An overview of the use of health science in evaluating the CAA and air pollution standards, including the different types of science that contribute and the process for determining whether a particular pollutant causes a particular effect.
For nearly 50 years, the United States has been implementing the U.S. Clean Air Act (CAA) to identify key air pollutants of concern and take action to reduce exposure to those pollutants, with substantial success. At the core of this success has been the creation of an extensive body of scientific literature on the health effects of air pollution, the critical evaluation of that literature by the U.S. Environmental Protection Agency (EPA), the application of that literature to setting National Ambient Air Quality Standards (NAAQS), and identification and targeting control of pollutant emissions.

The creation and evaluation of this science has been a central strength of the CAA, and at the same time a source of continued controversy, especially as standards and requirements for pollution control have become more and more stringent. Given that, we seek here to review the basis in the CAA for the use of this health science, the different types of science that contribute, and the process for assessing whether the accumulated science enables the EPA and its science advisors to determine that a particular pollutant causes a particular effect. This scientific process has by most measures worked well over many years, but there have been continuing questions and new developments; we seek to assess these as well.

The Clean Air Act and the Setting of Air Quality Standards

Beginning with the 1970 Amendments of the CAA, Title I of the Act has set specific requirements for the review of exposure and health science on the major air pollutants found in the United States, commonly known as “criteria pollutants.” For each of these pollutants—currently ozone, particulate matter, sulfur oxides, nitrogen oxides, carbon monoxide, and lead—Section 108 of the CAA requires EPA to establish air quality criteria that “shall accurately reflect the latest scientific knowledge useful in indicating the kind and extent of all identifiable effects on public health or welfare which may be expected from the presence of such pollutant in the ambient air.”

Section 109 of the CAA then calls upon the EPA Administrator to set national primary air quality standards “the attainment and maintenance of which in the judgment of the Administrator, based on such criteria and allowing an adequate margin of safety, are requisite to protect the public health.” (emphasis added) It is these primary NAAQS which have set the basis for the great majority of air pollution control actions, with the determination from the health science literature of what levels are “requisite” to protect public health with “an adequate margin of safety” at the very center of the debate for the setting of each NAAQS.

The exact steps of the process to develop this science and make NAAQS decisions have evolved over the years. As illustrated in the figure on the opening page of this article, it today involves three major technical steps: (1) an Integrated Science Assessment (ISA) of all of the latest air pollution exposures and health science; (2) a Risk/Exposure Assessment (REA) that applies that science to estimate public health implications at current and potentially new levels of the NAAQS; and (3) a Policy Assessment (PA) that recommends whether the current NAAQS protects public health with an adequate margin of safety, and recommends changes to the NAAQS if appropriate. To ensure that the science is assessed independent of its policy implications, the ISA is prepared by EPAs Office of Research and Development (ORD) and the REA and PA are prepared separately by the EPA Office of Air and Radiation (OAR).

At each of these stages, the documents are subjected to detailed and public review by the seven-member Clean Air Scientific Advisory Committee (CASAC) created by Section 109 of the CAA. CASAC is required to “complete a review of the criteria published under section 108 of this title and the national primary and secondary ambient air quality standards promulgated under this section and shall recommend to the Administrator any new national ambient air quality standards and revisions of existing criteria and standards.” The Act also requires that every five years, the EPA administrator will review and revise the NAAQS, as appropriate, in view of evolving science and other information.

How Does Health Science Contribute?

Several different types of air pollution health studies are considered in each ISA, typically involving critical review and evaluation of thousands of individual peer-reviewed scientific papers. Chief among these are:

- **Animal and toxicology studies** (i.e., studies exposing cells and laboratory animals to air pollutants and pollutant mixtures). These can contribute to the understanding of potential biological mechanisms of how air pollutants can cause effects, although the issues of relevance to actual human effects must always be examined.

- **Human Epidemiology Studies** (i.e., studies of human population to determine whether, even when attempting to control for other factors that might cause health effects, such as smoking, obesity, and other “confounders,” there is a robust association of air pollution exposure with specific health effects). These can take many forms, from small “panel” studies of carefully selected subjects to large population studies of selected population cohorts ranging to very large administrative data sets (e.g., Medicare recipients). These studies, if well designed, can help determine “concentration-response relationships” that can be important to determining the lowest levels at which effects are observed—and thus the potential level at which to set a NAAQS. At the same time, challenges in exposure assessment, control for all possible...
confounders, and differing statistical techniques can introduce uncertainty in the results.

• **Controlled Human Exposure Studies** (i.e., studies of exposure of informed human volunteers to specific pollutants and levels in carefully controlled chambers). These studies also have limitations; they do not represent exposure to pollution mixtures which are most common, and ethical considerations preclude the ability to test those who may have the highest susceptibility. However, they do provide direct evidence of whether there are effects in humans from specific pollutants, and can do so at levels relevant to actual ambient levels.

**Assessing Causality**

The final stage in evaluation of scientific evidence is the complex process of synthesis and integration of evidence, reaching scientific conclusions, and determining causality. That is, are the associations observed in various studies real or artefactual and, if real, to what extent are they influenced by coincidental factors (confounders)? Epidemiology—representing real-world conditions—is particularly susceptible to such problems, while other kinds of studies have their own limitations in terms of representativeness of the population, species or dose studied. The ISA integrates the various lines of evidence, taking into account the strengths and limitations of each line of evidence.

Bradford Hill in 1965 laid out a framework for ascertaining various aspects of causality in epidemiology and public health, and this framework has been adapted, with many modifications, by EPA and other organizations. The ISA uses a five-level hierarchy that classifies the weight of evidence in terms of causality. In such determinations, EPA systematically assesses and integrates evidence from the various kinds of health studies described above and with different endpoints, and with short- and long-term exposures at levels relevant to current conditions. In addition, EPA also evaluates the quantitative relationship between exposure to the pollutant and health response.

In recent years, formal, statistical tests for determining causality have been developed. Although these may be valuable, it is difficult to foresee how a single statistical test could readily supplant EPA’s comprehensive approach to evaluate the overall strength and weight of evidence. Refinements to the current ISA framework, including possibly more formal methods for causality determination, may serve to enhance the current process; such changes are topics of discussion and debate.

**Recent Developments**

The process of reviewing and drawing conclusions from the NAAQS-relevant health science has evolved substantially since 1970, with an explosion of new studies, development of new techniques for systematically identifying and evaluating the scientific evidence, and calls for more rigorous assessments of the weight of causal evidence from CASAC and others. This has included the development of the Health and Environmental Research Online (HERO) database by EPA, the most comprehensive, regularly updated database on environmental and health research available worldwide today. It also has included more cogent summaries of the evidence contained in the ISAs, and the development and implementation of the much more systematic assessment of causality described above, which was first applied in the review of evidence of nitrogen oxides in 2008.

Most recently, there have been two major efforts to revise the process.

The first, issued on April 30, 2018, was a Notice of Proposed Rule Making for “Transparency in Regulatory Science,” which proposed to restrict the use of science for which all data was not available in “a manner suitable to allow for independent validation” and proposed additional requirements for the evaluation of “dose–response” relationships. This proposal has been the subject of extensive comments from a diverse set of parties and is currently under review. While there are many reasons for enhancing access to underlying data, and many organizations have been advocating this in recent years (including our organization the Health Effects Institute, which
has had a data access policy for over two decades\textsuperscript{9}), many of the studies relevant to NAAQS considerations are older and relied on subject confidentiality agreements that cannot be readily altered, leading to the prospect that such a rule—should it be finalized—could preclude the use of otherwise high-quality studies in the NAAQS review process.

Second, on May 9, 2018, the then-EPA Administrator Pruitt issued his “back-to-basics” memo for the NAAQS process.\textsuperscript{9} This memo called for several key steps:

1. Completing review of the NAAQS for particulate matter and ozone by 2020, closer to or meeting the statutorily required five-year deadline (which has often not been met).
2. Asking CASAC to consider all of the CAA provisions for their review and advice, especially noting that they had not in the past been asked to “advise the Administrator of any adverse public health, welfare, social, economic, or energy effects which may result from various strategies for attainment and maintenance of such national ambient air quality standards,” as noted in Section 109 of the CAA.
3. Directing a streamlining of the NAAQS review process (i.e., by combining the development and review of the ISA, REA, and PA), while at the same time calling for differentiation between the science and policy judgments in the process.

This latter memo has also sparked controversy,\textsuperscript{10} extensive work to move ahead in the near term to streamline the process, and attempts to reconcile the somewhat contradictory requests to on one hand combine the science evaluation and policy-setting steps, while at the same time calling for stronger differentiation between science and policy considerations. The directive to more actively consider the CAA provisions seeking CASAC advice on, among other things, the “social, economic, or energy effects” has also sparked considerable controversy as the CAA has routinely been interpreted by the courts to not allow the explicit consideration of costs and other economic factors in the setting of the NAAQS.\textsuperscript{11}

**Ensuring Public Health is at the Center of NAAQS Decisions**

Through nearly 50 years, the process of developing and applying health science to inform air quality and public health decisions has worked well to distill the best evidence and contribute to substantial improvements in public health. Those improvements are now being documented in accountability, or intervention, studies of actual health benefits.\textsuperscript{12,13}

At the same time, the process has not been static: it now conducts much more systematic reviews of the literature and applies a rigorous framework for assessing causality based on a diverse literature. And the entire process is conducted in public view, with ample opportunity for public review and comment, and independent scientific peer review from CASAC. In the global work on control of air pollution, the U.S. approach is unique and much admired.

There are always opportunities to improve any such process, and the newest developments should be taken as an opportunity to make further improvements. But it is critical, in further enhancing the process, to not undermine the high-quality scientific process that it is in place, and its significant success. \textsuperscript{em}

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**References**


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