Integrated Science Assessment for Particulate Matter

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Cardiovascular Effects Consistent with the 2009 PM ISA, this ISA concludes there is a causal relationship between short-term PM2.5 exposure and cardiovascular effects (Section 6.1). The strongest evidence comes from epidemiologic studies that reported consistent, positive associations between short-term PM2.5 exposure and cardiovascular-related ED visits and hospital admissions across studies that used different approaches to control for the potential confounding effects of weather (e.g., temperature), particularly for ischemic heart disease (IHD) and heart failure (HF), as well as cardiovascular-related mortality. Recent examinations of potential copollutant confounding generally indicate that the associations observed between PM2.5 exposure and cardiovascular effects in single-pollutant models remain relatively unchanged in copollutant models, providing evidence that the observed associations with PM2.5 are not artifacts due to confounding by another air pollutant. The independence of a PM2.5 cardiovascular effect is further supported by recent experimental studies. Controlled human exposure studies expand upon previous findings and demonstrate PM2.5-induced changes in endothelial function, which is coherent with animal toxicological studies demonstrating the same effect. Moreover, experimental evidence demonstrating decreased cardiac contractility and altered left ventricular pressure is coherent with epidemiologic studies observing positive associations between ambient PM2.5 and ED visits and hospital admissions for HF. Thus, the collective body of experimental evidence supports and provides biological plausibility for epidemiologic studies reporting associations, particularly between short-term PM2.5 exposure and IHD and HF outcomes, as well as a range of other cardiovascular-related effects (e.g., arrhythmia, thrombosis) that can result in more severe outcomes, possibly including death.

The 2009 PM ISA, as well as the current PM ISA, concluded there is a causal relationship between long-term PM2.5 exposure and cardiovascular effects (Section 6.2). Epidemiologic studies of multiple recent U.S.-based cohorts along with reanalyses of these cohorts provide strong evidence of consistent, positive associations between long-term PM2.5 exposure and cardiovascular mortality. These studies used a variety of exposure assessment and statistical techniques and examined various spatial domains (e.g., 1 × 1-km grid cells, census tract, etc.) in many locations where mean annual average PM2.5 concentrations are ” 12 µg/m3 . Recent epidemiologic studies of cardiovascular morbidity have greatly expanded upon the body of evidence available at the completion of the 2009 PM ISA by focusing on populations with distinct demographic characteristics (e.g., postmenopausal woman, male doctors, etc.) and extensively considering potential confounders (e.g., socioeconomic status [SES]). Although an

extended analysis of the Women's Health Initiative (WHI) cohort strengthened the initial observation of a relationship between long-term PM2.5 exposure and coronary events among postmenopausal women, additional cohorts of women similar to the WHI cohort did not report consistent, positive associations with coronary heart disease (CHD), myocardial infarction, or stroke. Longitudinal studies examining the progression of atherosclerosis in relation to long-term exposure to PM2.5 reported inconsistent results that were dependent upon the vascular bed examined, but there was evidence of PM2.5-associated coronary artery calcification, a strong predictor of CHD, within a study focusing on the progression of atherosclerosis in a healthy population (i.e., Multi-Ethnic Study of Atherosclerosis and Air Pollution [MESA–Air]). A limited number of epidemiologic studies examining other cardiovascular effects provide some evidence of associations with HF, blood pressure, and hypertension, as well as subclinical cardiovascular biomarkers. Recent studies also reduce the uncertainty associated with potential copollutant confounding by reporting that associations between long-term PM2.5 exposure and cardiovascular mortality remained relatively unchanged or increased in copollutant models adjusted for O3, NO2, SO2, and PM10−2.5. Evidence from animal toxicological studies further supports a direct PM2.5 effect on the cardiovascular system and provides coherence with effects observed in epidemiologic studies. For example, animal toxicological studies demonstrating atherosclerotic plaque progression in mice is coherent with epidemiologic studies of atherosclerosis, and animal toxicological studies reporting increased coronary artery wall thickness, decreased cardiac contractility and output, and changes in blood pressure are coherent with epidemiologic studies of HF. Furthermore, when considering the collective body of evidence, there are biologically plausible pathways by which long-term exposure to PM2.5 could lead to a continuum of effects potentially resulting in death.