air Pollutants Is Essential to Understand Adverse Health Effects. *American Journal of Respiratory Cell and Molecular Biology*, 49(5), 691-696.

particular ozone-mortality effect estimate can reliably be used to predict mortality reductions that would ensue from specific ozone reductions.

The authors also cautioned that it is possible that the appearance of an association at low ozone levels may be due to the effect of co-pollutants, or an artifact caused by differences between personal and ambient exposure.

The HREA estimated risk based on a mix of positive ozone associations from single-city studies and Bayes-adjusted city-specific effect estimates from selected multi-city studies. Even so, the total ozone-attributable mortality risk in most of the 12 cities evaluated upon attaining the current standard is not statistically significant and the change in risk from attaining a 70 ppb standard is small and non-significant in almost all the cities. For example, as evident in Table 7-7 of the HREA,[130] the counts for total ozone-attributable deaths at the current standard in 8 of 12 cities are not statistically significant for either the 2007 or 2009 base years. Similarly, the change is ozone-attributable deaths going from the current standard to a 70 ppb standard is not statistically significant in 8 of 12 cities using 2007 as the base year. When 2009 is used as the base year, the change in ozone-attributable deaths is small, positive, but not significant in 6 of the 12 cities, is zero in one city, and is actually negative, but non-significant in 2 cities, and significantly negative in 1 city. Thus, there is much uncertainty as to whether the there will be any mortality benefit from a 70 ppb standard.

If the unadjusted city-specific associations from any one of the multi-city studies were used, the risks would vary from positive to actually negative, covering a range that is biologically impossible. AIR previously demonstrated that model selection uncertainty is extremely large compared to the EPA estimates of risk and that there is a temporal and spatial pattern to the data that is not consistent with ozone causality. Since epidemiology studies cannot be used to identify a threshold because of exposure uncertainty, EPA's extrapolation of risk to low ozone concentrations is not justified.

By assuming ozone mortality extends down to zero ozone and by using selected ozone-mortality associations from the literature, the HREA calculates what appears to be a substantial burden of mortality even when man-made emissions are taken away. The proposal sums the total mortality risk from the 12 urban areas modeled and reported in Table 7-7 of the HREA and in Table 3 of the Proposed Rule.[131] The impact of reducing the level of the standard from 75 to 70 is only a small portion, a few percent, of the total risk. When compared to the total incidences of death in the 12 selected cities during their ozone seasons, as derived from Table 7A-1 of the HREA, the change in mortality with an alternative standard is very low, the order of 6 or 7 parts in 10,000. Due to the assumptions made in the analysis, the bulk of the risk comes from mid-range and lower ambient ozone concentrations that are not responsive to the massive precursor controls modeled by the Agency. Due to the NO_x inhibition effect, the massive emission reductions actually result in <u>increases</u> in mean ozone levels in some central cities. Thus, the potential changes in mortality are very small and uncertain. The changes in morbidity are also small and uncertain.

[130] HREA, supra note 10, at 7-53.
[131] Proposed Rule, supra note 1, at 75277.

The Proposed Rule discounts the results of the observational-based risk assessment, giving it less weight than the results for the human clinical-based risk assessment, noting:[132]

> Compared to the weight given to HREA estimates of exposures of concern and lung function risks, ….. the PA places relatively less weight on epidemiologic-based risk estimates. In doing so, the PA notes that the overall conclusions from the HREA likewise reflect less confidence in estimates of epidemiologic-based risks than in estimates of exposures and lung function risks. The determination to attach less weight to the epidemiologic-based estimates reflects the uncertainties associated with mortality and morbidity risk estimates, including the heterogeneity in effect estimates between epidemiologic study areas, the potential for epidemiologic-based exposure measurement error, and uncertainty in the interpretation of the shape of concentration-response functions at lower O_3 concentrations.

Because of the uncertainties acknowledged by the Agency and the additional uncertainties and problems with the observational studies as documented in Section V.B, the epidemiologic-based risk estimates are even more uncertain than acknowledged by the Agency and, hence, should be given little or no weight in the setting of the primary standard.

3. Summary of the Risk Assessment

Based on the risk assessment using the clinical studies, the current primary ozone standard is highly protective of public health. The risk assessment using even EPA's favored epidemiological associations and assumptions shows that the risk of mortality effects is small and highly uncertain. When the full range of associations in the literature are considered, along with the lack of biological plausibility for such serious effects below the level of the current standard, the epidemiological risk assessment should not be considered in setting the primary standard. Therefore, retention of the current standard should be considered as a health-protective alternative in the current review.

4. Beneficial Effects of Tropospheric Ozone Ignored

The Proposed Rule notes that EPA was directed to consider the potential beneficial health effects of ozone in shielding the public from the effects of solar ultraviolet (UV) radiation, as well as adverse health effects.[133] The Rule notes that EPA responded to the court's remand in 2003, deciding that any plausible changes in UV–B radiation exposures from changes in patterns of ground-level ozone were too uncertain to quantify and would likely be very small from a public health perspective.

In the current review, the ISA discusses this issue in Chapter 10, with the same result, concluding:[134]

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[132] Ibid., at 75276.
[133] Ibid., at 75239.
[134] ISA, supra note 52, at 10-32.

> EPA has found no published studies that adequately examine the incremental health or welfare effects (adverse or beneficial) attributable specifically to changes in UV-B exposure resulting from perturbations in tropospheric O_3 concentrations. While the effects are expected to be small, they cannot yet be critically assessed within reasonable uncertainty. Overall, the evidence **is inadequate to determine if a causal relationship exists between changes in tropospheric O_3 concentrations and effects on health and welfare related to UV-B shielding.**

In discussing this issue, the ISA notes that tropospheric ozone makes up a relatively small portion (~10%) of the total column of ozone over mid-latitudes, but it does play an important role in the overall radiation budget. In addition, the ISA notes that tropospheric ozone plays a disproportionate role in absorbing UV-B radiation compared with stratospheric ozone on a molecule per molecule basis.[135] The higher shielding effect per molecule for ozone in the troposphere results from the higher atmospheric pressure present in the troposphere, resulting in higher concentrations of gas molecules present that can absorb or scatter radiation.

While an increased exposure to UV radiation that would accompany reductions in tropospheric ozone to meet a revised air quality standard might have several possible effects, the main concern is for increased skin cancer incidences and deaths. The ISA notes that exposure to UV radiation is considered to be a major risk factor for all forms of skin cancer.[136]

Although the ISA indicates that EPA found no published studies that examined the effects of perturbations of ozone related to UV exposures, Chapter 10 does discuss a study by Madronich et al. (2011)[137] that used the CMAQ model to estimate the UV radiation response to changes in tropospheric ozone concentrations under different control scenarios, describing the study as follows:[138]

> This study focused on southeastern U.S. and accounted for spatial and temporal variation in tropospheric O_3 concentration reductions, an important consideration since most controls are focused on reducing O3 concentrations in populated urban areas. The contrasting control strategies considered in this study included a historical scenario designed to meet an 84 ppb 8-h daily max standard and a reduced scenario designed to bring areas predicted to exceed a similarly designed 70 ppb standard into attainment. A biologically effective irradiance was estimated by multiplying the modeled UV irradiance by a sensitivity function (action spectrum) for the induction of nonmelanoma skin cancer in mice corrected for human skin transmission, then integrating over UV wavelengths.
>
> The average relative change in skin cancer-weighted surface UV radiation

[135] Ibid., at 10-2.
[136] Ibid., at 10-26
[137] Madronich S, Wagner M, and Groth P. (2011) Influence of Tropospheric Ozone Control on Exposure to Ultraviolet Radiation at the Surface, *Environ. Sci. Technol*., 45, 6919-6923.
[138] ISA, supra note 52 at 10-29.

> between the two scenarios was 0.11 ± 0.03% over June, July and August. Weighting by population, this estimate increased to 0.19 ± 0.06%. Madronich et al. (2011) report that their estimated UV radiation increment is an order of magnitude less than that reported in an earlier study by Lutter and Wolz (1997) with the main reason for the discrepancy coming from the overly-simplified uniform 10 ppb reduction in O_3 concentrations assumed in the former study. Madronich et al. (2011) did not attempt to link their predicted increase in UV radiation to a predicted increase in skin cancer incidence, however, due to several remaining and substantial uncertainties.

The ISA goes on to indicate that:

> Quantitatively estimating human health and welfare effects directly attributed to changes in UV-B penetration resulting from changes in ground-level O_3 concentrations will require both (a) a solid understanding of the multiple factors that define the extent of exposure to UV-B, and (b) well-defined and quantifiable links between UV-B exposure and human disease and welfare effects.

Although Madronich et al. did not link their predicted increase in UV radiation to a predicted increase in skin cancer incidence, EPA has developed and applied models to link increases in UV radiation due to stratospheric ozone depletion to skin cancer incidences and mortality.

The Executive Summary of a 2006 EPA report indicates that the Agency uses its Atmospheric and Health Effects Framework (AHEF) to evaluate certain human health impacts associated with reduced emissions of ozone-depleting substances (ODS) under the Montreal Protocol and associated amendments, noting:[139]

> Specifically, the AHEF estimates the probable increases in skin cancer mortality and incidence in the United States that result from ODS emission scenarios.

The EPA report also indicates that the modular nature of the AHEF enables the model to be easily adapted to predict changes in skin cancer incidence and mortality resulting from almost any scenario involving a change in ozone concentrations. The results for various scenarios involving the Montreal Protocol and its amendments are given in Tables 7 and 8 for incidences of melanoma, basal cell, and squamous cell carcinoma, and deaths from melanoma. Such calculations have been used by the Agency in rulemakings for ozone-depleting substances and for a proposed fleet of supersonic aircraft.

Thus, when it comes to estimating the morbidity and mortality benefits of proposed rules, the Agency quantifies the benefits, but when it comes to UV-related dis-benefits from precursor

[139] U.S. Environmental Protection Agency, (2006) Human Health Benefits of Statospheric Ozone Protection Peer Reviewed Report, prepared for Global Programs Division, Office of Air and Radiation, April 24, 2006, at ES-1.

controls as in the current Proposed Rule, the Agency claims that there is too much uncertainty to make quantitative estimates. This is an unacceptable double standard.

A comparison of the substantial effort to estimate premature mortality from ozone in the HREA with the lack of even passing reference to potential increases in skin cancer morbidity and mortality from a revised standard demonstrates, again, a double standard. In both cases, the effects are small and uncertain. However, the UV-related skin cancer effects at current ozone column levels are acknowledged by the scientific community and EPA as real, while the assumption of ambient ozone causing mortality with no threshold is not biologically plausible. The uncertainty over whether a revised standard will have a net benefit or dis-benefit for morbidity and mortality is, therefore, an additional reason to heavily discount the observational studies in the final decision.

Appendix 1 -- APHENA O_3 Comments

The combined results of the large and comprehensive APHENA study are not consistent with ozone having a causal role in mortality or morbidity below the current standard.

In October, 2009, the Health Effects Institute (HEI) published the results of the *Air Pollution and Health: A European and North American Approach (APHENA)*[140] study. The APHENA project was designed to take advantage of the largest databases available. These had been developed by the three groups of investigators for earlier studies: 1) the *Air Pollution and Health: A European Approach* Phase 2 (APHEA2) study involving 32 cities; 2) the National Morbidity, Mortality, and Air Pollution Study (NMMAPS), conducted in the 90 largest U.S. cities; and 3) multicity research on the health effects of air pollution in 12 Canadian cities. Each database included air pollution monitoring data for particulate matter and ozone, health outcome data in the form of daily mortality for all ages, for persons younger than 75 years, and for persons 75 years or older (from all nonaccidental causes [all cause]), cardiovascular disease, or respiratory disease) and daily hospital admissions for persons 65 years or older (for cardiovascular and respiratory disease). Other database variables used for APHENA included weather data and a number of socioeconomic and other variables known or suspected to influence mortality or hospital admissions.

In the original studies, each of the three groups used different modeling methodologies and entered different variables into their models. Although each group found positive and significant relationships between PM_{10}/O_3 and mortality and some morbidity endpoints, the magnitude of the relationships differed by geographic region. One goal of APHENA was to use common methodologies and variables and reanalyze their data sets. They intended to create a central repository for all three of the time-series databases and use a common quality assurance approach. In addition, they would conduct analyses on a combined, pooled dataset to study a variety of sensitivity issues including effect modification. They would then investigate the sensitivity of the estimates to a variety of smoothing methods and to the number of degrees of freedom. They also intended to explore reasons for the geographical heterogeneity of the effect estimates seen in their original studies. Another important goal of the program was to understand the extent of coherence between mortality and hospitalizations using data from cities in North America and Europe.

In the original analyses, all three groups used a two-stage approach. In the first stage, risks were estimated for the individual cities, and in the second stage, evidence across the cities were combined. Each group used different methods to perform both stages in the original analyses. In APHENA, the investigators wanted to identify a preferred way to do both stages and apply common methodologies to the three data sets. For the first stage, they identified two smoothing techniques, natural splines (NS) and penalized splines (PS), and decided to use a number of

[140] Katsouyanni K. and Samet, J. (2009). Air Pollution and Health: A European and North American Approach (APHENA), HEI Report 142, October, 2009.

degrees of freedom choices. They chose to use 3, 8 and 12 degrees of freedom and also the number of degrees of freedom chosen by minimizing the partial autocorrelation function (PACF).

For the second stage analyses, the two approaches used in original NMMAPs and the European studies represented the two major approaches used at the time to pool estimates. NMMAPS used Bayesian hierarchical regressions models while the Europeans used metaregression models. However, they could not determine which was the best method, so they decided to use the models interchangeably.

Using the two smoothing techniques together with the four choices for the degrees of freedom and three choices of lags (0-1 day, 1 day and distributive lags which provided the cumulative effects of days 0 through 2) for each health outcome, the investigators ran a total of 24 different models for ozone. In addition, subsets of these choices were also used to examine the effects of controlling for PM_{10} and seasonal variations.

The results showed that the differences between the PS and the NS were very small in most cases and that the number of degrees of freedom tended to give similar results when greater than 6-8 degrees of freedom where used.

The overall modeling results for the mortality models and the morbidity models are summarized in Table 1 and 2, respectively. The denominator in the tables is the total number of different models that were run for each health effect outcome examined and the numerator is the number of models that resulted in a positive and statistically significant relationship between ozone and the health effect outcome. The way to interpret these tables is as follows. High ratios are suggestive of a robust and consistent relationship while low ratios are suggestive of no significant relationship. Intermediate values of the ratio suggest inconsistent and non-robust relationships that are dependent upon the model selected. Since there is no a priori way to determine the "correct" model, it is not possible to determine whether a small number (low ratio) significant and positive relationship represents real causal relationship or if they are false positives that can occur by chance or by confounding.

The all cause, all ages mortality results indicate a consistent relationship with ozone in Canada but somewhat less consistent relationships in Europe and the US. When the results for the two different age groups are examined, the interpretation of the results becomes even less clear. For $\geq$ 75 years of age, a consistent relationship still holds in Canada, but the European and US relationships become less consistent. When compared to the results for the < 75 years of age group, the results are implausible as they suggest that ozone is affecting the younger group more than the older group which goes against conventional wisdom. Controlling for PM makes the positive relationship for the older group disappear in all three locations, but the positive effect remains for the younger group except in the US where no relationship is evident. At all three locations a consistent summertime relationship is seen but vanishes in Europe and the US when PM is controlled. PM controlled model results were not presented for the Canadian data. In any event, the results are not consistent with the existence of a causal relationship between ozone and all cause mortality.

The cardiovascular mortality/ozone modeling results are somewhat confusing. A clear positive relationship was found only in Canada and only for the ≥ 75 years of age group. Few significantly positive relationships were found for either age group for the other locations and no relationship was found in Canada for the younger age group. When PM is controlled for, few significant relationships remain. The summer only results suggest significant relationships in Europe and the US, but they vanish when PM is controlled. Taken altogether, these results do not support a causal relationship between ozone and cardiovascular mortality when the models are controlled for PM.

The cardiovascular hospital admissions/ozone results are also confusing. The annual results show a few significant model-dependent relationships in Canada and the US but none in Europe. When PM is controlled for, a few significant, model-dependent relationships remain in Canada, disappear in the US, but become consistently significant in Europe. The European results defy logic and were dismissed by the APHENA authors as a strong positive relationship was evident for respiratory hospital admissions and PM_{10}. The summer only results at all three locations show no significant relationships. Thus the weight of evidence from these results is consistent with the mortality results and does not suggest a causal relationship between ozone and cardiovascular hospital admissions.

In contrast to the cardiovascular mortality results, the respiratory mortality modeling results consistently show no relationship with one exception. None of the annual results at any location show any significant relationship between ozone and respiratory mortality. However for the summer, consistent significant results are found but only in Canada. Significant model-dependent results are seen in Europe and the US, but they disappear when controlled for PM. PM controlled results for Canada were not presented. Nevertheless, the weight of evidence of all the ozone/respiratory mortality model results does not support a causal relationship.

The respiratory hospital admissions show consistent significant relationships with ozone in Canada that disappears when PM is controlled. In the US and Europe, a few significant, model-dependent relationships are seen that persist when PM is controlled. However, during the summer when ozone is the highest and the strongest relationships would be expected, no significant relationships are found in either the US or in Europe. Consequently, the weight of evidence does not support a causal relationship between ozone and respiratory hospital admissions.

In summary, the APHENA results do not support EPA's claims of causal relationships between ozone and mortality or between ozone and hospital admissions.

Cause of Death	Canada	Europe	United States
All Cause – all ages	24/24	15/24	12/24
≥ 75 yrs	23/24	2/24	6/24
< 75 yrs	18/24	22/24	10/24
All Cause PM controlled – all ages	4/8	8/16	0/16
≥ 75 yrs	0/8	3/16	0/16
< 75 yrs	5/8	14/16	0/16
All Cause – summer only	9/9	18/18 (4/12)*	18/18(0/12)*
Cardiovascular – ≥ 75 yrs	24/24	3/24	2/24
< 75 yrs	0/24	8/24	2/24
Cardiovascular –PM controlled ≥ 75yrs	0/8	0/16	0/16
< 75 yrs	0/8	5/16	2/16
Cardiovascular – summer only	0/6	8/12(0/8)*	11/12(0/8)*
Respiratory – all ages	0/24	0/24	0/24
≥ 75 yrs	0/24	0/24	0/24
Respiratory – PM controlled – all ages	0/8	0/16	0/16
≥ 75 yrs	0/8	0/16	0/16
Respiratory – summer only	6/6	4/12(0/8)*	2/12(0/8)*

*Denotes the PM controlled ratio

Table A1: APHENA modeling results for mortality. The numerators represent the number of models that showed a positive and statistically significant relationship between O_3 and mortality while the denominator is the total number of models run.

Type of Admission	Canada	Europe	United States
Respiratory	18/24	8/24	7/23
Respiratory – PM controlled	0/8	7/16	5/16
Respiratory – summer only	3/3	0/4	0/4
Cardiovascular	5/24	0/24	3/24
Cardiovascular – PM controlled	3/8	16/16	0/16
Cardiovascular – summer only	0/4	0/4	0/4

Table A2: APHENA modeling results for hospital admission for patients 65 years and older. The numerators represent the number of models that showed a positive and statistically significant relationship between O_3 and admissions while the denominator is the total number of models run