Comments for the authors of
"Review of the National Ambient Air Quality Standards (NAAQS)
for Particulate Matter (PM):
Policy Assessment of Scientific and Technical Information.
OAQPS Staff Paper — First Draft,"
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There have long been two, competing hypotheses to account for the oft-observed, weakly positive correlations between ambient concentrations of particulate matter (PM) and rates of disease and death. The first is that some components of ambient, pollution-derived PM, at current concentrations in the U.S., cause disease and death. The corresponding EPA policy response has been that total respirable PM must be further reduced, through size-range-specific, but otherwise undifferentiated, PM NAAQS. The second hypothesis is that pollution-derived PM, at current U.S. levels, is only a marker (*i.e.*, a co-variate) of other factors that cause disease and death, and not itself a cause: if so, then reducing concentrations of ambient PM *per se* in the U.S., through a PM-based NAAQS, would not improve public health.

If the first hypothesis were correct, well-studied mixtures such as particulate matter from diesel engine exhaust (DPM) or concentrated ambient particles (CAPs) should by now have been shown to sicken or kill laboratory animals at levels reasonably close to ambient. Despite concerted attempts by scores of researchers, they have not. Alternatively, some particularly toxic metals, organic compounds, or other pollution-derived ingredients of PM, studied alone or in mixtures, should have been shown to cause disease or death at levels close to U.S. ambient. Again, they have not.

Instead, controlled, experimental studies of PM have shown one of two things: some particularly toxic, pollution-derived mixtures, such as residual oil fly ash (ROFA), cause disease and death in laboratory animals, but do so only at concentrations vastly in excess of ambient. Because there is so little ROFA in U.S. air, ROFA does not explain why ambient PM as a whole

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correlates with rates of disease and death. Other chemicals and mixtures, such as DPM, are present at higher concentrations in ambient U.S. air, but their toxic potencies have proven to be rather low, so again there is a wide margin between U.S. ambient levels and levels demonstrated to harm health.

It is time to admit that the first hypothesis appears to be incorrect. The most parsimonious explanation for the data is instead the second hypothesis: current, low levels of ambient, pollution-derived (as opposed to biological) PM correlate, weakly and positively, with rates of disease and death *not* because they cause these things, but only because they co-vary with agents and factors that do. These confounding factors — such as ambient temperatures, differences in rates of smoking cessation, stress, and other determinants of disease — are not ingredients of pollution-derived PM, and reducing ambient PM (except for bacteria, viruses, and the like) through a NAAQS will not reduce disease burdens in the United States.

This is not to say that EPA's NESHAP program, for example, that regulates emissions of dozens of forms of PM (*e.g.* arsenic, beryllium, cadmium, chlorinated dioxins and furans, and hydrochloric acid) is not appropriate and health-protective. To the contrary, it is. We mean to make clear instead that a NAAQS for PM as a whole (differentiated only according to size-range) is neither appropriate, health protective, nor based on sound scientific judgment.

Virtually all other aspects of EPA's Clean Air Act programs (and underlying legislation) recognize that PM is not PM is not PM. Thus, the list of 188 hazardous air pollutants (HAPs) contains scores of individual, specific, liquids and solids present in air: there is nothing so crude as undifferentiated $PM_{2.5}$ or PM_{10} on such a list. In further refinements according to toxicity and exposure-levels, such as under EPA's Air Toxics Strategy, the Agency has identified 33 specific airborne chemicals or mixtures that pose "the greatest threats to public health in urban areas." This list again includes specific liquid and solid forms of PM derived from stationary and mobile sources; and again, there is, appropriately, no listing of fine PM as a whole. Moreover, it is the Agency's position that emissions standards, rather than ambient standards, are the more efficient and appropriate means for achieving cleaner air in urban settings.

Some details of the scientific bases for our opinion are as follows. Please also see the attached papers (Green *et al.*, 2002; Green and Armstrong, 2003, in press; Valberg, in press).

Toxicologic, clinical, and epidemiologic studies of hundreds of forms of particulate matter demonstrate, as expected, vast differences in health-risks, according to specific chemical, physical, and biological properties. As a result, health-based recommendations and regulations concerning air in the workplace — such as those recommended by the National Institute of

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Occupational Safety and Health [NIOSH] or the American Conference of Governmental Industrial Hygienists [ACGIH], or promulgated by the Occupational Safety and Health Administration [OSHA] and the Mine Safety and Health Administration [MSHA] — are based on the specific chemical (and sometimes physical) forms of PM to which workers may be exposed. Thus, hundreds of disparate forms of PM — such as ammonium sulfamate, arsenic, barium oxide, beryllium, carbon black, carbaryl, cotton dust, crystalline silica, diesel engine exhaust particulate matter (DPM), mineral oil mist, nickel, phosphoric acid mist, pyrethrum, rhodium, sulfuric acid mist, and tin — are each regulated according to distinct, chemical-specific (or mixture-specific) standards intended to protect health. NIOSH-recommended exposure limits (RELs), for example, range from concentrations as stringent as 0.0005 mg/m^3 for beryllium to levels as generous as 10 mg/m^3 for ammonium sulfamate.

Toxicologists, industrial hygienists, physicians, and others working in, or knowledgeable about, occupational health — and so aware of the very different kinds and extent of health effects and risks due to the hundreds of different kinds of industrially-derived PM — are mystified at U.S. EPA's current position that a single standard, expressed as a NAAQS, is appropriate for all of the countless forms of $PM_{2.5}$ (or PM_{10}) in ambient air. Such a notion seems to them and to us to be profoundly unscientific. More disturbingly, because compliance with such a standard could be achieved by reducing any harmless form of PM, such a standard is quite unlikely to improve public health, except perhaps by accident. It would be as if workplaces in which airborne levels of arsenic, for example, were too high, could "come into compliance" by substantially reducing airborne concentrations of sodium chloride. Total mass-based concentrations of respirable PM would indeed be reduced, but to no health benefit.

Instead, health-based standards for particular matter in ambient air should be based on the specific chemical forms or mixtures of PM known or reasonably expected to harm health. Virtually all of the forms of PM regulated by OSHA or MSHA (and/or evaluated by NIOSH and ACGIH) are also detected in outdoor, ambient air, but most are present (at least in most ambient air in the U.S.) at levels too small to pose significant risks to health, and so are not properly regulated by NAAQS. Some forms of PM, however, are or may be present in ambient air at significantly risky levels: the task for scientists and policymakers in the NAAQS program, then, is to determine which forms of PM these are, and then to design one or more NAAQS (if

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appropriate, and if not managed better under NESHAP or other programs) to control exposures.[1]

To address this question, one would do well to adopt the approach taken by Valberg (in press) and by U.S. EPA in its Air Toxics Strategy, and examine two sets of data. The first set would be the list of U.S. EPA Reference Concentrations (RfCs), which concentrations are, essentially, the Agency's scientific judgment regarding acceptable airborne limits for priority pollutants or pollutant-mixtures: these RfCs are intended to protect the health of the U.S. population, including sensitive subpopulations (with respect to non-cancer effects). This set could be augmented with the larger sets of occupational health-based recommendations, adjusted downward to account for differences between workplace exposures and ambient exposures, and, as needed, between the possibly greater susceptibilities of members of the general public relative to members of working populations. The set could be augmented further still with toxicologic and epidemiologic data on forms of PM prevalent in ambient air — such as ammonium sulfate and ammonium nitrate — for which no RfCs or occupational recommendations or standards have been derived.

The second set of data consists of air quality measurements made by EPA, the States, and others, reflecting average and maximum ambient air concentrations of priority pollutants and other chemicals/mixtures in the U.S.

Given these two lists, one could calculate, for each substance or mixture appearing on both lists, the margin of safety (or lack thereof) between current air quality and acceptable air quality. Obviously, substances present in ambient air in the U.S. at concentrations of the same order of magnitude, or higher than, acceptable concentrations, might well be candidates for regulation under the Clean Air Act (whether under the NAAQS program or otherwise).

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[1] As always, the extremes are easy to discern: certain forms of ambient PM clearly cause disease and death at current U.S. levels; other forms are apparently safe. In the first category are biological forms of PM, such as certain viruses and bacteria in air (both outdoors and indoors): indeed, influenza and pneumonia are currently the seventh leading cause of death in the United States. In the second category are airborne forms of PM such as sodium chloride and calcium chloride, which are enriched in ambient air near the Atlantic, Pacific, and Gulf coasts, and which are apparently harmless at ambient concentrations. Of course, each of these "extreme" forms of PM — microbial or marine — is due not primarily to pollution, and so not controllable by the NAAQS program (or other regulatory interventions). Nonetheless, they are part of ambient PM as currently defined, measured, and studied.

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Valberg (in press, and attached) has presented analyses along this line, and found that for all pollutant-derived forms of PM — with one exception — margins of safety between ambient concentrations and acceptable concentrations are quite large. As such, these forms do not appear to require regulation under the NAAQS program.

For diesel engine exhaust particulate matter (DPM), however, the margin of safety between current ambient concentrations, at least in some areas of the U.S., and acceptable concentrations (defined by U.S. EPA's RfC) may be rather small. As such, DPM *might* be a candidate for further consideration under the NAAQS program. Whether DPM would *in fact* merit regulation under this program would depend on a careful review of the scientific evidence — and careful applications of scientific and policy judgments — in order to determine acceptable concentrations for ambient air in the U.S., and appropriate policies for achieving these concentrations.[2]

The point, however, is this: to design valid NAAQS, one must evaluate and extrapolate from reliable and holistic scientific bases. Unfortunately, for PM, currently defined and measured only as a size-range-specific total mass, the Agency has not done this. It saddens us to note that EPA has instead disregarded, discounted, or misinterpreted vast amounts of toxicologic, epidemiologic, and clinical data — and seems to have abandoned the much more reasoned approach it took in designing the NAAQS for the individual molecular gases.

In different contexts (EPA, 2002; IRIS, 2003), EPA has thoroughly reviewed the abundant scientific literature on DPM — and, more generally, on diesel engine exhaust as a mixture of gases and particles (since it is this mixture to which people and lab animals alike have been exposed). Oddly, none of the Agency's considerable knowledge of DPM has yet been brought to bear with regard to the NAAQS program and PM, even though ambient DPM is, of course, a component of PM in cities studied epidemiologically.

The toxic effects of diesel engine exhaust — both DPM and the gases and vapors that comprise the bulk of the exhaust — have been evaluated in numerous acute and chronic studies. Laboratory animals are believed to be good models for humans with regard to their responses to

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[2] Of course, DPM is a complex mixture — or, more precisely, thousands of different complex mixtures — and current and future changes in the sulfur content of diesel fuels — and in diesel engines, catalytic converters, and other modifiers of emissions — are expected to change the qualities and quantities of DPM in various ways. Whether and how these changes affect the toxic potency of DPM remain to be elucidated.

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DPM (U.S. EPA, 2002; ILSI, 2000), and some 17 chronic studies, involving laboratory rats, mice, hamsters, guinea pigs, cats, and monkeys, have evaluated the respiratory and systemic effects of exposure to DPM (U.S. EPA, 2002; IRIS, 2003). DPM has little acute toxicity; chronic exposures, however, to large concentrations of DPM (in the presence of diesel engine exhaust gases) consistently cause inflammation, fibrosis, and functional changes in the respiratory system, and very large concentrations cause premature death.

Inflammation of the rat lung from chronic exposures to DPM is assumed, by the Agency, to be relevant for human health, and the exposure-response data from the rat studies form the basis of EPA's RfC for DPM. In particular, in evaluating DPM, the Agency has utilized these data to derive an Effective Concentration$_{50}$ (EC_{50}) of 3,100 ug DPM/m^3 "human equivalent concentration." From this, using several safety factors, the Agency estimates an RfC of 5 ug/m^3. Of course, depending on one's view of ancillary information,[3] the Agency's safety factors might be viewed as either too large or too small; but, to a first approximation, a chronic RfC would be the value to use if one were designing a NAAQS.

The question then becomes, what are current U.S. ambient concentrations of DPM, and how do they compare to the RfC? Ambient concentrations of DPM can be approximated from ambient concentrations of elemental carbon (U.S. EPA, 2002). Based on results from the EPA's 2002 fine particulate matter speciation monitoring program (U.S. EPA, 2003), the mean annual average concentration of elemental carbon in the U.S. is about 0.6 ug/m^3, with the highest annual

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[3] Some studies suggest that DPM at ambient levels, in conjunction with biological antigens, may provoke some attacks of asthma, but other studies contradict this idea. Additional research is needed. In another regard, it should be noted that laboratory rats, though not other test species, develop lung tumors during lifetime exposures to very high concentrations of DPM. As noted by U.S. EPA (IRIS, 2003), the mechanism by which these tumors arise involves "particle overload and consequent persistent inflammation and cell proliferation, [which] supports a nonlinear mode of action for lung cancer in the rat (ILSI, 2000). The nonlinear cancer response is further characterized as occurring at relatively high exposures of diesel exhaust (>3500 ug DPM/m^3), which is far beyond the range of environmental levels. The rat tumor occurrences, thus, are not particularly influential in judging the hazards at environmental levels of exposure." EPA also notes (IRIS, 2003), "While the weight of evidence indicates that DE [diesel engine exhaust] has the potential to pose a lung cancer hazard to humans at anticipated levels of environmental exposure, as shown by occupational epidemiology studies, a confident dose-response relationship based on occupational exposure levels is currently lacking." Again, the issue is far from settled.

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averages being less than 2 *u*g/m^3. Based on conversion factors used to extrapolate DPM levels from ambient elemental carbon measurements — which range from about 0.6 to 1.3 (U.S. EPA, 2002) — it is unlikely that average ambient levels of DPM exceed 5 *u*g/m^3 anywhere in the U.S. Thus, if EPA's RfC is in fact protective of all citizens, including sensitive subpopulations, no additional regulation appears warranted. In other words, DPM concentrations in U.S. ambient (non-occupational) air appear to be already acceptably small.

Note that the abundant rodent data on lifetime exposures to diesel engine exhaust contradict the notion that chronic exposures to tiny concentrations of PM cause premature death. In particular — as EPA (2002) noted in reviewing DPM — the experimentally-derived LOEL for premature death due to *lifetime* exposure to DPM has been reported to be 6,330 *u*g DPM/m^3 in F344 rats (Nikula *et al.*, 1995) and 4,240 *u*g/m^3 in NMRI mice (Heinrich *et al.*, 1986); other rodents tested in other laboratories showed no decreased survival even given lifetime exposures of some 7,000 *u*g DPM/m^3 (Mauderly *et al.*, 1984, 1987, and 1996; Heinrich *et al.*, 1995). None of the extensive toxicologic data on DPM provides a basis for assuming that current ambient concentrations of DPM, which average less than 2 *u*g/m^3, cause premature death in humans, let alone that reducing such concentrations would prevent premature deaths.

Is there *any* form of pollution-derived PM in ambient air — other than lead, for which a chemical-specific NAAQS has long existed — for which a health-based NAAQS is needed? If there is, we cannot think of what it might be. The important, pollution-derived solids, liquids, and fibers (such as asbestos) in ambient air are already regulated (or soon to be regulated) under more than 70 federal emissions standards and related programs. Additional forms of harmful PM in ambient air may yet be discovered, but these too will likely be better controlled by regulations directed at specific emission sources, rather regulation of ambient air under the NAAQS program. In our judgment, enforcement of the PM NAAQS, as currently constructed, is not likely to reduce disease or avert death.

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