

Commentary: Flawed Scientific-Evidence Standards Delay Diesel Regulations

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Of 188 government-monitored air toxics, diesel particulate matter (DPM) causes seven times more cancer than all the other 187 air toxics combined, including benzene, lead, and mercury. Yet, DPM is the only air toxic not regulated more stringently under the Clean Air Act, as a hazardous air pollutant (HAP). One reason is that regulators use flawed standards of scientific evidence. The article argues (1) that DPM meets all six specified evidentiary criteria, any one of which is sufficient for HAP regulation and (2) that regulators' standards of evidence for denying HAP status to DPM (no DPM unit-risk estimate, inadequate dose-response data, alleged weak mechanistic data) err logically and scientifically, set the evidence bar too high, delay regulation, and allow 21,000 avoidable DPM deaths annually in the U.S.

Keywords: cancer, cause, diesel, hazardous air pollutant, particulate matter, PM, unit risk estimate

INTRODUCTION

Is the U.S. Carmaheaven, where Americans have unlimited auto access and enjoy the freedom of the open road? Or is it Carmageddon because on-road vehicles produce a massive amount of atmospheric carbon monoxide, nitrogen oxides, diesel particulate matter (DPM), and climate-change pollutants?

A key determinant of the answers to the two preceding questions is the debate over diesel vehicles and fuels. On one hand, diesel vehicles appear cheaper than gasoline because of their greater fuel efficiencies. On the other hand, gasoline vehicles are better than diesel for reducing oil use and global

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climate-change pollution. And although U.S. gasoline vehicles are far greater in number, diesel vehicles cause a far higher percentage of health harms, including lung cancer and adverse neurological, reproductive, cardiovascular, and respiratory health effects (Pope and Dockery, 2006; Block and Calderón-Garcidueñas, 2009; Wilhelm et al., 2012; Nelin et al., 2012; Valavanidis et al., 2013; CATF, 2014, 2005a,b).

For instance, government scientists say that in Los Angeles County, mobile sources like vehicles generally cause 90% of the total cancer risk, but DPM alone causes 70% of this risk, 70% of Los-Angeles County cancers (SCAQMD, 2005; MATES III, 2008; CAL-EPA, 2008a). Throughout the U.S., vehicles and especially diesel trucks, cause most cancer deaths, with average air-pollution-caused U.S. cancer deaths at 36 per million people. However, in areas of heaviest DPM pollution, such as Los Angeles County, this rate jumps to 63 per million, double the national average. And near intermodal-freight-transport facilities in southern California, for instance, containers come into Long Beach, are loaded onto trucks, and then transported to “East Yards” in Commerce, California where they are loaded onto trains or other trucks at the intersection of several rail and truck depots. Because of DPM, the cancer rates in the largely-minority community of East Yards are as high as 700 in a million, 19 times higher than average-US rates, and 11 times higher than already-high Los Angeles rates (EPA, 2013c; CAL-EPA, 2008a, p. 15; see Rosenbaum et al., 2011).

America’s tens of millions of diesels, mostly trucks, but also buses, trains, and docked ships, emit pollutants that lead to 21,000 premature U.S. deaths each year, with a disproportionate number of deaths occurring in places like East Yards, California; the cancer risks from U.S. diesel vehicles are seven times greater than the combined risk of all 187 other air toxics that the U.S. Environmental Protection Agency (EPA) tracks (CATF, 2005a; see EPA, 2014c; MATES III, 2008). In the U.K. and other nations, DPM causes similar problems, such as 29,000 preventable U.K. deaths each year (COMEAP et al., 2010).

In spring 2014, vehicle DPM became so bad in Paris, worse than in Beijing and far worse than what damages human health, that it obscured the Eiffel Tower and put a hazy dome over the city. In response, the government temporarily banned (from Paris and its 22 surrounding towns) all vehicles whose license plates ended in even numbers. It also made mass transit free, lowered speed limits for remaining vehicles, and offered free parking in Paris suburbs (Barnard, 2014; Blaise, 2014; Mathiesen, 2014).

For decades the European Union has recognized DPM harms. It now requires all new models of on-road vehicles, including passenger cars, light-duty vehicles, and heavy-duty vehicles to have DPM filters. By January 2015, the E.U. says all existing diesel engines must be retrofitted with DPM filters (European Commission, 2013). In the U.S., only heavy trucks since 2007 must

have the DPM filters. However, unlike the E.U., the U.S. requires no DPMs on medium-duty and passenger vehicles, and no retrofit for 80% of the 15 million heavy-duty-diesel-transport trucks, long-lived vehicles that have lives of about one million miles or 30–40 years. These weaker U.S. regulations mean that 11 million older and dirtier, long-distance, diesel trucks, the source of most U.S. DPM, remain largely unregulated. Unless the U.S. EPA requires full retrofits as the E.U. does, or names DPM a hazardous air pollutant (HAP), 80% of the dirtiest U.S. polluters can continue spewing out hundreds of tons of DPM per day, for another 30–40 years (Bienkowski, 2013).

BACKGROUND: DPM AND PM

Why aren't U.S. DPM regulations as protective as those in Europe? To begin to answer this question, consider the nature of DPM, PM, and their hazards. Any type of PM is an air-suspended mixture of solid or liquid particles that vary in number, size, shape, surface area, chemical composition, solubility, and origin (Pope and Dockery, 2006). It originates from stationary and mobile anthropogenic sources as well as from natural sources such as windblown dust and wildfires (EPA, 2009). All PM is classified into three main size categories, coarse, fine, and ultrafine. PM of 2.5 to 10 μm (PM_{10}) is inhalable coarse particles. PM of 2.5 to 0.1 μm ($\text{PM}_{2.5}$) is inhalable fine particles, and PM of 0.1 μm or less ($\text{PM}_{0.1}$) is inhalable ultrafine particles. PM has no safe dose and exhibits a linear concentration-response relationship (Pope and Dockery, 2006; Schwartz and Zanobetti, 2000; Daniels et al., 2000; Dominici et al., 2002; Dominici et al., 2003; Pope, 2002; Laden, 2006). As mentioned, PM is associated with carcinogenic, neurological, reproductive, cardiovascular, and respiratory health harms (Pope and Dockery, 2006; Block and Calderón-Garcidueñas, 2009; Belleudi et al., 2010; Wilhelm et al., 2012; Nelin et al., 2012; Valavanidis et al., 2013).

Ultrafine is the most dangerous type of PM because it can easily pass into the nose, through the blood-brain barrier, and directly into the brain (Oberdorster et al., 2004; Cassee et al., 2013). Ultrafine PM also is much more potent, than fine and coarse PM, in inducing oxidative stress, reactive oxidative species (ROS), and inflammation (Li et al., 2003; R ckerl et al., 2007; Delfino et al., 2009; Li et al., 2009; Song et al., 2010), all of which can cause cardiovascular, neurological, immune, and other problems (e.g., Franck et al., 2011; Kleinman et al., 2008).

Because DPM or soot is mostly ultrafine, DPM is the most dangerous type of PM. Both the World Health Organization (WHO) and the International Agency for Research on Cancer classify diesel exhaust, including DPM, as carcinogenic to humans, although the U.S. does not do so. Two-thirds of all PM emissions come from diesel-powered vehicles and equipment (IARC, 2012; Union of Concerned Scientists, 2008)

Because most DPM is ultrafine, it has four ultrafine characteristics that make it especially deadly. These include its small size, large surface area and thus inflammatory properties, being a Trojan-Horse pollutant, and its ability to travel great distances. Its first or small-size characteristic enables it to enter either the nose then the brain, or the lungs, bloodstream, and all bodily organs, where it can cause chronic inflammation and organ degeneration (CATF, 2005b; Peters et al., 2006; Terzano et al., 2010). Its small size, in turn, leads to its second characteristic, relatively larger surface areas. For the same mass, smaller ultrafine or fine particles like DPM have much larger numbers and surface areas than do coarse particles. As a result, DPM has much greater opportunity to interact with cell surfaces and cause inflammatory damage (EPA, 2013a).

A third ultrafine and DPM characteristic, being a Trojan-Horse pollutant, means that the DPM attracts other diesel-exhaust carcinogens, toxins, and metals such as arsenic, cadmium, formaldehyde, polyaromatic hydrocarbons (or PAHs), and zinc. They adhere to the ultrafine PM, form fine PM, enter the brain or lungs, and can travel to all bodily organs, where they can cause chronic inflammation leading to diseases such as Alzheimer's, autism, birth defects, cancer, Parkinson's, and even death (Costa et al., 2014; Deng et al., 2009; Bush et al., 1994; Rivera-Mancia et al., 2006; Szewczyk, 2013; Aizenman et al., 2000; Dineley et al., 2002; James et al., 2011; Kleinewietfeld et al., 2013; Pentylala et al., 2010; Trumbo et al., 2001; Visjkina et al., 2008; Yang et al., 2013; CATF, 2005b; Araujo, 2011; Terzano et al., 2010; Krivoshto et al., 2008; Pope and Dockery, 2006; CATF, 2005b; Block and Calderón-Garcidueñas, 2009; CATF, 2005b).

A fourth ultrafine PM and DPM characteristic is its ability to linger in the air, travel great distances, and thus harm people hundreds of kilometers from its emissions source. When other particles are adsorbed onto ultrafine PM, it can persist much longer and travel farther, up to thousands of kilometers from its emissions source (Amann et al., 2006; EPA, 2009).

BACKGROUND: DPM REGULATIONS

Despite the four characteristics of ultrafine PM and thus DPM that cause its special health threats, the U.S. EPA does not regulate it any differently than other PM. As a result, there are at least six U.S. DPM regulatory gaps.

- Although U.S. EPA has a Reference Concentration (RfC) for diesel exhaust, it has *no RfC for DPM*, the most dangerous part of diesel exhaust.
- The *RfC for diesel exhaust is too high* because as already noted, no DPM dose is safe, and because the U.S. EPA RfC for diesel exhaust is 5 $\mu\text{g}/\text{m}^3$, 5 times higher than the fine DPM increase that has been shown to annually

cause a 3% increase in coronary hospitalization and a 6% increase in coronary mortality (Gan et al., 2011).

- U.S. EPA uses the diesel-exhaust RfC as a benchmark to try protect against chronic non-carcinogenic health effects, but *the diesel RfC is not binding and has no regulatory status*.
- *The diesel RfC takes account of no carcinogenic effects*, although as already shown, DPM causes about 70% of the total cancers in some areas.
- Although DPM is included under the National Ambient Air Quality Standards (NAAQS) for both fine and coarse PM, *NAAQS standards for DPM and ultrafine PM underestimate harm because they are based on PM mass concentrations*. Basing PM hazards on mass concentrations grossly underestimates ultrafine and DPM hazards because it ignores particle numbers and surface areas, to which PM harm is proportional, not mass concentrations, and because most DPM is ultrafine. Per unit of mass, ultrafine PM can be about 65 times more hazardous than coarse or fine PM, although flawed U.S. regulations do not take account of these worse hazards (Sager and Castranova, 2009).
- *U.S. PM regulations ignore the greater hazards of ultrafine PM* because they are the same for fine and ultrafine PM. These mass-based standards are $150 \mu\text{g}/\text{m}^3$ for coarse PM, and $35 \mu\text{g}/\text{m}^3$ for fine and ultrafine PM, both for 24-hour emissions, averaged over three years (EPA, 2012).

The six preceding DPM, ultrafine PM, and NAAQS regulatory gaps mean that despite the four characteristics that make DPM more hazardous than the same mass of other PM, there are no specific regulations for the most hazardous of all air pollutants, DPM. However, U.S. EPA has attempted to reduce DPM in several other ways. Beginning in 2010, it required year-2007-and-later heavy trucks to use ultra-low-sulfur-diesel fuel, something that also reduces ultrafine-PM (SCAQMD, 2007). Trains, boats, construction, and farm engines had to begin using it in 2012. In addition, since 2007 EPA has required diesel particulate filters (DPFs) for all new U.S. heavy-duty highway diesel vehicles or heavy-duty trucks, but not also for medium-duty and passenger vehicles, as the E.U. requires. These EPA regulations for new, on-road diesel engines are 0.01 g/brake-horsepower-hour (bhp-hr), that is, horsepower measured by the amount of braking needed to stop the vehicle. For long-haul-diesel trucks of 600 horsepower, this means regulations allow each DPF truck to release 6 g PM/hour and 48 g or 0.11 pounds of PM during an eight-hour day. But because there are 15 million U.S. diesel trucks, even if they all had DPFs, the latest 2007 regulations allow them together to release roughly 1.6 million pounds or 825 tons of PM, for each eight-hour day of travel. But because DPF filters are required only on all 2007-and-later U.S. trucks, and because diesels have very

long lifetimes, up to 11 million heavy-duty trucks, 80% of the U.S. freight fleet, will remain without filters for 30–40 years (Integer, 2014; EPA/NCDC, 2013).

Despite the 2007 regulatory improvements because 80% of U.S. diesel freight trucks are not subject to the 2007 requirements, for 30–40 years, EPA will allow far more than 825 tons of PM/day for a pollutant that has no safe dose. Pre-2007 diesel vehicles remain in use and free of either retrofitting, strict regulation, or DPFs. Of course, if EPA named DPM a HAP, it would have to be regulated under the 1990 Clean Air Act Amendments, and EPA would have to set better standards for DPM (EPA, 2014d; CFR Title 42, 2012a).

DPM MEETS HAP CRITERIA

In other words, one reason the U.S. does not regulate DPM more strictly is that EPA has not named it one of the 187 HAPs. This section of the article outlines criteria for HAP designation and begins to assess why EPA denies HAP status to DPM. According to the U.S. Clean Air Act, HAPs are “pollutants which present, or may present, through inhalation or other routes of exposure, a threat of adverse human health effects (including, but not limited to, substances which are known to be, or may reasonably be anticipated to be, carcinogenic, mutagenic, teratogenic, neurotoxic, which cause reproductive dysfunction, or which are acutely or chronically toxic).” Thus, any pollutant that is “reasonably anticipated to be “carcinogenic, mutagenic, teratogenic, neurotoxic,” or a “cause [of] reproductive dysfunction,” fits any one of the criteria that is sufficient for being named a HAP (CFR Title 42, 2012a).

Moreover, the Clean Air Act specifies that if “standards . . . applicable to a . . . pollutant (or pollutants) classified as a known, probable, or possible human carcinogen do not reduce lifetime excess cancer risks to the individual most exposed to emissions . . . to less than one in one million, the Administrator shall promulgate standards under this subsection for such source category”; in other words, any pollutant classified as a known carcinogen must be regulated so that it causes less than one in one million cancers, if one million people were all exposed to this level over a lifetime of 70 years (CFR Title 42, 2012b). In sum, therefore, the Clean Air Act requires that if a pollutant is likely a carcinogen, mutagen, teratogen, neurotoxin, or cause of reproductive dysfunction, it fits the criteria for being declared a HAP and, if it is a probable carcinogen, it should be regulated so that it causes less than one cancer in a million people exposed over a 70-year lifetime.

Given these Clean Air Act criteria for HAP designation, and the current absence of NAAQS standards for ultrafine PM and therefore most diesel PM, there is a puzzle about the fact that EPA has not named DPM a HAP. The puzzle is that the U.S. EPA says on its website that a HAP is an air toxin or toxic air pollutant, and it uses the three terms—HAP, air toxin, toxic air

pollutant—interchangeably, as synonyms (EPA, 2013b). Yet, DPM is the only one of all of the roughly 1,100 mobile-source air toxics (187 of which government tracks) that EPA has not also named a HAP (EPA, 2014a). Thus either EPA seems wrong to use the terms HAP, toxic air pollutant, and air toxin synonymously, or it seems wrong not to classify DPM as a HAP.

Should EPA name DPM a HAP so that it can be regulated more strictly under the Clean Air Act? At least four different reasons suggest that it should. (1) As a probable and known carcinogen and mutagen that causes more than one in a million cancers, DPM meets three different sufficient conditions for being named a HAP or regulated under the Clean Air Act. (2) By causing teratogenic and reproductive effects, DPM meets an additional two, singly sufficient, conditions for being named a HAP. (3) By causing neurotoxic, cardiovascular, and respiratory harms, DPM meets yet another sufficient condition for being named a HAP. (4) The evidentiary standards, used by EPA to deny HAP status to DPM, are questionable. Consider these four reasons.

A CARCINOGEN-MUTAGEN HARMING MORE THAN ONE-IN-A-MILLION PEOPLE, DPM MEETS THREE DIFFERENT SUFFICIENT HAP CONDITIONS

DPM meets at least two different, singly sufficient conditions for being named a HAP, namely that it is a carcinogen and mutagen, as established by the Interagency Review Group on Cancer (IARC) of the WHO. IARC has a three-part classification for carcinogens, 1, 2A, and 2B, respectively, that are definitely, probably, and possibly known to be carcinogenic to humans. In 2012, IARC and WHO classified diesel exhaust and DPM as “carcinogenic to humans (Group 1)” (IARC, 2012, p. 1), the classification that expresses the highest level of scientific confidence in its carcinogenicity. The head of the IARC assessment said the decision was unanimous and that evidence showed diesel exhaust, and thus DPM, exposure should be reduced worldwide (PAHO, 2012). As late as 2014, however, the U.S. EPA classified diesel exhaust and DPM as merely a group-2 carcinogen, as “likely to be carcinogenic to humans” (EPA, 2014c). Nevertheless, for IARC’s 2012 unanimous group-1 decision, it relied on a massive amount of evidence (e.g., Bruske-Hohlfeld et al., 1999; Finkelstein et al., 2004; Garshick et al., 1987, 1988, 2004; Gauderman et al., 2004; Guo et al., 2004; Hoppin et al., 2004; Muzyka et al. 2004; Steenland et al., 1990, 1992, 1998), to draw its conclusion that DPM is a definitive human carcinogen (e.g., see Olsson et al., 2011; Raaschou-Nielsen et al., 2013).

This IARC evidence included not only animal experiments that showed “strong mechanistic evidence” for carcinogenicity, but also human epidemiological evidence, and evidence that DPM can induce lung cancer in humans through genotoxic mechanisms (IARC Monograph, 2012, p. 464). Not only is

DPM genotoxic *in vitro* (EPA, 2002), but IARC confirms that DPM induces “DNA damage (e.g., oxidative lesions and bulky adducts), gene mutations, DNA strand breaks, chromosomal alterations (e.g., chromosome breaks, sister chromatid exchange, and aneuploidy) and morphological cell transformation *in vivo* and *in vitro*” in mice, rats, rodent primary cells, rodent and human cell lines, and gene mutations in bacteria (IARC Monograph, 2012, p. 461). Thus DPM clearly meets two different sufficient conditions for being named a HAP, namely, it is a possible carcinogen and a possible mutagen, DPM also meets a third sufficient condition for being named a HAP, namely, that it causes cancer risks greater than one in a million, as shown by the California EPA, IARC, and WHO. Cal-EPA says that in Southern California alone, DPM contributes more than 70% of the area’s total cancer risk (CAL-EPA, 2008a; see CATF, 2005b). Depending on where they live, Los Angeles County residents have a cancer risk that is 438–700 times greater than EPA’s acceptable cancer level of 1 in a million (CATF, 2014; CAL-EPA, 2008a, p. 15).

Therefore, DPM meets at least three of the conditions, any one of which is sufficient for being named a HAP. That is, DPM is at least a possible human carcinogen, is at least a possible genotoxin, and has a cancer risk in some areas that is hundreds of times greater than one per million. Thus several different grounds show that DPM meets Clean Air Act criteria for HAP designation.

CAUSING TERATOGENIC AND REPRODUCTIVE EFFECTS, DPM MEETS TWO ADDITIONAL, SINGLY SUFFICIENT, HAP CONDITIONS

Although the possible link between DPM and teratogenic and reproductive effects is less clear because it has been discovered more recently than the cancer link, DPM also is clearly tied to teratogenic and reproductive effects. Despite the fact that ambient air often contains many pollutants whose effects are difficult to differentiate, nevertheless researchers report human epidemiological associations between exposure to various DPM contaminants and birth defects, such as neural-tube defects and congenital heart defects (Lupo et al., 2010; Ren et al., 2011; Bowen et al., 2009; see McKenzie et al., 2014). Animal experiments also clearly show that DPM can cause birth defects (e.g., Simsek et al., 2012), including disruption of locomotive activity and the monoaminergic system (e.g., Suzuki, 2010), perhaps as a result of increased inflammation and oxidative stress (Raveenthiran, 2012).

Regarding reproductive effects, human epidemiological studies also have linked both PM and DPM to endocrine disruption and to possible low birth weight and preterm birth (Brink et al., 2014; Ballester et al., 2010; Brauer et al., 2008; Dadvand et al., 2013; Ghosh et al., 2012; Llop et al., 2010; see Ritz and Wilhelm, 2013; Wilhelm et al., 2012; Bell et al., 2011). Animal experiments likewise show similar DPM reproductive effects. DPM exposures, at roughly

the levels found on many U.S. interstates, can cause reproductive dysfunction. In multiple animal experiments, typical levels of vehicle DPM in urban air have caused increases in inflammatory cytokines, testosterone, estradiol, estrus cycles, miscarriage, but decreases in fertility, pregnancy, offspring birth weight, follicle-stimulating hormones, luteinizing hormones, and sperm production (e.g., Auten et al., 2011; Hougaard et al., 2008). Watanabe and Oonuki, 1999d; Veras et al., 2009; Irvin and Martin, 1987). Because both animal experiments and human epidemiological studies link DPM to these harms, DPM satisfies at least two additional (the fourth and fifth) conditions, any one of which is sufficient for being named a HAP and hence for being regulated more strictly; namely, it causes possible teratogenic and possible reproductive harms.

CAUSING NEUROTOXIC, CARDIOVASCULAR, AND RESPIRATORY HARMS, DPM MEETS ANOTHER SUFFICIENT CONDITIONS FOR HAP DESIGNATION

In addition, DPM meets a sixth condition that also is alone sufficient for being named a HAP, namely, that it causes neurotoxic, cardiovascular, and respiratory harms. Regarding neurotoxic effects, DPM fits the HAP criterion insofar as it “may reasonably be anticipated to be . . . neurotoxic” (CFR Title 42, 2012a). In both humans and animals, the lowest levels of DPM inhalation exposure, only 5% of typical freeway levels, trigger inflammation, and dopaminergic neurotoxicity, including activation of microglia or immune cells of the brain. (Block and Calderón-Garcidueñas, 2009; Block et al., 2004). Even at these low DPM levels, human epidemiological studies show reduced levels of verbal learning for both men and women (Gatto et al., 2013; Power et al., 2011). One reason is that because of DPM’s easy access to the brain, via the nose, it has been implicated in the inflammation and oxidative stress that lead to Alzheimer’s and other neurodegenerative diseases (Levesque et al., 2011; Krivoshto et al., 2008). Numerous well-controlled animal and human studies, including brain autopsies, show that increased DPM levels are associated with increased neuroinflammation, cytokines, oxidative damage, diffuse amyloid plaques in the brain, DNA damage in the olfactory bulb, and brain pathology like Alzheimer’s and Parkinson’s (Cave, 2012; Block and Calderón-Garcidueñas, 2009; Shwe et al., 2008; Yokota et al., 2013).

DPM and PM are associated not only with neurodegenerative diseases, but also with cardiovascular disease and strokes. Uncontroversial epidemiological evidence links DPM and PM exposure with increased cardiovascular mortality and ischemic heart disease (Nawrot et al., 2011; Brook et al., 2010; Rich et al., 2012). Even a 10 $\mu\text{g}/\text{m}^3$ reduction in fine PM would avoid thousands of hospitalizations for heart failure (Dominici et al., 2006), partly because even a 1 $\mu\text{g}/\text{m}^3$ increase in a city’s fine DPM is associated with a 3% increase in

coronary hospitalization and a 6% increase in coronary mortality (Gan et al., 2011). A recent Harvard study showed that the PM-concentration-response relationship is linear down to the lowest PM doses; it found that each increase in $10 \mu\text{g}/\text{m}^3$ of PM is associated with a 14% increased risk of all-mortality, 26% increased risk of cardiovascular mortality, and 37% increased risk of lung-cancer mortality (Lepeule et al., 2012). One mechanism behind at least some of the DPM organ damage appears to be epigenetic harms, partly heritable changes in methylation that lead to a cascade of inflammation, including creation of reactive oxygen species and atherosclerotic plaque vulnerability (Valavanidis et al., 2013; Nelin et al., 2012; Ho et al., 2012; Brook et al., 2010; Brauer et al., 2007; Nemmar et al., 2002, 2003, 2013).

FLAWED EVIDENTIARY STANDARDS BEHIND FAILING TO NAME DPM A HAP: THE URE ARGUMENT

DPM meets six different sufficient conditions for being named a HAP, namely, that it is a probable carcinogen, mutagen, cause of cancer risk greater than one in a million, teratogen, reproductive toxin, and neurotoxin. Why has U.S. EPA not designated it as a HAP and thus regulated it more stringently?

EPA says that “in considering both the currently available health-effects evidence, and the air-quality data . . . information [are] still too limited to provide support for a distinct PM standard for ultrafine [thus most DPM] particles” (EPA, 2013a, p. 3122). More specifically, in complaining about limited DPM and ultrafine data, EPA appears to have three main scientific objections to naming DPM a HAP. It says (1) it is unable to develop a unit risk estimate (URE) for DPM, something it says it needs for regulation; (2) because there is no reliable cancer dose-response curve, EPA cannot estimate DPM cancer potency; and (3) EPA has no reliable mechanism of action for DPM induction of cancer. Considering these three scientific rationales in order, this section of the article shows why each objection fails logically and scientifically because of the scientific standards of evidence that it employs.

The first stated or URE scientific argument against naming DPM a HAP is that although DPM is a “likely” human carcinogen, the exposure-response data in human studies are too uncertain to develop a carcinogenic URE (EPA, 2014b; CATF, 2005b). EPA also says that “the available data are not sufficient to develop a confident estimate of cancer unit risk (i.e., unit risk estimate or URE). Therefore, EPA cannot provide a quantitative estimate of potential cancer risk associated with environmental exposures to diesel particulate matter The Agency has concluded that national average lifetime cancer risks from exposure to diesel exhaust may exceed one in one hundred thousand (1/100,000) and could be as high as one in one thousand (1/1,000)” (EPA, 2010a). Other scientists also claim uncertainty about a DPM URE as follows:

“One possibly high-risk HAP that was not included in our analysis is diesel exhaust. Diesel particulate matter is a significant exclusion from our HAPs list. A sample calculation using the 1999 NATA ambient concentrations for diesel PM and a recommended inhalation unit risk from OEHHA gives us a risk of 2.7×10^{-4} , which is on the order of the dioxin risk. The difficulty with diesel PM is that it is more difficult to quantify in measurement studies, because usually elemental carbon is used but only as a proxy, so we chose to exclude it” (Loh et al., 2007, p. 1166).

However, there appear to be at least seven problems with EPA’s URE argument against naming DPM a HAP. The first problem is that, as the EPA quotation itself reveals, EPA suggests the DPM URE range is between one-in-one-thousand and one-in-one-hundred-thousand. But because both ends of the URE range are still 10–1,000 times higher than the EPA acceptable risk level of one-in-one-million, EPA could lower DPM risks by a factor of 10, and yet still be within the range in which regulation is required, even if the URE is one-in-one-hundred-thousand. In other words, even those lacking confidence in a DPM URE nevertheless realize that the lowest DPM risk still is very high, on the order of dioxin risk, and high enough to require Clean Air Act regulation as a HAP (Loh et al., 2007, p. 1166). Moreover, EPA defines the URE as “the upper-bound excess lifetime cancer risk estimated to result from continuous exposure to an agent at a concentration of $1 \mu\text{g}/\text{m}^3$ in air” (EPA, 2014d). Therefore, because even the lowest estimate of excess lifetime cancer risks is above the level at which regulation should occur, EPA ought to be able to regulate DPM as a HAP without having a point estimate for the URE—because it can be reasonably confident that it is not overregulating.

A second scientific problem with EPA’s URE argument is that a DPM-effects range of uncertainty of two orders of magnitude, one-in-one-thousand to one-in-one-hundred-thousand, is still a relatively narrow range. Admittedly EPA’s reference doses often have a range within only one order of magnitude, but there are no obvious grounds for EPA’s assuming that it needs a cancer range less than two orders for magnitude, in order to regulate a presumed carcinogen DPM as a HAP. After all, risk assessors typically assume that interspecies uncertainties or variations are an order of magnitude or factor of 10, and that child-to-adult uncertainties or variations are another order of magnitude or factor of 10. Just to deal with both of these uncertainties/variations, risk assessors routinely must face an uncertainty range of 100, the same as that indicated by EPA for DPM effects. In this context, a risk range of 100 does not seem so large that it precludes regulation. If it did preclude regulation, then logically, regulations to protect children would be suspect because they involve uncertainties of two orders of magnitude.

A third scientific problem with EPA’s rejecting DPM regulation as a HAP, because of no precise URE, is that such precision appears largely irrelevant, given that DPM is an admitted carcinogen, hence presumably has no

safe dose, and has independently been documented as having no safe dose (EPA, 2010b). If so, the obvious regulatory stance is to reduce DPM insofar as possible/practical, regardless of the specific URE. Indeed, for threats that have no safe dose, any URE may be beside the point.

A fourth scientific problem is that EPA's own guidance on risk assessment recommends expert elicitation or expert judgment in cases of uncertainty (EPA, 2005, p. 3–32). Yet, if one uses expert elicitation in the DPM case, then it seems reasonable to rely on the unanimous judgment of the WHO, IARC, and CAL-EPA that DPM is a known human carcinogen and ought to be regulated very, very strictly, as already suggested. After all, IARC Director Christopher Wild said that IARC's 2012 DPM-cancer "conclusion sends a strong signal that public-health action is warranted" (IARC, 2012, p. 2). At the least, if EPA rejects the expert judgment of IARC and says DPM is only a "likely" human carcinogen, it ought to say precisely how and why it is doing so, why public health does not need this protection, and on what grounds its analysis, rather than that of IARC or the state of California, ought to be preferred.

After all, while the U.S. EPA says it cannot develop a URE for DPM, the state of California has long been able to do so. In 1998 and 2008, the Scientific Review Panel for the California Air Resources Board estimated the unit cancer risk for DPM as 3 cancers per 10,000 persons per μg DPM (CAL-EPA, 2008b; CATF, 2005b). This URE is 2 orders of magnitude higher than required to trigger federal HAP regulations, and other scientists have confirmed that the URE for DPM is at least this high (Rosenbaum et al., 2011). Yet, the US EPA has not named DPM a carcinogen or a HAP. At a minimum, U.S. EPA needs to say precisely why "the available data are not sufficient to develop a confident estimate" of this URE (EPA, 2010a), given that California scientists for the South Coast Air Basin calculated a URE of 12,000 per million, or 4 orders of magnitude higher than required to trigger federal regulation, 84% from diesel exhaust (MATES III, 2008), is wrong. U.S. EPA likewise needs to say precisely what is wrong with California scientists' calculations of the West Oakland, California DPM URE of at least 10 per million (CARB, 2008c). Otherwise, EPA seems to ignore the expert elicitation that it endorses.

A fifth scientific problem with U.S. EPA's demanding a precise DPM URE is that this demand seems contrary to its endorsement of a "weight of evidence" (WOE) approach to carcinogenic risk assessment. The National Toxicology Program (NTP) and the IARC also use WOE assessment, and both of them classify DPM as carcinogenic (ATSDR, 2005, 8.3.1). EPA does not do so, although its own carcinogen risk assessment dictates relying on WOE and not demanding point-estimate certainty in the URE before regulating something (EPA, 2005, p. 3–33). EPA says WOE focuses on "a collective evaluation of all pertinent information so that the full impact of biological plausibility and coherence is adequately considered" (EPA, 2011, p. 6; Krimsky, 2005, p. 133). Because U.S. EPA specifically warns that no single "assessment factor" (EPA, 2011, p. 230),

such as a precise URE, is necessary in the WOE approach, it is unclear why it demands a precise URE for DPM, especially given the obviously high risk of DPM.

In demanding a precise URE, EPA is demanding certainty about the precise level of DPM harm, rather than knowledge of DPM harm beyond a reasonable doubt, and the two are not the same. One can know beyond a reasonable doubt that *x* is carcinogenic without knowing with certainty the precise level of harm. In fact the U.S. Occupational Safety and Health Administration (OSHA) made exactly this point when it explained OSHA action in another case, involving the carcinogenicity of wood dust. OSHA said that

In response to those commenters who argued that none of the studies described by OSHA presented sufficient dose-response data to be used as a basis for establishing a [precise, numerical, regulatory] limit, the Agency emphasizes that it is not relying on any single study to determine . . . a significant risk of material health impairment. Instead, OSHA is making this determination [of harm] on the basis of the findings in . . . dozens of studies . . . The Agency finds the results of these studies biologically plausible and their findings reproducible and consistent. It is true that some of these studies, like all human studies, have limitations of sample size, involve confounding exposures, have exposure-measurement problems, and often do not produce the kind of dose-response data that can be obtained when experimental animals are subjected to controlled laboratory conditions. What the large group of studies being relied upon by OSHA to establish the significance of the risk associated with exposure . . . do show is that the overall weight of evidence that such exposures are harmful and cause loss of functional capacity and material impairment of health is convincing beyond a reasonable doubt. (CFR Title 29, 1989; see Krinsky, 2005, p. 1334)

In demanding a precisely certain URE, rather than a URE beyond reasonable doubt, EPA appears to be using a particular “conceptual framework for weighing the evidence” (Krinsky, 2005, p. 135). EPA’s particular framework seems doubtful because in science, one often knows that something is the case, long before one knows precisely the degree to which it is the case. Scientists knew that climate change is the case, for instance, long before they knew the tempo and mode of climate change (Oreskes, 2007). Just as knowing the precise contributors to someone’s harm is not necessary for knowing that she has been harmed, so also, knowing the precise URE is not necessary for knowing beyond a reasonable doubt that DPM is a carcinogen and a HAP.

A sixth scientific problem with EPA’s not naming DPM a HAP is that in focusing on the precise cancer probability and URE for DPM, EPA may be overemphasizing cancer probability at the expense of cancer consequences. As EPA puts it, in its own guidelines for cancer risk assessment, “the data that support cancer assessments generally are not suitable for numerical calculations of the probability that an agent is a carcinogen” (EPA, 2005, p. 2–53). If not, EPA might name DPM a known carcinogen and HAP without knowing

its precise cancer probability and URE. Besides, in some situations, the consequences of a potential carcinogen's harm, such as numbers of people affected, might be more important than its probability of cancer. A majority of Americans either lives close to a freeway or travels to work or school on a freeway. This means that DPM exposures affect nearly everyone and thus are virtually unavoidable. And in cities like London, 91% of ultrafine pollution comes from diesel vehicles; "diesel vehicles are the worst contributors to harmful air pollution in London" and other cities (Moore, 2012, p. 12). Given such dire DPM consequences, EPA seems wrong to ignore them and instead to require a precise probability and URE before regulating DPM as a HAP, especially because its own risk criteria emphasize something more than probabilities. EPA specifically says that "weighing of the evidence includes addressing not only the likelihood of human carcinogenic effects of the agent but also the conditions under which such effects may be expressed, to the extent that these are revealed in the toxicological and other biologically important features of the agent" (EPA, 2005, p. 1–12). In other words, given a situation in which a pollutant is able to harm many people, the conditions under which the effects are expressed, the consequence of widespread harm might be just as important as the precise probability of harm. If so, the claimed absence of a URE need not be grounds for denying HAP status to DPM.

A seventh scientific problem with EPA's not naming DPM a HAP is that EPA may be partly swayed by political considerations. After all, the diesel industry and powerful trucking industry repeatedly have used the courts to try to block clean-air and PM standards and have long lobbied against naming DPM a HAP; both also have tried to block diesel and DPM studies and yet argued, at the same time, that such studies are needed prior to any additional DPM regulation (Monforton, 2006; see Crump and Landingham, 2012). "From early days," says a prominent journal editor, DPM studies have "been subject to a series of legal actions initiated by industry bodies concerned about the methods and implications, which has delayed the publication of these [DPM] papers" (Ogden, 2010, p. 727). Indeed, this industry delay has been especially obvious in the classic studies of how DPM harms miners (e.g., Stewart et al., 2010; Coble et al., 2010; Vermeulen et al., 2010a, 2010b; Monforton, 2006). Obviously, however, science, not industry pressure, ought to determine the outcome of DPM assessment. If so, there appear to be adequate scientific grounds for naming DPM a HAP.

FLAWED SCIENTIFIC GROUNDS FOR NOT NAMING DPM A HAP: THE DOSE-RESPONSE ARGUMENT

Besides the URE rationale, a second scientific reason that EPA gives for not naming DPM a HAP is that it says there are inadequate DPM human data at

low-exposure levels (Cogliano, 2002, p. 8). Hence, EPA says there is an “absence of a confident cancer dose-response curve,” both of which prevent estimation of DPM cancer potency (Ris, 2007, p. 229). However, a key problem with this EPA argument is that many well-known, highly regulated carcinogens, such as ionizing radiation, have long had inadequate data at the low-dose end of exposure. Yet, this low-dose-knowledge gap has not kept government from naming and regulating them as potent carcinogens.

Ionizing radiation, for instance, was discovered in the 1895, and discovered to be a carcinogen in the 1920s (Martland and Humphries, 1929). Yet, more than 80 years later, scientists were still trying to measure low-dose radiation effects. They were still debating whether there was a threshold for harm at the low-dose end of the ionizing-radiation-exposure curve, whether the curve was linear, whether the curve was quadratic, and what the effects of low-dose radiation exposures were. Indeed, this low-dose-radiation debate has never really been settled empirically, because of the difficulty of experimentally tracing effects of low-dose radiation exposure. (And low-dose effects are an experimental difficulty for any low-dose carcinogen, including DPM.) Instead, considering all the theoretical evidence about ionizing radiation, the U.S. National Academy of Sciences settled the low-dose-radiation debate in 2006 by claiming that, for theoretical biological reasons, the consensus hypothesis is that low-dose radiation exposures have linear, no-threshold effects (U.S. NRC, 2006). Thus, a full 80 years after radiation was known or regulated as a carcinogen, scientists were still debating its low-dose effects, and the shape of the radiation dose-response curve, just as they are now doing with DPM. Meanwhile, the more that is discovered about ionizing radiation, the stricter radiation standards have become. But if so, the absence of low-dose information and a full DPM dose-response curve is no reason to delay naming DPM a HAP and regulating it under the Clean Air Act.

FLAWED SCIENTIFIC GROUNDS FOR FAILING TO NAME DPM A HAP: THE MECHANISM ARGUMENT

Besides the URE and the dose-response objections, a third scientific reason EPA gives for not naming DPM a HAP, and not regulating it under the Clean Air Act, is that EPA says it lacks a reliable mechanism of action for DPM induction of cancer, particularly lung cancer, long known to be associated with DPM (Ris, 2007, p. 235). Yet, EPA claims that unknown mechanistic considerations are important for estimating DPM risk (Cogliano, 2002).

The problem with this third EPA argument against naming DPM a HAP is that one can know something is a carcinogen or a hazardous air pollutant, without knowing all the precise mechanisms by which the agent exercises its harmful properties. Indeed, the history of science and medicine is full of stories

of how people learned that something was harmful, and avoided it, long before they ever knew the precise mechanisms through which the harm occurred. For instance, a full decade before there was ever a germ theory of disease, physician John Snow recognized that cholera in London spread through contaminated water. Hence, Snow convinced officials to remove the pump handle from the water pump, so that more people would not die, although he did not know the mechanism responsible for the deaths. Had Snow waited for knowledge of the mechanism behind the contaminated water, thousands more Londoners would have died of cholera. The same is true for DPM. If EPA has to know the complete mechanisms through which DPM harm has occurred, before taking steps to stop the harms, far more people will die.

In addition, it is misleading for EPA to claim that the mechanisms of lung cancer caused by DPM are unknown. In fact, people have long known that cancer occurs in part as a result of chronic inflammation (Balkwill and Mantovani, 2002; Coussens and Werb, 2002), and that PM causes inflammation wherever it settles in the body (Davies, 1995; Brown and Neher, 2010; Levesque et al., 2011). Even EPA itself admitted, more than a decade ago, that possible DPM cancer mechanisms included chronic inflammation, production of reactive oxygen species, and so on, all established cancer mechanisms (Cogliano, 2002, p. 17).

Still another scientific reason that lack of full knowledge (of a DPM cancer mechanism) ought not cause EPA to delay in naming DPM a HAP is that its own cancer risk assessment guidelines argue for doing so. As these guidelines state, “when the weight-of-evidence evaluation of all available data are insufficient to establish the mode of action for a tumor site and when scientifically plausible based on the available data, linear extrapolation is used as a default approach, because linear extrapolation generally is considered to be a health-protective approach” (EPA, 2005, p. 3–21). Thus, even if EPA cannot name a mechanism for DPM cancer harm, its own procedures dictate that it should follow a default approach, assume a linear DPM harm, and proceed from that assumption, so as to protect people.

ETHICAL VALUES AND GOVERNMENT STANDARDS FOR REGULATORY SCIENCE

Thus, as this article shows, apart from the fact that regulatory agencies use flawed standards of scientific evidence and therefore appear not to have not named DPM a HAP, some agencies like EPA also seem to be ignoring their own professed regulatory goals and values, such as using “health-protective” science. For instance, in demanding precise knowledge of mechanisms before strictly regulating carcinogenic DPM that is already known to be extremely harmful, EPA appears to have made an ethical judgment to promote epistemic values, such as scientific accuracy and precision, ahead of ethical values, such

as protecting public health or promoting equal protection under the law. Yet, sometimes non-epistemic values ought to override epistemic values, especially in regulatory science, mainly because its goal is often to avoid human harm, not just to attain scientific precision (Elliott and McKaughan, 2014). And especially when they do science, all scientists arguably have duties not only to protect epistemic values, but also to protect public welfare, particularly in areas related to their expertise (Shrader-Frechette, 2012).

Insofar as EPA frequently privileges epistemic over ethical values, it sometimes may have allowed regulatory science to succumb to paralysis through analysis, being manipulated by regulated entities who demand unnecessary scientific precision, simply in order to slow health-protective regulatory processes (Michaels, 2008). One antidote for such paralysis and overprivileging epistemic values would be for regulatory agencies like EPA to adopt explicit policies about ethical values. One policy might require EPA to examine the social costs and benefits of regulating, versus failing to regulate, in cases such as DPM, and then to use these social costs and benefits, as well as epistemic values, in its regulatory decision-making.

To promote ethical as well as purely epistemic values, Carl Cranor (1995) has argued for adopting quicker, less accurate, risk-assessment methods instead of the lengthy, more accurate, current methods. His reasoning is that the social costs of lengthy risk assessment, and thus delayed human-health regulations, are higher than the social costs of expedited assessment; insofar as human-health harms are concerned, economists say the social-cost ratio, of false-negatives to false-positives, is 10:1. For instance, when the California Environmental Protection Agency used an expedited risk-assessment methodology, Cranor noted that it was able to estimate the human-carcinogenic potency of 200 known animal carcinogens within 8 months. Yet, the traditional methodology was 22 times slower, allowing assessment of only 70 animal carcinogens in 5 years. Although the expedited approach was slightly less accurate, Cranor argues that it saved far more lives and money than the traditional approach. If he is right, the earlier scientific analyses of DPM suggest that EPA might increase emphasis on ethical values and decrease emphasis on purely epistemic values, in part by expediting scientific assessments likely to have great human-health consequences (Cranor, 1995; Elliott and McKaughan, 2014).

Likewise, in high-stakes areas of regulatory science such as DPM, where special interests have repeatedly used the courts and lawsuits to block implementation of health-protective, clean-air standards, EPA's emphasis on ethical values should include special attention to minimizing conflicts of interest that could jeopardize social welfare. As David Resnik (2007a,b, pp. 116–129) notes, although it is not realistic to expect scientific research related to regulation or litigation to be free from conflicts of interest, it is possible to minimize the impacts of these conflicts. He suggests requiring full disclosure of information

needed for independent evaluation of research, prohibiting financial relationships between regulatory agencies and those they regulate, and prohibiting paying expert witnesses for specific research results or testimony (Resnik, 2007a,b).

Of course, U.S. EPA has improved its conflict-of-interest policies. Nevertheless, it still has not required full disclosure of all conflicts. Current EPA conflict-of-interest policies have many loopholes, including not asking for all information that the U.S. Government Accountability Office (GAO) says is relevant to assessing possible conflicts of interest, and not publicizing these conflicts, as preeminent journals (such as *Environmental Health Perspectives*), do (Shrader-Frechette, 2007). If EPA followed the ethics advice of Resnik, GAO, and others, it might require all those who play a role in government regulatory science to publish (along with their research, opinions, or court cases) full disclosure of competing financial interests and any relationship that could be seen as potentially influencing their position. Such disclosures arguably would help reduce the sorts of scientific problems on which this article has focused.

CONCLUSION

What does this brief overview of DPM research reveal? Despite the fact that DPM is a carcinogen, mutagen, neurotoxin, reproductive toxin, and so on, EPA has delayed regulating DPM as a HAP under the Clean Air Act. Yet, this article shows that DPM meets at least six of the conditions specified in U.S. regulations, any one of which is sufficient for regulating DPM as a HAP. It also shows that none of EPA's three scientific reasons for its regulatory delay are convincing because they rely on flawed criteria for scientific evidence, namely, requiring a precise and complete URE, dose-response curve, and mechanism for harm, before regulating DPM as a HAP. Yet, these questionable evidentiary standards are not required by the Clean Air Act and appear instead to be supported mainly by regulated industries. Given the massive health harms of DPM, including cancer risks in areas like East LA that are 700 times higher than those triggering mandatory regulations, EPA does not need perfect and complete science in order to regulate DPM. It needs only science beyond a reasonable doubt. This article shows that adequate science exists, provided that EPA uses adequate evidentiary standards. Therefore, EPA should name DPM a HAP.

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