Vaccine: Volunteer Melissa Harting, from Harpersville, New York, receives a COVID-19 vaccine injection from nurse Kathe Olmstead. Harting is participating in the world's largest study of a possible COVID-19 vaccine, developed by the National Institutes of Health and Moderna Inc.

DOI: 10.1377/hlthaff.2020.01732

After A COVID-19 Vaccine: Collaboration Or Competition?

As COVID-19 vaccines and therapies emerge, critical questions remain about access and affordability around the world.

BY HARRIS MEYER

Effective international collaboration not only could end the coronavirus disease 2019 (COVID-19) pandemic and restore the global economy but also could lead to revolutionary improvements in vaccine and therapeutic drug development, drug regulation, clinical trial design, and health care delivery. Alternatively, lack of cooperation and coordination by governments, nongovernmental organizations, and manufacturers could prolong the pandemic, producing an outcome where more people die and economic devastation continues indefinitely.

Those sharply different scenarios both remain possible as some wealthy nations like the US move to lock up future supplies of experimental COVID-19 vaccines through individual deals with manufacturers even as other countries pool their resources to develop and equitably distribute vaccines through the World Health Organization (WHO)–sponsored COVID-19 Vaccine Global Access Facility (COVAX).[1,2]

Experts discussed these unprecedented opportunities and challenges at a Health Affairs online symposium, "Promoting Innovation and Equity as COVID-19 Vaccines and Treatment Emerge," presented August 24, 2020.

There was excitement among the speakers about the rapid, pandemic-driven advances in science, clinical trial, and regulatory processes and collaborations among governments, manufacturers, and nongovernmental organizations that could improve global health in the future. But there were deep concerns about whether the US, China, and other countries will be able to transcend nationalist rivalries to defeat their common viral foe and whether profit incentives will get in the way.

"We can choose to collaborate and bring the world back to health equitably, or we can compete and exacerbate inequities," Orin Levine, director of Global Delivery Programs at the Bill & Melinda Gates Foundation, said in his opening remarks. "A moment is coming soon when we have a breakthrough on a lifesaving vaccine. Then humanity will be tested on the question of equity."

'Missed Opportunity'

On September 1, 2020, a White House spokesperson said that the US would not join COVAX to develop and equitably distribute a vaccine because the effort is "influenced by the corrupt World Health Organization and China."[3]

Meanwhile, Germany, Japan, and the European Commission have announced their participation, although the terms of their cooperation remain undisclosed. A total of seventy-eight higher-income countries and ninety-two lower-income countries have expressed interest in participating, according to Gavi, the Vaccine Alliance, which co-leads COVAX

Photograph by AP Photo/Hans Pennink

with the WHO and the Coalition for Epidemic Preparedness Innovations (CEPI) (Gavi spokesperson, personal communication, September 16, 2020). Countries had until September 18 to make a binding legal commitment—a date that was pushed back from the original August 31 deadline.

Resistance from wealthy nations reportedly forced the COVAX sponsors to redesign the program and delay the deadlines. Among the changes made is a more flexible payment model enabling countries to opt out of vaccines they already have acquired through individual purchase deals and to trade any excess vaccines from their own deals through a COVAX exchange platform.[4]

Many public health experts lamented the Trump administration's decision not to join COVAX, which some criticized as vaccine nationalism. "If COVID has taught us anything, it's that we're all interdependent," Nicole Lurie, a CEPI strategic adviser and former Department of Health and Human Services assistant secretary who spoke at the symposium, said in an emailed comment. "This is a huge missed opportunity to change the way the world works together to respond to pandemics."

The COVAX initiative grew out of the world's experience in dealing with the H1N1 influenza pandemic in 2009, when the US delayed for months in sharing with less wealthy nations the vaccine it had developed to combat that virus.[5]

The initiative's approach is for wealthier countries to provide up-front funding and purchasing guarantees to a range of COVID-19 vaccine developers with the stated goal of guaranteeing all countries enough doses of proven vaccines to inoculate at least 20 percent of their populations.[2] Advocates claim that everyone wins: Wealthier countries get the promise of guaranteed access to a broader pool of potentially effective vaccines, and the entire world's population gets vaccinated, enabling the global economy to reopen.

"With infectious disease, no one is safe until everyone is safe," Seth Berkley, Gavi's chief executive officer, wrote in July 2020.[6]

COVAX currently is providing research, development, and manufacturing funding for nine candidate vaccines, seven of which are now are in clinical trials, with a pledge to buy those that prove effective. The nine candidates include vaccines being developed by Moderna, AstraZeneca, Inovio, and Novavax.

One of those potential vaccines, developed by AstraZeneca and the University of Oxford, suffered a setback in early September when Phase III trials in the US were put on hold because of a suspected serious adverse reaction to the product by a participant in the United Kingdom.[7] Although the hold could be temporary, it may delay efficacy results as trials of other candidates race ahead.

An additional nine candidate vaccines are being evaluated for inclusion by COVAX. Governments, vaccine manufacturers, other organizations, and individuals have committed $1.4 billion toward vaccine research and development so far, but an additional $1 billion is needed to move the research and development portfolio forward, according to the WHO.

At the same time, wealthy nations have struck their own deals with manufacturers to develop and purchase COVID-19 vaccine candidates should they be approved, potentially locking up billions of doses. The Trump administration's Operation Warp Speed initiative has reached deals for at least seven candidates in various stages of development, including products being developed by Moderna and Pfizer that are in Phase III clinical trials in the US.[8]

The European Commission, negotiating on behalf of all twenty-seven European Union states, has agreed to buy at least 300 million doses of AstraZeneca's potential vaccine, with an option to buy an additional 100 million doses. That product has just started Phase III trials in the US.[9]

In total, the US, the European Union, Japan, and the United Kingdom have agreed to buy more than three billion doses of various vaccine candidates, whereas China and India, which are working on their own vaccines, likely will keep much of their production for their own populations.[10]

"If these giant bilateral deals result in hundreds of millions of doses being hoarded by rich countries, that's a threat to achieving global herd immunity," Gavin Mark Yamey, a professor of global health at Duke University who spoke at the symposium, said in an interview.

In a new paper, Yamey and several Duke colleagues urge that such deals include provisions to promote the sharing of data and technology with other manufacturers and countries, enabling others to rapidly produce and distribute effective vaccines throughout the world.[11]

"There are dramatic opportunities for all to win, and also dramatic opportunities for all to lose," said David McAdams, an economics professor at Duke who coauthored the paper.

'The Same Access Questions'

Food and Drug Administration (FDA) Commissioner Stephen Hahn recently said that he will consider granting emergency authorization for a COVID-19 vaccine even before clinical trials have been completed if the benefits outweigh the risks. "This is going to be a science, medicine, data decision," Hahn recently told the *Financial Times*, even though he previously acknowledged he is under pressure to deploy a vaccine as fast as possible. "This is not going to be a political decision."[12]

Robert Redfield, director of the Centers for Disease Control and Prevention (CDC), recently urged states to get their vaccine distribution sites ready by November 1.[13] State and local officials say that will be a daunting challenge, given vaccine cold storage requirements, lack of vaccine administration tracking tools, public health departments' limited staffing and resources, and other logistical issues.[14]

Vaccines are hardly the only tough issue. Symposium speakers stressed the importance of rapidly testing and producing therapeutic products for COVID-19 and making them affordable for people all over the world. There are 184 treatments for COVID-19 in clinical trials, as well as forty-three antiviral products in trials, according to the Biotechnology Innovation Organization, a pharmaceutical industry trade group.

Many of the COVID-19 therapeutics in development are monoclonal antibodies—biologically derived treatments that can cost more than $100,000 a year. Previously approved monoclonal antibody treatments for other diseases, such as for rheumatoid arthritis, are largely unavailable in poorer countries and

even to Americans lacking good health insurance. At the symposium, Mark Feinberg, CEO of IAVI, a not-for-profit research organization focused on global health, urged stronger efforts to broaden access to these products, which may hold promise for COVID-19 prevention and treatment.

"We need to map out what is necessary to make sure people can benefit from these products, and deal with the same access questions as for vaccines," Feinberg said.

One approach to making COVID-19 therapies more affordable is repurposing off-patent or generic drugs. Rena Conti, an associate professor of markets, public policy, and law at Boston University, and colleagues found that of about 300 drugs in development for COVID-19 treatment, one-third were products that had lost patent protection.[15]

But manufacturers have shown little interest in exploring these drugs for COVID-19 treatment because "there's no money in it," Conti said at the symposium. She called for the US government to take a more prominent role in testing and manufacturing existing drugs for treating coronavirus disease.

The government also needs to design policy to make expensive orphan drugs that show potential in for treating coronavirus, such as nivolumab and ruxolitinib, far more affordable, Conti and Kao-Ping Chua wrote in a recent Health Affairs Blog post.[15] Among the possible policy options are revoking the 340B exemption for orphan drugs, encouraging generic and biosimilar competition, and advance market deals between the government and manufacturers for reduced prices in exchange for volume purchasing and other benefits to companies.

"We need an all-in strategy to develop and repurpose existing therapeutics for the pandemic now and to address other pandemics in the future," Conti said.

'Imagine'

Standardized trial protocols and streamlining of regulatory processes also would speed development of vaccines and treatments and reduce their costs for the current and future pandemics, said Esther Krofah, executive director of FasterCures at the Milken Institute.

If and when safe and effective vaccines are developed and approved, there will be major challenges in distribution, allocation, and prioritization of who gets them.

She advocated the master protocol model, in which a single infrastructure and trial design is used to simultaneously evaluate multiple products in multiple substudies. For example, the WHO used a master protocol in its international Solidarity trials to rapidly evaluate the potential COVID-19 treatment hydroxychloroquine, finding it ineffective. The Adaptive COVID-19 Treatment Trial master protocols, established through the National Institutes of Health, studied remdesivir. The British master protocol study, RECOVERY, provided definitive evidence that dexamethasone decreased mortality for severely ill patients with COVID-19.

Other research and regulatory innovations, such as greater use of telemedicine and real-world evidence, also would help strengthen clinical trials, Krofah added.

In a recent op-ed, University of Pennsylvania physician and bioethicist Ezekiel Emanuel and two colleagues contrasted the major COVID-19 research results produced in Great Britain through large, simple, randomized trials with the dearth of pathbreaking research in the US, where researchers lean toward smaller, complex trials.[16]

"Imagine a world post-COVID where these kinds of master protocol trials could be helpful for rare diseases as well as conditions like Alzheimer's," Krofah said. "Once the public health declaration [for COVID-19] has ended, will these innovations also end, or can we work them into our normal practice?"

The pharmaceutical industry, however, isn't necessarily enthusiastic about master protocols, Lurie said. If a company's vaccine candidate doesn't perform as well as others in an apples-to-apples comparison, it may become a lot more difficult for a manufacturer to make the case for its product.

Phyllis Arthur, the Biotechnology Innovation Organization's vice president for infectious diseases and diagnostics policy, who spoke at the symposium, said in an interview that manufacturers do accept the need for comparable data on each COVID-19 vaccine candidate to streamline regulatory review, although her organization has not taken a position on master protocols for COVID-19 products. She added that manufacturers might not find master protocols appropriate for commercial products outside the COVID-19 space.

She also rejected the idea that manufacturers, as part of the COVAX framework, should be required to share technology with other countries and manufacturers to accelerate development and production of vaccines around the world. "Companies already are solving this issue through their own partnerships with manufacturers in other countries to make sure there is global access," she said. "There's no need for any required technology transfer."

'Science By Press Release'

If and when one or more safe and effective vaccines are developed and approved, there will be major challenges in distribution, allocation, and prioritization of who gets them. And it's not clear whether enough Americans and people in other countries will trust the safety and efficacy of the vaccines and get vaccinated. It's estimated that as much of 70 percent of the population will have to get vaccinated to achieve herd immunity.[17] A vaccine must only be 50 percent effective to win FDA approval.[18]

Multiple symposium speakers expressed fears that there may be far-reaching consequences if political considerations intrude into government approvals of COVID-19 therapies and vaccines. They cited recent Trump administration announcements and decisions on potential COVID-19 treatments—notably, hydroxychloroquine and convalescent plasma therapy—that later were withdrawn or widely criticized because of a lack of scientific evidence.[19] The appearance of political interference and haste could limit the public's willingness to get vaccinated at a time when there already is significant popular resistance to

vaccines in general.

Seventy-eight percent of Americans worry that the COVID-19 vaccine approval process is being driven more by politics than science, according to a recent survey by the Harris Poll and STAT.[20] Another recent Harris Poll survey found that about 30 percent of Americans said they were unlikely to seek a COVID-19 vaccine.[21]

"We're unfortunately seeing science by press release," Margaret Hamburg, foreign secretary of the National Academy of Medicine and former FDA commissioner, said at the symposium. "I worry this is adding a new form of vaccine hesitancy, even for the most sophisticated vaccinologists."

Vaccine hesitancy remains particularly problematic in poor and minority communities in the US, where decades of racism, discriminatory medical treatment, and infamous medical abuses like the Tuskegee syphilis experiment have seeded a deep skepticism of medical authority.

Vaccine trials in the US so far have failed to recruit enough people of color to match their percentage of the population.[22] This shortcoming persists despite the high rate of COVID-19 cases among Blacks, Hispanics, and Native Americans, which is more than 2.5 times the rate among Whites; hospitalization rates for those groups are four to five times higher those of Whites, and death rates among Blacks are twice as high as for Whites, according to the CDC.[23]

It probably didn't help that the Trump administration dubbed its vaccine development effort "Operation Warp Speed," stressing haste over safety.

Multiple symposium speakers expressed fears that there may be far-reaching consequences if political considerations intrude into government approvals of COVID-19 therapies and vaccines.

"Why are these communities hesitant, especially with that hyperbole?" said Garth Graham, vice president and chief community health officer at CVS Health. "Because this may be moving at a speed that's not beneficial to them."

The Department of Health and Human Services recently announced that it will launch a major public awareness campaign in the media focusing on vaccine safety and efficacy.[21] But Graham said that public health officials and providers need to embed themselves deeply in communities to correct misinformation and build vaccine trust.

"If you want to reach the community, you need to be in the community and use trusted people," Graham said. "Years of systemic racism have shaped these communities. We have to understand their experiences."

CVS, for example, has made COVID-19 testing available at nearly 1,000 store locations and partnered with free clinics, community colleges, and federally qualified health centers to provide tests in underserved communities at no cost, Graham said.

'The Other Side'

Even as the fate of the international vaccine effort remains uncertain, many experts hold out hope that the world's efforts to combat the COVID-19 pandemic will lead to major advances in global health. At the very least, the crisis has exposed weaknesses in public health systems, clinical research and regulatory processes, national social safety nets, and international collaborative structures, potentially spurring reforms.

The Gates Foundation's Levine pointed to how the pandemic has sped up efforts to expand the availability of medical oxygen to children in lower-income countries suffering from pneumonia. Historically, such children have died by the millions as a result of a lack of access to this life-saving therapy. Given the urgent need for treatment of patients with COVID-19 with medical oxygen, countries and organizations such as the United Nations Children's Fund are working to improve supply chains, financing, and training of health care workers for this therapy, with the benefits spilling over to kids with pneumonia.

"It's hard right now, when everyone is in emergency mode with their lizard brain firing, to look at the horizon," Levine said in an interview. "There is an opportunity to come out the other side better than where we went in." ■

The *Health Affairs* symposium described in this article was supported by Anthem Inc., Amgen Inc., Avalere, Kaiser Permanente, Pharmaceutical Research and Manufacturers of America (PhRMA), Gilead, McKesson, Quest Diagnostics, Dynavax, Alexion, and Danaher. **Harris Meyer** (harris_meyer@yahoo.com) is a freelance writer based in Chicago, Illinois. [*Published online September 28, 2020.*]

NOTES

1 Callaway E. The unequal scramble for coronavirus vaccines—by the numbers. Nature. 2020; 584(7822):506–7.

2 World Health Organization [Internet]. Geneva: WHO; 2020. Press release, 172 countries and multiple candidate vaccines engaged in COVID-19 vaccine Global Access Facility; 2020 Aug 24 [cited 2020 Sep 10]. Available from: https://www.who.int/news-room/detail/24-08-2020-172-countries-and-multiple-candidate-vaccines-engaged-in-covid-19-vaccine-global-access-facility

3 Rauhala E, Abutaleb Y. U.S. says it won't join WHO-linked effort to develop, distribute coronavirus vaccine. Washington Post [serial on the Internet]. 2020 Sep 1 [cited 2020 Sep 10]. Available from: https://www.washingtonpost.com/world/coronavirus-vaccine-trump/2020/09/01/b44b42be-e965-11ea-bf44-0d31c85838a5_story.html

4 Mancini DP, Peel M. "Vaccine nationalism" delays WHO's struggling Covax scheme. Financial Times [serial on the Internet]. 2020 Sep 2 [cited 2020 Sep 10]. Available from: https://www.ft.com/content/502df709-25ac-48f6-aee1-aec7ac03c759

5 World Health Organization. Main operational lessons learnt from the WHO pandemic influenza A (H1N1) vaccine deployment initiative [Internet]. Geneva: WHO; 2012 [cited 2020 Sep 10]. Available from: https://apps.who.int/iris/handle/10665/44711

6 Berkley S. In the COVID-19 vaccine race, nobody wins unless everyone wins. Fortune [serial on the Internet]. 2020 Jul 8 [cited 2020 Sep 10]. Available from: https://fortune.com/2020/07/08/covid-19-vaccine-alliance-update-cooperation-coronavirus-vaccines/

7 Robbins R, Feuerstein A, Branswell H. AstraZeneca Covid-19 vaccine study put on hold due to suspected adverse reaction in participant in the U.K. STAT [serial on the Internet]. 2020 Sep 8 [cited 2020 Sep 10]. Available from: https://www.statnews.com/2020/09/08/astrazeneca-covid-19-vaccine-study-put-on-hold-due-to-suspected-adverse-reaction-in-participant-in-the-u-k/

8 Hancock J. They pledged to donate rights to their COVID vaccine, then sold them to pharma. Kaiser Health News [serial on the Internet]. 2020 Aug 25 [cited 2020 Sep 16]. Available from: https://khn.org/news/rather-than-give-away-its-covid-vaccine-oxford-makes-a-deal-with-drugmaker/

9 Guarascio F. EU agrees first COVID-19 vaccine deal with AstraZeneca in WHO blow. U.S. News & World Report [serial on the Internet]. 2020 Aug 14 [cited 2020 Sep 10]. Available from: https://www.usnews.com/news/top-news/articles/2020-08-14/eu-reaches-deal-with-astrazeneca-for-at-least-300-million-doses-of-potential-covid-19-vaccine

10 Shah S. In race to secure Covid-19 vaccines, world's poorest countries lag behind. Wall Street Journal [serial on the Internet]. 2020 Sep 1 [cited 2020 Sep 10]. Available from: https://www.wsj.com/articles/in-race-to-secure-covid-19-vaccines-worlds-poorest-countries-lag-behind-11598998776

11 McAdams D, McDade KK, Ogbuoji O, Johnson M, Dixit S, Yamey G. Incentivizing wealthy nations to participate in the COVID-19 Vaccine Global Access Facility (COVAX): a game theory perspective [Internet]. Durham (NC): Center for Policy Impact in Global Health; 2020 Aug [cited 2020 Sep 10]. Available from: http://centerforpolicyimpact.org/wp-content/uploads/sites/18/2020/08/COVAX-Facility_Game-Theory-Analysis_FINAL.pdf

12 Stacey K. FDA head says he is willing to fast-track Covid-19 vaccine. Financial Times [serial on the Internet]. 2020 Aug 30 [cited 2020 Sep 10]. Available from: https://www.ft.com/content/f8ecf7b5-f8d2-4726-ba3f-233b8497b91a

13 Wilner M. "Urgent" request sent to states in push for coronavirus vaccine delivery by Nov. 1. Centre Daily Times [serial on the Internet]. 2020 Sep 2 [cited 2020 Sep 10]. Available from: https://www.centredaily.com/news/coronavirus/article245406245.html

14 Szabo L. Health officials worry nation's not ready for COVID-19 vaccine. Kaiser Health News [serial on the Internet]. 2020 Sep 2 [cited 2020 Sep 10]. Available from: https://khn.org/news/health-officials-worry-nations-not-ready-for-covid-19-vaccine/

15 Chua K-P, Conti RM. How orphan drug policy could impede access to COVID-19 treatments. Health Affairs Blog [blog on the Internet]. 2020 Jun 25 [cited 2020 Sep 10]. Available from: https://www.healthaffairs.org/do/10.1377/hblog20200623.498157/full/

16 Emanuel EJ, Zhang C, Diana A. Where is America's groundbreaking Covid-19 research? New York Times [serial on the Internet]. 2020 Sep 1 [cited 2020 Sep 10]. Available from: https://www.nytimes.com/2020/09/01/opinion/coronavirus-clinical-research.html

17 O'Keefe SM. One in three Americans would not get COVID-19 vaccine. Gallup [serial on the Internet]. 2020 Aug 7 [cited 2020 Sep 10]. Available from: https://news.gallup.com/poll/317018/one-three-americans-not-covid-vaccine.aspx

18 Food and Drug Administration. Development and licensure of vaccines to prevent Covid-19 [Internet]. Silver Spring (MD): FDA; 2020 Jun [cited 2020 Sep 10]. p. 14. Available from: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/development-and-licensure-vaccines-prevent-covid-19

19 Hamburg MA, Sharfstein JM. The FDA must stand up for itself and for science, not politics. Washington Post [serial on the Internet]. 2020 Aug 25 [cited 2020 Sep 16]. Available from: https://www.washingtonpost.com/opinions/the-fda-must-stand-up-for-itself-and-for-science-not-politics/2020/08/25/7c253742-e70c-11ea-bc79-834454439a44_story.html

20 Silverman E. Poll: most Americans believe the Covid-19 vaccine approval process is driven by politics not science. STAT [serial on the Internet]. 2020 Aug 31 [cited 2020 Sep 10]. Available from: https://www.statnews.com/pharmalot/2020/08/31/most-americans-believe-the-covid-19-vaccine-approval-process-is-driven-by-politics-not-science/

21 Hopkins JS. A Covid-19 vaccine problem: people who are afraid to get one. Wall Street Journal [serial on the Internet]. 2020 Aug 28 [cited 2020 Sep 10]. Available from: https://www.wsj.com/articles/covid-19-vaccine-hesitancy-is-a-growing-concern-for-researchers-health-officials-11598607002

22 Johnson CY. Large U.S. covid-19 vaccine trials are halfway enrolled, but lag on participant diversity. Washington Post [serial on the Internet]. 2020 Aug 27 [cited 2020 Sep 16]. Available from: https://www.washingtonpost.com/health/2020/08/27/large-us-covid-19-vaccine-trials-are-halfway-enrolled-lag-participant-diversity/

23 Centers for Disease Control and Prevention. COVID-19 hospitalization and death by race/ethnicity [Internet]. Atlanta (GA): CDC; [last updated 2020 Aug 18; cited 2020 Sep 10]. Available from: https://www.cdc.gov/coronavirus/2019-ncov/covid-data/investigations-discovery/hospitalization-death-by-race-ethnicity.html