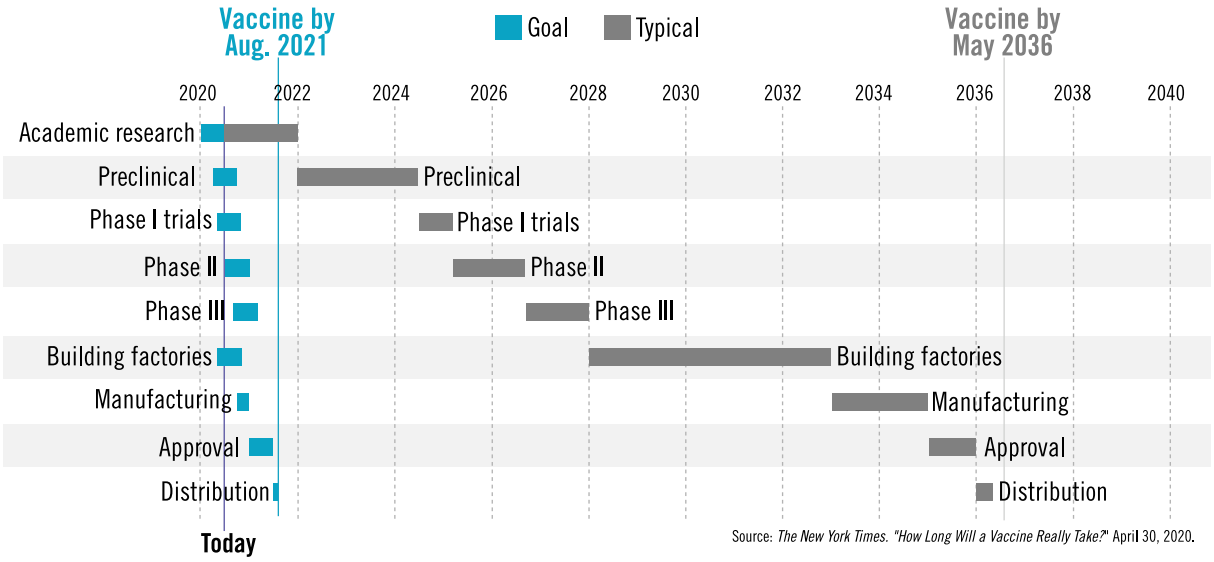
ADVOCATES' GUIDE: The risks and benefits of expedited COVID-19 vaccine research

AVAC
25 Years and Counting

Developing COVID-19 vaccines at "pandemic speed" depends both on an unprecedented global research effort and on a number of innovative strategies to shorten the vaccine testing and distribution timeline. Each of these strategies should be weighed against its relative risks and benefits, along with its potential to speed COVID-19 vaccine research. ***Speed is important, but not at the expense of ethics, safety, robust engagement, equitable access, and scientific rigor including independent peer and regulatory review.***

THE RACE FOR A COVID-19 VACCINE



Source: *The New York Times. "How Long Will a Vaccine Really Take?"* April 30, 2020.

STRATEGIES TO SHORTEN THE COVID-19 VACCINE TIMELINE

- Multiple vaccine approaches
- Concurrent testing
- Rapid data sharing
- Emergency regulatory approval
- New approaches to funding and research collaboration
- Early manufacturing scale-up
- A global sense of urgency

Testing multiple vaccine approaches simultaneously

More than 140 COVID-19 vaccine candidates have entered preclinical and human studies. Because of the extraordinary global interest in developing safe, effective and easy-to-produce COVID-19 vaccines as quickly as possible, the candidates represent a broad array of approaches (e.g., DNA, RNA, live-attenuated, inactivated, subunit and viral vector vaccines).

BENEFITS

- Testing a variety of vaccine approaches simultaneously can identify the strongest candidates more quickly and ensure that there are alternative approaches to consider when products fail.
- This approach may also lead to the development and distribution of multiple COVID-19 vaccines, with different product profiles and mechanisms of action.

RISKS

- It is possible that this rapid, multi-pronged approach means some potentially promising vaccines could be discarded too quickly.
- Significant resources could be spent researching weak candidate vaccines that would not have entered human clinical trials under less-urgent circumstances.

TAKEAWAY

Simultaneous testing of large numbers of candidates across multiple platforms increases the chances of quickly finding a safe and efficacious vaccine.

Run different study phases concurrently

The traditional approach to vaccine testing runs preclinical and then Phase I, II and III studies in sequence, sometimes with gaps between each study. To speed timelines, some COVID-19 vaccine studies are advancing to the next phase of research as soon as data show the vaccine is promising and safe, even while the previous study phase is still underway.

TAKEAWAY

Accelerating preclinical and clinical testing must not be done at the expense of safety.

BENEFITS

- Compressing traditional research timelines produces faster results without eliminating any steps in the research process.

RISKS

- Executing research steps in parallel, before confirming a successful outcome, results in significant elevated financial risk for product developers and taxpayers.
- Normally, researcher conduct trials in animals over the course of months to identify a range of safety issues and to rule out the possibility of disease enhancement, the rare occurrence where the vaccine actually makes the disease worse once a vaccinated person is naturally infected. Expedited research may limit scientists' ability to identify enhancement, or other potential safety issues, in animals before moving to humans.
- Governments and/or vaccine developers may be tempted to shorten, or eliminate, Phase 3 testing, which is critical to proving efficacy and testing safety in larger numbers of people, as China and Russia have done.

Rapid data sharing

Traditionally, the results of scientific studies are published in peer-reviewed academic journals or presented at research conferences following months of preparation. Because COVID-19 vaccine science is progressing so rapidly, some journals are shortening or eliminating the review process and publishing data in an initial "preprint" form that makes data available rapidly, but with little or no review by outside researchers. Bypassing outside review can also lead to "science by press release", in which summary results are released directly to the media, with extremely limited data or without necessary context on the research's limitations.

BENEFITS

- Shorter data review periods make study results available faster, guiding the next phases of research and speeding vaccine development timelines.
- Many researchers and advocates welcome the transparency and fast access to information that preprints provide.

RISKS

- Reducing or eliminating peer review—the careful scrutiny of a study by outside experts—can reduce opportunities to identify errors or raise important questions about a study's findings.
- Publication by press release can be used to manipulate public reaction, generate funding or hide information that is critical to interpreting study findings.
- When results are misrepresented or the tentative nature of preprints is not clearly communicated, there is the potential to damage public trust in scientific findings and vaccines in general.

TAKEAWAY

Expedited data sharing must include a minimum data set and be paired with careful public framing around the tentative nature of preprints and followed by the opportunity for rigorous peer-review in advance of decision-making.

Emergency regulatory approval

Regulatory review by agencies such as the US Food and Drug Administration (FDA) or the European Medicines Agency (EMA) is traditionally a methodical, rigorous process that can take many months. HIV advocates have played a vital role in speeding review of new treatment and prevention options for HIV and AIDS, creating innovative and patient friendly trial designs and the compassionate use and emergency access systems being used today to help ensure rapid access to potential prevention and treatments for COVID-19.

TAKEAWAY

Regulatory review can only be accelerated to a point; it must be based on adequate data and allow for the thoughtful, informed and unbiased decision-making that is central to the product approval process.

BENEFITS

- Faster access to safe and effective prevention or treatments in development could save lives.
- Under certain conditions, emergency access paired with research can also provide data to help speed the study of promising products.

RISKS

- Completed Phase III trials are essential to determining if a candidate vaccine is safe and effective. Approval without a complete Phase III study reduces the possibility of identifying whether a vaccine is truly effective, and subtle and rare side-effects that may not have been identified in earlier, smaller studies.
- If an emergency approval appears to have been influenced by politics—for example, when political leaders indicate support or "belief in" a particular treatment without scientific evidence—public faith in regulatory review can be damaged, resulting in decreased uptake.

New approaches to funding and research collaboration

The COVID-19 vaccine response has ushered in a new era of collaboration in research and research funding. Based on models developed in HIV research, collaboratives such as ACTIV, ACT-A, Operation Warp Speed and others are pursuing different approaches to speed COVID-19 vaccine development by collaborating on COVID-19 vaccine science and funding. This includes advance purchase commitments, where public-sector and philanthropic funders negotiate a price and plan to purchase and distribute vaccines before the vaccine testing process is completed.

BENEFITS

- Pooling funding and sharing research data and expertise can speed scientific innovation.
- Collaborative research and funding can help to build and strengthen research infrastructure and expertise in the global South.
- Advance commitments can give manufacturers the confidence to scale up production capacity for vaccines in development and reduce delays in access once a vaccine has been proven safe and effective.

RISKS

- Depending on the makeup of the collaboration, some partnerships may encourage overly nationalistic vaccine development efforts, which allow wealthy countries to prepurchase doses for their own citizens, reducing availability for low- and middle-income countries.

TAKEAWAY

Research collaborations should clearly articulate a commitment to the rational, equitable and global distribution of safe and effective vaccines.

Scaling up production while vaccines are tested

Vaccines can be complex to produce, package and distribute. This is why there is usually an extended interval from the time a vaccine is proven effective until it is available for large-scale use. With early manufacturing capacity scale-up, private and public entities fund the production of large quantities of the most promising vaccine candidates before testing on those vaccines is complete.

TAKEAWAY

Early scale-up of manufacturing capabilities can dramatically reduce the lag time between when a vaccine receives regulatory approval, and when it is available for wide use

BENEFITS

- Scaling up vaccine production in advance could save tens of thousands of lives and help end the pandemic faster.
- Early scale-up can help to identify and address any manufacturing challenges in advance of licensure.

RISKS

- Scaling up production costs hundreds of millions of dollars, and if a vaccine is not safe or effective, it uses up money that could have been spent on other global health needs.
- If production scale-up is concentrated in wealthier nations (as is currently the case, with the exception of India), it could exacerbate unequal access to an eventual vaccine in countries with less vaccine manufacturing capacity.

A global sense of urgency

COVID-19 has produced an unprecedented global commitment to rapid biomedical research. Signs are emerging, however, that an emphasis on speed may make some people anxious about COVID-19 vaccine safety.

BENEFITS

- The global sense of urgency fuels all the innovations outlined here: from innovative research timelines to scientific and funding collaboration to precommitments for vaccine production.
- This collective sense of urgency could fuel positive changes in research processes, and commitments to make lifesaving technologies available, for years to come.

RISKS

- Pressure to accelerate vaccine development, combined with language such as "Operation Warp-Speed", may raise concerns that safety will be sacrificed for speed and exacerbate vaccine hesitancy.
- If language about speed is not matched with information reinforcing the commitment to the highest quality of scientific research, confidence in vaccines may falter.
- The urgency to enroll large-scale clinical trials of vaccines cannot interfere with the need to ensure the informed consent of participants or broad community engagement in study design and implementation.

TAKEAWAY

Speed is important, but not at the cost of safety or meaningful community engagement.

What advocates can do

The rapid pace of COVID-19 vaccine development presents challenges that HIV advocates are uniquely qualified to meet. To help ensure that the COVID-19 vaccine development effort is not only the fastest in history, but also one of the safest and most inclusive, HIV advocates can:

Promote the GPP Principles in research

Guidelines for the ethical design and conduct of research such as the Good Participatory Practice (GPP) Guidelines for HIV Prevention Research, Good Participatory Practice Guidelines for TB Vaccine Research, Good Participatory Practice Guidelines for TB Drug Trials and Good Participatory Guidelines for Emerging Pathogens (GPP-EP) emphasize the centrality of community consultation and provide ethical guidelines that can be quickly and effectively adapted to COVID-19 research.

Insist on high-quality community engagement

Phase III trials of COVID-19 vaccine candidates will seek to enroll tens of thousands of participants rapidly. These studies may face pressure to reduce their community engagement and participant education efforts in order to speed the process. Decades of experience show, however, that the only way to ensure successful clinical research is to invest in thoughtful, thorough and inclusive outreach to ensure community input into study design and processes, and true informed consent by study participants. Inclusion of community advocates on protocol teams will result in more patient-friendly, ethical protocols and more expeditious resultsAVAC, TAG and ITPC have created the Covid Advocates Advisory Board (CAAB) to strategically engage civil society and community representatives in COVID R&D—consider joining us! (*www.covidadvocates.org*)

Ensure that affected communities lead

Like HIV, COVID-19 is not an equal opportunity virus. Poorer communities and Black and Brown communities around the world are more seriously affected and have poorer outcomes from the disease. These are also the communities in which much of the later stages of COVID-19 vaccine research will take place. It's essential, for the quality of the research, the safety of participants and public support for any vaccine that emerges from these studies that the communities most impacted by COVID-19 play clear leadership roles in the engagement efforts that can make COVID-19 vaccine research successful.

Resist the politicization of science

Advocates' messaging should be clear: political leaders can build public support for vaccine research, support funding efforts and ensure that regulatory and other systems work efficiently to ensure rapid, high-quality research and broad, affordable access to vaccines. Advocates must speak out, however, when politicians promote misinformation about the disease or research timelines, encourage stigma or favor particular products outside of the scientific process.

Help to rebuild public faith in vaccines

Community involvement in the process is key to strengthening public faith in vaccines and other products of biomedical research. Visible, engaged advocates can help to explain research processes, (including new approaches necessitated by COVID-19), counter misinformation, frame preliminary and fast-moving science, relay community concerns and help ensure the true community engagement help ensure true community engagement. That engagement will be critical to developing COVID-19 vaccines that work not just in the lab, but actually help to end the pandemic worldwide.

About AVAC

AVAC is a non-profit organization that uses education, policy analysis, advocacy and a network of global collaborations to accelerate the ethical development and global delivery of new HIV prevention options as part of a comprehensive response to the pandemic. For more information, visit ***www.avac.org***.