



September 15, 2026

Lee Zeldin, Administrator
U.S. Environmental Protection Agency
William J. Clinton Building
1200 Pennsylvania Avenue, NW
Washington, DC 20460

Re: EPA's Draft Integrated Science Assessment to Support the Review of the Primary National Ambient Air Quality Standards for Oxides of Nitrogen (Docket EPA-HQ-OAR-2023-0317)¹

Our organizations strongly support the conclusions of the draft Integrated Science Assessment (ISA) conducted to support the review of health-based Primary National Ambient Air Quality Standards (NAAQS) for nitrogen dioxide (NO₂) and related oxides of nitrogen (NO_x). We offer the following comments and urge EPA to ensure a thorough and timely review process that considers all the comments it receives from the public.

Our organizations represent patients and communities who rely on clean air to breathe as well as healthcare and public health professionals working to prevent, identify and treat diseases caused or exacerbated by air pollution. Many of our organizations have long engaged throughout the NAAQS process with the goal of ensuring that EPA's ultimate decision on the standards reflects what the scientific evidence shows is necessary to protect health with an adequate margin of safety, particularly for at-risk populations including children, seniors and people with chronic diseases.

We find the draft ISA to be a rigorous assessment of the current scientific evidence on the health effects of exposure to NO_x and to provide a strong foundation for the current NO₂ NAAQS review process. It reflects a comprehensive analysis of the available scientific literature that has substantially expanded since the last ISA of 2016. The current ISA incorporates an additional decade of research data and provides a more comprehensive evaluation of multiple health outcomes including respiratory, cardiovascular, reproductive and developmental, metabolic, nervous system, mortality and cancer endpoints. This assessment appropriately synthesizes evidence from epidemiologic studies, controlled human exposure studies, toxicological investigations,

¹ <https://www.regulations.gov/document/EPA-HQ-OAR-2023-0317-0004>

exposure science, dosimetry research and mechanistic studies using EPA's established causal assessment framework.

EPA's Causality Framework and Determinations

We strongly support EPA's application of its long-standing weight-of-evidence framework in its causal inferences. This framework effectively considers the totality of evidence across multiple scientific disciplines in determining whether a pollutant causes adverse health effects. In this ISA, the EPA appropriately evaluates consistency, coherence, biological plausibility, exposure-response relationships, and integration of evidence across epidemiology, controlled human exposure, toxicological and mechanistic studies on the health effects of NO_x exposures. EPA also properly bases its causal conclusions on the convergence of multiple independent lines of scientific evidence across multiple studies.

Epidemiologic Evidence

The ISA appropriately weights epidemiologic evidence in evaluating health effects of NO_x. Epidemiological data provide evidence of health impacts under real-world exposure conditions and exposure patterns including those of susceptible populations that the Clean Air Act requires EPA to protect. The overall body of evidence presented in the ISA demonstrates consistency and coherence across multiple study designs and disciplines.

At-Risk Populations

The Clean Air Act requires setting of primary NAAQS at levels that protect public health with an adequate margin of safety to safeguard the health of vulnerable populations such as children, elderly, and individuals with preexisting respiratory conditions. The draft ISA conducts a thorough assessment of populations at increased risk from NO_x exposure, which is essential in informing the later stages of the NAAQS review, including the Policy Assessment.

Summary

The draft ISA thoroughly evaluates currently available scientific evidence which strengthens and expands the conclusions from the last review in 2016 on the health impacts of NO_x exposures. It provides a more extensive evidence base, additional mechanistic support, enhanced understanding of exposure and dosimetry and continued evidence of adverse health effects associated with NO_x exposure under contemporary conditions. The annual NO₂ NAAQS has never been revised since initial promulgation in 1971 and the 1-hour NAAQS has not been revised since 2010. This ISA's strengthened evidence base supports a careful reevaluation of whether existing standards provide the required margin of safety for children, seniors, people with respiratory illnesses and other susceptible populations.

We urge the Clean Air Scientific Advisory Committee (CASAC) to recognize the scientific record on the health impacts of NO_x exposures and affirm the causal inferences presented in the ISA. We recommend that EPA fully incorporate the ISA's health findings in evaluating whether the current NO₂ NAAQS provide public health protection with an adequate margin of safety.

Allergy & Asthma Network

Alliance of Nurses for Healthy Environments

American College of Chest Physicians

American Lung Association

American Public Health Association

International Society for Environmental Epidemiology-North America Chapter

Medical Students for a Sustainable Future (MS4SF)

National Association of Pediatric Nurse Practitioners

Oncology Advocates United for Climate and Health - International

Physicians for Social Responsibility