VIEWPOINT

The Advisory Committee on Immunization Practices and Its Role in the Pandemic Vaccine Response

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More than 3.7 million infections and more than 140 000 deaths due to coronavirus disease 2019 (COVID-19) have occurred in the US in the past 6 months. As case counts continue to increase, robust vaccine development efforts unprecedented in scale and speed are being pursued. More than 130 COVID-19 vaccines are in preclinical development using a variety of established and new platforms, and 17 candidate vaccines are undergoing evaluation in clinical trials in the US, Europe, and China.[1] The US government has invested in the development of 5 vaccines as part of Operation Warp Speed.[2] On June 25, the Chinese government approved the first COVID-19 vaccine (Ad5-nCoV) for use in the military population.

In the US, the Advisory Committee on Immunization Practices (ACIP) provides recommendations on the use of vaccines for effective control of vaccine-preventable diseases in the US civilian population on licensure by the Food and Drug Administration (FDA).[3] ACIP is a federal advisory committee, established in 1964, composed of 15 members who provide guidance on the optimal use of vaccines to the director of the Centers for Disease Control and Prevention and the secretary of the US Department of Health and Human Services. Thirty-three national organizations representing various aspects of the immunization delivery system (eg, health care and clinician organizations, pharmacies, immunization registries, health insurers, state/county public health) and 8 ex officio members (Centers for Medicare & Medicaid Services, Department of Defense, Department of Veterans Affairs, FDA, Health Resources and Services Administration, Indian Health Service, National Institutes of Health, and the Office of Infectious Disease and HIV/AIDS Policy) are also represented.

As a federal advisory committee, ACIP meetings are open to the public, committee documents are made available, and written and oral public comments are shared; hence, the ACIP process ensures transparency in decision-making regarding recommendations for vaccine use. In 2010, the committee formally adopted the Grading of Recommendations Assessment, Development and Evaluation framework to facilitate a standardized approach for evaluating scientific evidence. Furthermore, ACIP uses the evidence-to-recommendation framework as a tool for communicating deliberations and judgments it makes in formulating recommendations, based on burden of disease; efficacy and effectiveness; safety; the quality and certainty of evidence reviewed; values of the target population; resource use; acceptability (ethically, programmatically, financially, etc) among patients, clinicians, and immunization programs; and implementation issues.[4] ACIP recommendations are linked to access through the Vaccines for Children program, which provides vaccines at no cost for Medicaid-insured, underinsured, and uninsured children. Under provisions of the Patient Protection and Affordable Care Act (ACA), ACIP recommendations are also covered by health insurers and employer-sponsored health plans established after the passage of the ACA, although significant gaps remain for some insured, uninsured, or underinsured adults.

Policy making about vaccine use in the COVID-19 era highlights some unique challenges. The burden of severe disease is highest among older adults and American Indian/Alaska Native, Black, and Hispanic/Latinx populations, regardless of age.[5] Candidate populations for vaccine use may vary regarding risk of exposure (eg, congregate settings, health care settings) and risk for morbidity/mortality (eg, older age, race/ethnicity, presence of comorbidities, access to health care). Depending on the characteristics of each vaccine, such as effectiveness, number of doses required, durability of immunity, and safety profile, certain vaccines may be preferable in some populations over others. The timing of availability of different COVID-19 vaccines, as well as initial vaccine supply constraints relative to demand, will result in intense scrutiny of recommendations for use.

ACIP vaccine policy for endemic diseases is generally undertaken after decades of research to elucidate the epidemiology of the disease, transmission patterns, and risk factors, as well as to understand the immunology of infections and vaccines. Hence, evidence regarding the benefit-risk balance is generally ample. Furthermore, the majority of routinely recommended vaccines focus on children in the context of well-established schedules and delivery systems. The scientific uncertainties inherent in a newly emerged infection and newly developed vaccines at the onset of a pandemic and the need for rapid, equitable, and transparent distribution of vaccines present unique challenges for policy development. Simultaneously, these very characteristics make it even more important to provide evidence-based recommendations consistently. The ACIP had such a role during the 2009 influenza H1N1 pandemic, anticipating the need for recommendations that prioritized certain groups for early vaccination when vaccine supply was expected to be limited. An emergency ACIP meeting was convened in July 2009 to finalize these recommendations. The adoption of these recommendations allowed early engagement of state, tribal, territorial, and local public health authorities; hospitals and health systems; pharmacies; health insurers; community groups; and other organizations involved in vaccine delivery to support distribution and ensure consistent communication.

The ACIP COVID-19 Vaccine Workgroup was established in April 2020 to help inform evidence-based approaches to COVID-19 vaccination policy, using an open and transparent process for decision-making, with the

intent of providing draft recommendations to the full ACIP for consideration and a formal vote. The work group includes 41 members with expertise in epidemiology, vaccine safety, vaccinology, infectious diseases, immunology, general medicine, geriatrics, pediatrics, obstetrics, immunocompromised hosts, vaccine administration/delivery, public health/surveillance, ethics, health equity, communications, and emergency preparedness. The goals of the COVID-19 work group are to evaluate the available evidence and make recommendations regarding the safety and effectiveness of COVID-19 vaccines; the likelihood of vaccines to reduce transmission, morbidity, and mortality of COVID-19 disease; the potential of vaccines to help minimize disruption to society and economy, including maintaining health care capacity; and the approaches to help ensure equity in vaccine allocation and distribution.

ACIP convened an open meeting on June 24, 2020, to discuss the epidemiology and clinical characteristics of severe acute respiratory syndrome coronavirus 2 infection, immune responses to infection, vaccine candidates, and considerations for ACIP recommendations. Given the many unknowns, the emerging evidence base, and the need to make decisions under conditions of uncertainty, the ACIP developed several guiding principles to inform decision-making. First, safety was deemed to be of paramount importance, with the understanding that the concept of safety reflects the balance of benefits and risks of disease and vaccination, and that these risks may vary in different populations. Monitoring effectiveness and safety in real time will be critical to ensure that recommendations can be revised or adapted as new data emerge. Second, the importance of diversity in clinical trials (eg, race and ethnicity, comorbidities, older age, pregnant women, children) was emphasized as fundamental for ensuring that future recommendations are based on safety and efficacy data reflective of all of the populations who may benefit from COVID-19 vaccines. Third, efficient and equitable distribution of vaccines was highlighted as critical to minimize the compounding inequities already observed with COVID-19 disease in the US and long-standing disparities in adult vaccination coverage, as observed with influenza vaccines.[6]

On June 30, 2020, the FDA published guidance for industry on the development and licensure of vaccines, given the current state of knowledge about COVID-19 immunology, with the goal of pursuing traditional approval via direct evidence of vaccine safety and efficacy in protecting humans from infection and disease.[7] Recognizing the operational challenges of conducting trials in the setting of a public health emergency, the guidance recommended a primary relative efficacy end point of greater than 50% for a placebo-controlled trial, with a lower bound of the confidence interval around the primary efficacy end point of greater than 30% and stated safety evaluations should be no different than for other preventive vaccines for infectious diseases. Accelerated approvals might be considered if sufficient knowledge were generated about how vaccine immune responses correlate to protection. The FDA also included requirements for issuing an emergency use authorization for unapproved medical products in circumstances in which no other alternatives are available, although lower levels of evidence for "effectiveness" are needed for an emergency use authorization compared with traditional licensure approaches. Regardless of the pathway used, ACIP will continue to review all available evidence on the efficacy and safety of COVID-19 vaccine candidates to support near real-time decision-making on the benefit-risk balance of recommending use in targeted populations.

Although ACIP focuses on vaccine recommendations, the implementation of these recommendations will rely on strong partnerships with public health (eg, Association of State and Territorial Health Officials, National Association of County and City Health Officials), immunization registries, health care systems, pharmacies, health insurers, community groups, faith-based organizations, and others to help control the pandemic, reduce morbidity and mortality, and ensure that at-risk populations have timely and equitable access to COVID-19 vaccines. Furthermore, public engagement will be crucial throughout the deliberation process to help clarify values and preferences and to identify the most effective strategies.[8] Rapid, accurate, transparent, and timely communication efforts targeting both health care clinicians and the public are necessary to enhance trust, particularly because policies will need to adapt to reflect rapidly changing circumstances and new knowledge.

For many years, ACIP has played a central role in recommending vaccines for children, adolescents, and adults in the US. As part of the pandemic response, the process for decision-making and the use of transparent and evidence-based approaches to formulate recommendations have never been more critical. Given the many challenges ahead, maintaining public trust will be crucial before, during, and long after COVID-19 vaccines are deployed for use. Ensuring support for robust public health surveillance systems to monitor vaccine effectiveness and vaccine safety should help to enable a dynamic decision-making process that seeks to improve health, mitigate inequities, and restore stability to society and the economy.

ARTICLE INFORMATION

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