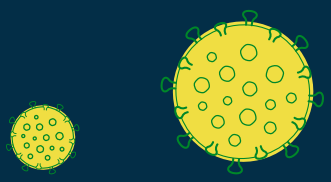
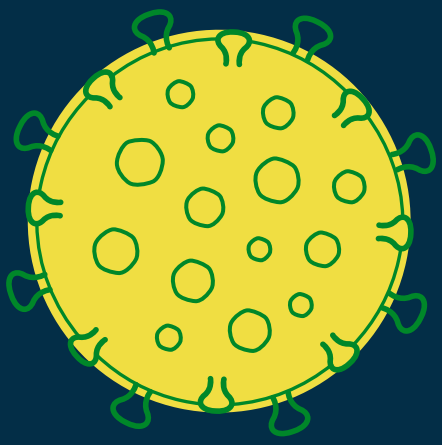
Influenza Vaccines R&D Roadmap





A Research and Development (R&D) Roadmap for Influenza Vaccines

Looking to the Future

EXECUTIVE SUMMARY

Threats from seasonal and pandemic influenza persist in a world still battling the COVID-19 pandemic. As another highly contagious respiratory virus, influenza causes a spectrum of disease, ranging from mild to fatal. Globally, it causes up to 1 billion infections annually and kills an estimated 290,000 to 650,000 people each year. The regular appearance of seasonal influenza outbreaks year after year can dull public concern for the significant amount of severe illness and death caused by the virus, particularly among the elderly and young children, and for those living in low- and middle-income countries (LMICs).

The chronic lack of urgency to address such a heavy burden may be compounded by the apparent absence of seasonal influenza during the COVID-19 pandemic. Experts also worry that the COVID-19 crisis is obscuring the very real threat of a pandemic caused by another respiratory disease, such as influenza, and that we are missing out on the opportunity to prepare for a future crisis that could be at least as deadly and disruptive as COVID-19, if not more so. Public health experts have estimated, for example, that the influenza pandemic of 1918-19 killed more than 50 million people globally.

At the same time, new advances and insights generated during COVID-19 vaccine development could prove instrumental in managing the risks of seasonal and pandemic influenza. Many of the advances in vaccinology, immunology, technology, and manufacturing that rapidly produced highly effective vaccines for fighting COVID-19 also provide an opportunity to gain the upper hand against influenza.

Now, at this unique moment in the history of global health, an international collaboration, initiated 3 years before the arrival of COVID-19, is offering an exciting opportunity to do just that. In 2017, at a time when influenza loomed as the biggest threat of sparking a global pandemic, an international partnership known as the *Global Funders Consortium for Universal Influenza Vaccine Development* concluded that global influenza preparedness required a vaccine research and development (R&D) roadmap that would provide a clear vision for organizing existing efforts and attracting new partners.

Over the next 2 years, the Wellcome Trust supported an effort led by the Center for Infectious Disease Research and Policy (CIDRAP) at the University of Minnesota to work in partnership with the World Health Organization (WHO), Wellcome Trust, the Sabin Vaccine Institute, the Bill & Melinda Gates Foundation, the Task Force for Global Health, and an expert taskforce to develop the Influenza

Vaccine R&D Roadmap (IVR). The steering group engaged more than 100 stakeholder organizations—representing diverse perspectives from 29 countries—in extensive discussions and consensus building to explore different components of influenza vaccine development.

The IVR addresses the significant barriers and opportunities for preventing influenza and lays out a concise 10-year plan to leverage the lessons from the COVID-19 pandemic and reduce the threat of influenza globally through two significant goals:

- **Improving the production and effectiveness of strain-specific seasonal influenza vaccines.** Even incremental improvements in the effectiveness of today's seasonal vaccines could translate into far fewer deaths and severe disease from influenza.
- **Advancing the development, licensure, and production of universal influenza vaccines.** Universal influenza vaccines would radically alter the battle against influenza by protecting against all influenza viruses that infect humans and those circulating in animals that risk crossing to humans and causing a pandemic.

The IVR provides a focused blueprint for action that will allow the world to apply the lessons learned from COVID-19 vaccine development as a springboard for launching a new era for influenza vaccine R&D.

Why It's Time to Update Influenza Vaccines

Rapid development of safe and effective influenza vaccines is critical to fighting influenza, especially given the need for a rapid response to pandemic strains. Every year, seasonal influenza vaccines prevent many deaths and limit the severity of disease in those infected. But current influenza vaccines are nowhere near as effective as they need to be.

Applying the lessons learned from the success of COVID-19 vaccine development will be critical to the development of improved influenza vaccines. COVID-19 vaccine development benefited from many years of research on messenger RNA (mRNA) platforms to rapidly produce highly effective vaccines in record time. By comparison, the vast majority of influenza vaccines available today are based on a reliable but outdated technology developed in the 1940s that involves growing vaccine strains in chicken eggs.

The IVR recognizes that while important gaps remain in our knowledge of influenza viruses and immune responses, influenza vaccines can be much more effective and production processes much faster. However, to achieve this requires embracing a new level of political commitment, partnerships, and investments—the same combination that accelerated the development of COVID-19 vaccines.

The IVR Blueprint for Action

The IVR is organized around six key areas of R&D, each of which contains specific technical milestones for measuring progress:

Vaccinology for Universal Vaccines

This is an achievement that would end the need for seasonal vaccinations and strengthen pandemic preparedness. **While many promising universal influenza vaccine candidates are under study, clinical development requires overcoming a variety of significant technical and logistical challenges**, such as conducting clinical trials over multiple seasons with different circulating viruses.

Vaccinology for Seasonal Influenza Vaccines

One strategy for improving efficacy of seasonal vaccines is to develop rapid production methods, which means vaccines can be produced closer to the influenza season, thereby making forecasting of dominant circulating strains more accurate. Faster production may be achievable via one of the vaccine approaches or platforms validated in COVID-19. The IVR also identifies potential approaches for improving the effectiveness of seasonal vaccination formulations for preventing infection and severe disease.

Virology

The goal of the virology work is to gain more insights into the changes occurring in influenza viruses as they circulate in humans and animals around the world. **The IVR focuses on research aimed at improving our understanding of influenza virus evolution and our ability to identify novel viruses with pandemic potential.**

Immunology and Immune Correlates of Protection

A major barrier to developing better influenza vaccines is that **scientists still don't know enough about how to generate a durable immune response to influenza infections and how to accommodate the effects of preexisting partial immunity in the population.** The research community also wants to clarify the role of T cell responses (i.e., cellular immunity) in infection and protection. T cell responses to COVID-19 vaccination may play an important role in preventing severe disease, but current influenza vaccines do not produce robust cellular immunity.

Animal and Human Influenza Virus Infection Models

Experimental animals used in influenza research—including mice, ferrets, swine, and non-human primates—are critical tools for accelerating vaccine development. But **they need further refinement to more accurately reflect human responses to influenza viruses and vaccines. The IVR identifies several strategies for improving insights from animal models.** It also encourages scientists to explore safe and ethical human challenge trials in which human volunteers are vaccinated with a new vaccine candidate and then "challenged" with an influenza virus.

Policy, Financing and Regulation

The IVR **calls for new communications and advocacy efforts targeting policy makers, funders, researchers, and the public health community to highlight the benefits of developing improved vaccines for seasonal and pandemic influenza**, including for use in LMICs. The IVR also calls for efforts to explore the feasibility of creating new public-private partnerships with sustainable funding, aimed at mission-driven R&D for universal influenza vaccines. This section also advocates for a global strategy to support the growing focus on establishing and expanding sustainable vaccine R&D and manufacturing in LMICs. Finally, this section highlights the importance of improved data sharing for R&D and the need for clarity regarding regulatory requirements for licensing broadly protective or universal influenza vaccines.

Leveraging COVID-19 Advances

The IVR provides a much-needed framework for organizing the efforts of existing influenza researchers while identifying a wide range of opportunities that will encourage new partners to play a role. The roadmap has the backing of many major supporters of influenza research and represents a vision for coordinated, integrated influenza research in an accountable, inclusive and critical global endeavor.

When work began on the roadmap, no one involved imagined their efforts would conclude in the middle of the most serious global health challenge of the last 100 years. But there is a significant upside of providing such an ambitious plan for influenza vaccines at time when COVID-19 has energized the entire field of vaccine development. Now it's time to learn from COVID-19 and tackle influenza.