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A COVID-19 Vaccine at 'Warp Speed' Raises Myriad Ethical Questions

By Melinda Young

The United States is at a challenging and possibly dangerous crossroad as the desire for speedy development of a COVID-19 vaccine might be pushing political concerns ahead of safety, efficacy, and the regulatory process, bioethicists and researchers say.

In May, President Trump launched Operation Warp Speed, including agreements with pharmaceutical companies and a \$12 billion federal investment in six vaccine candidates with the intention of shaving years off the typical decade-plus vaccine development process.¹

In early August, President Trump said he expected a coronavirus vaccine to be ready by the Nov. 3 general election. In the first week of September,

the Centers for Disease Prevention and Control (CDC) asked state governors to be ready for vaccine distribution by early November, before the general election.²

These signified the election was possibly affecting the regulatory process and scientific research. Several national research organizations raised objections and concerns.

“The idea is that perhaps one of these COVID-19 vaccines in development might be prematurely released for use — via an emergency use authorization [EUA] order — on political grounds,” says **Alison Bateman-House**, MPH, PhD, assistant professor in the division of medical ethics at NYU Grossman School of Medicine in New York City.

“THE IDEA IS THAT PERHAPS ONE OF THESE COVID-19 VACCINES IN DEVELOPMENT MIGHT BE PREMATURELY RELEASED FOR USE ON POLITICAL GROUNDS.”

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The Food and Drug Administration (FDA) should decide whether to approve a vaccine for public use based on the apolitical grounds of science, as it has historically, Bateman-House says.

“That accounts for the anger and revulsion that has been evinced toward the idea of partisan politics influencing FDA decision-making,” she adds.

On Sept. 8, nine chief executive officers of biopharma companies signed a pledge stating they are committed to developing and testing potential vaccines in accordance with high ethical standards and sound scientific principles. They pledged to only submit their investigational vaccine for approval or for emergency use authorization after a Phase III clinical study demonstrated safety and efficacy.³

The research community, FDA, and IRBs should make decisions about vaccine trials based on the four ethical principles of autonomy, beneficence, nonmaleficence, and justice, Bateman-House says. (*See story on following ethical principles in vaccine study decision-making in this issue.*)

In August, the Infectious Diseases Society of America and the HIV Medicine Association asked the FDA to allow vaccine trials to go through the full licensure process and not be made available through an EUA, which allows for far less scrutiny of trial data. “Cutting corners with respect to the evaluation of safety and effectiveness must not be done,” the organizations wrote.⁴

Regulatory Ambiguity

COVID-19 research has proliferated and received a lot of public and governmental attention.

This has led to some ambiguity in how regulatory agencies are handling it.

“This is a unique pathway of activities with COVID. Rarely do we get that amount of [research attention], and rarely do we get lot of ambiguity,” says **Chris Weir**, CIP, IRB operations manager at Fred Hutchinson Cancer Research Center in Seattle.

For instance, IRBs and research organizations might view risks and benefits of a clinical trial differently when it involves a therapeutic or vaccine needed for a public health emergency and/or pandemic.

“If you put COVID on it, you could argue that any activities are in the public health realm,” Weir says.

This does not mean IRBs should make decisions that bow to political or other pressure because the studies might be labeled as for the public good.

There would be no reason not to issue a vaccine EUA if all clear conditions were met, says **Herschel Nachlis**, PhD, research assistant professor of government and policy fellow in the Rockefeller Center for Public Policy and Social Sciences at Dartmouth College in Hanover, NH.

“It’s true that prior EUAs, like for hydroxychloroquine, were probably not great for the agency or for public health,” Nachlis says. “But there is no reason to not issue EUA for a vaccine if conditions are met.”

These conditions include trials enrolling quickly, providing successive doses of vaccine fast enough, and enrolling sufficient numbers of people in the treatment control arm. “If the average treatment effect is very large, efficacy is clear in data, and safety is clear in the data, then that’s what we should all be praying for,” Nachlis says. “If everyone agrees on data, that would be wonderful.”

But if a vaccine receives an EUA from the FDA, there should be robust, rigorous, and detailed post-marketing surveillance. “This is not something the agency has historically put at the top of its agenda,” he adds. “If we get an EUA before a Phase III trial is done, it will be done based on less data than a full trial. Because of low probability and high-impact safety concerns, there has to be really robust post-marketing surveillance.”

Evidence from ongoing SARS-CoV-2 vaccines could be discussed at the Oct. 22 meeting of the Vaccines and Related Biological Products Advisory Committee. (*More information is available at: <https://bit.ly/3kgYHdt>.*)

“Having the meeting 13 days before the presidential election is less than ideal,” Nachlis notes. “The committee can make a recommendation to the agency and commissioner, and that is nonbinding. But they’re typically followed 80% of the time, and that meeting will be public and, possibly, livestreamed, so we’ll see that discussion and the evidence.”

The decision ultimately rests with the FDA commissioner. No one knows what the current FDA commissioner will decide, but some say politics could play a big role in this decision because of the president’s repeated claims that a vaccine will be released before the election.

There is much “nonsense” about coronavirus vaccines, said **Arthur Caplan**, PhD, professor of bioethics at NYU Grossman School of Medicine and founding director of the division of medical ethics. Caplan is on the World Health Organization’s emergency use investigation committee and has advised two companies with vaccine candidates — work for which he is unpaid and has no equity or stock. Caplan spoke at the Aug. 5

WIRB-Copernicus Group webinar on vaccine development.

“The White House says they’ll expect to see a vaccine in a few months, and now we hear we may get a vaccine by the fall,” Caplan said. “I think there has been a lot of nonsense about vaccine availability. I don’t believe we’ll see a vaccine this year.”

Starting with animal studies, it takes many years to get to Phase III trials. The mumps vaccine was produced in four years, but most vaccines take at least 10 years, Caplan explained.

There is no guarantee a vaccine will come to fruition. For instance, decades of work on potential vaccines for HIV and hepatitis C have come up empty, he added.

“As a historian of medicine, I share some of the concerns about Operation Warp Speed because in the past, speed has been associated with mishaps,” says **Susan E. Lederer**, PhD, professor of medical history and bioethics at the University of Wisconsin-Madison. “We live in a period of vaccine hesitancy. There has been vaccine resistance since the smallpox vaccine.”

It took decades for the United States to develop the current research standards and FDA evaluation process for the marketing of safe and effective vaccines. “Now, we’re just going to ignore that to beat Election Day?” Lederer asks. “I think the same thing is going on with convalescent plasma that the FDA gave an emergency use authorization when it’s not proven. I thought it would be subjected to rigorous clinical trials, but we haven’t finished that, and people are deviating from accepted standards.”

In addition to vaccine reluctance among many Americans, there is the potential for a coronavirus vaccine mishap to set back all vaccine acceptance, Lederer adds.

“I think the term ‘Operation Warp Speed,’ is one that I, as a health communication person, would not have used as a slogan,” says **Aisha Langford**, MPH, PhD, assistant professor in the department of population health at NYU Grossman School of Medicine, and co-director of the Clinical and Translational Science Institute at NYU Langone Health. “On the one hand — and this is a good thing about COVID-19 trials, in general — is these vaccine trials have aspects of the research process that are being done quicker than usual. There is a lot more collaboration than usual because we’re in the middle of a pandemic.”

Research organizations are learning to be more collaborative and to cut out some of the nonessential steps that make clinical trials take longer than needed. “A lot of people, including the general public and scientists, want to do well-conducted, very sober, step-by-step science,” Langford says.

Promising a COVID-19 vaccine by a set date, rushing the vaccine through the FDA approval process, or bypassing Phase III clinical trials and making a vaccine available via EUA can lead to public trust issues.

“To make an announcement or overpromise and make things available before they’re actually ready is not a good idea because we don’t want to jeopardize public trust for when a vaccine is available, or erode public trust for other treatments,” Langford explains. “The public needs to know we have ethics review boards, and we need safety and efficacy first.”

Scientists should follow their process and not let politics dictate the process. “All regulatory decisions are a combination of policy and politics,” Nachlis says. How much a decision is based on policy, law, and politics is a

continuum, and it depends on where it sits on the continuum, he explains.

“What’s unique about this president is his willingness to mobilize public pressure on expert regulatory agencies in a way that other presidents have been less likely or interested in doing,” Nachlis continues. “President Trump has been comfortable and excited about using the bully pulpit and going public to move the needle on the political side of regulatory policymaking.”

From a bioethical standpoint, coronavirus vaccine research cannot skip Phase III trials, Bateman-House says.

“We might allow some high-risk

people to get access to an unapproved vaccine through expanded access, but there is no way to approve this for use on only Phase II data,” Bateman-House says. “That sometimes happens in oncology trials, but only for dying patients who have no other option. Vaccines are for healthy people, and I cannot fathom a situation in the United States where a COVID-19 vaccine is approved on Phase II data. It’s too small and short of a time to have a real gauge of efficacy and safety.” ■

REFERENCES

1. The White House. President Donald J. Trump is using every available

resource to deliver a safe and effective vaccine to the American people. Aug. 11, 2020.

<https://bit.ly/2DRwyyg>

2. Kaplan S, Wu KJ, Thomas K.

CDC tells states how to prepare for COVID-19 vaccine by early November. *The New York Times*, Sept. 2, 2020.

<https://nyti.ms/3mq2MT>

3. Sanofi. Biopharma leaders unite to stand with science. Sept. 8, 2020.

<https://bit.ly/32tT7yB>

4. Infectious Diseases Society of

America. Infectious diseases

specialists to FDA: Don’t cut corners in COVID-19 vaccine approval. Aug. 26, 2020. <https://bit.ly/35nXhpt>

Vaccine Trials Should Follow the Four Ethical Principles

All human research, including COVID-19 vaccine trials, should be guided by the four ethical principles of autonomy, beneficence, nonmaleficence, and justice. When researchers, data safety monitoring boards, or the Food and Drug Administration (FDA) decide to stop a clinical trial or expedite approval or use of an investigational product, these principles still apply, says **Alison Bateman-House**, MPH, PhD, assistant professor in the division of medical ethics at NYU Grossman School of Medicine in New York City.

“When we’re talking about approving a new medical product, there is the possibility of benefit to those who are helped by that product and who really needs that product to be approved,” Bateman-House says. “There is also a risk of harm if something is approved prematurely.”

Americans are particularly enamored with the idea of autonomy, she

notes. “There already are ideas from people that we should just allow the public to get access to these drugs, even if they’re not approved,” Bateman-House says.

The attitude is “I know it’s not approved, but I want it anyway.”

“If people want this product, is it the role of the government to protect them from themselves?” she asks.

Ensure Justice

It could be argued COVID-19 investigational therapeutics and vaccines are beneficial because of the potential of curing the disease or preventing it. But investigational drugs also can cause adverse events and harm. The fourth ethical principle of justice applies to how equitably the clinical trial investigators are enrolling subjects. If they are enrolling disproportionately fewer minorities, it could be argued

the trials are not meeting the standard of justice.

Justice also applies to how quickly investigational products are made available to the public. “On the grounds of justice, we could push this product out quickly,” Bateman-House explains. “Do we have a justice-based obligation to get these products out of trials and to individuals through compassionate use programs or approving the product as soon as possible?”

All these ethical claims are reasonable, but they also can compete when the research community, public health officials, and governmental agencies debate policy during a pandemic. “I think this is the debate happening right now,” Bateman-House says. “You can’t have four competing claims at once.”

Some have put forth the idea that people should decide the risks for themselves when potential cures and

vaccines are under investigation, she notes. “Other people say individual risk tolerance has no place in public health interventions when a population intervention is at stake.”

In the United States, the general reckoning on ethical principles has been in favor of the gold-standard clinical trial process with limited exceptions in which seriously ill or terminally ill people might obtain an investigational treatment through expanded access, Bateman-House says.

“We don’t do this for healthy people,” she says. “The precedent for a vaccine is we wouldn’t release it before it’s fully approved by the FDA, but these are not normal times.”

What is imperative is that any decision made about emergency use authorizations, compassionate use access, and early approval of a COVID-19 therapeutic or vaccine be made based on science, not with any political influence, Bateman-House says.

“That accounts for the anger and revulsion that has been evinced toward the idea of partisan politics influencing FDA decision-making,” she adds.

Bateman-House suggests IRBs take these actions when reviewing clinical trials, particularly when they are related to COVID-19:

- **Ask more questions.** “When you see a protocol for a COVID vaccine or for any therapeutic or intervention, I would encourage you to look at who the recruited population is and ask, ‘Why?’” Bateman-House says.

“Typically speaking, IRBs are looking to make sure vulnerable subjects are protected and there is no undue inducement of people,” she adds. “In terms of justice and equity, they also need to know who is and is not recruited for this trial, and whether there is a rational reason for that.”

For instance, if investigators only recruit men, are there evidence-based reasons for excluding women? “I would go back to the investigator to make sure there’s a really good reason for that and not just go along with it,” Bateman-House says.

- **Check and update policies.** One difference between research before and after COVID-19 is that investigators are experimenting with study design, sometimes in ways

that might go against IRBs and institutional policies. For example, researchers in Boston are performing self-experimentation, vaccinating themselves with a potential COVID-19 vaccine candidate.¹

“This gets back to the autonomy question,” Bateman-House says. “The attitude is ‘If I want to and I’m a highly educated scientist and I understand the risks and benefits, let me make a decision.’”

But this type of situation might break institutional rules. They also could sow further distrust in the research community, she notes.

“Any sort of deviation from the norm is worthy of concern because people may misconstrue it,” Bateman-House says.

It could contribute to society fracturing in its response to an eventual coronavirus vaccine, she adds. ■

REFERENCE

1. Regalado A. Some scientists are taking a DIY coronavirus vaccine, and nobody knows if it’s legal or if it works. *MIT Technology Review*, July 29, 2020. <https://bit.ly/2ZAYgrl>

COVID-19 Misinformation Affects Everyone in Research Community

Clinical trial recruitment for COVID-19 studies faces a new challenge: Rampant misinformation.

“We’ve found that misinformation crowds out everything else,” says **Tim K. Mackey**, MAS, PhD, associate professor at the University of California, San Diego School of Medicine, and director of healthcare research and policy at UC San Diego Extension.

Since COVID-19 was declared a national emergency and pandemic, fake news, false cures, ill-informed posts, and conspiracy theories have dominated the social media space. People were urged to spend \$99 for a 14-day cure from COVID-19 or to mix their saliva with a pawpaw tree and garlic. Posts claimed they could order a do-it-yourself coronavirus test kit. Photos of hydroxychloroquine

tablets were listed for sale, as were personal protective equipment (PPE).¹

On Facebook, thousands of people shared a conspiracy theory that claimed Microsoft co-founder Bill Gates planned the COVID-19 pandemic. Other posts falsely claimed that Gates, Anthony Fauci, MD, George Soros, and Jeffrey Epstein were investors in vaccine research that

received \$1 billion dollars from the federal government.²

Also, Gates, who appears to be a COVID-19 conspiracy theorist's favorite target, was claimed to have a plan to implant trackable microchips in Americans, via a coronavirus vaccine. A YouGov poll suggested 28% of Americans believed the outlandish claim.³

"As everyone knows, in addition to the actual pandemic going on, there's an infodemic where a lot of misinformation related to COVID-19 has been proliferating," said **David Rand**, PhD, professor of brain and cognitive sciences at the Massachusetts Institute of Technology. Rand spoke at an Aug. 19 WIRB-Copernicus Group (WCG) webinar for IRBs and the research community. "Partly on social media, part of it coming from tweets, and it's having a serious impact on our ability to deal with the pandemic."

One of the challenges from an IRB perspective involves informed consent and public trust in the shadows of the misinformation world. For example, rumors circulated in Chicago that white people would receive a COVID-19 vaccine, but Black people would receive placebo, says **Wenora Johnson**, a cancer research and patient advocate. Johnson also spoke at the Aug. 19 WCG webinar.

"It just leaves me at a loss for words," Johnson says. "Misinformation impacts minority communities the hardest. Period."

Because of both factual historical research atrocities, such as the Tuskegee syphilis experiment, and rumors and misinformation, minority communities are less willing to participate in research, Johnson says. (*See story on disparities in COVID-19 research in this issue.*)

Early in the pandemic, misinformation on Chinese social media feeds

filled the gap of what people knew and did not know. There was little science-based information about how to deal with COVID-19, so China's Weibo posts spread erroneous information, Mackey says.

"The lack of information creates the environment for misinformation to grow and spread later on," he explains.

The same phenomenon of false information also spread in the United States, beginning in early 2020. This misinformation was mostly about unsubstantiated herbal remedies. "Not enough was known about the disease," Mackey says. "What people were peddling were preventive treatment options that had no scientific basis."

As the outbreak continued, testing became the focus because misinformation followed the trajectory of the pandemic.

It is important that IRBs and the research community monitor and address the spread of misinformation because of the potential effect on prospective clinical trial participants.

"An IRB professional needs to know what information is out there so they can administer informed consent," Mackey says. "Hopefully, they are in a position to be a gatekeeper or someone who can combat some of the misinformation."

While this is not the typical role of IRB professionals and clinical trial staff, this also is not the usual research environment.

"Unfortunately, we're in the middle of a pandemic, and there's way more misinformation than good information," Mackey says. "It's way easier to say something fake about a pandemic than to give good information about what works and is tested."

Researchers will need to release evidence-based information about

COVID-19 to improve recruitment for clinical trials for vaccines and therapeutics, he notes.

"The IRB and clinical trial professionals are at the frontline of talking about misinformation and making sure that patients don't have misinformation impacting their participation in clinical research," Mackey says.

IRBs could even ask COVID-19 study investigators to address misinformation in their informed consent process.

"Should you bring up misinformation in an informed consent document? With COVID-related studies, I think you have to," Mackey says. "For other studies, it's subjective."

At the very least, IRBs should ask researchers how they plan to deal with misinformation and whether they are pointing potential research participants to correct resources and information. "If a person is exposed to misinformation, how does that impact their participation in the clinical trial?" he asks.

For instance, misinformation could cause participants to be lost to follow-up, or lead to reduced compliance with the study protocol or treatment regimen, Mackey says.

"If I'm an African American, and I enrolled in a COVID vaccine trial, and I heard that only white people get the treatment arm, then I may drop out," he says. "You should say to people that this rumor is misinformation, you're completely randomizing, and you don't have any bias in the study, but those are hard concepts to explain to someone."

One tactic research institutions could employ is to hold town hall meetings in communities where COVID-19 clinical trials are held, says **Aisha Langford**, MPH, PhD, assistant professor in the department of population health at NYU

Grossman School of Medicine, and co-director of the Clinical and Translational Science Institute at NYU Langone Health.

The broader issue in COVID-19 study recruitment is the general public does not know much about how clinical trials work. Everyone could benefit from town hall meetings and educational sessions about COVID-19 vaccine research, Langford says.

“There is some confusion and concern about vaccines, in general, so having educational sessions and town halls about COVID-19 vaccines will be very helpful for people,” she adds. “They can ask questions, express concerns, and get accurate information because there’s

a lot of bad information on the internet.”

Research organizations also can put accurate resources and links for COVID-19 on their websites and distribute brochures and pamphlets that explain how clinical trials and vaccine research work.

“I think it will be very important, even when a vaccine is proven to be safe and effective, that people have information about when to get vaccinated, where to get it, and why it’s safe,” Langford says. “Maybe it will be virtual town halls for a long time, but we need to have good health education and patient materials, including decision support tools and patient support tools to help people feel more comfortable

with taking a vaccine because it’s good for themselves and for society.” ■

REFERENCES

1. Mackey TK, Li J, Purushothaman V, et al. Big data, natural language processing, and deep learning to detect and characterize illicit COVID-19 product sales: Infoveillance study on Twitter and Instagram. *JMIR Pub Health Surveill* 2020;6:e20794.
2. Reuters. Fact check: Bill Gates is not responsible for COVID-19. Sept. 10, 2020. <https://reut.rs/2GTAoEf>
3. Goodman J, Carmichael F. Coronavirus: Bill Gates “microchip” conspiracy theory and other vaccine claims fact-checked. BBC News, May 30, 2020. <https://bbc.in/3bWTuVu>

Minority Recruitment for COVID-19 Trials Is Low While Disease Burden Is High

Death rate is higher for Black patients

More than 350,000 people said they were interested in volunteering for a COVID-19 vaccine trial in the United States, and only 10% of those who signed up are Black and Hispanic. Actual trial enrollment among two companies with large COVID-19 vaccine trials in the U.S. includes only one in five volunteers who are Black and Hispanic.¹

“The COVID pandemic had a disproportionately bad impact on minority communities. Some people are not interested in participating in clinical research, given historical research abuses,” says **Alison Bateman-House**, MPH, PhD, assistant professor in the division of medical ethics at NYU Grossman School of Medicine in New York City.

The authors of a new study examined two months of COVID-19 hospitalization data in 12 states. They found hospitalizations of white patients was much lower than their share of the population, while Black patients and Hispanic patients were overrepresented among those hospitalized.²

For example, in Virginia, 36.2% of hospitalizations were among Hispanic individuals, while they only account for 9.6% of the population. In Ohio, 31.8% of hospitalizations were among Black patients, while they account for 13% of the state population. These data suggest that even more Black and Hispanic people should be enrolled in clinical trials involving COVID-19 vaccines and therapeutics. Instead, their representation is lower.

There are multiple reasons why minorities are underrepresented, including historical research atrocities, says **Karla Haack**, PhD, lecturer of anatomy and physiology at Kennesaw State University in Kennesaw, GA. Haack also is chair of the diversity and inclusion committee for the American Physiological Society.

“We have a history in the United States of cruel studies like Tuskegee, using samples like Henrietta Lacks’ tissue, and unethical experiments on prison populations,” Haack says. “We have a historical precedence in the U.S. of mistreating Blacks when it relates to medical experimentation.”

Study recruitment problems also relate to systemic disparities in America, including the lack of Black and Hispanic professionals in clinical

trials, as well as in medical care, she notes.

“If we had more healthcare workers who reflected the communities they serve, then that in itself would be trust-building,” Haack says. “If someone comes from a similar community or background as you, it gives you a sense of being in an in-group with your healthcare provider.”

The racial disparities in COVID-19 trial enrollment is particularly disheartening considering the pandemic has disproportionately harmed Black and Hispanic communities.

Data show that Black and Hispanic Americans are three times more likely to become infected with SARS-CoV-2 than white Americans. (*More information is available at: <https://bit.ly/3k9PsvI>.)* Data from the COVID Tracking Project show Black people are dying at 2.4 times the rate of white people, and account for 21% of COVID-19 deaths where the race is known. (*Find out more at: <https://bit.ly/3hHm7aa>.)*

COVID-19 exploits existing health access and treatment disparities among Black and Hispanic populations, says **Wenora Johnson**, a cancer research and patient advocate. Johnson spoke at an Aug. 19 WIRB-Copernicus Group webinar.

“Without affordable wages, one cannot afford healthcare,” Johnson says. “When you don’t have insurance, your health suffers more and you become more susceptible to viruses like COVID-19.”

Persistent inequity throughout society leads to a healthcare system that exacerbates distrust among minorities, Haack says.

“We know that the doctor-patient relationship, particularly in the United States, has distrust

because of implicit or explicit biases that minority populations may experience,” Haack explains. “You have historical precedent and historic distrust and inequality to healthcare access. All of those things combined makes it unsurprising that there are fewer Black and Hispanic populations volunteering for vaccine trials than there are whites.”

Research organizations need to reach out to minority communities to increase representation in clinical trials across the board, perhaps even with TV commercials of actors representing clinical trial volunteers, Johnson says.

“I have yet to see one commercial with a person of color telling us about the clinical trial process. Let’s not do this in the future — it needs to be done now,” Johnson adds.

“Some of the conversations we’re having now are not unique to COVID, but the pandemic sets light on inclusion in clinical trials,” says **Aisha Langford**, MPH, PhD, assistant professor in the department of population health at NYU Grossman School of Medicine, and co-director of the Clinical and Translational Science Institute at NYU Langone Health. “Different racial and ethnic populations and others are disproportionately affected by COVID-19, including African Americans, Hispanics, older adults, and people in higher-risk occupations like grocery store workers, cleaners at hospitals, delivery drivers, people working in restaurants, and folks who have a lot of contact with the general public.”

Clinical trials need people from these groups to enroll in COVID-19 research. They should be openly recruited and asked to enroll, Langford says.

“A lot of times, racial and ethnic minorities are never really asked to

participate in trials,” she says. “Many times, they are not aware of clinical trial opportunities, and they are not explicitly invited.”

When researchers say they tried to include minorities, Langford says her questions include: “What is your method for recruitment? Did you get the work out? Did you invite people?”

With COVID-19 vaccine trials, much of the work is conducted at academic medical centers and not necessarily in communities where racial minority populations are receiving their medical care. “Many groups are starting to think about community engagement, and we need to start to think about how to partner with community-based organizations, federally qualified health centers, and community hospitals where people are getting their care,” Langford says.

If someone lives a 45-minute drive or subway ride away from the center that is conducting a COVID-19 vaccine trial, then that distance would be a barrier, she adds.

IRBs can help reduce disparities if they ask researchers about their efforts to recruit and reach out to minority communities. “If I were on an IRB, I would want to see at least the intention or solicitation of X number of volunteers coming from different racial and ethnic backgrounds,” Haack says.

Research organizations could partner with ethnic communities and groups. They also could contact college student populations to form partnerships and champion hiring these students onto research teams, she adds.

“It doesn’t take much for people to see themselves reflected on the other side of the table,” Haack says.

Taking concrete steps, including outreach to minority communities

and hiring minority students as interns, are good, concrete steps they could take to chip away at disparities, she says.

The COVID-19 pandemic gives IRBs and research communities a rare opportunity to work toward change and reducing healthcare and research disparities. “We are really at a tipping point, where I think it is impossible to not see

or recognize these longstanding, historic inequities that have existed in our country,” Haack explains. “Given the fact that the pandemic is disproportionately impacting communities of color, we really have an opportunity to reach out and fix some of those historic inequities.” ■

REFERENCES

1. Johnson CY. Large U.S. covid-19

vaccine trials are halfway enrolled, but lag on participant diversity. *The Washington Post*, Aug. 27, 2020. <https://wapo.st/32tq12p>

2. Karaca-Mandic P, Georgiou A, Sen S. Assessment of COVID-19 hospitalizations by race/ethnicity in 12 states. *JAMA Intern Med* 2020; doi:10.1001/jamainternmed.2020.3857. [Online ahead of print].

Lessons Learned — or Not — from Hydroxychloroquine Mishap

Public trust is hard to regain

The research community’s decades of work to build public trust in IRB oversight and the clinical trial process has reached one of its greatest challenges during the COVID-19 pandemic.

Misinformation spread through social media and some media outlets, as well as contradictory instructions and information from political and public health officials, have helped create distrust. When government agencies then take actions that some people believe are more politically motivated than evidence-driven, trust wavers.

For example, in mid-March, President Trump issued tweets promoting the antimalarial and lupus drug hydroxychloroquine as a treatment for COVID-19, based on a tiny French study. That study was quickly followed by other research showing no difference between hydroxychloroquine and placebo. Based on the findings, New York Gov. Andrew Cuomo signed an executive order in late March, instructing pharmacists not to dispense hydroxychloroquine as a COVID-19 treatment.¹

Through the spring of 2020, misinformation about hydroxychloroquine as a COVID-19 therapeutic proliferated after President Trump spoke about it as a cure, says **Tim K. Mackey**, MAS, PhD, associate professor at the University of California, San Diego School of Medicine and director of healthcare research and policy at UC San Diego Extension. Rumors circulated on social media that a couple connected to hydroxychloroquine manufacturing were murdered because they promoted the drug as a cure, Mackey notes.

“There was some weird stuff,” he adds. “One tweet said you don’t need a vaccine or mask because hydroxychloroquine works.”

Trump continued to promote the drug as a cure through April. In May, he said he was taking daily doses of hydroxychloroquine, presumably to prevent COVID-19.²

The Centers for Disease Control and Prevention (CDC) reported new prescriptions for hydroxychloroquine or chloroquine in March 2020 were

7.2 times higher than those in March 2019. New prescriptions in April 2020 were 3.3 times higher than in April 2019.³

The Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) for oral formulations of hydroxychloroquine sulfate on March 28. The EUA enabled distribution of the drug from the Strategic National Stockpile as a treatment for COVID-19. But on June 15, the FDA revoked its EUA, citing scientific evidence that showed the product did not meet EUA criteria for evidence-based effectiveness and benefits that outweigh risks.⁴

“Recent data from a large randomized controlled trial showed no evidence of benefit for mortality or other outcomes such as hospital length of stay or need for mechanical ventilation of HCQ treatment in hospitalized patients with COVID-19,” the FDA letter says.⁴

The FDA’s reversal suggests the agency should make improvements in its EUA process, according to the authors of a recent editorial, published in *JAMA*.⁵

During a public health crisis, like the COVID-19 pandemic, federal agencies might need to expedite their decision-making process, but they should be cautious of political influence.

“On the one hand, this is the most devastating public health pandemic of our lifetime, and we need to solve it efficaciously,” says **Herschel Nachlis**, PhD, research assistant professor of government and policy fellow in the Rockefeller Center for Public Policy and Social Sciences at Dartmouth College in Hanover, NH. “On the other hand, we have less than precise regulatory standards. The FDA learned the hard way with hydroxychloroquine because the last thing you want to do is put a product out there for consumers to use and then say, ‘We’re wrong. We shouldn’t have let that product out there.’”

One of the problems is the FDA has rarely issued EUAs for anything except diagnostic tests. The only vaccine ever made available through an EUA was for anthrax — and that vaccine already was on the market, Nachlis notes.

“A lot of people are saying we need to make these EUA standards clear and more transparent for the future,” he says.

If the FDA had waited a couple of months before issuing an EUA for hydroxychloroquine, it would have had data from every study, showing that it did not appear to have any effect on mortality and morbidity. Encouraging hospitals to use hydroxychloroquine with almost no positive data wasted everyone’s time: “It took bandwidth away from running trials on other things,” Nachlis says.

When everyone is focused on one possible cure that ends up not working, it ties up resources

that could have been devoted to therapeutics that might work well, he adds.

“It’s really sorry to watch the fate of hydroxychloroquine because it was a false hope,” says **Susan E. Lederer**, PhD, professor of medical history and bioethic at the University of Wisconsin–Madison in Madison. The public desperation for a cure is understandable and true of past epidemics, she says.

“When people were harmed by cholera in the 19th century, they’d try anything,” Lederer says. “It was a disease killing large numbers of people, and they’d try smoke enemas.”

But in the 21st century, treatments need to be evidence-driven. “We want to make sure they’re not hurting people by giving interventions that are unsafe and might have hastened long-term disability,” Lederer says.

This misstep could have been avoided. It has caused public skepticism toward the FDA, says **Alison Bateman-House**, MPH, PhD, assistant professor in the division of medical ethics at NYU Grossman School of Medicine in New York City.

“We’re already in a situation where people are leery of what is happening at the FDA,” she says.

The CDC also came under question by scientists and public health officials who claimed the agency was becoming more political under the influence of appointees at the U.S. Department of Health and Human Services. Some health officials claimed Trump appointees and partisans delayed *Morbidity and Mortality Weekly Reports*.⁶

The hydroxychloroquine mistake was followed up by the FDA issuing an EUA for COVID-19 plasma as a treatment, despite incomplete clinical

trials. National news reports noted the FDA gave emergency approval for COVID-19 blood plasma after bowing to pressure from President Trump.⁷ Then, Trump told the public that a coronavirus vaccine could be available by 2020 Election Day, and the FDA followed this up with letters to states, asking them to prepare for a vaccine by Nov. 1.⁸

“I just saw that the FDA commissioner sent out an email to all staff, promising that he would not interfere with a data-driven decision, and he has been on a tour of FDA divisions to say that in person,” Bateman-House says. “It’s a shame that this cleanup is having to happen because of public missteps that could have been avoided.”

The formerly sterling reputation of the FDA has suffered from these blows. Combined with the antivaccination movement and the president’s accusation that the FDA has slow-walked COVID-19 therapies and vaccine research, there is a toxic confluence of circumstances that could affect how the public views an eventual vaccine when it is approved, she explains.

“The idea is that a vaccine will get things back to normal. Even a 100% effective vaccine — there never has been one — will not get us to those desired results if people do not take it,” Bateman-House says. “If people don’t trust it, they won’t take it.”

Public trust in scientists and what science shows was on the rise through 2019. Results of a Pew Research Center study showed Americans had growing confidence in science, rising from 76% in 2016 to 86% in 2019.⁹ A different Pew survey from May 21 revealed trust in scientists is growing in the United States, but mostly among Democrats.¹⁰

Scientists and public health officials are at a disadvantage in

communicating their research findings through the social media filter. “It’s much easier to say ‘A drug works’ if someone is scared about COVID and to say ‘You can be cured,’ than it is to explain, ‘The FDA revoked its emergency use authorization, and here’s why,’” Mackey notes. “The messaging for misinformation is so much easier and impactful than the public health response. When you’re not bound by evidence or scientific facts, it’s much easier to communicate.”

President Trump understands how to communicate to certain audiences, and misinformation created in that wave is much more cognizant, Mackey adds.

Public erosion in trust of governmental scientists and public health officials could result in a failed coronavirus vaccine campaign, even if one of the vaccine trials succeeds. “If you have that concern about the scientific validity of the vaccine approval, then it will, of course, be picked up by the larger, antivaccine movement with people saying, ‘This is what we’ve been warning you about all along,’” says Bateman-House.

“You will have a situation in which you have people already opposed to vaccines feel validated, and people who formerly were


very big supporters of vaccines saying, ‘I’m for vaccines, but not this vaccine,’” she adds. “This is the foreseeable outcome of a politicized rush.”

While some people still will opt for the vaccine, the damage will be done. The potential benefits of national public health campaign to get people vaccinated against SARS-CoV-2 will be lost.


“This could transform access to all vaccines,” Bateman-House adds. ■

REFERENCES


1. Herper M. What if hydroxychloroquine doesn’t work? What if it does? Right now, we don’t know. *Stat*, March 27, 2020. <https://bit.ly/3hrxtiq>
2. Carvajal N, Liptak K. Trump says he is taking hydroxychloroquine though health experts question its effectiveness. *CNN*, May 19, 2020. <https://cnn.it/2FB0QSb>
3. Bull-Otterson L, Gray EB, Budnitz DS, et al. Hydroxychloroquine and chloroquine prescribing patterns by provider specialty following initial reports of potential benefit for COVID-19 treatment — United States, January–June 2020. *MMWR Morb Mortal Wkly Rep* 2020;69: 1210-1215.
4. Food and Drug Administration. Letter revoking EUA for chloroquine phosphate and hydroxychloroquine sulfate, June 15, 2020. <https://bit.ly/2RnwxkQ>
5. Thomson K, Nachlis H. Emergency use authorizations during the COVID-19 pandemic: Lessons from hydroxychloroquine for vaccine authorization and approval. *JAMA* 2020; doi: 10.1001/jama.2020.16253. [Online ahead of print].
6. Weiland N, Stolberg SG, Goodnough A. Political appointees meddled in the CDC’s “holiest of the holy” health reports. *The New York Times*, Sept. 15, 2020. <https://nyti.ms/35vZQtJ>
7. LaFraniere S, Weiland N, Shear MD. Trump pressed for plasma therapy. Officials worry, is unvetted vaccine next? *The New York Times*, Sept. 12, 2020. <https://nyti.ms/3mi3NYP>
8. Kaplan S, Wu KJ, Thomas K. CDC tells states how to prepare for COVID-19 vaccine by early November. *The New York Times*, Sept. 2, 2020. <https://nyti.ms/3mq2MT>
9. Funk C, Hefferon M, Kennedy B, et al. Trust and mistrust in Americans’ views of scientific experts. Pew Research Center, Aug. 2, 2019. <https://pewrsr.ch/3kcFWbk>
10. Funk C, Kennedy B, Johnson C. Trust in medical scientists has grown in the U.S., but mainly among Democrats. Pew Research Center, May 21, 2020. <https://pewrsr.ch/33Guxtu>




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CME/CE QUESTIONS

- 1. Which was a chief concern the research community raised about the Food and Drug Administration (FDA) approving a vaccine or issuing an Emergency Use Authorization (EUA) for a COVID-19 vaccine by November 2020?**
 - a. It would be too late for a vaccine to stop the pandemic.
 - b. European nations would approve a vaccine first.
 - c. A speedy approval might be based more on politics and not on clinical trial evidence.
 - d. Not enough doses would be ready to give out to the public.
- 2. What are the four ethical principles that should guide human research?**
 - a. Risks, benefits, subject compensation, fairness
 - b. Autonomy, beneficence, nonmaleficence, justice
 - c. Hippocratic oath, equity, accuracy, speediness
 - d. Justice, direct benefit, legality, equity
- 3. COVID-19 tracking data found minorities are dying from the disease at what rate when compared with white Americans?**
 - a. Black people are dying at 2.4 times the rate of white people.
 - b. Hispanic people are dying at five times the rate of white people.
 - c. Black and Hispanic people are dying at four times the rate of white people.
 - d. Black people are dying at 1.2 times the rate of white people.
- 4. On March 28, the FDA issued an EUA for oral formulations of hydroxychloroquine sulfate for treatment of COVID-19. But on June 15, the FDA revoked the EUA because:**
 - a. hydroxychloroquine led to several deaths.
 - b. research showed another treatment produced better outcomes for COVID-19 patients.
 - c. scientific evidence showed the product did not meet EUA criteria for evidence-based effectiveness and benefits that outweigh risks.
 - d. President Trump ordered the revocation based on lack of evidence of efficacy.