

Utah Physicians for a Healthy Environment (UPHE) is one of the largest civic organizations of healthcare professionals in the Western US, including about 450 physicians, some of whom are academics and researchers, but most of whom are clinicians, and 3,500 members of the lay public. We practice on the front lines of public health, 24/7, 365 days per year. Our patient care responsibilities provide us with a different perspective on pollution's health consequences from what EPA might get from other environmental groups or non-clinicians doing only research. We submit these comments for the purpose of demonstrating that EPA's proposed changes to the PM2.5 National Ambient Air Quality Standards (NAAQS) are inadequate to protect public health, do not reflect an overwhelming body of relevant science (most of which EPA already has at hand), and do not satisfy EPA's legal obligations to do both. We urge the EPA to adopt a 24-hour standard of 20µg/m<sup>3</sup> and an annual standard of 8 µg/m<sup>3</sup> for PM2.5.

## Executive Summary

### A. Introduction

B. Trends suggest air pollution will be an even larger health burden to the US population in the future.

1. The US population is aging.
2. The urban migration increases air pollution exposures.
3. The climate crisis is increasing multiple types of pollution.
4. Like previous research trends, future research is likely to show greater health impacts and show them with more accuracy.
5. Airborne plastic nanoparticles are adding to toxicity of particulate pollution (PM).
6. Incidence of cancer in young people is increasing. They will need more protection from PM.
7. PM increases morbidity and mortality from COVID, a disease likely to become endemic.
8. Life expectancy is dropping, and air pollution is connected to several contributing trends.

C. EPA's methodology is flawed.

1. The EPA standard for declaring causality is extreme.
2. Medical organizations have long called for stricter standards than the EPA eventually adopts; this proposal is an example of this disparity.
3. The form used to establish the 24-hour standard must be changed to 99<sup>th</sup> percentile.
4. The standard for nitric oxide and nitrogen dioxide (NO<sub>x</sub>, the nitrogen oxides most relevant for air pollution) has been virtually ignored; updating the PM2.5 standard will have ripple effect on NO<sub>x</sub>.

D. Clean Air Act (CAA) mandates that EPA establish stricter standards.

1. "Adequate margin of safety" is required, including for the public to engage in outdoor activities.

2. The EPA may not consider cost or feasibility.
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4. Setting standards is an expression of a value system, not just of science.

E. EPA Looks at the right science but draws the wrong conclusions.

1. Some EPA conclusions are wrong on their face and even defy common sense.
2. EPA methodology is arbitrary and eliminates too many valuable studies.
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  - g. EPA inappropriately discounts morbidity studies.
  - h. EPA gives inappropriate weight to controlled human exposure studies.
  - i. EPA is wrong to discount biochemical and histological studies and studies of subtle clinical outcomes.
  - j. The Clean Air Scientific Advisory Committee (CASAC) is correct that EPA is wrong to over emphasize the use of the “mean” in exposure studies.
  - k. CASAC is right in criticizing EPA for excluding areas impacted by wildfires and winter inversions.
3. We agree with CASAC that lowering the annual standard alone will leave many communities and subgroups without protection from short-term pollution hazards.
4. By relying on PM2.5 mass measurements, EPA is likely underestimating the toxicity of PM.
5. EPA’s standard for declaring causality is arbitrary and extreme.

F. A small fraction of the studies that compel stricter standards:

1. Supralinear dose/response relationship at low exposures.
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  - a. Mortality and long-term exposure.
  - b. Mortality and short-term exposure.
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  - b. Effect on heart electrophysiology.
  - c. Effect on blood pressure.
  - d. Association with pulmonary hypertension.
  - e. Association with heart failure (HF), morphologic changes, and blood clots.

4. PM2.5 and the brain and nervous system:
  - a. Interferes with brain development.
  - b. A significant contributor to stroke.
  - c. Impaired cognition.
  - d. Association with Parkinson's Disease.
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G. Economic considerations

1. The economic benefits of tightening the annual standard is overwhelmingly positive, nationally and in Utah  
Cost benefit analysis favors annual standard of 8 ug/m<sup>3</sup> over 9-10.
2. Economic benefits to the heavily populated areas of Utah

H. Conclusion

**A. INTRODUCTION**

On March 8, 2023, a worldwide news headline read, “Almost everyone in the world breathes unhealthy air.”<sup>215</sup> The report referenced a study published in *Lancet Planetary Health* that showed that virtually everyone across the globe is exposed to air pollution that exceeds the standards proposed by the World Health Organization (WHO).<sup>216</sup> The WHO states, “Air pollution is the greatest environmental threat to health and well-being at the global scale, and all populations are affected....”<sup>340</sup> It is from that general assessment that WHO makes recommendations for much stricter standards than EPA. In the three documents that form the scientific basis of EPA’s proposed changes, *2019 Integrated Science Assessment for Particulate Matter*, *2022 Supplement to the 2019 Integrated Science Assessment for Particulate Matter*, and *Preamble to the Integrated Science Assessments*, we see no scientific justification for EPA to adopt the standards they are proposing.

Although a wealth of science is available to guide EPA’s decision, in the end, setting the NAAQS is a discretionary act. The decision will be one of judgement and values, not technical analyses of the quality of the data. For the last 16 years, UPHE has kept very close track of the world’s air pollution and health research. When we see that time and again, EPA, under both Republican and Democratic administrations, makes standards that we and most other medical organizations believe to be too weak, standards that don’t adequately reflect the science that we are familiar with, we feel obligated to speak out.

Our interaction with patients and their families compels us to see this issue not on the abstract level of morbidity and mortality statistics and causality probabilities, but on the level of the human faces behind those numbers and equations. We interact personally with air pollution’s victims and their families. They experience real diseases, real economic losses and disability, loss of quality of life, real suffering, and sometimes irreversible tragedy and death from air pollution.

What are the risks and benefits of EPA’s options in establishing PM<sub>2.5</sub> NAAQS? EPA’s current proposal contradicts any reasonable risk/benefit analysis. If EPA sets NAAQS at 8 µg/m<sup>3</sup> annual and 20 µg/m<sup>3</sup> daily averages or lower, that would be unequivocally supported by current science, even if an argument can be made that the supportive science is still incomplete. If it turns out the science behind that decision was wrong or merely premature, and the end result was 330 million people breathed cleaner air than necessary or cleaner air than polluting industries were willing to acquiesce to in court, what is the societal cost? At the very most, a slim possibility of a reduction in some kinds of economic activity. However, EPA’s own cost analysis found that the benefits of pollution reductions afforded by EPA’s enforcing the Clean Air Act from 1990 to 2020 paid off at a rate of 30 to 1.<sup>1</sup> Is it logical that a slightly overzealous NAAQS PM<sub>2.5</sub> would have a reverse economic impact? The medical and economic literature certainly doesn’t support such a scenario.

From a public health standpoint, there is obviously no such thing as air that is too clean. There would also be a co-benefit of reducing CO<sub>2</sub> emissions, and we could ask another absurd rhetorical question, “Is there such a thing as too much climate protection?”

On the other hand, if EPA sets NAAQS that are too weak, it also risks economic consequences from increased healthcare costs, decreased worker productivity, and lost employment, but it obviously also risks quality of life, increased morbidity, shortened life expectancy, and directly increased mortality.

To be simpler and more direct, EPA failed to do its job in allowing 11 years and 17 years, respectively, to elapse since the annual and 24-hour PM2.5 NAAQS were last updated. As with justice, “public health protection delayed is public health protection denied.” When the EPA errs on the side of NAAQS that are too weak or delays updating them, public health consequences on a massive scale are the result. Tens of thousands of lives are shortened or lost, millions are victimized with life-altering morbidities, and virtually every US resident suffers to some degree, even if, for some, it is subclinical and not quantifiable. Even worse, establishing regulations that indisputably allow this as an end result codifies a cynicism and disrespect for human life into federal agency regulatory actions that tend to be perpetuated and normalized. Much of the world looks to EPA for guidance on environmental and public health protection, so the consequences of weak or delayed regulations reverberate throughout the world, affecting billions of lives.

## **B. TRENDS SUGGESTING AIR POLLUTION WILL BE A STEADILY LARGER HEALTH BURDEN IN THE FUTURE**

**B1. The US population is aging.** By 2050, the number of Americans over the age of 65 will double to nearly 90 million.<sup>4</sup> Overall, the US population five and ten years from now will be increasingly more vulnerable to the health consequences of air pollution from this demographic shift.

**B2. Urban migration increases air pollution exposures.** Globally, the world’s population is drifting toward urban centers. While this trend has slowed in the US, urban areas are still growing denser, and that means more people are exposed to more air pollution of all types. Among the fastest-growing US cities, growth from 2010 to 2020 ranged from 11% to 26%. As a result, other things being equal, the residents of these cities will all be experiencing higher concentrations of PM2.5 attributable to the urbanization trend.

**B3. The climate crisis is increasing multiple types of pollution.** In setting PM2.5 NAAQS, **EPA must consider the contribution of the climate crisis to future pollution exposure.** Global temperatures will undoubtedly continue to increase, and heat waves will have a dual enhancing effect on pollution and health. Warmer atmospheric temperatures will increase ground-level ozone globally. In Utah, for example, rural communities are experiencing ozone as high as Los Angeles, but many contributors to that problem are beyond the reach of state or federal regulations. Ozone’s health hazards largely overlap with those from PM2.5. Higher temperatures and drought in the US, especially in the Western US, are leading to increased pollution from wildfires, including PM2.5. Numerous studies have found that the consequences

of PM are enhanced in a setting of higher temperatures. A study of populations in Japan, Korea, and Taiwan found a synergistic effect between high temperature and air pollution on mortality, using a multicity time-series analysis.<sup>299</sup> A meta-analysis of 56 studies found moderate quality evidence for a synergistic adverse effect of high temperatures and air pollution.<sup>134</sup> In a study of over 2 million adults in New England, increasing temperature extremes and temperature variability had a synergistic effect with short-term PM<sub>2.5</sub> on hospital admissions.<sup>289</sup>

EPA should also factor into its decision that control of PM<sub>2.5</sub> will derive the co-benefit of reducing atmospheric greenhouse gas emissions, contributing to mitigation of the climate crisis. It will also produce the co-benefit of reduction of other criteria pollutants, such as NO<sub>x</sub> and carbon monoxide (CO), and other hazardous air pollutants such as polycyclic aromatic hydrocarbons (PAHs) and heavy metals. There is evidence that synergism exists in the adverse health effects precipitated among criteria pollutants. Reducing PM<sub>2.5</sub> will help address those possible synergistic effects.<sup>136</sup>

As temperatures and atmospheric carbon dioxide rise, both will contribute to increased air pollution from natural sources like plants and dust. On their own, biogenic volatile organic compounds (BVOCs) are benign. However, once they react with oxygen, they produce toxic organic aerosols. The organic aerosols and dust will increase PM<sub>2.5</sub>. A recent study found that an increase in global temperatures of 2° C will increase BVOCs and global dust (largely from the Sahara Desert) about 7%.<sup>236</sup>

**B4. Like previous research trends, future research is most likely to show greater health impacts and with more accuracy.** The history of pollution/health research has steadily moved in only one direction. **The more research advances, the stronger the association with death and the broader its association with disease.** The overwhelming likelihood is that research five or ten years from now will show that the standards that EPA is proposing are inadequate. Yet EPA's approach is almost purely reactive, insisting on an unrealistic standard of biological proof of harm before taking action. Proactive anticipation of that research trend's continuing should provide more impetus for a stricter standard. Not only does research continuously move in the direction of finding ever-greater harm from air pollution, but the research steadily becomes more accurate, especially regarding estimating concentrations of exposure. Populations in newer studies are more than ten times larger than those in studies used for previous reviews.<sup>2</sup>

**B5. Airborne plastic nanoparticles are adding to toxicity of particulate pollution.** When criteria pollutants became part of EPA's regulatory mandate, airborne plastic nanoparticles were not a recognized part of the toxic potential of air pollution. Now, however, we know that **plastic fragments of 5 microns in size and smaller are a ubiquitous component of global air, water, and soil pollution and are an increasing source of human health hazards.**<sup>141</sup> Exposure is possible through inhalation, ingestion, and dermal absorption. Thousands of different chemicals are used in manufacturing different plastics and are attached to these plastic fragments. Furthermore, they absorb other toxins, like PAHs and heavy metals, once released into the environment,<sup>142</sup> and can serve as a vector for microbial pathogens.<sup>143</sup>

Plastic nanofibers are resistant to biodegradation much like asbestos is, and can be deposited in terminal bronchioles, alveolar ducts, and alveoli, resulting in chronic inflammation, granulomas, or fibrosis. They are now detected in human stool, blood,<sup>144</sup> and many human organs.<sup>145</sup> The toxic potential of airborne microplastics is beyond the scope of our comments, but their presence is reason enough to engage in mitigation of the problem. EPA should consider that PM2.5 control will also help control human contamination by airborne plastic nanoparticles, a problem that is likely to accelerate, given the rate of global plastic use and production.

**B6. The incidence of cancers in people under 50 years old**—breast, colorectum, endometrium, esophagus, extrahepatic bile duct, gallbladder, head and neck, kidney, liver, bone marrow, pancreas, prostate, stomach, and thyroid—**has increased dramatically in multiple countries.**<sup>5</sup> Air pollution has been implicated in multiple cancers (to be addressed later in our comments), but it has also been implicated in decreased survival rates from cancer in general.<sup>6</sup> Stricter PM2.5 NAAQS would help tens of thousands of these young cancer victims survive.

**B7. Air pollution, PM2.5 in particular, has been shown numerous times to contribute to increased rates of hospitalization and death from COVID.**<sup>7,8,9</sup> A Harvard Chan study found an 11% increase in mortality with each 1 µg g/m<sup>3</sup> increase in long-term PM2.5 exposure.<sup>10</sup> The chances are high that COVID will become endemic to the United States, and other pandemics are likely to emerge, but stricter PM2.5 standards will save the lives of some who contract COVID. One new study has found that even in a setting of low pollution, median annual PM2.5 of 6.39 µg/m<sup>3</sup>, the risk of developing long COVID is increased with small increases in long-term PM2.5. For a PM2.5 increase of just 0.65 µg/m<sup>3</sup>, the odds of long COVID increased about 30%.<sup>371</sup>

**B8. Air pollution is among the reasons that life expectancy in America has been dropping,** down almost three years since 2025.<sup>3</sup> Many countries that are poorer than the United States now have higher life expectancies. American life expectancy is now nine years lower than Japan's. While COVID, vaccine misinformation, drug overdoses, and gun violence are contributing to the majority of that decline, increasing cardiovascular disease, metabolic disorders like obesity and diabetes—all morbidities significantly connected to air pollution—are as well. Even violence and crime have a connection to air pollution. For many Americans, a poor healthcare system contributes to this disturbing trend, and unfortunately, will likely continue to do so, given the current political climate and lack of political will to improve or expand it. In this setting, air pollution has an even larger impact.

### **C. EPA'S METHODOLOGY IS FLAWED**

**C1. The EPA standard for declaring causality is extreme.** Time and again, EPA's scientific reviews are characterized by being overly cautious in drawing conclusions that would force enhanced regulatory action. While we cannot expect that setting the NAAQS is an exercise in exact science, it is obvious that EPA often functions more as a political agency than as a public health agency. This was particularly true during the Trump Administration when, flying in the

face of overwhelming evidence, the NAAQS were not strengthened. Notably, it was during that time that CASAC was dismantled and reassembled with political appointees rather than public health and research experts.

EPA's methodology for establishing causality (and presumably, therefore, proof of benefit from intervention) is arduous, excessive, and incompatible with providing best available healthcare and public health protection. It is likely that EPA adopts this methodology as a precaution for the eventuality of being sued by polluting industries. But that will happen regardless of the standards adopted, and if those standards are no stronger than those proposed, health groups will almost certainly sue as well. In establishing NAAQS, EPA should function with the same focus on the best available information that physicians have to use.

**C2. EPA has a long history of repeatedly setting standards that the vast majority of the medical specialty societies and other health organizations believe are inadequate to protect public health.** At virtually every opportunity for engagement, the American Lung Association, American Thoracic Society, and the California Air Resources Board have called on EPA for stricter NAAQS than what EPA eventually adopts. This year, the following organizations have called for NAAQS stronger than what the EPA has proposed: Allergy & Asthma Network, Alliance of Nurses for Healthy Environments, American Academy of Pediatrics, American Lung Association, American Psychological Association, American Public Health Association, Asthma and Allergy Foundation of America, Children's Environmental Health Network, Health Care Without Harm, Medical Society Consortium on Climate and Health, Medical Students for a Sustainable Future, National Association of Pediatric Nurse Practitioners, National League for Nursing, Physicians for Social Responsibility, and Public Health Institute. That alone is strong evidence that EPA's proposal is inadequate. UPHE joins these and other groups in that assessment for this proposal. The World Health Organization's recommendation of a 24-hour standard of 15 and an annual standard of 5 may be unachievable, but it is thoroughly scientifically defensible.<sup>13</sup>

**C3. We also join these other groups in calling for EPA to revise the form of the short-term standard to the 99th percentile to effectively capture acute, short-term exposures.** The current form at the 98th percentile dates to 1997 and allows nearly 22 days in the 3-year review period to exceed the standard limit, in addition to days exempted for exceptional events, such wildfires.

**C4. It should be noted that the annual standards for nitrogen oxides and carbon monoxide have not been updated since their inception in 1971, over 52 years ago.** An arguably far-too-weak, one-hour daily standard for NO<sub>x</sub> was only added in 2010, and the last time the CO was even reviewed was in 1994. This is a profound failure on EPA's part. Because both the sources and health hazards of these other toxins greatly overlap with PM<sub>2.5</sub>, by selecting stricter standards for PM<sub>2.5</sub>, EPA also has a chance to add the co-benefit of simultaneously reducing nationwide NO<sub>x</sub> and CO to a more appropriate level.



## D. THE CAA MANDATES THAT EPA ESTABLISH STRICTER STANDARDS

D1. Under Section 109 of the Clean Air Act, **the primary NAAQS must be set at a level requisite to protect the public health with an adequate margin of safety** in order to prevent not just known, but even reasonably anticipated health-related effects from air pollution. It further mandates that EPA set the NAAQS at a level that allows the public to spend time outdoors engaged in their normal activities and that air will be clean enough to “protect the public’s health with an adequate margin of safety” during those outdoor activities.

This mandate “carries the promise that ambient air in all parts of the country shall have no adverse effects upon any American’s health.” 116 Cong. Rec. 81 (Dec. 18, 1970, remarks of Senator Muskie, floor manager of the conference agreement). Indeed, EPA has previously recognized this to be the case:

“Standards must be based on a judgment of a safe air quality level and not on an estimate of how many persons will intersect given concentration levels. EPA interprets the Clean Air Act as providing citizens the opportunity to pursue their normal activities in a healthy environment.”

44 Fed. Reg. at 8,210

D2. The CAA sets significant limits on the discretion granted to EPA in selecting a level for the NAAQS. **The EPA must err on the side of protecting public health and may not consider cost or feasibility** in connection with establishing the NAAQS. The D.C. Circuit summed up EPA’s mandate two decades ago in a suit by the American Lung Association:

D3. “Based on these comprehensive [air quality] criteria and taking account of the ‘preventative’ and ‘precautionary’ nature of the act, **the Administrator must then decide what margin of safety will protect the public health from the pollutant’s adverse effects – not just known adverse effects, but those of scientific uncertainty or that research has not yet uncovered.**” Then, and without reference to cost or technological feasibility, the Administrator must promulgate national standards that limit emissions sufficiently to establish that margin of safety.”

Am. Lung Ass’n v. EPA, 134 F.3d 388, 389

The CAA expressly requires EPA to consider the advice of the “statutorily-created” CASAC and rationally explain any important departure from their recommendations.

The precautionary and preventative nature of the NAAQS requires EPA to set standards that protect against health consequences that may go beyond those impacts that their analysis finds causally established by science. As the D.C. Circuit noted in another case, limited data cannot be an excuse for failing to establish the level at which there is an absence of adverse effect. To the contrary:

“Congress’ directive to the Administrator to allow an ‘adequate margin of safety’ alone plainly refutes any suggestion that the Administrator is only authorized to set primary air quality standards which are designed to protect against health effects that are known to be clearly harmful.”

EPA is legally bound to prioritize public health protection, not economic activity, industrial profit making, or societal convenience. It could be reasonably argued that given the strong evidence that there is no safe level of particulate pollution, having a standard at all actually backfires. Often, the standard is used to defend industry and proposed polluting projects and public policy with modeling that shows a certain standard will not be exceeded. The rationale of setting a standard (which is inadequate) is to ensure that by meeting this standard, public health will be protected. Meeting an inadequate standard does not promote safety.

D4. Given that a pollution standard will never fully protect public health, what is “adequate” protection must be used instead. **EPA standards then are not scientific expressions that establish thresholds differentiating between health and illness, but value system expressions,** i.e., how much pollution can a society accept to maintain the normal activities of modern civilization? To that extent, EPA standards must reflect what is reasonably possible to achieve, not what is easy, convenient, or inexpensive to achieve.

## **E. EPA LOOKS AT THE RIGHT SCIENCE BUT DRAWS THE WRONG CONCLUSIONS**

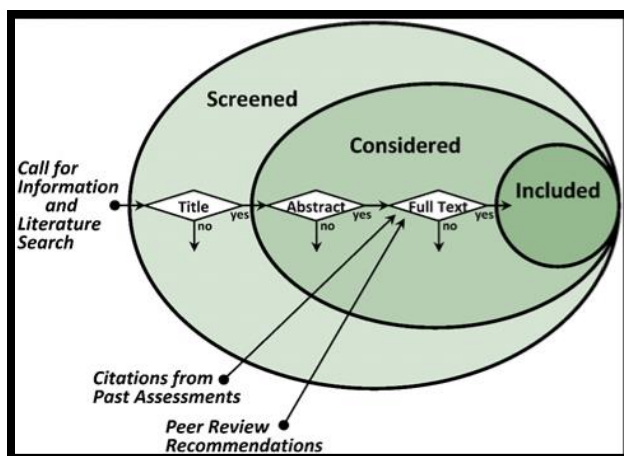
**E1. Some EPA conclusions are wrong and even defy common sense.** In the EPA’s trio of documents presumably used as the basis for their PM2.5 NAAQS proposal, the *2019 Integrated Science Assessment for Particulate Matter*, the *2022 Supplement to the 2019 Integrated Science Assessment for Particulate Matter*, and the *Preamble to the Integrated Science Assessments*, **we see a recurring pattern of referring to many of the appropriate scientific studies, yet being overly cautious in drawing conclusions from that science that should be driving regulatory action.**<sup>16</sup>

We find it ironic that EPA managed to compile over 2,300 pages in these companion documents that are highly detailed, with many hundreds of studies referenced, most of which we are familiar with, and still found a way to draw the wrong conclusions.

Some of the assertions in these documents are stunning to healthcare professionals. For example, on page 1-1 of the *2019 Integrated Science Assessment for Particulate Matter* it states, “Inadequate evidence exists to determine whether having diabetes, being in an older life stage (i.e., older adults), residential location (including proximity to source and urban residence), sex, or diet increase the risk of PM2.5-related health effects.” Every part of that statement contradicts the vast majority of relevant studies and the experience of virtually every front-line clinician.

Many of the recent, large, air-pollution epidemiologic studies are specific to the elderly, i.e., those on Medicare. For example, one study looked at the entire Medicare-eligible population of seven states and found that mortality increased 2.1% for each 1 $\mu\text{g}/\text{m}^3$  increase in PM<sub>2.5</sub>. The risk decreased with age. It also found increased risk for those that lived in lower-income zip codes, higher urban density, or had any of several chronic diseases or previous hospitalizations.<sup>47</sup> EPA's statement above also ignores the growing evidence that increased risk of diabetes itself is associated with air pollution.

**E2. EPA methodology is arbitrary and eliminates too many valuable studies.** Figure 3 in the *Preamble to the Integrated Science Assessments* offers a good example of EPA's flawed methodology.



What the figure above implies is that EPA sifts through the volume of relevant literature, and through a process of elimination, presumably by quality, narrows down the research they will consider to only small number of studies to draw the conclusions used to establish the NAAQS. But weight of evidence is related to both quality and quantity of the research. If EPA starts out with 100 studies and grades 60 of them C, 30 of them B, and 10 of them A, and ultimately only allows the A studies to be considered, then it is completely eliminating a great deal of available, important evidence. While quality of research is important and should be given a premium in consideration, quantity of research is also important, especially if the conclusions are in line with those considered of highest quality. To just eliminate the vast majority of “slightly lower quality” serves only to justify weaker standards.

The result of EPA's overly cautious approach to study inclusion and data/design scrutiny provides a veneer of scientific rationale for EPA to routinely offer only tepid public health protection.

E2(a). In a similar vein, **we are disturbed by EPA's apparent policy to downplay or even dismiss epidemiologic research that originates outside of North America.** The *Supplement to the 2019 Integrated Science Assessment for Particulate Matter* states, “studies examining

associations outside the U.S. or Canada reflect air quality and exposure patterns that may be less typical of the U.S., and thus less likely to be informative for purposes of reviewing the NAAQS. Therefore, within this Supplement the studies considered for inclusion are limited to those studies conducted in the U.S. and Canada.” We consider that policy and the rationale behind it scientifically inexplicable and indefensible.

The unwritten but implied EPA assumption is that pollution from other countries is often higher than in the US, sometimes significantly so, and that those studies, therefore, have no value in establishing EPA standards. While North American air pollution may have components and overall chemical composition slightly different than exists in other countries, to our knowledge there is no literature to support a contention that the toxic profile of foreign pollution is so different from domestic pollution that we can justify wholesale dismissal of research that examines foreign populations and foreign atmospheric-pollution data. The supralinear dose response relationship (more about that later) that has been repeatedly established in both the US and foreign-based research is more reason to consider studies of concentrations higher than are common in the US because they provide more data points on those same dose response curves.

Furthermore, this policy is inconsistent with other EPA policies. EPA states, “multicity studies can provide insight on potential confounding through the use of a consistent method to analyze data from across locations with different concentrations of copollutants and other covariates.” If “multicity” studies can provide insight, “multi-country” studies should be able to provide the same strength and quality of data benefit.

**No other branches or specialties of medical care, diagnosis, and treatment would discard large bodies of well-done research merely because it was done in other countries on foreign populations.** Indeed, nearly all drug makers routinely conduct early-stage drug trials outside the US because it is often less expensive. In fact, “a STAT analysis found that 90 percent of new drugs approved this year were tested at least in part outside the U.S. and Canada.”<sup>14</sup>

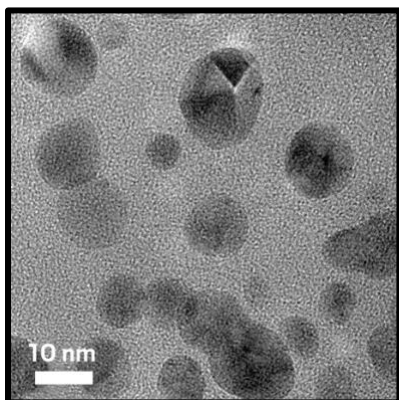
We do not see that kind of American exclusivity being applied to scientific research in non-medical disciplines. For EPA to limit what they regard as relevant or qualifying research to what is generated from North America seems like an ironic, hypocritical, unscientific excuse to restrict available scientific evidence.

E2(b). In many places, EPA states that it prioritizes studies that analyze conditions “at or near conditions relevant to ambient exposures.” But doctors part of Utah Physicians for a Healthy Environment practice medicine in a geographic area characterized by severe spikes in PM2.5 that are not typical of “ambient exposures” in many other places of the country. Those spikes sometimes represent the some of the highest PM2.5 levels in the world. What is relevant “ambient exposure” in New York is not more relevant to Utah than ambient exposure in Beijing would be. **EPA should not be limiting the research it “considers” to what is typical of ambient exposures for most of the US.** Indeed, it is those areas that may be exposure outliers that need

the most protection, given that the largest source of PM2.5 in some Western states is now wildfire PM2.5, with exposure delivered in short-term spikes.

**E2(c). Over emphasizing copollutant confounding is counterproductive to protecting public health.** EPA makes repeated reference to the importance of eliminating confounders and attributes much of the uncertainty in many studies that could be used to infer “causality” to the presence of “copollutant confounding.” While that concern is valid to a certain extent, that emphasis can be overwrought. For example, attributing health outcomes to one type of pollution, like PM2.5, when the atmosphere is also contaminated with other types of pollution, like NOx, may weaken the quality of the study because NOx would be considered a confounder. But both the sources and physiologic effects of the different pollutants significantly overlap. Furthermore, in most cases, regulatory control of sources of one type of pollution also provides control of other pollution components. If the goal is actually to protect public health, then this kind of obsessive differentiation does not serve that goal, but instead, is being used as an excuse to discount numerous valuable studies.

**E2(d). EPA demonstrates little consideration of the growing number of autopsy and tissue studies that have proven beyond any reasonable doubt that particulate pollution nanoparticles now contaminate virtually all human critical organs.** The first of these studies found high-temperature-combustion nanoparticles (magnetites), at the rate of millions per gram of tissue, in the brains of every human examined from two different cities, including the brains of children.<sup>137</sup>



This electron microscopy image shows magnetite particles extracted from a human brain sample.

That should be considered prima fascia evidence of unmitigated biological harm. In fact, EPA’s own review gives a detailed physiologic and biochemically plausible explanation of mechanisms of harm from this nanoparticle contamination of human organs, but ultimately downplays its significance and the significance of all the other epidemiologic and laboratory studies on brain function, labeling PM2.5 only “likely to be causal” in neurotoxicity (more about that below). The review even makes the case that 10% of particles landing on nasal mucosa would “translocate

to the olfactory bulb,” and that is only a “small fraction,” of those landing on the nasal mucosa, again downplaying its significance.

Subsequent studies have found even greater particulate pollution contamination of human heart tissue,<sup>138</sup> knee joints,<sup>350</sup> the placenta, including the fetal side of the placenta,<sup>139</sup> and black carbon nanoparticles in the lungs, livers, and brains of unborn, otherwise normally progressing fetuses.<sup>140</sup> The large surface area-to-volume ratio of the smallest PM allows them to be often saturated with other toxins like heavy metals, PAHs, and pathogens, allowing the PM to act as a Trojan horse carrying other co-pollutants into the body. Moreover, the attached co-pollutants may alter the surface of particles, increasing their reactivity and enhancing their intracellular bioaccessibility.<sup>351</sup> This information should be treated as clear justification for the tightest PM2.5 regulations possible, i.e., as a regulatory five-alarm fire, yet it doesn't seem to factor into EPA decision making.

**E2(e). EPA is inconsistent in their consideration of heterogeneity of studies.** There are likely slightly different toxic profiles of PM2.5 from one region in the US to another, from one state to another, from one county to another, even from one neighborhood to the next. Yet, in establishing regulatory thresholds, EPA does not make customized standards for each of these jurisdictions. We know full well there are different toxic profiles of PM2.5 depending on the source. Yet in state implementation plans, EPA allows state agencies to equate all types of PM2.5 as interchangeable in pursuing regulatory compliance.

Moreover, EPA explicitly recognizes there is significant heterogeneity in susceptibility among the US population. Therefore, there is also heterogeneity in causality. A criteria pollutant may be “causal” for heart disease in person A, but it may not be in person B. Nonetheless, EPA has an obligation to protect both.

We acknowledge that it would be absurd for EPA to have standards for each individual in the country, despite each individual's having their own susceptibility risk, even if that risk is quantitatively unknown. Likewise, It would be impractical to have separate NAAQS for each subgroup of vulnerability, even though that would provide better protection. For example, a set of NAAQS for pregnant mothers and a different one for adolescents is impossible even though it would make scientific sense. So on the one hand, EPA accepts heterogeneity of risk within the population, while having to establish a uniform standard that is required to be broadly protective of all. But inexplicably and arbitrarily, EPA rejects heterogeneity of populations and pollution characteristics in the studies that it will consider valid or informative based solely on the country of origin.

EPA states in its Nov. 2015, *Preamble to the Integrated Science Assessments*, “Consistency of findings across studies is informed by the repeated observation of effects or associations across multiple independent studies. Further strength is provided by reproducibility of findings in different populations under different circumstances.” Yet EPA arbitrarily eliminates research that would accomplish exactly that.

E2(f). **EPA cannot do its job functioning as an engineering firm, it must act with less than perfect knowledge.** Healthcare decisions seldom can be made with the same precision as physics or engineering decisions. Biologic systems are too complex to be accurately or adequately evaluated using merely mathematical equations. Physicians and patients don't have the luxury of waiting until all uncertainty calculations have been satisfied and all doubt is removed before diagnosis and treatment options must be engaged. As caregivers, we have to function on the basis of the best available information at the time, not perfect information or indisputable facts. The science often steers us toward multiple treatment options, with each one having competing risks and benefits. In evaluating knowledge offered by research and in establishing NAAQS, EPA should look at their responsibility in the same way healthcare providers do, as public health advocates do, not as engineering firms do.

E2(g). The CASAC review of the afore-mentioned documents implies that **EPA considers almost exclusively only mortality-based risk assessments, giving little consideration to morbidity risk.** It is bewildering and indefensible that EPA would arbitrarily limit their review to such a narrow adverse health outcome. A similar criticism was levied by the Natural Resources Defense Council against the EPA when it declined to strengthen the ozone standards. They said, "EPA's near-exclusive focus on lung function decrements demonstrated in controlled human experiments on healthy young adults arbitrarily overlooks important factors and sensitive populations for whom the standards must be protective with an adequate margin of safety."<sup>15</sup> We echo that criticism and go further. Ozone's adverse impact on the pulmonary system is only one small part of ozone's overall health consequences. Ozone has nearly as broad an influence on health as does PM2.5, affecting virtually every organ system, including having a mortality impact.

E2(h). **We also echo CASAC's critique on EPA's relying on controlled human exposure studies to identify a minimum concentration for which health can be expected from a 24-hour PM2.5 standard.** Those studies do not and cannot involve those most vulnerable to air pollution, i.e., the elderly, those with cardiovascular and pulmonary morbidities, children, and those in utero. **Most of those studies involved exposures much shorter than 24 hours, and none of those studies involve PM2.5 spikes that last several days in a row, as is typical in Utah.** They almost always involve a single pollutant, hardly ever matching a real-world pollution spike, and the concentrations required to elicit a response in the short term are usually unrealistically high.

E2(i). **EPA is wrong to discount biochemical and histological studies and studies of subtle clinical outcomes.** We disagree with this statement from the EPA and its implications in their decision-making process: "It is more difficult to determine the extent of change that constitutes adversity in more subtle health measures. These more subtle health effects include a wide variety of responses, such as alterations in markers of inflammation or oxidative stress, changes in pulmonary function or heart rate variability, or alterations in neurocognitive function measures."<sup>16</sup> Each one of these clinically subtle or biochemical outcomes is directly associated with definitive disease and disability. If A=B, and B=C, then A=C. By discounting the value or significance of these kinds of biochemical studies, the EPA is unnecessarily and inappropriately limiting the evidence for stricter standards.

Furthermore, EPA's statement, "The committee also observed that elevations of biomarkers, such as cell number and types, cytokines, and reactive oxygen species, may signal risk for ongoing injury and clinical effects *or may simply indicate transient responses that can provide insights into mechanisms of injury, thus illustrating the lack of clear boundaries that separate adverse from nonadverse effects*"<sup>16</sup> (italics added).

**This kind of characterization of the relevance of biochemical and histological hallmarks of injury and inflammation, and the claim that this "illustrates the lack of clear boundaries separating adverse from nonadverse effects" reflects a poor understanding or a deliberate discounting of their connection with real clinical disease.** Injury at the microscopic level means injury at the macroscopic level, even if it is difficult to measure.<sup>17</sup> For example, repeated episodes of airway inflammation may provoke airway remodeling, which occurs in asthma, and leads to irreversible reductions in lung function. Indeed, chronic or repeated episodes of inflammation are the ubiquitous root cause of atherosclerotic vascular disease.<sup>18</sup>

E2(j). We agree with CASAC's critique that the **EPA is being overly conservative for emphasizing use of "the mean" to define where the data provide the most evidence**, since quality data clearly indicate adverse effects below the mean in concentration-response functions.

E2(k). **CASAC is right in criticizing EPA for excluding areas impacted by wildfires and winter inversions.** CASAC's review states, "in an effort to exclude areas influenced by wildfire PM, areas where the 24-hour PM<sub>2.5</sub> standard is controlling due to wintertime stagnation and/or home heating by woodstoves were also excluded." Utah is a perfect example of EPA exclusion of major sources of our pollution. But in the same way, EPA is also ignoring the PM produced by "prescribed burns," which produce PM every bit as toxic as that from wildfires. In some parts of the country, EPA acknowledges that prescribed burns are the largest source of particulate pollution.<sup>135</sup>

**E3. Many communities and subgroups will not be protected from short-term pollution hazards by lowering the annual standard alone. We join CASAC in disputing that the annual standard guarantees or even implies adequate protection from short-term PM<sub>2.5</sub> spikes.** A simple analogy is worth considering. A home in Oklahoma's tornado alley could be destroyed by 10 seconds of 240 mph tornado winds, yet the average wind speed at the front door of that house over a 24-hour period might be completely normal. Regulating wind speed in Oklahoma based on an annual average would accomplish nothing. **PM<sub>2.5</sub> is a key component in abrupt spikes in pollution related to winter versions, wildfires, and industrial accidents and bypass events.** Independent of chronic exposure, it can result in multiple morbidity and mortality events, such as status asthmaticus, infections like pneumonia, cardiac arrhythmias and arrest, ischemic cardiac events, strokes, and other outcomes related to venous and arterial thrombi or to the disruption and friability of atherosclerotic plaque. Even brief exposures to air pollution triggering inflammation can have life-long consequences if they occur at the earliest life stages,



i.e., in utero during organogenesis. The genesis of all these listed events is not related to annual averages, and that fact is the reason there is a 24-hour PM 2.5 standard in the first place.

Most UPHE physicians are based in Utah on the Wasatch Front, where 2.5 million people live. Because of unique geographic circumstances, the majority of Utah's population lives in the greater Salt Lake Valley with mountain ranges on both sides. Therefore, most of Utah's population is subjected to significant short-term spikes of PM2.5. Because of that geography, our physicians group is particularly concerned that EPA is not proposing a tightening of the 24-hour standard.

A recent study found that Utah air pollution causes between 2,480 and 8,000 premature deaths every year, shortens median life expectancy up to 3.6 years, and triggers economic losses of \$750 million to \$3.3 billion annually, up to 1.7% of the state's gross domestic product.<sup>11</sup> This large impact on Utah's population is mostly due to short-term, i.e., days' to-weeks' long PM2.5 spikes from weather inversions, and where the nation's worst air pollution may be found for weeks at a time. Our state does not violate the annual average standard. In fact, we would likely not have violated the annual standard even if it were lowered to 9µg/m<sup>3</sup>. **Utah citizens will receive virtually no protection from only reducing the annual standard.**

We also believe that the EPA should not be allowing exemptions from the standards for "exceptional events." Utah's exceptional events are primarily regional wildfires. With the increasing intensity and duration of Western wildfires, exceptional events are no longer exceptional. In California, wildfire emissions nearly equal all their transportation emissions.<sup>12</sup>

Utah is heading in the same direction, with wildfire pollution now becoming a larger source of particulate pollution than our historic winter-inversion PM2.5 spikes. The belief of some EPA staff and a few CASAC members that tightening the annual standard would be enough to reduce the 24-hour standard is contrary to the experience in Utah. If you were to ask Utah's population, "Should the EPA do more to prevent or ameliorate our short-term pollution spikes?" you would almost certainly get nearly 100 percent responding adamantly, "Yes." We believe both the legal mandate via the Clean Air Act and the science compel the EPA to do exactly that.

In discounting the need to tighten the 24-hour standard and in EPA's afore mentioned documents, we see inadequate consideration of fetal, infant, and children's exposure to PM2.5. These are the critical developmental stages through which everyone must pass. A standard that is not sufficiently protective of these universal life stages cannot be considered acceptable from any standpoint. Children experience greater exposure for a given atmospheric concentration because of their higher metabolic rate, higher heart rate, and higher respiratory rate relative to adults. The adverse influence of pollution spikes on lifetime chronic disease vulnerability is also greater because of the ongoing organ development during all these early life stages.<sup>30</sup>

It is reasonable to conclude that the greatest public health impact of air pollution comes from its adverse impact during in-utero stages of development, considering the impact on

organogenesis and genetic and epigenetic function. Many of the studies that assess these connections found specific, sometimes short windows of vulnerability, e.g., during certain weeks of gestation.<sup>32</sup> Protection against these kinds of outcomes will be provided only by tightening the 24-hour standard.

To those EPA staff and CASAC members that argue against tightening the 24-hour standard, we say such a position implies an **unacceptable philosophy of “how much harm can citizens tolerate?” rather than a philosophy consistent with EPA’s mandate, which is, “how much harm can we prevent?”**

#### **E4. By relying on PM2.5 mass measurements, EPA is likely underestimating the toxicity of PM.**

We disagree with EPA’s assertion that “the evidence does not indicate that any one source or component is more strongly related with health effects than PM2.5 mass.”<sup>31</sup> Ultrafine particles (UFPs) are now widely recognized as the most toxic subset of PM2.5.<sup>20, 44</sup> Particle number concentration (PNC) is a common metric to measure smaller particles with little mass and are a much better marker of ultrafine concentration, and therefore, are a better marker of health hazard. This is common sense, given the axiom that the smallest particles are the most easily inhaled, the most difficult to exhale, the most easily translocated to the blood stream, and in turn, are the ones that most easily penetrate cellular membranes, including the nucleus of the cell. The majority of particles contributing to PNC in typical atmospheric systems are UFPs.

Therefore, measurement of PM2.5 via capture of PM2.5 mass on filters does not accurately reflect the toxicity of particulate pollution because it does not accurately reflect PNC or the surface area of the PM2.5. Regulating PM2.5 mass as a surrogate for PNC has been found to be inadequate because it correlates poorly with PM2.5 mass.<sup>21</sup> The study’s authors stated that the two metrics, “are not representative of each other; and regulating PM2.5 does little to reduce PNC.”

As long as EPA continues to use PM2.5 mass and not PNC as the regulatory benchmark, it is flying blind in determining the true health hazard of particulate pollution. This adds urgency to the need for EPA to tighten PM2.5 standards as much as possible in the hope of reducing PNC until it starts changing regulations based on PNC. Other studies draw similar conclusions.<sup>45</sup> PM2.5 tends to be more homogeneous within cities, impacted predominantly by regional and long-range transport. PNC is usually more variable, influenced by in-city sources, especially traffic emissions, things that are more amenable to local public policy control.

Furthermore, measuring merely PM2.5 mass also doesn’t distinguish between the different toxic profiles of the various elemental components of PM2.5<sup>46</sup> or the source. For example, for multiple physiologic and mechanistic reasons, wood smoke is the most toxic of the various types of PM2.5 that the average person is ever exposed to. Yet EPA conducts a certification program that perpetuates and even implicitly endorses wood stoves as acceptable sources of heat.

EPA's regulatory framework allowing states to consider all sources equally toxic fails to provide the public health with protection afforded by prioritizing control of the most toxic sources and types of PM.

**E5. The EPA standard for declaring causality is arbitrary and extreme.** We strongly disagree with many of the conclusions on causality in table ES-1, page ES-9 of EPA's *2019 Integrated Science Assessment for Particulate Matter*. Of all the organ systems and disease categories, the only ones that EPA acknowledges have an unequivocal causal relationship to short- and long-term particulate pollution are the cardiovascular system and mortality. The table labels the respiratory system for both short- and long-term exposure as only "likely to be causal." It labels the nervous system for long-term exposure only as "likely to be causal," and for short-term exposure only "suggestive of, but not sufficient to infer." It labels "metabolic effects," "male and female reproductive, and fertility" as "suggestive of, but not sufficient to infer," pregnancy and birth outcomes as "suggestive of, but not sufficient to infer," and cancer as "likely to be causal."

Given our familiarity with the many hundreds of epidemiologic studies from around the world that have firmly established strong connections with these outcomes, and the autopsy, biochemical, histologic, and animal toxicologic studies that provide biological plausibility, we consider EPA's standards for declaring "causality" far too rigid, arbitrary, and unscientific. They are an excuse to not pursue stricter standards. To put this in context, it is not possible to say in any one individual who is a lifetime smoker and got lung cancer, that smoking was the cause. Even though smoking increases the risk of lung cancer by at least 15 times, about 25-30% of lung cancers are triggered by air pollution (more about that later), and 3-14% are caused by radon. If the EPA was that patient's physician, using EPA's regulatory standard for establishing causality, Doctor EPA would not be willing to tell that patient they must "regulate smoking," that is, stop smoking, because there might have been another cause.

**EPA's rigid causality standard contributes to its over emphasis on cardiovascular disease and mortality while discounting all the other endpoints and providing cover for a weak proposal. Again, to us this suggests an underlying strategy more consistent with a philosophy of, "how much pollution-related harm can we tolerate?" rather than "how much can we prevent?"**

We note that in that same document, other health outcomes associated with particulate pollution are left out. There is no mention of the hundreds of studies that show connection to infections, inflammatory bowel disease, arthritis, immunosuppression, skin disorders, and acceleration of the aging process. There is inadequate attention paid to infant mortality or sudden infant death syndrome (SIDS).

## **F. A SMALL FRACTION OF THE STUDIES THAT COMPEL STRICTER STANDARDS**

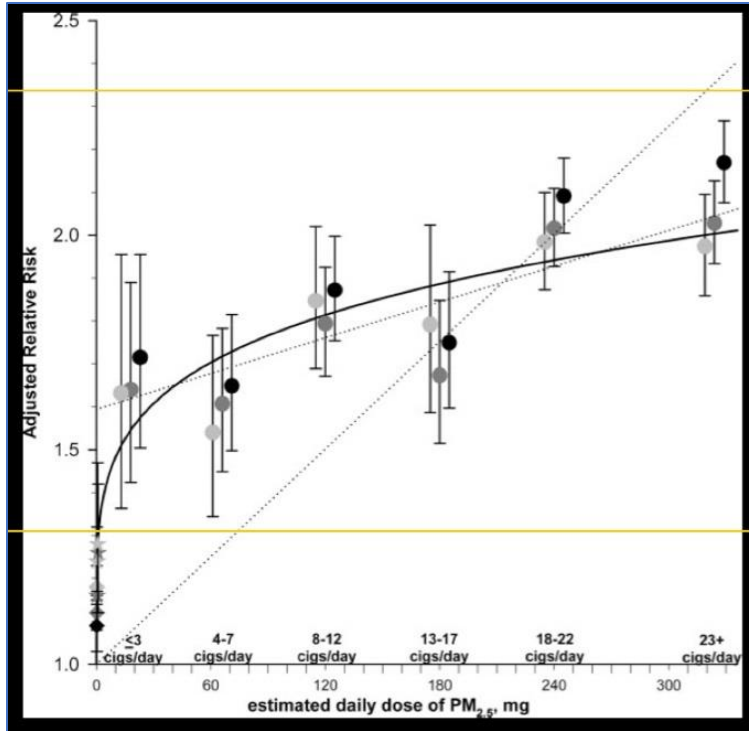
The totality of adverse health effects from particulate air pollution is staggering from both mortality and morbidity. Our comments in the remainder of this document are based on approximately 1,800 studies that we have reviewed. However, we cite here only those specific studies that were the most directly policy relevant, that provide quantitative exposure-response relationships, and that could be interpreted to specifically address the issue of whether to lower the annual and 24-hour PM2.5 standards.

Specifically, we excluded those that measured PM10 even though 50-70% of PM10 consists of PM2.5 in most cases.<sup>19</sup> We eliminated studies that only measured common co-pollutants of PM2.5, such as hazardous air pollutants (HAPs), black carbon, or PAHs, or studies that only measured certain sources of PM, such as diesel exhaust or pollution surrogates such as traffic density or distance from heavily trafficked roads, or only measured subsets of PM2.5, such as UFPs. Nonetheless, EPA should take into account that many studies of air pollution suggest that toxic chemicals like PAHs, although not regulated as criteria pollutants, are the most important hazards of a typical urban air pollution mix.<sup>22</sup>

We eliminated almost all animal studies. These other types of studies could be extrapolated to indict PM2.5 and should be considered in rule making. Our comments then are based on only a small fraction of the worldwide medical literature that reveals the extent of the public health hazard of PM2.5.

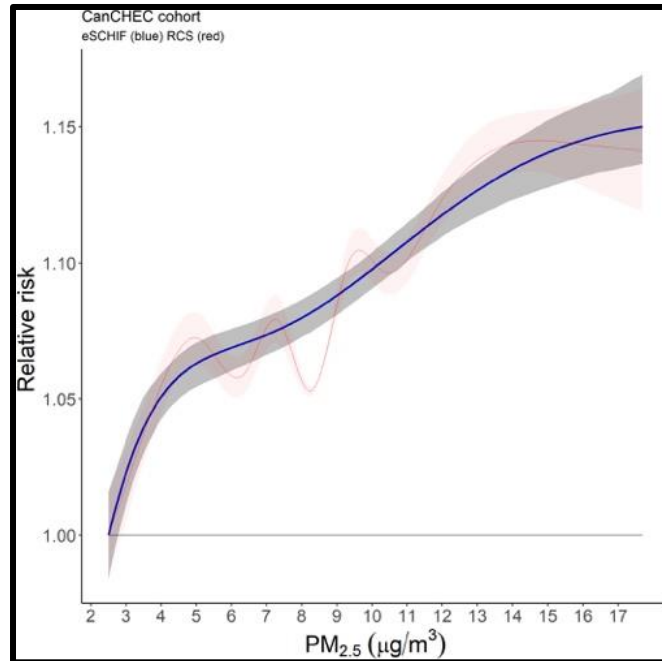
There is the temptation to look at these PM2.5 health outcomes in isolation. But regulators must keep in mind that there are additional adverse outcomes from ozone, NOx, sulfur oxides (SOx), VOCs, HAPs, etc., and that the overall nationwide health burden from air pollution is far greater than and much worse than the statistics we cite in the following pages. The EPA should not look at regulating PM2.5 in isolation. Regulating PM2.5 should be looked at as only one step of many needed to protect the public from the much larger overall air pollution hazard.

**F1. Supralinear dose/response relationship at low exposures:** Fundamental to setting the PM2.5 NAAQS at an appropriate level is the concept repeatedly confirmed by research over the last 15 years, that the relationship between disease and particulate air pollution is not linear but is supralinear. As this graph illustrates, from research published in 2009 in the journal *Circulation*, plotting concentration of three different types of air pollution (first-hand cigarette smoke, second-hand cigarette smoke, and community PM2.5), versus disease risk, it is clear that there is no safe level of air pollution, and that reducing pollution levels by a fixed amount has the greatest benefit at the lowest background levels.<sup>35</sup> The inclusion of smoking in this discussion is appropriate because smoking is merely personalized air pollution.



Many other studies have confirmed the same supralinear relationship.<sup>36</sup> For example, a meta-analysis found an RR of 1.08 per 10  $\mu\text{g}/\text{m}^3$  PM<sub>2.5</sub>, but also found a supralinear relationship at lower levels.<sup>37</sup> An analysis of European cohorts found the same pattern for “(1) natural- and cause-specific mortality including cardiovascular and nonmalignant as well as malignant respiratory and diabetes mortality; and morbidity measured as (2) coronary and cerebrovascular events; (3) lung cancer incidence; and (4) asthma and chronic obstructive pulmonary disease (COPD) incidence.... Associations mostly showed steeper slopes at low exposures with no indication of a threshold.”<sup>330</sup>

Most recently, a population-based cohort study of 7.1 million Canadian adults in one of the world’s cleanest environments for air pollution, followed between 1991 and 2016, revealed a supralinear concentration-response relationship between outdoor PM<sub>2.5</sub> and mortality at concentrations below 5  $\mu\text{g}/\text{m}^3$ . The mean PM<sub>2.5</sub> was 8.5  $\mu\text{g}/\text{m}^3$ , and 13.3% of the person-years in the cohort had outdoor PM<sub>2.5</sub> concentrations below 5  $\mu\text{g}/\text{m}^3$ . Each 10  $\mu\text{g}/\text{m}^3$  increase in long-term, average outdoor PM<sub>2.5</sub> concentration was associated with an 8.0% increased risk of nonaccidental mortality.<sup>367</sup> The dose mortality response curve is copied below.



A meta-analysis of 141 cohort studies found smoking one cigarette per day is nearly half as much cardiovascular and stroke risk as smoking an entire pack per day.<sup>38</sup> The risk of a premature death from smoking just one cigarette per day is 64% higher than if a person didn't smoke. By smoking just one cigarette per day, a person has a nine times greater risk of dying from lung cancer than a non-smoker has, while smoking ten cigarettes a day results in a 12 times greater risk.<sup>39</sup> These studies don't just speak to the risks of very light smoking, they are reflective of studies that correlate community PM<sub>2.5</sub> levels in a supralinear dose-response relationship with disease.

This same supralinear relationship is at the heart of the conclusions of the report commissioned by Environmental Defense Fund that concluded that an annual PM<sub>2.5</sub> standard of 8 µg/m<sup>3</sup> would save nearly 20,000 lives compared with an annual standard of 10 µg/m<sup>3</sup> that would save only 4,800 lives.<sup>23</sup>

Whether the annual standard should be tightened and to what degree is specifically addressed by a study of US veterans that found nine different causes of death were associated with air pollution (cardiovascular disease, cerebrovascular disease, chronic kidney disease, chronic obstructive pulmonary disease, dementia, type 2 diabetes, hypertension, lung cancer, and pneumonia), and that 99% of air pollution deaths occurred in counties where the annual PM<sub>2.5</sub> levels met current EPA standards.<sup>40</sup> This study is another reflection of the supralinear relationship between PM<sub>2.5</sub> dose and adverse health outcomes.

The knowledge that there is no safe level of air pollution, there is no threshold below which health effects are not seen, and that per unit of exposure, most major health consequences are greater at low concentrations calls into question not only the adequacy of current standards but also the efficacy of even having standards.

For example, in Utah and undoubtedly other states, invariably pollution discussions with state agencies end up at whether a proposal allows a community to be compliant with NAAQS. If modeling suggests that compliance will be achieved or maintained, then a project that will expose the community to more air pollution is almost certainly approved by the state. The existence of the standard in such a case provides a shield behind which state regulators can hide in approving more pollution. Instead of protecting public health, the standards actually undermine it. Because of that, the issue is not whether a new standard will be tight enough to eliminate public health impacts—no new standard ever will be. The issue is what does the society value? How much constraint of industry and personal fossil fuel use will society accept in pursuit of improved health?

There is a significant difference between genders and demographic groups on their risk of poor health outcomes from particulate pollution. Several studies show women have higher risk of cardiovascular disease from air pollution compared with men,<sup>41,42</sup> something that should be factored into the NAAQS. Reductions in PM2.5 are associated with increased life expectancy.<sup>43</sup>

**F2. PM2.5 and mortality:** PM2.5 has been identified as the sixth leading cause of premature death.<sup>34</sup> The scope of the of diseases and organ system damage from particulate pollution is nearly as broad as that from smoking cigarettes.

**F2(a). Mortality and long-term exposure:** The report commissioned by the Environmental Defense Fund mentioned above<sup>23</sup> also found that low-income Americans would see a 30% higher mortality benefit per capita from an 8  $\mu\text{g}/\text{m}^3$  standard than a 10  $\mu\text{g}/\text{m}^3$  standard.

In the largest study of its kind, using a cohort of over 60 million US Medicare beneficiaries followed for 12 years, with 460,310,521 person-years of follow-up, researchers found the risk of death from a 10  $\mu\text{g}/\text{m}^3$  increase in PM2.5 was 7.3%. But when the analysis was restricted to person-years of less exposure than 12  $\mu\text{g}/\text{m}^3$ , the same increase was associated with a 13.6% increase in risk of death. Subsets of that population—men, blacks, and Medicaid-eligible people had an even greater risk of death. This study is particularly striking because it provides information on the health effects of long-term exposure to low levels of PM2.5 in smaller cities and rural areas and among minorities or persons with low socioeconomic status.<sup>48</sup> This study also supports the supralinear dose/response relationship addressed above. In a study of similar size, each daily increase of 10  $\mu\text{g}/\text{m}^3$  in PM2.5 was associated with an increase in daily mortality rate of 1.05%.<sup>49</sup>

In an 11-year follow-up study of the famous Harvard Six Cities study, the authors found each average 10  $\mu\text{g}/\text{m}^3$  increase in PM2.5 was associated with increased risk of all-cause mortality of 14%. The concentration-response relationship was linear down to PM2.5 concentrations of 8  $\mu\text{g}/\text{m}^3$ .<sup>53</sup>

A Canadian cohort study of over 2 million people found similar results. Notable about this study was that exposures were predominantly lower than in previous studies: mean PM<sub>2.5</sub> exposure was 8.7 µg/m<sup>3</sup>.<sup>55</sup>

**F2(b). Mortality and short-term exposure:** Another study found an 18% increase in all-cause mortality, a 3% increase in cardiovascular disease, a 22% increase in heart attacks, a 76% increase in stroke, and a 71% increase in respiratory deaths in association with a mere 10 µg/m<sup>3</sup> increase in 2-day averaged PM<sub>2.5</sub>.<sup>54</sup>

Analyzing long- and short-term PM<sub>2.5</sub> via satellite, researchers found that even annual concentrations < 10 µg/m<sup>3</sup> and daily concentrations < 30 µg/m<sup>3</sup> were associated with increased mortality: 9.28% and 2.14% respectively. The relationship appeared to be linear for short-term exposure, but on annual exposure, a greater effect per unit of exposure appeared with concentrations above 6 µg/m<sup>3</sup>.<sup>56</sup>

Other studies of daily PM<sub>2.5</sub> and daily deaths in Boston found that the association was almost certainly causal.<sup>57</sup> Causal modeling of PM<sub>2.5</sub> in 135 US cities found that PM<sub>2.5</sub> from local pollution increased daily deaths 1.5% per 10 µg/m<sup>3</sup> PM<sub>2.5</sub> increase. Restricting the analysis to days with pollution below 25 µg/m<sup>3</sup> yielded a 1.7% increase, supporting again the supralinear association and that the current 24-hour PM<sub>2.5</sub> standard is not providing enough protection.<sup>290</sup>

An increase of 10 µg/m<sup>3</sup> PM<sub>2.5</sub> on the day of and the day prior to death is associated with a 1.56% increase in daily deaths. This association was found even in zip codes that meet the EPA's current annual standard. The effect of PM<sub>2.5</sub> below both EPA daily and annual standards was 2.08%. This study highlights that PM<sub>2.5</sub> affects even rural populations with low air pollution levels.<sup>58</sup> Schwartz, et al, estimated that a PM<sub>2.5</sub> increase of 6.32 µg/m<sup>3</sup> increased daily death totals by .9%, even when all days with PM<sub>2.5</sub> concentrations > 30 µg/m<sup>3</sup> were eliminated.<sup>59</sup>

In a nationwide study in Italy, data on causes of death were extracted for three years and correlated to daily PM<sub>2.5</sub> levels. There was a positive association with mortality from natural, cardiovascular, cardiac, respiratory, and nervous-system causes. For example, mortality from nervous system–related causes increased by 4.55% for 10 µg/m<sup>3</sup> increases in PM<sub>2.5</sub>, lag 0-5 days.<sup>335</sup>

**F2(c). Association with infant mortality:** The United States has one of the highest rates of SIDS of all middle and high income countries in the world. PM<sub>2.5</sub> is also associated with infant mortality, such as SIDS, and respiratory mortality. In a Korean study of 2.5 million births, an increase of 10 µg/m<sup>3</sup> PM<sub>2.5</sub> during the first two trimesters was associated with a 20% increased risk of SIDS.<sup>73</sup> A Massachusetts study of infant mortality among 466,000 births and postnatal lifetime PM<sub>2.5</sub> found a much stronger association with after-birth exposure. Per 1.3 µg/m<sup>3</sup> increase in PM<sub>2.5</sub>, the rates of total, respiratory, and SIDS mortality increased 266%, 336%, and 250% respectively.<sup>285</sup>



In a study of nearly 1 million African infants, a 10 µg/m<sup>3</sup> increase in PM<sub>2.5</sub> concentration is associated with a 9% rise in infant mortality. The authors noted, “This effect has not declined over the last 15 years and does not diminish with higher levels of household wealth.”<sup>291</sup> In another study of 360,000 births in Korea, an increase in gestational PM<sub>2.5</sub> exposure of 3.15 µg/m<sup>3</sup> was associated with a 53% increase in all-cause infant mortality, 315% for respiratory infant mortality, and 42% increase for SIDS.<sup>173</sup>

**F2(d). Association with ICU and COVID mortality rates:** Mortality rates in the intensive care unit are related to short-term PM<sub>2.5</sub> exposures. Per 10 µg/m<sup>3</sup> increase in PM<sub>2.5</sub>, mortality within 30 days increased 18%.<sup>305</sup>

As previously noted, COVID is likely to become endemic to the world’s population. It is still the third leading cause of death in the US. Numerous studies found PM<sub>2.5</sub> was associated with increased mortality from COVID. In 32 European cities, from 2020 through 2022, the highest death rates occurred during pollution peaks and varied in proportion to their intensity. A 550% increase in mortality was observed when PM<sub>2.5</sub> concentrations got close to 45 µg/m<sup>3</sup>. But an increase of just 1 µg/m<sup>3</sup> was associated with a 10% increase in mortality.<sup>50</sup> Other studies on short-term PM<sub>2.5</sub> exposure found similar results.<sup>312,337</sup>

Finally, reductions in PM<sub>2.5</sub> are associated with increased life expectancy.<sup>43</sup> Using 16 years of data on 68 million Medicare enrollees, a decrease in long-term PM<sub>2.5</sub> by 10 µg/m<sup>3</sup> was causally linked to a mortality decrease of 6-7%.<sup>308</sup>

The totality of adverse health effects from particulate air pollution is staggering from both mortality and morbidity. Taking into account the numerous studies that show genetic and epigenetic damage, which suggests transgenerational effects, makes the case even stronger for acting more aggressively than the EPA proposal on both the annual and 24-hour standard.

**F3. PM<sub>2.5</sub> and the cardiovascular system:** Air pollution’s impact on cardiovascular disease accounts for about 80% of air pollution–related mortality.<sup>323</sup> The pro-atherogenic influence of PM is based on several related pathophysiological processes: endothelial dysfunction,<sup>358</sup> impaired lipid metabolism,<sup>356</sup> increased oxidative stress and inflammatory reactions, and enhanced thrombogenesis and plaque friability. In addition, PM<sub>2.5</sub> causes subclinical damage to cardiac muscle cells by several mechanisms: apoptosis, oxidative stress, and decreased oxygen delivery due to coronary atherosclerosis and ischemic damage of myocytes.<sup>324</sup> Particulate pollution is a key contributor to accumulation of atherosclerosis. On the other hand, small reductions in PM<sub>2.5</sub>, 1 µg/m<sup>3</sup>, over less than five years, are associated with a slowing of atherosclerosis progression.<sup>84</sup>

As with cigarette smoke, the PM effects can be almost immediate. Within 15 minutes, inhaled pollution nanoparticles are detectable in the blood and urine and can still be detectable 3 months later. The amount detectable is inversely proportional to the size of the particles.<sup>52</sup> This implies that brief exposure to pollution nanoparticles can have prolonged inflammatory-based

health consequences. This alone makes for a strong argument to reduce the 24-hour PM2.5 as much as possible.

Furthermore, these nanoparticles preferentially accumulate at sites of vascular inflammation: in other words, at the worst possible locations.<sup>87</sup> This provides a plausible mechanism for the endothelial prothrombotic changes and friability of atherosclerotic plaques that are often the cause of strokes and heart attacks.

Other impacts of short-term PM2.5 exposure include alteration of electrical signaling within the heart, starting as early as infancy. Rates of arrhythmias, heart attacks, and strokes increase abruptly with air pollution spikes and are the primary cause for increased community mortality rates. Those rates correspond to hourly pollution concentrations and stay elevated for as long as 30 days after the exposure has ended. In patients who suffer from heart failure, short-term air pollution spikes reduce cardiac function further.

The studies referred to below provide quantitative information relevant to where PM2.5 NAAQS should be established.

**F3(a). PM2.5 is a key contributor to atherosclerosis, arteriole narrowing, plaque rupture, and cardiac ischemia.** The relationship between PM2.5 and cardiovascular disease is striking. Following over 136,000 healthy participants with no known previous history of cardiovascular disease for approximately 7 years, the risk of major cardiovascular events increased with higher PM2.5 in a linear relationship, 36% per 1 µg/m<sup>3</sup> chronic PM2.5 exposure. The air pollution effect was comparable to that from hypertension and diabetes mellitus.<sup>60</sup>

This winter, PM2.5 levels in the heavily populated areas of Utah were often above 50 µg/m<sup>3</sup>, a common wintertime occurrence. For one weekend, Utah had 7 of the top ten worst polluted cities in the country. Based on this study, the risk of heart attacks for most of Utah's population was increased by over 12% by short-term exposure to our winter inversion PM2.5 pollution.

In a review and meta-analysis of 12 global studies, angina pectoris risk increased .66% on the second day of exposure to a 10µg/m<sup>3</sup> increase in PM2.5.<sup>361</sup> Another meta-analysis showed a near-term increase in risk of heart attack of 2.5% for each increase of 10 µg/m<sup>3</sup> in PM2.5.<sup>51</sup>

Implementation of the first NAAQ for PM2.5 allowed researchers to track the difference in rates of cardiovascular (CV) mortality from before the standard was implemented and afterward. They found a 10% decrease in CV mortality for each 1 µg/m<sup>3</sup> decrease in long-term PM2.5. But counties with the greatest baseline pollution, and therefore the greatest reduction in PM2.5 after implementation saw the smallest reduction in CV mortality per unit decrease of PM2.5.<sup>61</sup> This is further evidence of the supralinear relationship between PM2.5 concentration and disease and further supports the need to continue tightening the PM2.5 standards.

The retina is the only place where direct vision of arterial vasculature is possible. This lends itself to valuable observations relevant to the entire arterial system. The value in reducing

PM2.5 by even small amounts was illustrated by a study showing that the diameter of arterial retinal vessels was reduced by an amount equivalent to 7 years of aging from chronic exposure to just 3  $\mu\text{g}/\text{m}^3$  PM2.5. The value of reducing even short-term exposure by 9  $\mu\text{g}/\text{m}^3$ , as determined by PM2.5 levels on the day prior to the exam, was associated with a reduction in vessel diameter equivalent to 3 years of aging.<sup>62</sup>

Rates of heart attacks are associated with exquisitely small increments in chronic PM2.5 exposure. Just .59  $\mu\text{g}/\text{m}^3$  increase in PM2.5 was associated with a 16% increase in the incidence of acute heart attacks.<sup>63</sup>

**In a retrospective cohort study of 3.7 million California adults followed for 10 years, there was a 12% increased risk of acute heart attack (acute myocardial infarction [AMI]), a 21% increased risk of ischemic heart disease (IHD) mortality, and an 8% increased risk of cardiovascular mortality associated with a 10  $\mu\text{g}/\text{m}^3$  increase in 1-year mean PM2.5. PM2.5 exposure at concentrations 10.0 to 11.9  $\mu\text{g}/\text{m}^3$  was associated with a 6% increased risk of AMI and 7% increased risk of IHD mortality compared with concentrations less than 8  $\mu\text{g}/\text{m}^3$ .**<sup>364</sup>

A retrospective study of 3.7 million people followed over 10 years found that chronic PM2.5 exposure was associated with an increased risk of heart attack, ischemic heart disease mortality, and cardiovascular disease mortality; these associations were more pronounced in low socioeconomic status communities. **PM2.5 exposure at moderate concentrations (10.0 to 11.9  $\mu\text{g}/\text{m}^3$ ) was associated with increased risks of incident AMI (6% [95% confidence interval (CI), 3%-10%]) and IHD mortality (7% [95% CI, 2%-12%]) compared with exposures < than 8  $\mu\text{g}/\text{m}^3$ .**<sup>64</sup>

Elevated PM2.5 contributes to the onset of acute coronary events, especially ST-segment elevation heart attacks. In a study done of Utah patients, researchers found that a same-day 10  $\mu\text{g}/\text{m}^3$  increase of PM2.5 to a level greater than 25  $\mu\text{g}/\text{m}^3$  increased the risk of an ST-segment elevation myocardial infarction 15%.<sup>65</sup> A 5  $\mu\text{g}/\text{m}^3$  increase in annual mean PM2.5 was associated with a 13% increased risk of coronary events.<sup>66</sup> In another study of fatal heart attacks, long-term PM2.5 increases of 5.3  $\mu\text{g}/\text{m}^3$  were associated with a 35% increase risk.<sup>67</sup> Even hourly PM2.5 concentrations of 36  $\mu\text{g}/\text{m}^3$  increase the risk of heart attack,<sup>68</sup> which speaks to the inadequacy of EPA's form used to calculate the 24-hour standard.

**F3(b). Effect on heart electrophysiology:** It is increasingly recognized that complex chronic diseases have their roots in early life development. Air pollution's effect on the heart begins in utero.

Normal heart rate variability is an indicator of a healthy heart's ability to respond to stress and is essential for optimal functioning of the cardiovascular, respiratory, and digestive systems and is also connected to psychological well-being and the ability to handle lifetime emotional stress. Decreased heart-rate variability, i.e., lower resting vagal tone, is an important indication of a heart's inability to respond appropriately to stress and is associated with increased risk of SIDS,

heart attack, arrhythmias, hypertension, metabolic syndrome, and psychological disorders in older childhood, adolescence, and adulthood.<sup>70, 71, 72</sup> **Examining heart and respiratory rates of six-month-old babies, and correlating that to air pollution levels inhaled by the mother during the pregnancy, a 1 µg/m<sup>3</sup> increase in PM<sub>2.5</sub> was associated with a 3.53% decrease in respiratory sinus arrhythmias, i.e., lower resting vagal tone.<sup>69</sup> This is an example of an important study with long-term implications that the EPA would likely not consider, given their arbitrary inclusion criteria.**

In adults, long-term PM<sub>2.5</sub> increases of 10 µg/m<sup>3</sup> increases the risk of abnormal heart electrical activity by 60-70%, depending on the type of abnormal rhythm.<sup>74</sup> Research on out-of-hospital cardiac arrest helps make the case for a stricter 24-hour standard. These typically fatal events occur 4% more often with an increase of 10 µg/m<sup>3</sup> in the day of and the day before the event.<sup>75</sup> Other studies showed similar results, such as the risk's increasing significantly with even a mild elevation of PM<sub>2.5</sub> (10-15 µg/m<sup>3</sup>) and further increasing with higher levels.<sup>76</sup>

**F3(c). Effect on blood pressure:** The relationship between air pollution and high blood pressure begins in utero. Prenatal air pollution exposure is associated with higher blood pressure in newborns. Increases in maternal PM<sub>2.5</sub> exposure of just 5 µg/m<sup>3</sup> was associated with a 2.4 mm mercury (Hg) higher systolic and a 1.8 mm Hg higher diastolic blood pressure (BP) at birth.<sup>77</sup> Another study showed similar results.<sup>78</sup> These are examples of studies excluded by EPA from consideration, but they have significant clinical implications.

Less than three days' exposure to 3.6 µg/m<sup>3</sup> PM<sub>2.5</sub> is associated with an increase in arterial stiffness in elderly men.<sup>79</sup> That, in turn, contributes to spikes in blood pressure. Elevated blood pressure is a health hazard both acutely and chronically, because it contributes to multiple adverse cardiovascular outcomes, like strokes and heart attacks. Short-term increases of 5.2 µg/m<sup>3</sup> PM<sub>2.5</sub> are associated with an 8.2 mm Hg higher mean systolic BP and 5.8 mm Hg higher mean diastolic BP.<sup>80</sup> Within just two hours of exposure to multiple types of pollution, including multiple sizes of particulate matter, BP rises.<sup>82</sup> Each 10 µg/m<sup>3</sup> increase in long-term PM<sub>2.5</sub> is associated with a 3% increased risk of hypertension.<sup>81</sup>

**F3(d). PM<sub>2.5</sub> is also highly associated with pulmonary hypertension.** Just a 3 µg/m<sup>3</sup> increase in chronic exposure is associated with a 438% increase in the risk of death or lung transplant from pulmonary hypertension.<sup>83</sup>

**F3(e). Association with heart failure (HF), morphological changes, and blood clots:** PM is also associated with HF. A highly cited meta-analysis found that a mean reduction of chronic PM<sub>2.5</sub> of 3.9 µg/m<sup>3</sup> would prevent 7978 HF hospitalizations and save a third of a billion US dollars per year just in HF expenses.<sup>85</sup> In a nationwide study by county, increased ambient PM<sub>2.5</sub> concentration level was associated with increased incidence of HF hospitalizations and mortality across the US. Every 1 µg/m<sup>3</sup> increase in annual PM<sub>2.5</sub> concentration was associated with an increase of 0.51 HF hospitalizations/1,000 Medicare beneficiaries, and 0.74 HF deaths/100,000 residents.<sup>349</sup>

PM2.5 is associated with increased risk of deep-vein thrombosis and pulmonary embolism, even in locations that meet the current annual standard of 12  $\mu\text{g}/\text{m}^3$ .<sup>86</sup>

In addition to atherosclerotic coronary artery disease, rhythm abnormalities, heart failure, and hypertension, chronic PM2.5 exposure is also associated with cardiac morphological abnormalities reflective of impaired pumping mechanisms. Using a cohort of almost 4,000 people without known cardiovascular disease, researchers estimated PM2.5 exposure five years prior to cardiac imaging studies. The mean PM2.5 value was 9.86  $\mu\text{g}/\text{m}^3$ . Per PM2.5 increase of 1.32  $\mu\text{g}/\text{m}^3$ , left ventricular end systolic volume increased 1.28%.<sup>88</sup> This cardiac parameter change is an indication of impaired heart function.

**Studies of hospitalizations make a similar strong case for reducing the annual standard to 8  $\mu\text{g}/\text{m}^3$ . In a nationally representative sample of Medicare enrollees, increasing exposure to PM2.5 from less than 8  $\mu\text{g}/\text{m}^3$  to between 8 and 12  $\mu\text{g}/\text{m}^3$  increased all-cause hospitalization rates by 15%.<sup>89</sup>**

**F4. PM2.5 and the brain and nervous system:** As with the cardiovascular system, particulate air pollution is associated with increased oxidative stress and inflammation in both the peripheral and central nervous system. In addition to the vascular system and crossing the blood brain barrier (BBB), PM2.5 and UFPs can directly access the central nervous system via the nasal mucosa and the olfactory nerves, and likely after oral ingestion, through the GI tract carried by the vagus nerve. These auxiliary pathways make the brain uniquely vulnerable to particulate pollution. Moreover, the systemic inflammation precipitated by PM causes a loss of BBB integrity and an increase in BBB permeability, initiating a vicious cycle of adverse impact on the brain.<sup>90</sup> Once UFPs penetrate brain parenchyma, their accumulation triggers local induction of oxidative stress and inflammatory responses, primarily manifested by reactive microgliosis and neuronal damage.

**F4(a). PM2.5 interferes with brain development:** PM nanoparticles can cross the placenta and interfere with brain development throughout intrauterine life. In a study where almost all PM2.5 measurements were below current NAAQS, prenatal exposure to small increments of PM2.5 (3 $\mu\text{g}/\text{m}^3$ ) was inversely associated with multiple metrics of functional neurodevelopment at two years. Exposures during mid to late pregnancy may be especially detrimental to neurodevelopment, which suggests the need for limiting air-pollution exposure, especially during the latter half of pregnancy.<sup>113</sup>

In a Chinese study of 2,435 infant mother pairs, increments of every composition of PM in prenatal exposure of 10  $\mu\text{g}/\text{m}^3$  PM2.5 [primary particles (black carbon, mineral dust, and sea salts) and secondary particles (NH<sub>4</sub><sup>+</sup>, NO<sub>3</sub><sup>-</sup>, SO<sub>4</sub><sup>2-</sup> and organic matter) was negatively associated with gross-motor and personal-social scores, and especially problem solving for all infants measured at age one.<sup>336</sup>

Neurodevelopmental disorders have repeatedly been shown to correlate with PM2.5 exposure during pregnancy. A 10  $\mu\text{g}/\text{m}^3$  increase in PM2.5 was associated with a 33% increased risk of

Autism Spectrum Disorder (ASD) in children. PM1 was even more tightly associated, with an increase of 10  $\mu\text{g}/\text{m}^3$  during pregnancy and the first year of life being associated with an increased risk of 364%.<sup>115</sup>

Other studies found similar results, such as a 15% increased incidence with an increased PM2.5 exposure of 4.68  $\mu\text{g}/\text{m}^3$ .<sup>116,117</sup> and even higher correlations, as high as 232% for an increase of 10  $\mu\text{g}/\text{m}^3$ .<sup>118,119</sup>

The association of PM2.5 with ASD is much stronger in boys, corresponding to the much higher incidence of ASD in males. Per 6.5  $\mu\text{g}/\text{m}^3$  increase in PM2.5 during the entire pregnancy, the risk increased 17%, and when occurring during the first year of life, the risk increased 21% and was specific to boys.<sup>120</sup>

Not only is PM2.5 associated with ASD, it is associated with long-term variations and disruptions in mitochondrial physiology in children with ASD.<sup>354</sup> The effect on mitochondria may be the route by which PM2.5 precipitates neurodevelopmental regression (NDR) in children with ASD, i.e., when a child loses previously acquired skills and develops ASD symptoms. A triggering event may or may not be involved. In a case control study, the risk of NDR was related to higher PM2.5 during 3 to 6 weeks of the NDR-event period, particularly in those without a trigger. Those that experienced NDR had a higher average exposure to PM2.5, both during the NDR-event period and reference periods, 12.2  $\mu\text{g}/\text{m}^3$  versus 11.2  $\mu\text{g}/\text{m}^3$ . Furthermore, those that had an NDR demonstrated a significant change in PM2.5 during the NDR event period relative to the reference period. The odds of having NDR without a trigger were significantly elevated when PM2.5 was higher, OR 1.041, per 1  $\mu\text{g}/\text{m}^3$ .<sup>355</sup>

Early-stage brain development is dependent on placental expression of appropriate genes, such as those that control the production of the brain-derived neurotrophic factor (BDNF)–signaling pathway. Prenatal exposure to PM2.5 impairs BDNF production. A 5- $\mu\text{g}/\text{m}^3$  increase in residential PM2.5 exposure during the first trimester of pregnancy was associated with a 15.9% decrease in expression of placental BDNF at birth.<sup>121</sup>

**F4(b). PM2.5 is a significant contributor to stroke:** A landmark study of PM2.5's association with four outcomes precipitating hospitalizations (stroke, cardiac arrhythmias, pneumonia, and heart attack) using a causal-model approach, accounting for multiple pollutants, identified important trends.<sup>309</sup> First, supporting the supralinear concept, the greatest increase in the risk of admissions per unit change in exposure occurs at lower concentrations of air pollutants for all four types of admissions. Second, PM2.5's association with increased risk for all four types of hospitalizations was especially true for elderly patients, contradicting an EPA as noted earlier. There was a nearly 1% increase in the risk of stroke for each 1  $\mu\text{g}/\text{m}^3$  increase in annual PM2.5.

Elevated levels of PM2.5 may trigger not only cerebrovascular events via short-term exposures but also increase the risk of future events via long-term average exposures.<sup>353</sup>

Particulate pollution contributes to about one-third of the global stroke burden and about one-fifth of the global burden of dementia.<sup>91</sup> Like heart attacks, strokes are highly associated with PM2.5. An increase of 6.6 µg/m<sup>3</sup> on the day of the stroke is associated with an increase in the risk of ischemic stroke of 10%.<sup>92</sup> A meta-analysis of long-term exposure to PM2.5 as a risk factor for stroke found a 6.4% (95% CI, 2.1–10.9%) increase in the hazard of admission for each 5-µg/m<sup>3</sup> increase in PM2.5 levels.<sup>310</sup>

In another study, the risk of stroke increased 34% following a 24-hour period of PM 2.5 15 µg/m<sup>3</sup> to 40 µg/m<sup>3</sup>, i.e., what is currently classified as moderate pollution and largely below the current 24-hour PM2.5 standard. The increase risk was greatest between 12 and 14 hours after exposure and was most closely associated with markers of traffic pollution, which suggests that ultrafine PM is a primary culprit. The same study found that as a continuous variable, 6.4 µg/m<sup>3</sup> PM2.5 increased stroke risk by 11%.<sup>93</sup> PM2.5 is also associated with the progression trajectory of strokes. A UK study of stroke incidence, post-stroke cardiovascular diseases, and subsequent death found that each 5 µg/m<sup>3</sup> increase in annual PM2.5 was associated with a hazard ratio (HR) for stroke of 1.24, and an HR of transition from pre-stroke to death of 1.30.<sup>332</sup>

**F4(c). PM2.5 is a significant contributor to impaired cognition:** Impaired cognition is a well-established consequence of both acute and chronic PM2.5 exposure at levels relevant to the issue of tightening the NAAQS. In a study of Salt Lake City, Utah, school children who were exposed to an average PM2.5 level of just over 8 micrograms per cubic meter, impaired school performance in math and English was associated with both chronic PM2.5 and short-term spikes that only reached as high as 23 µg/m<sup>3</sup>, well under the current 24-hour standard. Short-term spikes had a greater impact on academic performance than chronic levels.<sup>94</sup> An increase in PM2.5 exposure during adolescence of 7.73 µg/m<sup>3</sup> is associated with a loss of performance IQ of 3.08 points.<sup>114</sup>

In a study of nearly 58,000 3-4 year olds in low- and middle-income countries, a 5 µg/m<sup>3</sup> increase in annual PM2.5 was associated with an OR of cognitive delay of 1.17.<sup>347</sup>

In a meta-analysis of 86 studies, a 1 µg/m<sup>3</sup> increase in PM2.5 exposure was associated with reduced performance in general cognition, lower verbal fluency, and a decrease in executive functioning.<sup>342</sup> In a Chinese population of infants up to age 3, exposed to high levels of PM2.5, an increase of 16 µg/m<sup>3</sup> PM2.5 exposure was associated with a .19 decrement in motor-performance scores, and an OR of 1.06 for being diagnosed with “developmental coordination disorder” a neurodevelopmental disorder that affects children’s ability to execute coordinated motor actions, resulting in slow, clumsy, or inaccurate motor performances.<sup>343</sup>

In a study of workers in 6 different countries, over 12 months, office workers exposed to higher PM2.5 and lower ventilation rates demonstrated worse cognition. Each increase of 8.8 µg/m<sup>3</sup> was associated with slower response times and reduced accuracy for 8 out of 10 cognition-test metrics.<sup>95</sup>

PM2.5 adversely affects cognition in all age groups, but older adults are the most widely studied. In a racially diverse sample of older adults, an increase of 10  $\mu\text{g}/\text{m}^3$  annual average PM2.5 was associated with a 50% increase in cognitive errors on a mental-status questionnaire.<sup>122</sup> A 1.1  $\mu\text{g}/\text{m}^3$  increase in long-term PM2.5 exposure was associated with a decline in cognitive performance equivalent to about 14 months of aging.<sup>123</sup>

In a population of 19,409 US women aged 70 to 81 years, long-term exposure of 10  $\mu\text{g}/\text{m}^3$  PM2.5 was associated with a cognitive decline equivalent to 2 years of aging.<sup>96</sup> Another study of older women found that a three-year average PM2.5 increase of just 4.04  $\mu\text{g}/\text{m}^3$  was associated with associated accelerated declines in verbal learning and free-recall memory.<sup>97</sup> A meta-analysis of longitudinal studies involving over 12 million people found a risk of cognitive impairment of 8% per 5  $\mu\text{g}/\text{m}^3$  increments in exposure to PM2.5.<sup>98</sup>

**F4(d). PM2.5 is associated with Parkinson's Disease (PD):** PD is associated with PM2.5. The deposition of  $\alpha$ -synuclein ( $\alpha$ -Syn) in the brain is the pathological hallmark of PD. PM2.5 promotes the fibrillization of  $\alpha$ -Syn and the formation of  $\alpha$ -Syn fibrils with enhanced seeding activity and neurotoxicity.<sup>328</sup>

A population-based geographic study reported just weeks ago involving 22 million Medicare beneficiaries found not only an association, but there were geographic hotspots. The incidence of PD increased 25% with an annual average increase in PM2.5 exposure of 14  $\mu\text{g}/\text{m}^3$ .<sup>276</sup> This study found a "ceiling effect" at PM2.5 12 to 19  $\mu\text{g}/\text{m}^3$  consistent with the supralinear effect addressed earlier.

**F4(e). Association with dementia and Alzheimer's Disease (AD):** In a study of nearly 3,000 people with a mean age of 74.1 years, the risk of dementia increased 54% in association with an increase of .88  $\mu\text{g}/\text{m}^3$  PM2.5 during the previous 5 years at their residential address.<sup>99</sup>

Numerous other studies of dementia and long-term PM2.5 exposure showed a strong correlation. In a study with a mean 10-year average PM2.5 exposure of 10.1  $\mu\text{g}/\text{m}^3$ , each 1  $\mu\text{g}/\text{m}^3$  increase was associated with a 16% increased risk of dementia.<sup>100</sup> A meta-analysis of 12 studies found the risk of dementia increased 3% for each 1  $\mu\text{g}/\text{m}^3$  increase in long-term PM2.5.<sup>368</sup>

On the other hand, reduction in PM2.5 in later years reduced the risk of dementia. Older women free of dementia were followed for six years. A reduction in PM2.5 of 1.78  $\mu\text{g}/\text{m}^3$  was associated with a 20% reduction in the risk of dementia, equivalent to the risk reduction expected from being 2.4 years younger.<sup>101</sup> Other studies found similar, if less dramatic results.<sup>102,103</sup>

AD is significantly associated with PM2.5. A meta-analysis of nine studies showed long-term exposure of 10  $\mu\text{g}/\text{m}^3$  was associated with a 95% increased risk of AD.<sup>104</sup> Another study found a 138% increased risk of AD per increase of 4.34  $\mu\text{g}/\text{m}^3$  in PM2.5 over nine years.<sup>105</sup> In older females, averaging PM2.5 over three years, each of increase of 2.81  $\mu\text{g}/\text{m}^3$  declines in learning



and immediate recall were accelerated by 19.3%. Those same increments were associated with progressive atrophy of grey matter, as shown by MRI scans, indicative of increased AD risk.<sup>106</sup>

A meta-analysis of 49 studies published just weeks ago showed a positive association between 10  $\mu\text{g}/\text{m}^3$  increases in long-term PM2.5 and all-cause dementia, AD and PD, with pooled OR of 1.3, 1.65, and 1.17 respectively.<sup>363</sup>

Amyloid- $\beta$  (A $\beta$ ) plaques are considered an anatomic finding of AD. In a study that included more than 18 000 US participants with cognitive impairment who received an amyloid PET scan, air pollution was estimated 14 years before the scan and again 1 year before the scan. Living in areas with higher estimated PM2.5 concentrations was associated with a 10% higher likelihood of amyloid PET scan positivity per 4  $\mu\text{g}/\text{m}^3$  increase in chronic PM2.5.<sup>107</sup>

In a study of North Carolina residents, those living with chronic PM2.5 > 10  $\mu\text{g}/\text{m}^3$  were compared with a control group living with PM2.5  $\leq$  7.61 $\mu\text{g}/\text{m}^3$ . The group with greater exposure were found to have higher rates of mortality and hospital admissions for AD, non-AD dementia, and PD, including a pronounced increase in AD mortality (323/100,000 versus 257/100,000, respectively).<sup>108</sup> Another study tracked the relationship between long-term exposure to PM2.5 and time to first hospitalization for three common neurodegenerative diseases—dementia, AD, and PD. An increased risk for all three was found, ranging from 8% to 15% per 1  $\mu\text{g}/\text{m}^3$  increase in annual PM2.5.<sup>109</sup> Other studies tracked similar outcomes with short-term PM2.5. For each 10  $\mu\text{g}/\text{m}^3$  increase in two days' average of PM2.5, researchers found statistically significant increases in hospital admissions for PD 3.23% and for diabetes 1.14%.<sup>110</sup> Another study found an increase of 61% for the risk of hospitalization for PD, per 10  $\mu\text{g}/\text{m}^3$  increase in PM2.5 averaged over an eight-day period.<sup>111</sup>

Tracking the relationship between long-term PM2.5 and dementia, researchers found that a 4.8  $\mu\text{g}/\text{m}^3$  increase in PM2.5 was associated with a 4% increase in dementia over a 12-year period.<sup>112</sup>

**F4(f). Association with multiple psychiatric and tic disorders:** Air pollution is significantly associated with increased risk of psychiatric disorders. Multiple types of mental illness are highly associated with PM2.5. An increase of 10  $\mu\text{g}/\text{m}^3$  over 3 years was associated with an increased risk of depression of 44%.<sup>131</sup> In pregnant women, PM2.5 in the first 3 months of pregnancy was associated with increased risk of anxiety and depression, 23% and 25% respectively for a 10  $\mu\text{g}/\text{m}^3$  increase in daily PM2.5.<sup>339</sup> In a population-based longitudinal cohort study of nearly 9 million US Medicare enrollees older than 64 years, each 5  $\mu\text{g}/\text{m}^3$  increase in long-term mean exposure to PM2.5 was associated with an adjusted percentage increase in depression risk of 0.91%.<sup>362</sup>

On a daily basis, PM2.5 levels are associated with increases in emergency room visits for psychiatric disorders during the next three days. A 10  $\mu\text{g}/\text{m}^3$  increase in PM2.5 was associated with an increased risk of 7%.<sup>132</sup> In a French study, for periods of 6 days with PM2.5 above 20

$\mu\text{g}/\text{m}^3$ , hospital admissions for psychotic disorders was significantly increased.<sup>319</sup> Suicide risk is increased 4% per 6  $\mu\text{g}/\text{m}^3$  increase in PM2.5 two days before the event.<sup>270</sup>

Several studies have shown that particulate air pollution is associated with increased anti-social, aggressive behavior and crime. For example, one study found that over an eight-year period, a 10% increase in daily PM2.5 was associated with a 0.14% increase in violent crime, costing society \$1.4 billion. Notably, the effects increase until 20  $\mu\text{g}/\text{m}^3$  and then level off,<sup>133</sup> suggesting other pollution-related health outcomes with a supralinear relationship to dose.

Tic disorders in children are associated with PM2.5 exposure. In a Taiwan study of nearly 6,000 cases, tic disorders were positively associated with a 10  $\mu\text{g}/\text{m}^3$  increase in PM2.5 in a non-linear relationship. During pregnancy, the HR was 1.09, and during infancy it was 1.12. The vulnerable time window for infants with increased risk of tic disorders was 6-52 weeks after birth.<sup>348</sup>

**F4(g). Anatomic brain changes related to PM2.5:** Anatomic brain changes related to numerous pollution components, including PM2.5, have been documented even in children. Structural neuroimaging and cognitive function were investigated at 6 to 10 years of age in nearly 800 children and correlated with PM2.5 exposure of the mother during pregnancy. For each 5  $\mu\text{g}/\text{m}^3$  PM2.5 exposure, brain scans showed thinner cortex in several brain regions of both hemispheres, but primarily in the right prefrontal cortex.<sup>329</sup> These anatomic changes correlated to impaired childhood inhibitory control.<sup>124</sup>

MRI brain scans of 8-12 year olds were compared based on PM2.5 exposure of the mother during the third trimester of the pregnancy. A 7  $\mu\text{g}/\text{m}^3$  increase in PM2.5 was linked to a 5% decrease in corpus callosum volume. This anatomic aberration was associated with a higher rate of hyperactivity.<sup>125</sup>

In a study of 332 youth ages 6-14 years, brain imaging was correlated with PM2.5. "Researchers found progressively higher exposures were associated with greater disruptions in local volumes, tissue organization, metabolite concentrations, and blood flow throughout cortical and subcortical brain regions and the white matter pathways interconnecting them. Together these affected regions comprise cortico-striato-thalamo-cortical circuits, which support the regulation of thought, emotion, and behavior."<sup>126</sup>

In a study evaluating susceptible windows of exposure, from conception to preadolescence, via brain imaging of 9-12 year olds, markers of neurodevelopmental aberrations (fractional anisotropy and mean diffusivity) on MRI scans correlated with 5  $\mu\text{g}/\text{m}^3$  increases in PM2.5 during pregnancy and childhood.<sup>369</sup>

In the largest brain imaging/air pollution study done so far, including over 10,000 9-10 year old US children from across the country, median PM2.5 exposures ranged from 5.1 to 10.4  $\mu\text{g}/\text{m}^3$ . Increased PM2.5 exposure was associated with changes in brain morphology. A 5  $\mu\text{g}/\text{m}^3$  increase in PM2.5 was associated with hemispheric-specific differences in gray matter across

cortical regions of the frontal, parietal, temporal, and occipital lobes as well as subcortical and cerebellum brain regions. The authors said, “an increase of 5- $\mu\text{g}/\text{m}^3$  was associated with differences in cortical thickness on the magnitude ranging from 0.01 to 0.04 mm, suggesting that continual exposure to PM<sub>2.5</sub> during childhood and adolescence could substantially impact an individual’s brain-growth trajectories with potentially lifelong consequences.”<sup>344</sup>

In a cohort of people over 60 years old without a history of stroke or dementia, a 2  $\mu\text{g}/\text{m}^3$  increase in PM<sub>2.5</sub> was associated with a with -0.32% smaller total cerebral brain volume, (a marker of age-associated brain atrophy) and a 46% increased risk of covert brain infarcts.<sup>127</sup> Older women chronically exposed to PM<sub>2.5</sub> of just 3.49 $\mu\text{g}/\text{m}^3$  had an average loss of total brain volume of 6.23 $\text{cm}^3$ , equivalent to 1 to 2 years of brain aging.<sup>128</sup>

The hippocampus is an important area of the brain involved in memory processing. Researchers found that long-term exposure to PM<sub>2.5</sub> below 10  $\mu\text{g}/\text{m}^3$  correlated with reduced volume of the hippocampus.<sup>129</sup>

The prefrontal cortex is a key area of the brain involved in neurodegenerative and neuropsychiatric diseases. In a study of over 18,000 adults that had brain MRI scans, who were chronically exposed to an average PM<sub>2.5</sub> of less than 10  $\mu\text{g}/\text{m}^3$ , there was an inverse association between PM<sub>2.5</sub> exposure and prefrontal brain volume.<sup>130</sup>

#### **F5. PM<sub>2.5</sub> and reproductive toxicity, fetal development/chromosomal integrity:**

The numerous studies that show PM’s strong connection to genetic and epigenetic damage (suggesting adverse transgenerational effects), toxicity at multiple points in human reproduction, and to fetal development, together makes the case even stronger for acting more aggressively than EPA proposal on both the annual and 24 hr standard.

PM can adversely affect virtually all phases of human reproduction and early life development, causing sperm DNA damage, decreases in sperm count<sup>327</sup> and motility,<sup>315</sup> decreased rates of fecundability, increases in the rates of male and female infertility,<sup>269,280</sup> decreased fertilization and menstruation, and increases in miscarriages and other adverse reproductive outcomes.

**F5(a). Preconception toxicity impairs fertility and organogenesis:** Infertility is becoming a global public health problem, affecting at least 10% of all reproductive-aged couples worldwide. The World Health Organization estimates that pure male factors, mainly poor semen quality, could account for 50% of infertility cases. Stark changes in sperm concentration, count, and motility over a relatively short period suggest that the global trend of deteriorating semen quality is more likely to be related to environmental factors than genetics. While there are undoubtedly multiple environmental contributors, air pollution is certainly among the most important.

The risk of PM to fetal and child organ development can begin preconception. Preconception PM<sub>2.5</sub> exposure of parents, especially during the first 18 years of life, is associated with

increased risk of early onset respiratory diseases in their offspring.<sup>375</sup> Preconception PM2.5 exposure of the mother increases the risk of congenital heart malformations.<sup>374</sup>

Babies are essentially born pre-polluted by the air breathed by the mother during pregnancy. Particulate matter and the chemicals attached to it can cross the placenta and contaminate and interfere with fetal organ development. Air pollution breathed by a pregnant mother at critical stages in the development of the human embryo or during early infancy can cause genetic and epigenetic changes, increase the risk of birth defects like neural tube defects, and cause the baby, as an adult, to experience an increased likelihood of multiple chronic diseases, including those of the heart, lungs, immune system, brain, and even obesity, diabetes, cancer, rheumatoid arthritis,<sup>298</sup> and shortened life expectancy.

Pregnant women exposed to more particulate pollution give birth to babies with significantly more chromosomal aberrations, including shorter telomeres and epigenetic changes, which can be passed on to multiple subsequent generations.

Below are numerous studies that specifically relate quantitatively to dose/response relationships relevant to setting the PM2.5 NAAQS.

**F5(b). Quantitative consequences of preconception exposure:** Short-term PM2.5 increases are associated with decreased fecundability. An increase in PM2.5 of 10 µg/m<sup>3</sup> prior to attempted conception is associated with a 22% decrease in fecundability.<sup>266</sup>

In a highly exposed maternal population, **each 10 µg/m<sup>3</sup> increase in periconception PM2.5 exposure was associated with a 2% increase in the rate of congenital heart disease.**<sup>374</sup> One study determined the monthly average values of PM2.5 for each birth for five different monthly time periods: one and two months before/after conception, and the month of conception. Births with any congenital anomaly had a higher mean PM2.5 exposure level compared to non-anomalous births across all periconception months. **Per 10 µg/m<sup>3</sup> increase in PM2.5 during the month before conception, the month of conception, or the month after, the risk of congenital malformation increased 13 to 39%. Increasing PM2.5 exposure levels occurring one month prior to conception consistently demonstrated the highest risk, i.e., a 17% increased risk per 4.9 µg/m<sup>3</sup> increase in PM2.5.**<sup>146</sup>

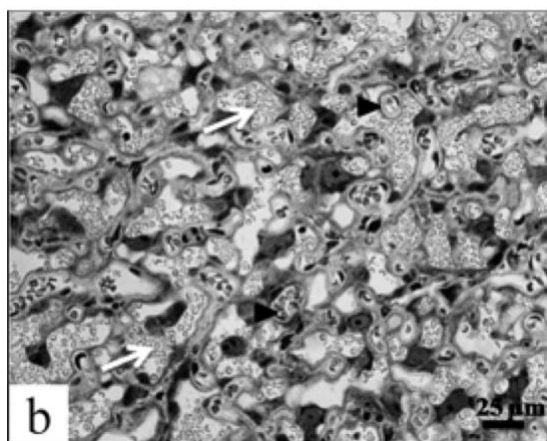
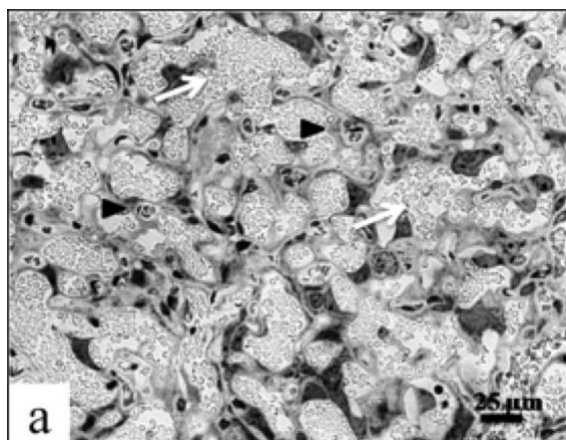
**F5(c). Prenatal exposure to PM2.5 increases the risk of birth defects:** Numerous studies have shown an effect of maternal PM2.5 exposure on the risk of birth defects. For example, in Taiwan, PM2.5 exposure of the pregnant mother measured during the first three months after conception revealed a 29% increased risk of hypospadias for each 15.6 µg/m<sup>3</sup> increase in PM2.5.<sup>149</sup> While this threshold is greater than the current or proposed annual PM2.5 standard, extrapolation to lower thresholds suggests that a significant reduction in birth defects would be expected by lowering the PM2.5 annual standard to 8 rather than 10 µg/m<sup>3</sup>. A 10 µg/m<sup>3</sup> increase in PM2.5 at the time of birth is associated with several different types of congenital cardiac malformations.<sup>150</sup>

F5(d). **The effect of exposure to PM2.5 on telomeres:** Telomere length is a marker of biological aging that may provide a cellular memory of exposures to oxidative stress and inflammation. Telomere length at birth has been related to life expectancy. In 641 mother/newborn pairs, a 5- $\mu\text{g}/\text{m}^3$  increment in PM2.5 exposure during the entire pregnancy was associated with 8.8% shorter cord blood leukocyte telomeres and 13.2% shorter placental telomere length.<sup>147</sup> This means nothing less than that **PM2.5 programs a person by the time of birth to a shorter life span.**

Among a group of elderly adults exposed to annual PM2.5 in a range between 15 and 23  $\mu\text{g}/\text{m}^3$ , increases of 5  $\mu\text{g}/\text{m}^3$  were associated with decreases in telomere length of 16.8% and decreases in mitochondrial DNA content of 25.7%.<sup>148</sup> An increase in annual average PM2.5 exposure of just 1  $\mu\text{g}/\text{m}^3$  in African-American youth was associated with a decrease in absolute telomere length.<sup>198</sup> In a review of 7 observational studies correlating PM2.5 with telomere length, most found shorter telomeres with PM exposure.<sup>271</sup>

F6. **PM2.5 and Pregnancy and Birth Outcomes:** Virtually every type of poor pregnancy outcome or complication is associated with particulate pollution, from still births and birth defects to premature births and placental rupture. This is understandable, given that one of PM2.5's most significant impacts is vascular inflammation, and the placenta can be regarded as the vascular of all human organs.

The pathologic effect on placental vasculature was illustrated by a study on mice.<sup>151</sup> The microscopic photo of a near-term placental section on the left (a) is from a mouse that breathed filtered air, PM2.5 6.5  $\mu\text{g}/\text{m}^3$ , during the pregnancy. On the right (b) is the same from the placenta of a mouse that breathed unfiltered Los Angeles air, with PM2.5 27.5  $\mu\text{g}/\text{m}^3$ . The vascular congestion, reduction of volume, and narrowed capillaries, is obvious. On the fetal side of the placenta, vascular dilatation occurred in an apparent attempt to compensate for the vascular narrowing on the maternal side, resulting in an increase in surface area. Similar, but slightly less dramatic results were found when the exposure was preconception rather than during the pregnancy. Both periods of exposure led to significantly smaller fetal weights.



The placental vascular compromise from maternal PM2.5 exposure illustrates a likely mechanism by which PM causes impaired fetal development and poor pregnancy outcomes, as many other studies have demonstrated.

Other studies provide more detail on PM2.5's pathologic changes in the placenta, such as a significant increase of blood mononuclear cells (PBMC); platelets; the inflammatory marker, interleukin-6; vascular thrombi; and chorioamnionitis.<sup>152</sup>

Below are some of the studies that provide dose/response information relevant to setting the NAAQS.

**F6(a). PM2.5 impairs fetal growth:** Examining placentas from 361 mothers, methylation of the fetal growth hormone, leptin, in the placenta was reduced with daily PM2.5 exposures during the pregnancy, 1.4% lower for each 7.5  $\mu\text{g}/\text{m}^3$  PM2.5.<sup>153</sup>

Fetal growth restriction is not only a major determinant of perinatal morbidity and mortality but also leads to adverse health effects in later life. Each 10  $\mu\text{g}/\text{m}^3$  increase in maternal PM2.5 exposure increases the risk of fetal growth restriction.<sup>154</sup>

Numerous studies have found an association between particulate pollution and various parameters of fetal growth. For example, a study of 3 million births across Canada found that a 10- $\mu\text{g}/\text{m}^3$  increase in PM2.5 over the entire pregnancy was associated with a 4% increased risk of small-for-gestational-age (SGA) and reduced-term birthweight of 20.5 g.<sup>155</sup> Similar results were found in a US population.<sup>156</sup>

**F6(b). PM2.5 is associated with premature birth.** "Evidence has consistently shown that adult survivors of preterm birth have increased risks of chronic disorders involving various organ systems, including cardiovascular, endocrine/metabolic, respiratory, renal, neurodevelopmental, and psychiatric disorders, which either persist from childhood into adulthood or sometimes first manifest in adulthood. These disorders also lead to moderately (30% to 50%) increased mortality risks during early to mid-adulthood among persons born preterm compared with full-term, and even higher risks among those born at the earliest gestational ages."<sup>376</sup>

Numerous studies found significant associations between PM2.5 exposure and low birth weight (LBW) and premature birth (PMB). For example, this meta-analysis of 18 studies found the risk of premature birth increased 13% per 10  $\mu\text{g}/\text{m}^3$  increase in PM2.5 during the entire pregnancy.<sup>157</sup>

Another meta-analysis of 25 studies found a 10  $\mu\text{g}/\text{m}^3$  increase in PM2.5 was associated with a 5% increased risk of LBW, a 10% increased risk of PMB, and a 15% increased risk of SGA based on entire pregnancy exposure. The pooled estimate of decrease in birth weight was 14.58 g.<sup>158</sup> Another meta-analysis showed similar results.<sup>159</sup>

Another study showed not only an association between PMB and PM2.5, a 9.6% increased risk for each 6.45  $\mu\text{g}/\text{m}^3$ , but also that the association existed for both primary and secondary PM.<sup>160</sup>

Intrauterine inflammation (IUI) is a known contributor to poor birth outcomes, including LBW and PMB. IUI is highly associated with PM2.5 exposure. Estimates of the prevalence of IUI range from 25% to 50% of preterm births. For all exposure periods (each trimester), including the three months prior to conception, PM2.5 is associated with risk of IUI. In this study, for example, per interquartile increase in PM2.5 over the entire pregnancy ( 3.31  $\mu\text{g}/\text{m}^3$ ), the risk of IUI increased 38%.<sup>161</sup> Estimated exposures to PM2.5 during the period of the entire pregnancy were below the federal annual standard of 12  $\mu\text{g}/\text{m}^3$  for nearly 70% of the participants. There was no threshold below which an association was not seen.

Even short-term PM2.5 is associated with PMB. This study found a 6% increased risk for an increase of 10  $\mu\text{g}/\text{m}^3$  on the day prior to birth.<sup>162</sup>

A meta-analysis of 84 studies of acute and long-term PM2.5 exposure during pregnancy found that per 10  $\mu\text{g}/\text{m}^3$  long-term increase during the pregnancy, PMB risk increased 8.4%. For short-term exposure, pre-term birth risk of .3% was associated with a 10  $\mu\text{g}/\text{m}^3$  increase in PM2.5 on lag day 2 and 3.<sup>163</sup> Globally, PM2.5 has been estimated to account for 18% of premature births. This is a tremendous liability to public health in general.<sup>164</sup>

Assessing gestational age at birth offers another metric of gestational health. Each 5  $\mu\text{g}/\text{m}^3$  increase in PM2.5 in the third trimester was associated with a reduction of gestational age at birth of 4.2 days.<sup>165</sup>

**F6(c). PM2.5 and other pregnancy, birth complications:** Particulate pollution increases the risk of stillbirth. In one study, for each 4  $\mu\text{g}/\text{m}^3$  increase in PM2.5, stillbirths increased over 2%.<sup>166</sup> In another study, the risk of stillbirth increased 18% for each 10  $\mu\text{g}/\text{m}^3$  increase in PM2.5.<sup>167</sup>

Gestational hypertension is strongly associated with PM2.5. In a US study, there was a 10% increased risk for hypertensive disorders with each increase of 5  $\mu\text{g}/\text{m}^3$  in PM2.5. An effect threshold was found at 9  $\mu\text{g}/\text{m}^3$ , and the authors calculated that 8.1% of cases were attributable to PM2.5.<sup>168</sup> A meta-analysis of studies of hypertension in pregnancy found that a 10  $\mu\text{g}/\text{m}^3$  increase in PM2.5 was associated with an increased risk of hypertension of 52% and an increased risk of pre-eclampsia of 31%.<sup>169</sup>

Gestational glucose intolerance and diabetes is another pregnancy complication associated with particulate pollution. A study of Boston pregnant mothers with a mean PM2.5 exposure of 10.9  $\mu\text{g}/\text{m}^3$  in the second trimester found that a 2.6  $\mu\text{g}/\text{m}^3$  increase in PM2.5 was associated with a 82% increased risk of glucose intolerance.<sup>240</sup> A meta-analysis of 11 studies found that an increase of 10  $\mu\text{g}/\text{m}^3$  PM2.5 was associated with a 4% increase in the risk of gestational diabetes.<sup>170</sup>

Premature rupture of membranes (POM) is associated with PM<sub>2.5</sub> exposure. Per 10 µg/m<sup>3</sup> increase, the risk of POM increased 35% for the whole pregnancy. Preterm POM was even more strongly associated with an increased risk of 53% for each increase in PM<sub>2.5</sub> of 10 µg/m<sup>3</sup> for the whole pregnancy, and with further positive trends for the last week and day of pregnancy.<sup>171</sup>

A position that the 24-hour PM<sub>2.5</sub> standard does not need to be tightened ignores research that shows a significant correlation between acute spikes and spontaneous abortion. A 20 µg/m<sup>3</sup> spike in PM<sub>2.5</sub> three days prior was associated with an 18% increase in the risk of pregnancy loss.<sup>172</sup>

**F7. PM<sub>2.5</sub> and the lung:** Prenatal and childhood exposure to PM can restrict lung growth and permanently reduce size, capacity, and function, including replacing the number of alveoli (air sacs) in the lungs with essentially scar tissue. Even one weekend of severe pollution during prenatal life or infancy can increase the risk of asthma many decades later in adulthood.<sup>189</sup>

PM triggers oxidative stress in the lung, inducing lung injury and scarring. PM causes, complicates, or exacerbates virtually all pulmonary diseases, from mild reactive airways disease to fatal pulmonary fibrosis. PM is associated with increased rates of serious lower respiratory infections, hospitalization, and death from most respiratory diseases, from neonates to the elderly.

Brief exposure to PM can temporarily reduce lung function even in young, healthy adults, and the reduction can last for a week after the pollution exposure is over. PM causes DNA damage, oxidative stress, and multiple avenues of cell death to lung epithelial cells.<sup>174</sup> Wildfire smoke may be ten times more toxic to the lung than other sources of particulate pollution.<sup>377</sup>

We cite the research below for its specific applicability to establishing the PM<sub>2.5</sub> NAAQS.

**F7(a). PM<sub>2.5</sub> and parameters of lung function:** All fractions of PM are associated with increases in the rate of respiratory and cardiovascular hospitalizations. Short-term increases in PM<sub>2.5</sub> of 10 µg/m<sup>3</sup> (lag 0-5 days) were associated with a 36% increase in respiratory hospitalizations.<sup>175</sup>

There are few things that correlate more closely with ultimate longevity than lung function.<sup>378</sup> Multiple studies have found reduced lung function in the general population with minimal long-term and short-term PM<sub>2.5</sub> exposure. Below are just a few of those studies.

Measuring subchronic PM<sub>2.5</sub> exposure, i.e., over 2 months, in children ages 6 to 15, researchers found that a 12 µg/m<sup>3</sup> increase was associated with a loss of lung function and lung capacity, as measured by forced expiratory volume (FEV<sub>1</sub>), forced vital capacity (FVC), and the ratios FEV<sub>1</sub>/FVC and maximal mid-expiratory flow (MMEF)/FVC.<sup>181</sup>



In over 6,000 adults in the Northeastern US, the association between long-term PM2.5 exposure and lung function and age-related lung function decline found that each 2 µg/m<sup>3</sup> increase in average of PM2.5 was associated with a 13.5 millimeter (ml) lower FEV1 and a 2.1 ml/year faster decline in FEV1. There were similar declines in FVC.<sup>182</sup>

A 5-µg/m<sup>3</sup> increase in PM2.5 concentration in 1-day average before lung function testing was associated with 7.9 cubic centimeter (cc) lower FEV1 (a measure of lung air flow over time).<sup>176</sup> Researchers also found linear relationships between 1- and 2-day averages of PM2.5 and FEV1 and FVC (lung capacity measurement) but not for longer-moving averages of exposure, suggesting that adverse effects on lung function occur acutely within 24 to 48 hours.

The authors stated, “Our study suggests that the general population, not just ‘unusually sensitive’ people, may experience respiratory effects from PM2.5, NO<sub>2</sub>, and ozone [O<sub>3</sub>] exposure in the ‘moderate’ range. However, these values represent the average effect estimate for a distribution of effects within the study population. Acute inflammatory responses to air pollution resulting in reduced lung function may be part of the triggering mechanism for the reported association between short-term air pollution exposure and respiratory hospitalization and mortality. The magnitude of the associations we found between short-term pollutant exposure and lung function is comparable to those reported by studies that included pollution levels above current EPA standards.” A similar result was found in a study of nearly 6,000 6-8-year-old children in Europe.<sup>177</sup>

The original Gauderman studies that established the loss of lung function in children exposed to air pollution were followed up 13 years later with studies that showed improved air quality was associated with improved lung function. In children followed for 4 years for lung function growth, the mean growth in FEV1 increased by 65.5 ml per decrease of 12.6 µg/m<sup>3</sup> in long-term PM2.5 exposure.<sup>183</sup> In a similar study in Stockholm, a decrease in median PM2.5 from 8.24 to 5.21 over 15 years was associated with an improved lung function growth rate of 4.63 ml/yr for FEV1 and 9.38 ml/yr for FVC.<sup>379</sup>

Deterioration of lung function and vulnerability to disease was well illustrated by a UK study of over 265,000 people without lung disease who were followed for 12 years. Per 5 µg/m<sup>3</sup> increase in long-term PM2.5 exposure, HR was 1.31 and 1.27 for progression from healthy to incident chronic lung disease and from incident chronic lung disease to chronic lung multimorbidity. The HR was 1.32, 1.24 and 1.91 for mortality risk from healthy, incident chronic lung disease, and chronic lung multimorbidity, respectively.<sup>360</sup>

An increase of 13.4 µg/m<sup>3</sup> PM2.5 in the day prior to testing was associated with an oxygen saturation decrease of .18% in elderly subjects.<sup>180</sup>

**F7(b). PM2.5’s effect on COPD and asthma:** COPD is associated with city-level PM2.5. One study found COPD prevalence increases 52% per 5 µg/m<sup>3</sup> increase in chronic PM2.5.<sup>199</sup> The

risks of hospitalization for COPD increased 9%, for an increase of 10  $\mu\text{g}/\text{m}^3$  PM2.5 measured as a moving average over 60 months.<sup>202</sup> Evaluating the relationship between short-term exposure to PM2.5 and COPD hospitalizations and mortality, a statistical summary of 12 studies, a 10  $\mu\text{g}/\text{m}^3$  increase in daily PM2.5 (lag days 0-7) was associated with a 3.1% increase in COPD hospitalization and a 2.5% increase in COPD mortality.<sup>185</sup>

In a study of 51,000 women in the US, self-reported wheeze, chronic cough, and doctor-diagnosed asthma were correlated with annual average PM2.5 estimated at their home address. An increase of 3.6  $\mu\text{g}/\text{m}^3$  increased the risk of asthma 20% and of wheezing 14%.<sup>178</sup>

Assessing the relationship between bronchitic symptoms (daily cough for three consecutive months) and improvements in PM2.5 in Southern California, researchers found that for a reduction of 6.8  $\mu\text{g}/\text{m}^3$  average PM2.5, symptoms decreased 32%.<sup>187</sup>

Multiple studies show an association between PM2.5 and various metrics of asthma. Annual average concentrations at the home address were associated with an increase in the incidence of an asthma diagnosis of 4% per exposure increase of 5  $\mu\text{g}/\text{m}^3$ .<sup>184</sup>

Among adults with active asthma, measuring PM2.5 for a 14-day average,  $\text{PM}_{2.5} \geq 7.07$   $\mu\text{g}/\text{m}^3$  was associated with a 4-5% higher asthma symptom prevalence. Even in the very low range of 4.00-7.06  $\mu\text{g}/\text{m}^3$  PM2.5, each 1- $\mu\text{g}/\text{m}^3$  increase was associated with a 3.4% increase in symptom prevalence.<sup>188</sup>

A meta-analysis of 87 studies found that with short-term PM2.5 exposure, an increase of 10  $\mu\text{g}/\text{m}^3$  was associated with a 2.3% increased risk of an asthma emergency room (ER) visit or hospitalization.<sup>186</sup> Other studies showed generally similar results for all types of respiratory hospitalizations.<sup>190,200,201,203</sup> A nationwide study of respiratory admissions in Italy over 3 years found that with daily increases of 10  $\mu\text{g}/\text{m}^3$  in PM2.5 (lag 0-5 days), hospitalizations for multiple types of respiratory illness increased 22%. The most at risk were the elderly, and strong effects were found even in non-urbanized areas.<sup>204</sup>

In a study of the association between PM2.5 at very low levels and asthma morbidity, children of low birthweight and an increase of 5.9  $\mu\text{g}/\text{m}^3$  in daily-measured PM2.5, experienced an 8% increased risk for an ER visit, hospitalization, or observational visit for wheezing or shortness of breath. The median PM2.5 concentration was only 7.8  $\mu\text{g}/\text{m}^3$ .<sup>195</sup>

**F7(c). PM2.5 and respiratory infections:** In a study of children in Atlanta, Georgia, PM2.5 was correlated to ER visits for pneumonia and upper respiratory infections in children less than five years old. A three-day moving average PM2.5 increase of 8.8  $\mu\text{g}/\text{m}^3$  prior to the hospital visit increased the risk of an ER visit of about 2%.<sup>179</sup>

A study of 146,000 Utah children, most younger than 2 years old, found that the risk of an acute lower respiratory infection increased within one week of an elevation in PM2.5 and peaked after 3 weeks with a cumulative 28-day odds ratio of 1.15 per 10  $\mu\text{g}/\text{m}^3$  increase in PM2.5.<sup>196</sup>

In a case-crossover study including 20,017 medical visits for infant bronchiolitis and 42,336 for otitis media, infant bronchiolitis risk was elevated for PM2.5 exposure on same day by 7% and 4 days prior to clinical encounter by 4%, per 10 µg/m<sup>3</sup> increase in PM2.5. Risks for pre-term infants were substantially increased.<sup>193</sup>

In a Utah study of patients admitted through ERs for pneumonia, researchers found PM2.5 increases of 10 µg/m<sup>3</sup> within the 6 days prior to presentation of pneumonia, increased risk of pneumonia 35%, and pneumonia-related mortality 50%, for levels above 12 µg/m<sup>3</sup>.<sup>194</sup>

A 10 µg/m<sup>3</sup> increase in daily PM2.5 concentrations was associated with a 6% increase in the risk of infant mortality from all causes, including pneumonia and congenital heart disease, and a 10% increase in the risk for post-neonatal mortality.<sup>197</sup>

Analyzing a total of 8,023,590 hospital admissions from 2011, researchers investigated the relationship between air pollution and outcomes from hospitalization and mechanical ventilation for acute respiratory distress syndrome. They found that for each 10 µg/m<sup>3</sup> increase in PM2.5 exposure, the mortality risk was increased 8%.<sup>191</sup>

**F7(c). PM2.5 and idiopathic pulmonary fibrosis:** Idiopathic pulmonary fibrosis is a devastating, invariably fatal pulmonary disease of mostly unknown origin. Investigating the relationship between air pollution and the natural progression of the disease, researchers found that mortality was significantly associated with long-term PM2.5. An increase of 10 µg/m<sup>3</sup> was associated with a nearly 800% increased risk of earlier mortality.<sup>192</sup>

**F8. PM2.5 and cancer:** Environmental contaminants are responsible for 70-90% of cancers,<sup>226,227</sup> and particulate pollution is one of the primary toxins with carcinogenic potential. Particulate pollution is associated with higher rates of breast, lung, prostate, cervical, brain, nasal, pharyngeal, esophageal, liver, pancreatic, and stomach cancer and with adult and childhood leukemia. Prenatal pollution exposure is associated with increased rates of multiple childhood cancers. World health experts now believe that as much as 30% of lung cancer is due to air pollution.<sup>206,225</sup>

The WHO has declared air pollution a leading environmental cause of cancer,<sup>207</sup> more important than second-hand cigarette smoke. The WHO placed it in the same category as asbestos and ionizing radiation.

Researchers recently discovered at least one mechanism for air pollution's role in causing lung cancer.<sup>205</sup> A combination of PM2.5 exposure and common mutations in the epidermal growth factor receptor (EGFR) and Kirsten rat sarcoma virus (KRAS) genes, likely a consequence of aging, are seen in about half of people with lung cancer who have never smoked. PM2.5 exposure promoted rapid changes in airway cells that had the mutations, driving them toward a cancer stem cell-like state. Particulate pollution triggers an influx of macrophages that release

the inflammatory mediator, interleukin-1 $\beta$ , promoting the expansion of cells with the mutations.

The studies cited below are directly relevant to the discussion of how far to strengthen the PM2.5 NAAQS.

**F8(a). PM2.5 and increased risk of cancer:** A recent study found reducing air pollution in 257 metropolitan areas would have as much of a reductive effect on the incidence of 12 difference smoking-related cancers as completely eliminating smoking in the population.<sup>33</sup> Those cancers included lung cancer, stomach cancer, kidney cancer, bladder cancer, pancreatic cancer, liver cancer, cervical cancer, oral cancer, colon cancer, esophageal cancer, cancer of the larynx, and acute myeloid leukemia.

In a Canadian study, each long-term 10  $\mu\text{g}/\text{m}^3$  increase in PM2.5 concentrations over a 20-year exposure period was associated with an increase in lung cancer incidence of 29% per 10  $\mu\text{g}/\text{m}^3$  increase in mean PM2.5.<sup>208</sup>

Analyzing 1,510,027 person-years in the Nurses Health Study, estimating average PM2.5 exposure for 72 months, a 10  $\mu\text{g}/\text{m}^3$  increase was associated with a 6% increased risk for lung cancer.<sup>211</sup>

A meta-analysis of 18 studies found that a 10  $\mu\text{g}/\text{m}^3$  increase in chronic PM2.5 exposure was associated with a 9% increased risk of lung cancer.<sup>212</sup> Another systematic review and meta-analysis of prospective studies found similar results,<sup>214</sup> but others have found much stronger associations.<sup>218</sup> In a Canadian study with a median PM2.5 exposure of just 9.1  $\mu\text{g}/\text{m}^3$ , a prospective study of 90,000 women found that an increase of 10  $\mu\text{g}/\text{m}^3$  was associated with an increased risk of lung cancer of 34%.<sup>220</sup>

The liver is another organ plausibly affected by PM due to its role in detoxifying xenobiotics embedded in PM. Rates of liver cancer are increased with long-term exposure to PM2.5. An increase of 10  $\mu\text{g}/\text{m}^3$  was associated with an increased risk of 34%.<sup>221</sup> Survival from liver cancer is also associated with long-term PM2.5 exposure. In a study of over 22,000 patients with liver cancer in California, for every 5.0  $\mu\text{g}/\text{m}^3$  increase in long-term PM2.5, all-cause mortality in these patients increased 18%.<sup>222</sup>

In a study of 11 European cohorts, a long-term increase in PM2.5 of 5  $\mu\text{g}/\text{m}^3$  over 14 years was associated with a 38% increased risk of gastric cancer and a 5% increased risk of upper digestive tract cancers.<sup>224</sup>

In an 18-year follow-up, bladder cancer was associated with long-term PM2.5. Per 5  $\mu\text{g}/\text{m}^3$  increase, the risk of cancer increased 9%.<sup>235</sup> Death from kidney and bladder cancer is associated with long-term PM2.5 exposure—an increase of 4.4  $\mu\text{g}/\text{m}^3$  was associated with an increased risk of both of about 14%.<sup>223</sup>

Several childhood cancers are associated with various types of air pollution. An increase of 7.84% in PM2.5 during the pregnancy was associated with an increased risk of leukemia, ependymoma, embryonal tumors, medulloblastomas, retinoblastomas, and Wilms tumors.<sup>213</sup>

**F8(b). Decreased rate of cancer survival:** Exposure to PM2.5 after diagnosis is associated with a significant increase in the risk for mortality among adult patients with lung, breast, kidney, bladder, and liver cancer, even after controlling for multiple confounders such as socioeconomic status, race, and stage at diagnosis.<sup>222,223, 231,233</sup> Proposed mechanisms for PM2.5's enhancing cancer mortality are similar to those that induce or promote the original cancer, "including genotoxic and epigenetic alterations, inflammation, xenogeneic effects or hormone dysregulation, or by reducing the immune system's ability to fight the cancer."<sup>226</sup> These biologic pathways may also reduce the malignancy's response to cancer treatment. PM2.5 may be associated with overall recurrence, with more aggressive recurrent cancers, and mortality from these recurrent cancers.<sup>232</sup>

Air pollution is associated with decreased survival in patients with all types of cancer, especially breast cancer, including those treated for cancer. Air pollution decreases the efficacy of chemotherapy. Lung and cardiovascular diseases are important non-cancer causes of death among cancer patients and survivors, both of which are enhanced by air pollution. Childhood cancer survivors treated with chemotherapy have significantly higher risk for a respiratory hospitalization after exposure to PM2.5 than the general public does.<sup>234</sup>

In an analysis of 21 cohort studies from around the globe, the risk of lung cancer morbidity or mortality increased 7.23% for every 10 µg/m<sup>3</sup> increase in chronic PM2.5.<sup>217</sup>

Lung cancer mortality was assessed among 188,699 lifelong never-smokers drawn from the nearly 1.2 million Cancer Prevention Study-II participants enrolled by the American Cancer Society in 1982 and followed prospectively through 2008. Each 10 µg/m<sup>3</sup> increase in mean PM2.5 was associated with a 15-27% increase in lung cancer mortality.<sup>209</sup>

In a whole-population Chinese cohort study, long-term exposure to PM2.5 reduced survival rates of lung cancer patients. An increase of 10 µg/m<sup>3</sup> was associated with an increased mortality rate of 6.5%.<sup>334</sup>

In a California study of over 255,000 cases of breast cancer, long-term PM2.5 exposure was significantly associated with breast cancer survival rate. Per 5 µg/m<sup>3</sup> long-term exposure, there was an 86% higher likelihood of early mortality, controlling for numerous other variables.<sup>210</sup>

In a broader study of cancer mortality's association with annual average PM2.5, 67,000 patients were followed for 10 years. The study found that an increase of 10 µg/m<sup>3</sup> PM2.5 was associated with an increased risk of mortality of 22% for multiple types of cancer.<sup>219</sup>

**F9. PM2.5 and metabolic, endocrine, and kidney disease:** PM2.5 promotes the development of inflammation in lungs, gut, and hypothalamus, and in turn, alters adipose tissue homeostasis.<sup>331</sup> More exposure to PM, even short term, decreases insulin sensitivity and

glucose tolerance, increases rates of Type I<sup>357</sup> and Type II diabetes, promotes obesity,<sup>359</sup> and increases lipid deposition and risk of metabolic syndrome.<sup>317</sup>

The biological pathways linking particulate pollution to diabetes include “endothelial dysfunction, dysregulation of the visceral adipose tissue through inflammation, hepatic insulin resistance, elevated hemoglobin A1c level, elevated blood pressure, alterations in autonomic tone,”<sup>244</sup> and vascular insulin resistance by inducing pulmonary oxidative stress.<sup>246</sup>

Prenatal exposure to PM has a particularly strong association with childhood obesity. Metabolic function can be evaluated by measuring leptin and adiponectin; both are adipocyte-secreted hormones important in energy, glucose, and lipids homeostasis. Elevated levels in cord blood are considered potential predictors of the early development of obesity.

Lipid metabolism is impaired, good cholesterol (HDL) is decreased, and bad cholesterol (LDL) is increased with more air pollution.<sup>345</sup> Air pollution impairs thyroid function in pregnant mothers, thyroid development in the fetus, and thyroid function in newborns. Impaired thyroid function is a likely mechanism for air pollution’s causing LBW and can impair fetal brain development. Diesel exhaust impairs liver function.

A few studies have now associated maternal PM exposure with abnormal thyroid hormone levels.<sup>254</sup> The clinical significance of that is not clear yet, but given the critical role that the thyroid plays in fetal development, especially of the brain, it only adds to the reasons for tighter EPA regulations.<sup>259</sup>

PM impairs kidney function,<sup>296</sup> and kidney disease is one of the top 10 causes of death worldwide. It is also an important risk factor for cardiovascular disease. Early evidence shows PM2.5 impairs kidney function at the microscopic level through direct particle accumulation, inflammation, oxidative stress, apoptosis, DNA damage, autophagy, and endothelial dysfunction. It impairs the renin-angiotensin system, and immune complex deposition.

The studies cited below have quantitative relevance to tightening the PM2.5 NAAQS.

**F9(a). PM2.5 and the risk of type II diabetes and glucose intolerance:** An average increase in PM2.5 during pregnancy of 3.2 µg/m<sup>3</sup> was associated with an 11% increase in umbilical cord adiponectin levels.<sup>247</sup> Umbilical cord plasma insulin levels are increased with maternal exposure to PM2.5. Following nearly 600 mother/infant pairs, cord plasma insulin levels increased 15.8% for each 2.4 µg/m<sup>3</sup> increase in PM2.5, corresponding to a pre-pregnancy 9 kg/m<sup>2</sup> higher BMI. The average PM2.5 exposure was 13.7 µg/m<sup>3</sup>.<sup>250</sup>

In a study of Los Angeles, California, Latino children, ages 8 to 15 years, that were at increased risk of diabetes because of obesity, the children were followed for 3.4 years. During that time, a 4 µg/m<sup>3</sup> higher long-term PM2.5 was associated with a 3.3% faster decline in insulin sensitivity and a 28.5% higher acute insulin response to glucose at age 18.<sup>249</sup>

In more than 4,200 Chinese children ages 6-13, fasting blood glucose was 2.3% higher per 10  $\mu\text{g}/\text{m}^3$  increase in PM2.5, measured 186 days prior to the blood draw.<sup>253</sup> In a study of over 38,000 adults in rural China and three-year-averaged PM2.5 exposures, a 1  $\mu\text{g}/\text{m}^3$  increase in PM2.5 was associated with an OR for type II diabetes of 1.02, and the black carbon component of PM2.5 was the most responsible constituent.<sup>341</sup>

In a study of glucose metabolism in over 7,000 non-diabetic adults, increases of 5.7  $\mu\text{g}/\text{m}^3$  in 28 day mean averages of PM2.5 were associated with higher blood glucose levels, i.e., 0.91 mg/dL, and a 4.0  $\mu\text{g}/\text{m}^3$  increase over 91 days was associated with an increase in HbA1c of .07 pp.<sup>251</sup>

In a 2010 US study, diabetes prevalence increased with increasing PM2.5 concentrations. A 1% increase in diabetes prevalence was seen with a 10  $\mu\text{g}/\text{m}^3$  increase in PM2.5 exposure, even for counties with air quality within the annual PM2.5 NAAQS (15 $\mu\text{g}/\text{m}^3$  at that time). Those counties with the highest exposure showed a > 20% increase in diabetes prevalence compared with that for those with the lowest levels of PM2.5, an association that persisted after controlling for diabetes risk factors.<sup>237</sup> Stronger associations have been found since.

In a study of over 24,000 nurses and a 5-year annual mean of PM2.5 exposure, a 3.1  $\mu\text{g}/\text{m}^3$  increase in PM2.5 was associated with an 11% increase risk of type II diabetes.<sup>245</sup>

Tracking six years of PM2.5 exposure to 62,000 non-diabetic adults, a Canadian study found that an increase in PM2.5 of 10  $\mu\text{g}/\text{m}^3$  was associated with an increased risk of an eventual diagnosis of type II diabetes of 11%.<sup>238</sup> Two other meta-analyses found nearly identical results.<sup>241,256</sup> Another meta-analysis of 10 cohort studies found an increased risk for type II diabetes of 39% per 10  $\mu\text{g}/\text{m}^3$  increment in PM2.5,<sup>243</sup> and another meta-analysis of 11 cohort studies found that a 10- $\mu\text{g}/\text{m}^3$  increase in PM2.5 in long-term exposure increased the risk of type II diabetes by 25%.<sup>248</sup>

In a Canadian study of 2.1 million adults with a long-term mean PM2.5 exposure level of only 8.7  $\mu\text{g}/\text{m}^3$ , a 10  $\mu\text{g}/\text{m}^3$  increase was associated with an increased risk of diabetic-related mortality of 49%. The monotonic change in risk persisted to PM2.5 concentration < 5  $\mu\text{g}/\text{m}^3$ .<sup>239</sup> A meta-analysis of 12 studies found that an increase of 10  $\mu\text{g}/\text{m}^3$  long-term PM2.5 was associated with a 12% increased risk of diabetic mortality.<sup>242</sup>

**F9(b). Obesity, metabolic syndrome, and thyroid dysfunction:** Obesity is associated with PM2.5. In a study population followed for eight years, annual PM2.5 increases of 4.5  $\mu\text{g}/\text{m}^3$  were associated with a 4.53% higher fat mass.<sup>328</sup>

Metabolic syndrome (defined as central obesity plus two out of four additional risk factors, i.e., elevated triglycerides, reduced high-density lipoprotein cholesterol, elevated blood pressure, or elevated plasma glucose) is associated with PM2.5. Comparing metabolic syndrome at baseline and again 5 years later, researchers found a mean annual PM2.5 increase of 1.5  $\mu\text{g}/\text{m}^3$  was associated with an 19% increased risk of developing metabolic syndrome.<sup>252</sup>

Metabolic dysfunction–associated fatty liver disease is associated with every size fraction of PM. For long-term PM<sub>2.5</sub>, increases of 10 µg/m<sup>3</sup>, the risk increased 29% among 90,000 people in China.<sup>257</sup>

In over 2,000 California newborns, prenatal monthly averages of PM<sub>2.5</sub> were associated with total thyroid hormone TT4 levels. An increase of 16.3 µg/m<sup>3</sup> PM<sub>2.5</sub> was associated with a 1.2-µg/dL increase in TT4.<sup>254</sup> Increases of 5 µg/m<sup>3</sup> in PM<sub>2.5</sub> short-term exposure during the first trimester of pregnancy were associated with a 21% increased risk of hypothyroxinemia in pregnant women.<sup>255</sup>

**F9(c). PM<sub>2.5</sub> and chronic kidney disease:** Globally, nearly 7 million people are estimated to have chronic kidney disease attributable to PM<sub>2.5</sub>.<sup>295</sup> In a Chinese population of 47,000 with a 2-year mean PM<sub>2.5</sub> exposure of 57.4 µg/m<sup>3</sup>, an increase of 10 µg/m<sup>3</sup> in PM<sub>2.5</sub> was associated with a 28% increased risk of chronic kidney disease.<sup>258</sup> In a US Medicare population of 1.1 million, county-measured PM<sub>2.5</sub> showed an association of 4 µg/m<sup>3</sup>, with an increased risk for chronic kidney disease of 3%.<sup>260</sup> In an observational cohort study of nearly 2.5 million veterans, chronic PM<sub>2.5</sub> exposure was linked to multiple metrics of diminished kidney function and kidney disease. The median baseline exposure was 11.8 µg/m<sup>3</sup>, and a 10 µg/m<sup>3</sup> increase in PM<sub>2.5</sub> over nearly 9 years of follow-up was associated with a 21-26% increased risk of diminished glomerular filtration rate, diagnosis of chronic kidney disease, and kidney failure.<sup>284</sup> In a Chinese cohort of over 2,000 followed for 5 years, each 10 µg/m<sup>3</sup> of long-term PM<sub>2.5</sub> exposure was associated with an 84% increased risk of chronic kidney disease.<sup>333</sup>

Chronic PM<sub>2.5</sub> exposure is also associated with increased mortality in patients with chronic kidney disease. The mortality HR per PM<sub>2.5</sub> increase of 4.0 µg/m<sup>3</sup> was 1.97 for ischemic heart disease and 1.42 for kidney disease among those patients concomitantly with hypertension.<sup>338</sup>

PM<sub>2.5</sub> is also associated with mortality rates of patients on dialysis. Short-term increases of PM<sub>2.5</sub> of 10 µg/m<sup>3</sup> are associated with a mortality increase of 7%.<sup>325</sup> There was no evidence of a threshold in the exposure-response relationship.

**F10. Miscellaneous health impacts of PM<sub>2.5</sub>:** Air pollution exposure rapidly increases reactive oxygen species production, causes systemic oxidative stress,<sup>262,273</sup> triggers an inflammatory chemical cascade,<sup>283</sup> increases in serum concentrations of the stress chemicals cortisol, cortisone, epinephrine, and norepinephrine,<sup>282</sup> endothelial cell death, cytotoxicity,<sup>267</sup> macrophage infiltration, and triggers the release of damaging extracellular vesicles.<sup>316</sup> PM penetrates intracellular structures, including the nucleus of the cell, interfering with chromosomal and mitochondrial function<sup>264</sup> and causing DNA damage, changes in DNA methylation,<sup>265, 317</sup> and epigenetic damage.<sup>283,318</sup> The consequences are widespread.

In addition to what has been addressed so far, PM has been associated with delayed maturation of the fetal immune system and immune suppression,<sup>373</sup> alteration of the gut microbiome beginning in infancy,<sup>370</sup> inflammatory bowel disease,<sup>288,314</sup> childhood obesity,<sup>304</sup> numerous types of bacterial and viral infections,<sup>272,274,278,292,320</sup> lupus, juvenile and adult



arthritis,<sup>263,300</sup> endocrine-disrupting effects on developmental puberty,<sup>277</sup> osteoporosis,<sup>286,303,311</sup> and sleep apnea.<sup>378</sup> Air pollution can induce liver toxicity<sup>268</sup> and accelerate liver inflammation<sup>281</sup> and steatosis. Pollution exposure in utero or in infancy increases the likelihood of osteoarthritis and rheumatoid arthritis decades later in adulthood.<sup>298</sup> PM is able to penetrate the skin, cause damage to the skin and corneas,<sup>307,313</sup> and increase rates of autoimmune skin disorders;<sup>346</sup> it is associated with age-related eye diseases like glaucoma.<sup>322</sup> PM accelerates the aging process<sup>271</sup> and decreases life expectancy.<sup>297</sup>

Studying over 95 million Medicare inpatient claims for 13 years, short-term PM<sub>2.5</sub> exposure was associated with increased risk of hospitalization for multiple diseases, including those not frequently studied, such as septicemia, fluid and electrolyte disorders, urinary tract and skin and subcutaneous infections, acute and unspecified renal failure, and intestinal obstruction without hernia, phlebitis, thrombophlebitis, and thromboembolism.<sup>301</sup> For each 1 $\mu$ g/m<sup>3</sup> increase in PM<sub>2.5</sub>, lag 0-1, the absolute increase in risk of hospital admissions for all these disease groups ranged from 0.02 to 0.68 per 10 million people at risk per day, and the relative percentage increase in risk of these hospital admissions ranged from 0.05% to 0.40%. **When restricting the analysis to days with daily PM<sub>2.5</sub> concentrations of 25  $\mu$ g/m<sup>3</sup> or less, absolute and relative percentage increases in risk of hospital admission remained consistent with the main analysis for most disease groups.**

Furthermore, each unit increase in lag 0-1 PM<sub>2.5</sub> was associated with an annual increase of 5,692 hospital admissions, 32,314 days in hospital, and 634 deaths at discharge. It was also associated with \$100 million annual inpatient and post-acute care costs, and \$6.6 billion in the value of statistical life due to the lives lost at discharge.

C-reactive protein is a marker of systemic inflammation and is associated with numerous chronic diseases. A 3- to 7-day moving average of PM<sub>2.5</sub> is positively associated with C-reactive protein concentrations. A 5  $\mu$ g/m<sup>3</sup> higher 5-day moving average of PM<sub>2.5</sub> was associated with 4.2% higher circulating C-reactive protein.<sup>279</sup>

In a study of multimorbidity status based on 41 physical and mental conditions, over 364,000 people with a mean age of 52 were assessed and correlated to their PM<sub>2.5</sub> exposure. A 1.71  $\mu$ g/m<sup>3</sup> increase in PM<sub>2.5</sub> was associated with an OR of 1.21. It is notable that the threshold between the third and fourth exposure quartiles was only 10.56  $\mu$ g/m<sup>3</sup>.<sup>366</sup>

In preschool-age children, short-term spikes in PM<sub>2.5</sub> were associated with symptom onset of juvenile arthritis. Per 10  $\mu$ g/m<sup>3</sup> increase in 3-day lag moving average, the risk increased 76%.<sup>275</sup>

PM aggravates inflammatory autoimmune disorders like lupus erythematosus (LE).<sup>287</sup> In a group of 237 patients with LE, a 10  $\mu$ g/m<sup>3</sup> increase in PM<sub>2.5</sub> averaged over 48 hours prior to a clinic visit, there was a 34% higher risk of serum-specific autoantibodies and a 28% increased number of renal tubular cellular casts, i.e., markers of LE disease activity.<sup>261</sup>

Sleep apnea is a steadily increasing public health problem, now affecting over 25% of American adults. The incidence of sleep apnea correlates with long-term PM2.5. A 5 µg/m<sup>3</sup> increase in annual PM2.5 was associated with 60% greater odds of being diagnosed with sleep apnea.<sup>293</sup>

Uterine fibroids may afflict as many as 60% of women; they are a common reason for hysterectomies. The incidence of uterine fibroids correlates with PM2.5. In a cohort-based, case control study over 10 years in Taiwan, an increase in long-term PM2.5 of 10 µg/m<sup>3</sup> was associated with a 10.5% increase in the risk of being diagnosed with uterine fibroids.<sup>294</sup>

In six low- and middle-income countries, frailty (defined by the frailty index) in older adults correlates to long-term PM2.5 exposure. Each 10 µg/m<sup>3</sup> increase in PM2.5 was associated with a 30% increase in frailty.<sup>306</sup>

Numerous studies have been published showing not just mortality risks quantifiable to PM2.5 exposure, but shortened life expectancy. In a nationwide study of Taiwan over 7 years, 10 µg/m<sup>3</sup> long-term exposure was associated with a shortened life expectancy of .3 years.<sup>297</sup>

**F11. Environmental justice:** Populations of color and the economically disadvantaged bear a disproportionate burden of health impacts associated with PM2.5 exposure.<sup>24,25,26</sup> While this is not likely to be based on different physiologic response to environmental toxins, it nonetheless mitigates for stricter standards than what would otherwise be indicated by studies of large heterogeneous populations. Not only are these groups disproportionately impacted by similar concentrations of PM2.5 and other pollutants, but these same groups are invariably exposed to higher concentrations, adding to the need for stricter standards.<sup>27</sup> They are particularly exposed to higher short-term PM2.5.<sup>321</sup>

A recent study by the Center for Air, Climate, and Energy Solutions found that the disparity in soot exposure between White, Black, Latino, and Asian Americans was consistent throughout the country, in both rural and urban settings, and at all income levels. Seventy-five percent of Black Americans are exposed to PM2.5 concentrations greater than 8 µg/m<sup>3</sup> each year, compared to 59% of white Americans. “Low-income populations currently have 49% higher likelihood of living in areas that exceed 12 µg/m<sup>3</sup> in comparison with wealthier populations. This difference drops to low-income populations having a 5% higher likelihood of living in areas that exceed 8 µg/m<sup>3</sup>.”<sup>23</sup>

Low-income populations have a 49% higher likelihood of being chronically exposed to the current annual standard 12 µg/m<sup>3</sup> or greater, compared with wealthier populations. This difference drops to low-income populations’ having a 5% higher likelihood of living in areas that exceed 8 µg/m<sup>3</sup>. Furthermore, Black populations over 65 years old have three times as many PM2.5-attributable deaths per capita compared to all other races. ER visits for asthma show an even starker contrast for risk based on race, with a 600% higher asthma ER visit rate for non-white and white Hispanic populations compared to Caucasians.<sup>28</sup>

In a review of 124 articles that explored race and air pollution as risk factors for poor pregnancy outcome, 13% specifically compared pregnancy outcomes among two or more racial groups. “Findings across all reviewed articles showed more adverse pregnancy outcomes (pre-term birth, SGA, LBW, and stillbirths) related to exposure to air pollution among Blacks and Hispanics than among non-Hispanic Whites.”<sup>365</sup>

Even within areas of similar economic, minority, and ethnic composition, there are large discrepancies in the spacial distribution of pollution, such that people can experience dramatically different levels within the same monitoring district. Severe hot spots of pollution can be completely missed by state monitoring networks. For example, a household downwind of a neighbor burning wood for heat during the winter can experience Beijing, China, levels of pollution, while an upwind neighbor can enjoy clean air. Studies from California show that within a single square kilometer of a residential area, concentrations of wood smoke can vary as much as 2,500 times. The highest measured concentrations were up to 100 times higher than the community average.<sup>29</sup> Similar distribution discrepancies are in play within neighborhoods adjacent to freeways or near industrial facilities.

There is a difference between genders in air pollution risks. Women are not thought of as a disadvantaged demographic, but statistically they are more likely to have cardiovascular complications related to air pollution. For example, several studies show women, especially post-menopausal women, have higher risk of cardiovascular disease from air pollution compared to men,<sup>41,42,380</sup> Women have smaller coronary arteries and are more likely to develop disease in the coronary microvasculature.<sup>382</sup>

A meta-analysis of 25 studies found the women-to-men RRR of ischemia heart disease (IHD) was 1.05 per 10  $\mu\text{g}/\text{m}^3$  increment in PM<sub>2.5</sub> exposure, indicating significant excess risk of IHD in women.<sup>381</sup> This should be factored into the NAAQS.

## **G. ECONOMIC CONSIDERATIONS**

### **THE ECONOMIC BENEFIT OF TIGHTENING THE ANNUAL PM<sub>2.5</sub> STANDARD IS OVERWHELMINGLY POSITIVE, NATIONALLY, AND IN UTAH**

Prior to the COVID pandemic, the World Health Organization concluded that air pollution is the leading avoidable cause of death worldwide, including tobacco smoking, alcohol use, road accidents and transmissible diseases such as AIDS, malaria, and tuberculosis.<sup>384</sup> This health hazard associated with air pollution has prompted the adoption of increasingly stringent environmental regulations, but disagreement remains over how stringent those regulations should be.

In the United States, even though the Clean Air Act forbids it, the EPA still sees air quality standards as requiring a difficult tradeoff between their benefits to health and the costs that they impose on the economy, as investment capital is diverted from productive activities towards pollution control. The tradeoff is conventionally framed as one of jobs versus the environment. Recent research, however, shows that it is more accurate to first analyze the tradeoff between the direct economic or “market” benefits of reducing pollution exposure and its economic or “market” costs, before adding avoided healthcare costs and “welfare” benefits to the equation. Doing so reveals that the balance tilts heavily toward tighter air pollution controls, especially when it involves PM2.5.

G1(a). There are four channels through which PM2.5 pollution can reduce aggregate economic activity:

- Reducing the number of workers (through deaths and migration).
- Reducing the number workhours per worker, if they are too sick to work or have to miss work to care for a sick relative.
- Reducing the productivity of workers during workhours
- Reducing the quality of natural capital, which is an input into production in particular in the agriculture sector.

Recent advances in econometric modelling and available data show that the effect of changes in PM2.5 concentrations on the first three channels is much greater than previously estimated. Typically, in cost-benefit analyses supporting air pollution control policies, the estimated “market” benefits (e.g., reduced absenteeism at work), are minor compared to estimates of non-market impacts such as avoided deaths. For example, the US Environmental Protection Agency estimated that total benefits of the Clean Air Act Amendments between 1990 and 2020 amounted to \$12 trillion (2006 dollars). It attributed 85% of these benefits to reduced premature mortality.<sup>385</sup> Similarly, recent analysis by the OECD estimates that the total annual market costs of outdoor air pollution (including reduced agricultural yields, absenteeism at work and health expenditures) amount to 0.3% of global GDP in 2015 while the costs from non-market impacts represent 6% of total income.<sup>386</sup>

A series of micro studies, however, shows that PM2.5 exposure can cause very substantial direct reductions in labor productivity by impairing cognitive or physical ability. (For a summary of these studies see Graff Zivin and Neidell, 2018).<sup>387</sup> These studies primarily observe the changes in individual worker productivity caused by concurrent exposure to high concentrations of PM2.5. For example, air pollution has been shown to decrease workers’ productivity at a large farm in California,<sup>388</sup> at a garment manufacturing facility in India,<sup>389</sup> or at a Chinese call center.<sup>390</sup> There is also evidence that pollution affects productivity in high-skill tasks, such as student performance in standardized high-school examinations<sup>391</sup> or investors’ performance at the New York Stock Exchange.<sup>392</sup> Most recently, a large-scale study using data taken from the near-universe of manufacturing plants in China found evidence that a 1 $\mu$ g/m<sup>3</sup> increase in average annual PM2.5 concentration (up from a mean of 53  $\mu$ g/m<sup>3</sup>) reduces value added per worker (worker productivity) by 1.1%.<sup>393</sup>

For the most part, these studies evaluate impacts of PM2.5 on specific workforces in developed countries (e.g. box packers, stock traders) or in less developed countries with high pollution levels (China, India). A 2020 study entitled “The Economic Cost Of Air Pollution: Evidence From Europe,” (OECD Study)<sup>394</sup> conducted by the economic research staff of the Organization of Economic Co-operation and Development, avoids the heterogeneity of the earlier studies by estimating the impact of variations in PM2.5 exposure on general levels of economic activity in a developed country context, using regional data from Europe.

The OECD Study finds that changes in annual PM2.5 concentrations cause changes in GDP levels per worker, and per capita, for the European Union member countries. By analyzing the response of aggregate economic output, this approach avoids the difficulties of modelling idiosyncratic populations as well as potential productivity displacement effects within a year, and factor reallocation across firms. This high resolution study uses data from European NUTS3 regions (analogous to counties in the United States), between 2000 and 2015. It thereby reflects the effects of PM2.5 on developed economies in a contemporaneous period. It also uses a hybrid of weather satellite and on-ground observations to estimate PM2.5 concentrations.

The OECD Study employs a two-stage regression model. A set of two instrumental (proxy) variables are used as explanatory variables in the first stage. One is the number of days in a given “county,” in a given year. The other is shifts in wind direction. These data on inversion event frequency and shifts in wind direction were regressed on PM2.5 concentrations. The response of PM2.5 concentrations to changes in inversion-event frequency and to changes in wind direction each was highly statistically significant, and robust to changes in weather control variable specification, and fixed geographic and time effects.

Inferred PM2.5 concentration is the explanatory variable used for the second stage regression. The dependent variable is per capita GDP. As noted above, PM2.5 pollution can affect aggregate economic activity through its impact on three labor-related quantities-- population size, presence at work, and productivity at work. Table 4 of the OECD Study shows that increasing PM2.5 concentration by 1  $\mu\text{g}/\text{m}^3$  (approximately a 10% increase) decreases output per capita by 1.1%. It can be inferred from the table’s point estimates that 96% of the effect on output per capita is due to reduced labor productivity, while the remainder is due to a decrease in the population available to work. This inference is consistent with the medical literature that finds that PM2.5 pollution primarily affects the mortality of old people and young children (neither of which contribute significantly to economic activity in developed economies), but rarely affects mortality among working-age individuals.

The response of GDP for the EU countries to annual changes in PM2.5 concentrations was highly statistically significant, and robust to geographic subsampling, to the removal of geographic fixed effects, and to the presence of a control variable for SO2 concentrations—the pollutant most highly correlated with PM2.5 concentrations

Using the OECD Study's baseline GDP-weighted estimates, it found that a 1  $\mu\text{g}/\text{m}^3$  decrease in PM2.5 concentrations increases Europe's GDP by 1.1%. While large relative to previous studies of labor productivity effects, this result is comparable to those reported in the emerging literature that focuses on the aggregate productivity effects of pollution. As of 2020, only three peer-reviewed studies estimated the effects of long-term exposure to PM2.5 on a general population, but their findings are consistent with the OECD Study results.

In a study that includes nearly all Chinese manufacturing plants, Fu et al. estimate that a 1  $\mu\text{g}/\text{m}^3$  increase in PM2.5 concentrations causes a decrease in labor productivity of 1.1%.<sup>395</sup> Since this increase represented only a 2.2% change from baseline PM2.5 concentrations, compared to the 10% change from baseline investigated by the OECD Study, it estimates a much higher labor productivity response. This suggests that air pollution has a substantial impact on productivity even at much lower concentration levels than those observed in China, and the effect is non-linear. Borgschulte et al. focus on PM2.5 pollution peaks in the US caused by forest fires. They estimate that spending one day exposed to a smoke plume increases PM2.5 concentration by 4  $\mu\text{g}/\text{m}^3$ , which causes a reduction in income of 10% across all workers.<sup>396</sup> If the effect is linear, this would imply that a 1  $\mu\text{g}/\text{m}^3$  increase in pollution causes a 2.5% reduction in income, which is over twice as high as the OECD Study's estimate.

As noted, the OECD Study estimates that a 1  $\mu\text{g}/\text{m}^3$  decrease in annual PM2.5 concentrations increases GDP by 1.1%. In 2022, the European Union's GDP was \$16.6 trillion (USD). Applying the OECD Study result to that GDP amount implies that a reduction in PM2.5 concentrations of 1  $\mu\text{g}/\text{m}^3$  would increase the EU's GDP by \$182.6 billion. In 2022, the GDP of the United States was roughly \$26 trillion. Applying the OECD Study result to the considerably larger GDP amount **for the United States implies that 1  $\mu\text{g}/\text{m}^3$  decrease in its annual PM2.5 concentrations would increase its annual GDP by \$286 billion.**

Whether reducing an NAAQS annual standard for PM2.5 by 1  $\mu\text{g}/\text{m}^3$  actually results in a reduction in national average annual PM2.5 concentrations by that amount depends on the baseline concentration of PM2.5 as well as the spatial and temporal distribution of PM2.5 emissions—a complex modelling exercise beyond the scope of these comments. The EPA, however, has made estimates that allow the benefits and costs of tightening the annual PM2.5 by 1  $\mu\text{g}/\text{m}^3$  (from 9 micrograms to 8 micrograms) to be inferred.

The EPA estimates that reducing the annual PM2.5 standard from the current 12  $\mu\text{g}/\text{m}^3$  to 9  $\mu\text{g}/\text{m}^3$  would require additional compliance measures in 51 counties across the nation and avoid \$43 billion in annual health-related costs. Separately, it estimates that reducing the current annual PM2.5 standard from 12 to 8  $\mu\text{g}/\text{m}^3$  would require additional compliance measures in 141 counties and avoid \$95 billion in health-related costs. These estimates from the EPA Policy Assessment are summarized in the January 9, 2023, edition of the E&E News.<sup>397</sup> Because the EPA separately estimates the benefits and costs of tightening the current standard to 9 micrograms, and then estimates the benefits and costs of tightening the current standard to 8 micrograms, it allows us to estimate the by 1 microgram by simply finding the difference between those two estimates.

G2. The arithmetic needed to find the difference in impact between the two tightened standards is as follows: The EPA estimates that the health-related benefits associated with tightening to 9 micrograms is \$43 billion. It estimates that the health-related benefits associated with tightening the standard to 8 micrograms is \$95 billion. The difference between the two is \$52 billion ( $\$95 - \$43 = \$52$ ). **\$52 billion is the estimated benefit from tightening the annual standard to 8 ug/m<sup>3</sup> instead of 9, if the dose response curve is linear.**

A more complete estimate of the benefit of tightening the annual PM<sub>2.5</sub> standard from 9  $\mu\text{g}/\text{m}^3$  to 8  $\mu\text{g}/\text{m}^3$  requires that effects on labor productivity be taken into account. As discussed above in connection with the OECD Study, **a 1  $\mu\text{g}/\text{m}^3$  decrease in annual PM<sub>2.5</sub> concentrations can be expected to increase national GDP by \$286 billion due to a 1.1% increase in labor productivity.** Therefore, a more complete estimate of the benefit of tightening the annual PM<sub>2.5</sub> standard from 9 to 8 micrograms should take both health-related cost reductions and productivity increases into account. These benefits are separate and distinct. Summing them yields a plausible comprehensive estimate of \$338 billion ( $\$286 + \$52 = \$338$ ) in annual benefits that would be realized by tightening the annual PM<sub>2.5</sub> standard to 8  $\mu\text{g}/\text{m}^3$  instead of 9  $\mu\text{g}/\text{m}^3$ . The case for tightening the annual PM<sub>2.5</sub> standard to 8  $\mu\text{g}/\text{m}^3$  becomes even more compelling when the benefits are compared to the EPA's estimate of the associated annual compliance costs.

### **THE ECONOMIC BENEFITS TO THE WASATCH FRONT OF TIGHTENING PM<sub>2.5</sub> STANDARDS FAR OUTWEIGHT THEIR COMPLIANCE COSTS**

With respect to air quality, the Greater Salt Lake City Metropolitan area is beleaguered. It has never met federal attainment levels for ozone or 24-hour PM<sub>2.5</sub> pollution. Its severe nonattainment status has earned it consistent “F” ratings by the American Lung Association for both measures. The concurrent negative impact of exceedances by both pollutants makes it especially important that the EPA use all the tools in its toolbox—tightening both its annual and its 24-hour standard—to mitigate the harm to area residents’ health and their economy from currently excessive concentrations of PM<sub>2.5</sub>. According to the American Lung Association’s 2019 State of the Air report,<sup>398</sup> the Salt Lake Metro Area ranked 7th out of 217 metropolitan areas for highest 24-hour PM<sub>2.5</sub>, and 11th out of 228 metropolitan areas for highest ozone pollution. For 24-hour PM<sub>2.5</sub>, this report ranks Salt Lake next below Los Angeles.

The Salt Lake metro area now faces three sources of increases in PM<sub>2.5</sub> going forward. As the regional climate rapidly heats up and dries out, it faces the likelihood that the adjacent Great Salt Lake will completely dry up over the next decade, exposing its vast, toxin-laced lakebed to wind erosion. This can be expected to massively increase particulate pollution in the metro area—some of it PM<sub>2.5</sub>. The hotter, drier climate also is increasing the frequency and scale of forest fires in the West, greatly increasing the Salt Lake metro area’s episodic exposure to PM<sub>2.5</sub>. In addition, the Utah State government has announced plans to transform Salt Lake into an international logistics hub. If these plans succeed, it will dramatically increase the number of diesel-powered trucks and trains moving within the metro area, and their emissions of PM<sub>2.5</sub>.

Seasonal factors are central to understanding why the Salt Lake area's air is as bad as it is. Like many metropolitan areas in the Western United States, Salt Lake is situated in an atmospheric basin that is surrounded by mountains. In the winter, cold air at ground level can get trapped beneath warmer air as a result of temperature inversions. These often occur after a snowstorm, when snow cover cools ground level air, or shortly after dusk and throughout the night, when there's no direct sunlight.

In winter, Salt Lake residents often find themselves trapped in a "bottle" of cold, stagnant air. The pollutants in that air have no outlet, causing pollution to build until the weather changes. Consequently, winter months can have more than five times the PM2.5 concentration as summer months. December, January, and November are typically Salt Lake's worst months for air quality. In 2019, they had Air Quality Index ratings of 60, 57, and 39, respectively, which are clearly unhealthy under the federal guidelines. June, May, and April are Salt Lake City's best months for air quality, with AQI ratings of 10, 10, and 11, which are clearly within federal guidelines.<sup>399</sup> Nevertheless, if the Salt Lake area's air quality were only evaluated and regulated from the perspective of annual averages, the Salt Lake area's air quality would appear to fall in the AQI "good" range. If averaged over all of 2019, the Salt Lake area's daily AQI would have been 25. Looked at only from the standpoint of annual averages, Salt Lake's air quality would raise no regulatory concerns, and provided no grounds for federal regulatory relief.

Annual averages conceal the intense but transient pollution events which commonly afflict the Salt Lake area, causing measurable harm to its residents on a substantial number of "unhealthy air" days each year. Between 2016 and 2018, for example, the Salt Lake area experienced a weighted average of 25.7 days of unhealthy ozone and 11.5 days of unhealthy PM2.5. NAAQS targets a weighted average of no more than 3.2 days of unhealthy pollution a year.<sup>400</sup>

Such frequent violations of the NAAQS target, and the harm that flows from them, would be overlooked, unregulated, and unmitigated if only the annual PM2.5 standard were applied to the Salt Lake area. Interactive graphs published by the Utah Department of Environmental Quality,<sup>401</sup> show that the Salt Lake area (as indicated by the data points (labelled "Near Road," "Rose Park," and "Hawthorn")) is safely within attainment of the current 12  $\mu\text{g}/\text{m}^3$  annual NAAQS standard for PM2.5 and likely would remain in attainment if that standard were tightened to 10  $\mu\text{g}/\text{m}^3$  or 9  $\mu\text{g}/\text{m}^3$ . They also show that historically, Salt Lake has been in nonattainment for the 24-hour PM2.5 standard of 35  $\mu\text{g}/\text{m}^3$ , but has been trending steadily toward attainment of that standard. In this docket, the EPA proposes not to tighten its obsolete 24-hour PM2.5 standard to reflect the overwhelming weight of recent epidemiological research. If it adheres to that approach, the Salt Lake area may soon have no help from the EPA in mitigating the serious harm to public health and the local economy that it continues to suffer from intense, transient spikes of PM2.5 pollution.

Current concentrations of PM2.5 in the Salt Lake area are particularly harmful to its children, the elderly, and those with heart and lung diseases such as COPD, asthma, and lung cancer. The Salt Lake area has over 600,000 residents that are categorized as especially susceptible to harm



from its unhealthy PM2.5 levels.<sup>402</sup> That harm comes from both long term and short term exposure.

If the EPA were to tighten the annual PM2.5 standard to 8  $\mu\text{g}/\text{m}^3$ , it would place the Salt Lake Metro Area in non-attainment status on that ground alone, as can be seen from the Interactive graphs published by the Utah Department of Environmental Quality,<sup>403</sup> Salt Lake and adjacent Wasatch Front counties would still have an obligation to adopt an SIP that would, at the least, require it to avoid further deterioration of its annual PM2.5 concentrations. If the EPA were to tighten the annual PM2.5 standard only to 10 or 9  $\mu\text{g}/\text{m}^3$ , the Utah DEQ's interactive graphs demonstrate that it is doubtful that the Wasatch Front counties would violate that annual standard or a 24-hour standard, going forward. This is likely to deprive the Wasatch Front of any federal assistance in improving its frequently unhealthy air quality.

The intermittent, transitory spikes in PM2.5 concentrations that plague Wasatch Front communities also harm the economy of the Wasatch Front.

The discussion above of the OECD Study and other research that focuses on the impact that PM2.5 has on aggregate economic activity concludes that if the EPA were to tighten the 24-hour PM2.5 standard from 9  $\mu\text{g}/\text{m}^3$  to 8  $\mu\text{g}/\text{m}^3$  it would likely result in an increase of \$52 billion in healthcare-related benefits nationally, and an increase in the nation's GDP of another \$286 billion, largely through an increase in labor productivity. That line of research also emphasizes that both the healthcare costs associated with PM2.5 pollution and the harm that they do to labor productivity are disproportionately large for economic sub-regions (such as the Wasatch Front) whose PM2.5 concentrations are above the economy-wide mean.

A simplistic estimate of the net benefit to the economy of the Wasatch Front of tightening the annual PM2.5 standard by roughly 10% (from 9  $\mu\text{g}/\text{m}^3$  to 8  $\mu\text{g}/\text{m}^3$ ) can be obtained by assuming that the economic costs and benefits of reductions in PM2.5 for the Wasatch Front will reflect the national average. As noted above, EPA estimates imply that, at the national level, health-related costs of \$52 billion could be avoided each year by tightening the annual PM2.5 standard from 9  $\mu\text{g}/\text{m}^3$  to 8  $\mu\text{g}/\text{m}^3$ . As calculated above, tightening the annual PM2.5 standard from 9  $\mu\text{g}/\text{m}^3$  to 8  $\mu\text{g}/\text{m}^3$  would also increase national GDP by \$286 billion annually. Nationally, the sum of these distinct benefits is \$338 billion, while the additional compliance cost associated with a 10% tightening is several orders of magnitude smaller.

The estimated increase in national GDP caused by each 1  $\mu\text{g}/\text{m}^3$  decrease in annual PM2.5 is closely analogous to the one measured for the EU because Utah and the EU have roughly the same annual average PM2.5 concentration baseline. Substantial proportions of both populations are subject to seasonal temperature inversions and, therefore, are subject to wide transitory variations in PM2.5 exposure. Both the United States and the European Union have similar demographic profiles, and both are at roughly the same advanced stage of economic development. For example, all of the 28 EU member states but Bulgaria have a very high Human Development Index according to the United Nations Development Program.<sup>404</sup>

It is reasonable to apply the same elasticity of GDP with respect to PM2.5 exposure estimated by the OECD model (1.1%) to the GDP of the United States generally, and to the Wasatch Front's GDP in particular. Doing so results in an estimated labor productivity increase from each 1  $\mu\text{g}/\text{m}^3$  decrease in annual PM2.5 along the Wasatch Front of \$2.475 billion. The calculations are presented below.

The Wasatch Front has 75% of Utah's population.<sup>405</sup> It is reasonable to presume that the Wasatch Front also produces 75% of Utah's GDP. Utah's GDP for 2021 was \$225 Billion.<sup>406</sup> The response of that GDP to a 1 microgram reduction in annual PM2.5 exposure is found by multiplying it by the 1.1% elasticity estimated by the OECD Study. The arithmetic is as follows:

$$\begin{aligned} & [0.011 \text{ GDP increase from a } 1 \mu\text{g}/\text{m}^3 \text{ decrease in PM}_{2.5}] \\ & \times [\text{Utah GDP of } \$225 \text{ billion}] \times [\text{WF share of Utah GDP of} \\ & .75] = \$2.475 \text{ billion increase in Wasatch Front GDP} \\ & \text{each year from increased labor productivity alone.} \end{aligned}$$

As noted above, the EPA estimates (by implication) that the healthcare-related cost avoided annually at the national level by tightening the annual PM2.5 standard from 9  $\mu\text{g}/\text{m}^3$  to 8  $\mu\text{g}/\text{m}^3$  would be \$52 billion. It is reasonable to assume that the Wasatch Front counties would receive at least a proportional share of this benefit, based on its share of the national population. As of the 2020 census, the population of the Wasatch Front counties (Cache, Weber, Davis, Salt Lake, and Utah Counties) was 2,602,693 million, the population of the United States was 331.4 million, and the Wasatch Front's share of the national population total was 0.785%. Therefore, the Wasatch Front's proportional share of the annual healthcare-related savings associated with a tightening of the annual PM2.5 standard from 9  $\mu\text{g}/\text{m}^3$  to 8  $\mu\text{g}/\text{m}^3$  would be \$408 million ( $\$52 \text{ billion} \times 0.00785 = \$408.2 \text{ million}$ ). Adding \$408.2 million in avoided health care costs to \$2.475 billion in increased labor productivity yields a total annual net benefit of \$2.883 billion to the Wasatch Front economy of tightening the annual PM2.5 standard from 9 micrograms to 8 micrograms. Since the EPA's estimate of the additional national compliance cost of this tightening was several orders of magnitude smaller than its benefits, the same can be presumed to be true for the local Wasatch Front economy.

An alternative calculation of the economic costs of PM2.5 pollution to the Wasatch Front community is provided in a study mentioned earlier in this report, published in 2020 in the journal *Atmosphere*. Entitled "Human Health and Economic Costs of Air Pollution in Utah: An Expert Assessment" (BYU Study),<sup>407</sup> the study has 23 co-authors. It employed an approach called expert assessment, which analyzes all available research and experience from published and unpublished scientific studies. Combining expertise from public health, atmospheric science, and economics, the researchers identified the types of disease and economic damage arising from Utah's air pollution and then quantified their impact.

The BYU Study focuses on the total burden of PM2.5 exposure on Wasatch Front residents, rather than the burden of an incremental tightening of the annual standard from 9  $\mu\text{g}/\text{m}^3$  to 8  $\mu\text{g}/\text{m}^3$ . The study found that economic losses ranged between \$750 million and \$3.3 billion,

including health care expenses, crop damage and lost earning potential, in addition to indirect costs such as loss of tourism, decreased growth and regulatory burdens. The mean of its estimates of the annual direct costs of this exposure is \$1 billion. The mean of its estimates of the indirect costs of this exposure is \$0.9 billion. The studies' mean estimate of PM2.5's share of these costs is 55%. Fifty five percent of the \$1.9 billion estimate of annual direct and indirect air pollution costs to the Wasatch Front counties comes to \$1.045 billion that is attributable to PM2.5.

Section 4.1 of the BYU Study offers a second approach to calculating the cost burden of exposure to air pollution along the Wasatch Front. It says that the market cost of air pollution scaled down from national to local levels of population and GDP are about \$2 billion, while this total swells to about \$7 billion when scaled down welfare costs are included. Fifty five percent of \$7 billion yields a rough estimate of the annual burden of exposure to PM2.5 along the Wasatch Front of \$3.85 billion. It should be borne in mind, however, that this estimates a total annual burden of PM2.5 exposure rather the 1  $\mu\text{g}/\text{m}^3$  increment analyzed above, nor does it account for the dominant component of PM2.5 exposure's market costs, which is its effect on aggregate labor productivity. The analysis of the net economic benefit from tightening the annual PM2.5 standard from 9 to 8 micrograms provided above, therefore, provides a more relevant guide to the EPA when considering how stringent PM2.5 NAAQS standards should be.

## H. CONCLUSION

Like with justice, "public health protection delayed is public health protection denied." The United States federal government has a long history of ignoring science and allowing businesses to manufacture products and create emissions that endanger the public long after the science has convincingly shown the associated health hazards. Lead, mercury, ionizing radiation, asbestos, and tobacco are just some of the toxins that were not banned or regulated until decades after their hazards were well established. Creation of the EPA was supposed to change that paradigm. But the fact that EPA has only banned eight substances in its history while the public is exposed to 140,000 industrial chemicals tells a disturbing story in and of itself. "Many of the most dangerous substances which faced bans in other countries, remained on the market for decades."<sup>383</sup> That pesticides kill plants and insects means they are poisonous to the same biologic world that humans inhabit and depend on. EPA now "manages" over 16,800 pesticides, including 1,200 active ingredients. In their entire history EPA has canceled the registration of only 37 pesticides, and in the last decade have only forced one pesticide off the market. Meanwhile the European Union has banned or restricted over 1,000 chemicals just since 2007.

Numerous books and investigative journalism articles by ProPublica, the Intercept, the Center for Public Integrity, Le Monde, and many others, have detailed why EPA has failed to protect the public from these poisons. EPA's default assumption is chemicals are innocent and treated

as such, until or unless proven--virtually without doubt--that they are guilty. And in the rare instance that happens, it is invariably after public health has seen prolonged harm on a mass scale. Just like with hazardous chemicals, EPA's long running modus operandi is to assume current NAAQS are safe unless there is near absolute proof that they are not.

Having closely followed the medical research on air pollution for the last 16 years, there is little doubt in our minds that the medical research will only continue to expand and become more convincing that current NAAQS PM2.5 standards and the EPA proposals are both too weak. We reiterate that EPA has not changed the PM2.5 24 hr. standard since 2006 and the annual standard since 2012. Consistent with both the science and EPA's legal mandate, we urge EPA to adopt a 24-hour PM2.5 standard of 20µg/m<sup>3</sup> and an annual standard of 8 µg/m<sup>3</sup>.

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