AMERICAN PUBLIC HEALTH ASSOCIATION

and

THE NATIONAL ACADEMY OF MEDICINE

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RESPONDING TO COVID-19: A SCIENCE-BASED APPROACH

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WEBINAR #15: COVID-19 VACCINE UPDATE -DEVELOPMENT, APPROVAL, ALLOCATION AND DISTRIBUTION IN THE U.S.

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WEDNESDAY
NOVEMBER 18, 2020

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The webinar convened at 5:00 p.m. Eastern Standard Time, Dr. Peggy Hamburg, Moderator, presiding.

PRESENT
PEGGY HAMBURG, MD, Former FDA Commissioner, Moderator
JAMES HILDRETH, PhD, MD, President and CEO, Meharry Medical College
LARRY COREY, MD, President and Director Emeritus, Fred Hutch
MARION GRUBER, PhD, Director, Office of Vaccine Research and Review, Center for Biologics Evaluation and Research, FDA
JAY BUTLER, MD, Deputy Director for Infectious Diseases, Centers for Disease Control and Prevention

ALSO PRESENT
LAURA DESTEFANO, Director of Communications, National Academy of Medicine

VICTOR DZAU, President, National Academy of Medicine

AGENDA

P-R-O-C-E-E-D-I-N-G-S

(5:01 p.m.)

MS. DESTEFANO: Good evening, or good afternoon for those out west. This is Laura DeStefano from the National Academy of Medicine. Welcome to our webinar on the COVID-19 vaccine update, development, approval, allocation, and distribution in the United States brought to you by the American Public Health Association and the National Academy of Medicine.

Today's webinar has been approved for 1.5 continuing education credits for CHES, CME, CNE and CPH. None of the speakers have any relevant financial relationships to disclose.

Please note that if you want continuing education credit, you should have registered with your first and last name. Everyone who wants credit must have their own registration and watch today's event in its entirety.

All of the participants today will receive an email within a few days from cpe@confex.com with information on claiming credits. All online evaluations must be submitted by December 16, 2020

to receive continuing education credit.

If you have any questions or topics you'd like us to address today or on future webinars, please enter them into the Q&A box or email us at apha@apha.org.

If you experience technical difficulties during the webinar, please enter your questions in the Q&A box. Please pay attention to the chat box for announcements about how to troubleshoot.

This webinar will be recorded and the recording and transcript will be available on covid19conversations.org. More information on the series and recordings of past webinars are also available at that link.

Now I'd like to introduce Dr. Victor Dzau, President of the National Academy of Medicine, to provide some opening remarks.

DR. DZAU: Thank you, Laura. Welcome, everyone, to the 15th webinar in the COVID-19 conversation series brought to you by the National Academy of Medicine and the American Public Health Association.

The purpose of this series is to explore the state of science on COVID-19 to inform policymakers, public health and health professionals, business leaders, scientists, and importantly, the public.

I'd like to thank my cosponsor, the APHA Executive Director Georges Benjamin, as well as the co-chairs of the Webinar Series Advisory Group, Carlos Del Rio of Emory University and Nicki Lurie, the former Assistant Secretary for Preparedness and Response.

Today's webinar will feature a dynamic discussion about a path to a COVID vaccine, including steps forward in development, approval, allocation, and distribution. You know vaccine is the hottest topic right now because we know that the pandemic will not truly end until we have a vaccine.

Pfizer announced today through a press release that their Phase III computer studies show a 95 percent effectiveness of their vaccine, and you'll hear more about this later, and last week, Moderna announced that their interim analysis showed that their vaccine is 94 percent effective.

You know, this may mean that we'll have one or two vaccines under emergency authorization as early as December. Now, this is good news, but a whole host of questions must be addressed.

Is the vaccine safe? Will people take the vaccines? If you have limited doses, what is the allocation framework? And also, how is the issue of global equity and access because a vaccine outbreak anywhere is an outbreak everywhere?

So, given the quick timeline to develop these vaccines and the fact there is likely to be vaccine hesitancy, I think it's really important to establish trust in the vaccine development and distribution process.

Now, the issue of trust cannot be understated because it doesn't matter how good the vaccine is if people don't believe in it.

So, to gain public trust, we need to make vaccine development and regulation rigorous and transparent, the allocation of vaccines equitable and prioritized, and the distribution effective, which is why we've brought together these experts today to hear more about how and where we

are in the vaccine development process and what steps can we expect from today's speakers.

So, first, I'd like to introduce our moderator today, Peggy Hamburg. Dr. Hamburg was the former Secretary of the National Academy of Medicine.

She's also a former Commissioner of the U.S. FDA. Peggy, she's a leading expert. She's my good friend. Let me turn it over today and frame today's discussion.

DR. HAMBURG: Wonderful, thank you so much, Victor, and thanks to the National Academy of Medicine and the APHA for hosting this series of COVID-19 conversations, and in particular, the timing for this one and the focus of this one could not be more significant.

You know, this is a very challenging time. We are seeing a resurgence of COVID disease and coronavirus infections across this nation and elsewhere in the world that are astounding. You know, we are seeing a surge that many anticipated, but I think no one anticipated that it would be quite so severe.

At the same time, we see great news, astounding news in the vaccine world in recent days. I think that it's really extraordinary when you realize that as 2020 began, we really did not even know that this novel coronavirus, SARS-Coronavirus-2, existed, and within a year, we likely will have two vaccines that have demonstrated a level of efficacy and safety to be authorized for broader use.

It's really, I think, quite astounding and remarkable the level of efficacy that has been reported on these two vaccines.

Of course, there are many vaccines that are in development in this country and around the world, and close to a dozen that are in the final stages of clinical testing.

So, we likely will have two vaccines in broader use in the very near future, but we'll hear more about that from one of our panelists, and how they get distributed and their uptake is going to be crucial.

We probably, we hope, at least, that we will have others as well, but this initial positive

news, I think, signals not only that vaccines can be successfully made against this novel coronavirus, that the spike protein is a target that works in terms of being able to generate an appropriate protective immune response, but with these first two vaccines that are nearing the finish line in terms of their large clinical studies, we also are seeing the entry of a completely novel vaccine technology coming to the forefront, the mRNA vaccines, which is enormously exciting because it suggests that this approach can be used to quite rapidly design, develop, and hopefully deploy vaccines to address this current global pandemic, but potentially against other serious pathogens and perhaps other disease conditions as well.

So, there's a lot to think about and a lot to talk about, a lot to feel good about, and this good news couldn't come at a more important time as we are thinking about how to manage, control, and hopefully quash this devastating global pandemic.

So, with that, let me introduce our expert presenters, and we really have a terrific panel

that can help us think about how the research is done, how it's overseen in terms of the regulatory framework, both leading up to authorization and/or approval, but the ongoing oversight of the vaccines as they move out into broader usage.

We have someone who is actually a participant in the trials as well as a great scientist, and we have someone to talk about distribution.

So, first, we have Larry Corey, an internationally renowned expert in virology, immunology, and vaccine development, and the former president and director of Fred Hutch out in Seattle.

Working directly with Dr. Anthony Fauci as part of the NIH COVID-19 Prevention Network, Dr. Corey is the head of a national operations center that runs large-scale clinical trials of vaccine candidates.

We also have with us James Hildreth, a distinguished immunologist and also the President and CEO of Meharry Medical College, the nation's largest independent historically black academic health sciences center.

And when I see him, I also have to always mention it's also the alma mater of my maternal grandfather who was a member of the class of 1901.

Dr. Hildreth is notably, and crucially at this moment in time, a member of the Vaccines and Related Biological Products Advisory Committee, which will review vaccine trial data and make recommendations as to whether a candidate vaccine should be authorized or approved. He also oversees a COVID vaccine clinical trial site at Meharry.

Then there is Marion Gruber, a longtime friend and colleague from the FDA. She's the Director of the Office of Vaccines Research and Review and the Center for Biologics Evaluation and Research at the Food and Drug Administration.

And in this role, she directs the review, monitoring, and evaluation of potential new vaccines, as well as research pertaining to the development, manufacturing, and testing of vaccines, and truly there probably is no one in the world more expert in this arena than her, or more dedicated.

And finally, Jay Butler is with us.

He's the Deputy Director for Infectious Diseases at the Centers for Disease Control and Prevention, and in this role, he provides leadership for CDC's three national infectious disease centers and helps to advance the agency's crosscutting infectious disease priorities, and needless to say, he has been deeply immersed in the response to COVID-19 and in the preparations for when a COVID-19 vaccine might be available.

So, I'd like to turn now to each of our panelists for remarks, and then we will open it up to the audience for questions and answers. So, Dr. Corey, why don't you get us started?

DR. COREY: All right, thank you, Peggy. It's really a pleasure to be able to be here and speak to people about the state of affairs, so why don't we go to the next slide?

This is a slide that they made up in April of 2020, actually very close to April 1 when I started working on this with Tony, and it was the conceptual framework for vaccine development knowing that BARDA -- as this was before Operation Warp Speed was conceived.

We had made this stake in having different platforms, I'll show them in a minute, and we knew that manufacturing, as the time frame in which those platforms would be able to be tested were going to be different, so, and also knowing that we had an enormous task here.

It's not just to vaccinate our country, but the necessity of vaccinating the world, and that we have 330 million people, 220 million adults, but the world essentially has 4.4 billion adults and we know children need vaccination also, so we're talking about seven billion people.

So, there's not one platform that could cover the world scientifically, and we needed to have a system that would allow the evaluation and the rapid evaluation of very scalable kinds of vaccines, and so how would we do that? Next slide.

Now, the platforms in the U.S. program, Operation Warp Speed, have been sort of the major platforms known for a long time. There's the making of the protein, the recombinant protein. Everything is validated now against spike, the monoclonal antibodies work against spike.

Now we have two vaccines that work against spike. So, that first guess of blocking the landing gear of the virus has turned out to be an appropriate and it looks like a very successful strategy.

So, we have two protein vaccines. That's the tried and true. It's often economically the best, good stability, transportability, but the hardest to manufacture, and that's the case. I'll show you that we haven't really started Phase III programs with that.

There's the soluble prefusion trimer and the transmembrane trimer, and a lot of the work and the success goes to the Vaccine Research Center, and Dr. Barney Graham, through working with RSV, then SARS-Coronavirus, recognized that it was the prefusion protein that really was the one that was most susceptible to neutralization, and they learned how to make it stably by mutating it in the crystal structure of the prefusion protein was generated by them, you know, almost within three or four weeks of the sequence.

The RNA and DNA technology, RNA vaccines is the way we've gone, and there are two recombinant

replication-defective viruses, one using the prefusion complex, that would be the Ad26 vector from Janssen recently licensed for Ebola, and the chimp ad using more of a protein, the spike also.

This slide is not to go over it. It's really to say that the immune responses in Phase I are all different, and despite having the same gene, and therefore the need to test them. So, next slide, the one that you had one is just fine.

How to do this, working with John Mascola, and Tony Fauci, and Francis Collins, we sort of outlined what we thought was a reasonably strategic approach through individual trials that were harmonized over time. Next slide.

And that's conceptually showing here by taking each of the platforms and putting it through a clinical trial that was harmonized, that was done by a collaborative network that would, you know, essentially keep the populations the same.

The laboratory is doing the correlates and the endpoints would be, again, centralized. There would be a correlates and protection analysis that we're going to now start seeing, again through

OWS-validated laboratories, and an important component, to have a common DSMB that would review, at least for Operation Warp Speed, all of the trials, so that decisions would be made in context because, again, the goal is to get as many vaccines as we can licensed, and we'll come through that as the talk goes on. Next slide.

We built on the infrastructure of HIV. It really has been this infrastructure that has created the Warp Speed labs, the statistical consultants in COVID, and the clinical trial sites that have been, you know, developed over the last 20 years in the HIV program and that Mike Cohen and myself have done and then the influenza program that Kathy Neuzil has led were all merged together into what is not the COVID-19 Prevention Network, and we did that all within a couple of months. Next slide.

We took on the task of essentially starting one 30,000-person trial a month. The Moderna and Pfizer trials started on July 27th and 29th. The AZ trials started early in September. The J&J trials started September 22, and the protein

vaccines have yet to start. They're scheduled to be early to late December. Next slide.

The main goal was to evaluate each candidate vaccine with high veracity for safety and the potential of efficacy in reducing COVID-19 disease. Each trial is approximately 30,000 persons. That was done essentially to double the number. 15,000 was sort of what was needed with a four percent incidence. We doubled it in order to, A, increase the safety profile, as well as speed the time to an answer, and it's been a remarkable timeline.

One hundred and fifty disease endpoints plus or minus is the final analysis. It was critical to enroll our Black, Latinx, and Tribal communities into each trial, and we've been relatively successful.

The academic clinical trial sites have been the ones that have done that and have passed off some of the learning to at least a few of the commercial sites.

It's essential, we felt, to evaluate vaccines in the epidemiological setting of persons

at greatest risk of its complications, including comorbidities, age, and race.

And the increased acquisition rate, still race is the biggest indicator of acquisition, and that relates to the epidemiological setting of these communities with respect to both work and living conditions. Next slide.

So, we have the task of needing over 125,000 volunteers to roll up their sleeves by the end of 2020. Next slide.

And when we plan the trials, this is sort of a typical trial. We would try and enroll it in eight weeks. You'd hit the potential intermediate endpoint at 16 weeks, 100 cases at 20 weeks, and get it all done in six months, and this is sort of how we design the trial. Next slide.

This is actually what's happened. The red line is the Moderna trial and the blue line here is how we designed and projected it, and you'll see essentially we're a month ahead. I guess that's, you know, good site selection and maybe unfortunate for the rate of the epidemic in our country, and this is how it's worked out.

The Moderna trial essentially took about ten weeks to enroll, then there was a tail to get more persons with health disparities, the Latinx and Black community in.

Frankly, where we projected 50, they actually had 95, and it looks like 150 will be achieved by Thanksgiving, and probably by the 1st of the year, we'll have over 200 by the time that things get collected. Next slide.

Now, it's been remarkable. This morning, I changed this slide or revised this slide from a couple of days ago. As far as the Pfizer vaccine and the Moderna vaccine, the prefusion spike transcript are the same. Each one says they have a little bit different repressor of, you know, the innate immune responses in a different spike protein.

The doses are a little bit different, but essentially the prefusion spike transcript is essentially the same. One is two doses 21 days apart. One is two doses 28 days apart.

Vaccine efficacy is 95 percent in the Pfizer vaccine. They report 162 cases of

symptomatic disease and eight in the vaccine group. They report ten cases of severe disease, nine in placebo, and one in the vaccine, and a VE of 94 percent in those greater than 65.

The interim analysis for the Moderna, they have two doses 28 days apart. The VE is essentially 95 percent. There were 90 cases of symptomatic disease, five in the vaccine group.

The Pfizer, when I had first has this slide before this morning, it was 90 and four. This one was 90 and five, but now it's at 162 and it holds, 11 cases of severe disease in the Moderna, all in the placebo group, so really pretty definitive data that the severity is -- which I think is of major importance in the efficacy value of this.

And there was no difference in VE by age and ethnicity, about 20 percent of the endpoints in each of these groups in the interim analysis for Moderna.

So, we're seeing what I'll call in the next slide astonishingly similar data. They have two large-scale efficacy trials enrolled, and completely independently which had similar results

is frankly remarkable.

The spike protein of the RNA transcript is essentially identical, allowing one, I think, to feel quite comfortable about the veracity of the efficacy data.

The safety data from the trials need to be made public so the public can evaluate it. At least available to me is the vaccines are pretty well tolerated, really quite well tolerated.

There are more side effects with the second dose than the first dose, and somewhat lower systemic severity of systemic effects in older persons as compared to younger persons.

I think the similarity of the data, meaning either vaccine can do the job, and should simplify the process of distribution. Whether it's the Pfizer vaccine or the Moderna vaccine, what gets into your arm, I don't think will make a difference to anybody, or shouldn't. Next slide.

This is marvelous, but I have to say we're not done. You know, vaccines don't save lives. Vaccinating people saves lives, and I think that's the next part and I think Dr. Butler and Gruber

will talk more about that, as well as Dr. Hildreth.

We know the USG contract for mRNA is about 100 million doses from each company. There are some options to buy more. The timeline is uncertain and I will say that these are data that are available to me. You know, I can't say with 100 percent veracity that this is what it is.

I can say that with reasonable confidence that this is an approximation that we will see 25 million doses by Pfizer and 15 million from Moderna in December, that we will see 30 million doses from Pfizer and 20 million from Moderna in January.

So, if you look at that, it basically is about 40 -- you know, it's two doses, so it's 40 million people, 40 to 50 million people can be vaccinated in December and get a second vaccine in January, approximately 35 million Pfizer and 25 million Moderna in February as well as in March.

So, if we look at the National Academy one group of around 90 million doses, we're really talking about the end of March with just RNA just to cover that group, and there are lots of other people left in the country, including kids, so that's

330 million minus, you know, let's say, round it up to 100 million, so we have another 200 million people to vaccinate.

So, we need the other vaccines for the rest of the adult population, as well as for kids and pregnant women where experience is much greater within the Ad26 vectors, as well as the protein-recombinant adjuvants, and it's really important to keep the ongoing trials as well as creating a way to test the recombinant protein if we're going to achieve our goals.

So, for us who are working on this, you know, it's wonderful. We can smell the roses for a week maybe, but that's about it. It's critical for us to get these trials continued to be enrolled.

The AZ and J&J trials have around 7,000 people each in it and we need to get them enrolled and keep the trials going we would estimate until the end of February and mid-March, and then we should have the kind of protected outcome. Whether the results will be the same is another story, but at least accrue the endpoints required for evaluation.

Next slide.

Now, I do want to raise an issue that we still have, as great as this success is, for everybody to recognize that there's still a gap, and what I'll consider a scientific gap in the OWS program, and it's conscious.

It's great to have this conversation, but we do not know if the vaccine reduces acquisition of infection, that the person can still get infected after vaccination, and so will they still be infectious to others?

Now, we've shifted -- the normal history of COVID-19 is 75 percent symptomatic and 25 percent asymptomatic. It varies with age, but that's sort of general. You know, are we now going to create five percent symptomatic and 95 percent asymptomatic?

If that's the case and there's a lot of asymptomatic acquisition, we need to know about the titer in the nose and onward transmission because community spread and population-based effects will be highly dependent on vaccine coverage.

We'll get incredible individual

benefit, but will we get population benefit? In HIV terms, you know, U equals U, undetected means uninfectious. In COVID-19 terms, does decreasing infectivity also mean no onward transmission?

And on an individual level, do I still need to wear a mask after vaccination? And until we find this out, I think the answer is yes. The infectivity of this pathogen is formidable and defining the effect of those vaccines on infectivity and onward transmission is the next frontier for us to investigate.

We're talking about designing these kinds of vaccines looking at college kids with high rates of acquisition and close community where could still do a placebo-controlled trial because they're not going to be eligible if we get this going in the next couple of months. Next slide.

They won't be on the first line though. Of course, they'll be eligible when vaccines get eligible, but we think we could still ethically do placebo.

So, I'm going to end right there. It's been a pleasure to work with my network collaborators,

the people from DAIDS and the Vaccine Research Center, obviously Tony and Francis Collins, and Moncef Slaoui and his organization with OWS. Thank you, and --

DR. HAMBURG: Thank you, excellent up to the minute overview, and I'd like to turn now to Dr. James Hildreth.

I mentioned his important role on the VRBPAC, the Vaccine Advisory Committee. He also is running clinical trials at his own institution. I believe he even personally participated in the clinical trial.

He also is an expert on issues of reaching out to minority communities and trying to engage people of color to participate in clinical trial research, and also thinking about how to increase trust and confidence in those communities in this kind of work and in the findings of this work, so he is uniquely positioned to provide additional insights to us now. Dr. Hildreth?

DR. HILDRETH: Thank you, Peggy, and thanks to the Academy and to the APHA for the chance to share some thoughts with you. I don't have any slides.

I want to put the context of our work out there first. You know, I'm the President of Meharry Medical College. It's one of four historically black medical schools in the country.

We were founded in 1876, just a few years after the civil war ended, as a place where African Americans could learn health and medicine to take care of each other.

So, our mission is really to provide opportunities for minorities and disadvantaged individuals to have access to care and to also have access to training in medicine.

So, as such, we are a trusted organization here in Nashville in middle Tennessee in terms of minority communities as it relates to research and medicine, and so when the pandemic struck the country, it was obvious that minority communities were going to be disproportionately burdened by the pandemic, so we decided we must jump into the fight.

Here in Nashville, we have three large hospital systems, Vanderbilt, St. Thomas, and HCA. They began to test their panels, patient panels

almost right away for COVID-19.

We wanted to make sure that minority communities had access to testing as well, so we set up an assessment center that eventually was absorbed into the city's sites.

We've been running the COVID-19 testing for the city of Nashville for the last several months, testing as many as 15,000 to 20,000 people a week.

But pertinent to the mission I shared with you, we've also been going to neighborhood churches, African American churches on weekends to do mobile testing there, again to make sure that those who really need access to testing would have it.

We've also been using that as an opportunity to inform and communicate to the community about the need to be tested, but also about the vaccine.

And I can just tell you that as an HIV researcher of long standing, I started working on HIV in 1987, I think, one of the lessons we learned was the importance of trusted messengers, and I need to tell you that it's hard to overstate the

apprehension and mistrust that is felt in some minority communities with respect to the vaccine and medical research generally.

There are a lot of reasons for that. Some of them are well known and well understood. One of the prominent reasons relates to the Tuskegee experiment that lasted from 1932 to 1972.

It was an atrocious deviation from ethical standards to the point that one of our sitting presidents had to apologize to the men who participated for that experiment.

So, what I've been trying to do is to make people understand that as egregious as Tuskegee was, it changed human subjects' research forever.

We had a national commission established to make sure there were ethical standards followed. We have informed consent, IRBs, data set and monitoring boards. All of those things to some extent can trace their origins back to the response to Tuskegee.

But the trusted messenger concept is the one that we've been focusing on, so we have

identified faith leaders, community organizers, and others to partner with to make sure we can deliver the message that African Americans and Latinx community members must get the vaccine because as you know, there's a huge gap in the burden of disease and death for those populations, and paradoxically, the ones who need it the most are least likely to accept the vaccines.

So, our challenge is to provide enough information from trusted individuals to allow people to make an informed decision about the vaccine.

And I'm often saying what you heard Dr. Corey say, which is that vaccines do not save lives, vaccinations do, and one of our biggest concerns is a perception that minorities have, and let me just share this with you.

Many of them believe that once the data was revealed that the pandemic was disproportionately burdening African Americans, Latinx individuals, and older individuals, the nation seemed to turn its attention elsewhere and go on with its business, and that was exacerbated by the murder of George Floyd, which again seemed

to suggest to those communities that not all lives matter as they profess to do by some leaders in our country.

So, we have the challenge of overcoming perceptions of bias, perceptions of not mattering in some of these communities, but I think that one of the answers is again to identify trusted messengers who are scientists, faith leaders, and community leaders to make sure they're fully informed about vaccines and how they work, why they work, and why they're needed.

And I think that although we know that immune systems work generally the same across races, there are some data to indicate that there might be some differences.

So, I've been emphasizing to my colleagues and to my communities that the only way to be sure that vaccines work in our communities is for us to participate in the studies of those vaccines, and I think we're having some success.

I think the numbers that we're seeing for the two vaccines that have made it to this point,

they have reasonable participation of Latinx and African Americans, but I think it could be a lot better.

But I am pleased to see that there is enough of those populations in these two studies to allow us to feel comfortable that they're going to work in those groups.

So, my perspective is one of someone who has been studying viruses since 1978. I did my PhD with Andrew McMichael studying the T cell response to influenza.

I've been working on HIV for a really long time and there are some things that emerged in that work, and one of them is to repeat that in order for this to be successful, people have to stick out their arms and get injected with the vaccine, and that's going to require an enormous effort across lots of different disciplines, and we're happy at Meharry to be one of the leaders in that.

We're about to launch a major media campaign here in middle Tennessee and the state of Tennessee with the messages that we think are

important to convince people in minority groups to participate.

So, I'm happy to have a chance to share a few thoughts and I'm looking forward to answering questions that people may have, so thank you, Peggy.

DR. HAMBURG: Well, thank you so much. Thank you for your work and for your leadership. Let me turn now to Marion Gruber. Marion's work has always been important, but it's probably never been as important as it is today, and never so much in the spotlight either.

But she is going to really talk to us about what is involved in a vaccine approval, particularly a COVID-19 vaccine approval, and sort of where we are, and what has been done, and what needs to be done. So, I'm going to turn it over to you, Marion.

DR. GRUBER: Well, yeah, thank you very much, Peggy. I want to first of all thank you all for having me here and to be able to participate in this very important webinar. Can I have the next slide, please?

So, what I wanted to do today is provide

you with a high level overview on the authorization and licensure of vaccines to prevent COVID-19. Next slide.

I think, you know, as we've heard, the development, the licensure, or authorization of vaccines against COVID-19 is critical to mitigate the current pandemic and hopefully prevent future disease outbreaks.

And it is our job at the FDA to ensure that the vaccines that are either approved or authorized under a so-called Emergency Use Authorization are supported by adequate scientific and clinical data.

And over the last couple of months, my colleagues in the Office of Vaccines have worked very hard to facilitate COVID-19 vaccine development.

They have provided expedited reviews of chemistry, manufacturing, and control information, preclinical and clinical protocols, and clinical trials data.

They have provided timely advice and guidance to sponsors to expedite proceeding to these

Phase III clinical trials for which we now have some very encouraging results.

And we also directed efforts at generating data to support access to investigational COVID-19 vaccines, and I'm going to talk about this in a couple of minutes. Can I have the next slide, please?

So, under the U.S. regulatory framework, there are several approaches for making COVID-19 vaccines available. First of all, we can license the vaccines. We can also make them available by doing clinical trials under the so-called Investigational New Drug applications or Expanded Access. I'm not going to be talking about this today, or we can issue an Emergency Use Authorization.

For all of these approaches, of course we need safety and effectiveness data supporting the use of these products to some differing levels as I will try to explain. Next slide, please?

When we consider COVID-19 vaccines and how they will be used, I think it's fair to state that they will likely be widely deployed and administered to millions of people, including

healthy people, and the public can expect that COVID-19 vaccines will be safe and effective, and that there is a low tolerance for vaccine associated risks.

So, COVID-19 vaccines that are either licensed in the United States or authorized under Emergency Use must meet applicable legal requirements and standards.

And the FDA would apply the same standards to grant a biologics license for a COVID-19 vaccine as for other preventive vaccines that we have already licensed or that are currently in development.

We have made great efforts to contribute to the expedited development of vaccines against COVID-19 by providing expedited reviews and regulatory advice, but we also have to acknowledge that we need to accrue the adequate manufacturing, safety, and effectiveness data that support potential widespread use, and that takes some time.

Next slide, please.

So, what is required in terms of data to support an approval of a COVID-19 vaccine or licensure? So, I'm using these terms

interchangeably here.

First of all, we need a manufacturing process that can assure us that the product can be made consistently and of adequate quality, right?

A great vaccine efficacy result is not doing you any good if you don't know how to make the product, so that means we need chemistry manufacturing and control data, and we need facility data.

We need data on the facility to assure us that the facility where the product is produced and manufactured is in compliance with good manufacturing practice requirements and regulations.

To support licensure, we also ask the vaccine manufacturer to give us non-clinical data. That is non-clinical safety and immunogenicity status derived from animal models, and for COVID-19 vaccines in particular, we also asked vaccine manufacturers to address the potential for vaccine-induced enhanced respiratory disease.

We need, of course, clinical data that

are adequate to support the proposed indication and use that is eventually written into the package insert for the vaccine. So, in other words, we need adequate efficacy and safety data.

And we have recommended and vaccine manufacturers have designed clinical endpoint that assess direct evidence of protection against SARS-CoV-2 infection or disease, and we also prespecified success criteria that had to be met regarding the vaccine efficacy point estimate.

We decided -- we recommended that a vaccine should be at least 50 percent effective against placebo, and fortunately, the data that we have available for two of the vaccines suggests that this point estimate is far exceeded, and we also need, appropriately, confidence of our lower bounds.

We asked manufacturers to also characterize the immune response induced by the vaccine, and that is important if we also want to make an assessment perhaps on duration of protection.

And if we license the product, we also asked vaccine manufacturers to develop a so-called

post-licensure pharmacovigilance plan. That's a plan by which the vaccine is further evaluated for safety once it is licensed because then we can have more and more safety data as the product is widely deployed. Next slide, please.

I want to talk briefly to Emergency Use Authorization. So, the Secretary of Health and Human Services earlier on this year made a declaration of a public health emergency that involves the COVID-19 virus, and based on that declaration, we can issue an Emergency Use Authorization once several requirements that are written in the law have been met.

The issuance of an Emergency Use Authorization or an EUA requires for FDA to determine that the known and potential benefits of the investigational vaccine outweighs its known and potential risks.

And I want to stress that an Emergency Use Authorization is not the same as vaccine approval. If we issue an Emergency Use Authorization for a vaccine, that vaccine is still deemed investigational. It's not approved yet.

If we make available a COVID-19 vaccine under an EUA, there is no requirement for informed consent. However, vaccine recipients need to be provided the so-called fact sheets, and these need to describe to the vaccine recipient the investigational nature of the vaccine, its known and potential benefits and risks, if there are available alternatives, and these people have, of course, the option to refuse vaccination. Next slide, please.

Now, an EUA for an investigational COVID vaccine may allow for rapid and widespread deployment for administration of these products to millions of individuals, including healthy people, provided, of course, that we have a sufficient number of doses available.

But because there is the likelihood for giving these products to millions of healthy individuals, we set the bar for issuance of an EUA for these vaccines rather high.

We want adequate manufacturing information to ensure the product's validity and consistency before we issue an EUA, and the

determination that the benefits of the products outweighs its risk need to be based on data from at least one well-designed Phase III clinical trial that demonstrate the safety and the efficacy of the product.

And of course, we take each vaccine into consideration and we make the decision regarding an EUA issuance on a case by case basis. Next slide, please.

The EUA request for a COVID-19 vaccine allows for a case-driven interim analysis from one or more clinical trials, and that was described by others here at the beginning of the webinar.

And to support a favorable benefit-risk determination, vaccine effectiveness needs to be supported even if we issue an EUA on clinical endpoints that assess for direct evidence of protection against COVID-19 infection or disease, and the vaccine efficacy endpoint estimate has to be the same in that it has to be at least equal or greater than 50 percent compared to placebo.

Now, if a COVID-19 vaccine, an

investigational product is made available under an EUA, there should be safety follow up, and that should not be only passive, but there should also be plans to allow for an active safety follow up of persons that are vaccinated under the Emergency Use Authorization because we want to learn more about the safety of the product.

Because as you've heard, these studies, these currently ongoing Phase III studies are a couple of months old right now and we would like to, of course, have longer term safety data, and so we encourage vaccine manufacturers to submit this as part of an EUA request submission their plans for safety follow up, including active safety follow up. Next slide, please.

And so to put that in writing, we sort of issued earlier this year, in June 2020, a guidance document entitled Development and Licensure of Vaccines to Prevent COVID-19, and then in October, this was followed by another guidance document that describes the data that are needed to support an Emergency Use Authorization for these products.

So, and the recommendations that we have

written into these guidance documents really reflects the advice that we have been providing to vaccine manufacturers and developers over the last year, and it describes, of course, the agency's current recommendations regarding data needed to support issuance of an EUA for vaccines to prevent COVID-19, as well as licensure, and thank you. This concludes my remarks.

DR. HAMBURG: Well, thank you very much, and I suspect there will be a few questions for you when we get to that part of our seminar as well, but I think very helpful to put this all into context, and of course now we turn to Dr. Jay Butler at the CDC.

And we focus a lot on the FDA with respect to the R&D and regulatory review, but CDC, of course, has always played a very important role in vaccines and their indications for use, as well as support for and design of vaccination programs.

And for COVID-19, this role becomes ever more important, and lots and lots of questions and concerns about how do we actually move from having a vaccine to actually getting people vaccinated,

and I think that Jay, you get to sort of start us out on that conversation this evening. Over to you.

DR. BUTLER: All right, well, thank you, Dr. Hamburg, and it really is my pleasure to be able to speak to you this evening, afternoon for those of you on the west coast.

We started with a description of how much has changed over the past year, and also disclosures of financial and commercial guide, which I have none, but I will have a disclosure of slide obsolescence.

So many things are changing so rapidly in this world, I know that what I'm going to be describing to you today at 5:50 Eastern Time on November 18, 2020, will be out of date within a few hours, but hopefully it will help paint a picture of the direction that I think we're going in in terms of getting the vaccines, once they are authorized and proven to be safe and effective, into arms. Susan, go to the next slide.

So, as Dr. Corey mentioned earlier, we have multiple platforms that are in development

or they're in Phase III trials in the United States now, and this is good news in that I think it helps hedge our bets in terms of having an adequate supply of vaccine.

It does complicate actual distribution of the vaccine because the handling requirements are different, particularly the mRNA vaccine.

The mRNA is a relatively unstable molecule and it has to be handled with great care and texture requirements that are outside of what we're accustomed to in the clinical world of administering vaccines.

But we also have viral vector platforms and protein subunits that will be a little more used to what we're accustomed to in handling vaccine.

I think it's very likely that the mRNA vaccines will be first. The Pfizer product in particular may be the first, and it also has some of the most challenging handling requirements, that it is store at minus 80 degrees Centigrade and it has to be maintained at that temperature during the shipping process.

Once it is thawed, it needs to be

administered within 120 hours, or that's five days, and once it's mixed with its diluent, that it needs to be administered within a period of a few hours.

Because of the extreme temperature requirements, it will be shipped in trays of 195 vials. Each vial will contain five doses. So, a minimal size shipment will be 975 doses.

That, of course, creates some unique challenges in terms of it will be going to places that will be able to handle that temperature and also be able to vaccinate a relatively large number of persons over a short period of time.

The additional challenge for most of the vaccines, with the possible exception of the Janssen and Johnson & Johnson viral vector vaccine, is that they will require two doses. In the mRNA vaccines, the Moderna product, two doses 28 days apart, and for the Pfizer product, two doses 21 days apart.

The actual physical logistics of shipping vaccine will be built primarily on a backbone that we're familiar with. The Pfizer vaccine, because it is so unique in its temperature

requirements, will be shipped to sites designated by the receiving jurisdictions by the manufacturers.

The others will be shipped building on the platform that is currently used to distribute vaccines under the Vaccine for Children Program, and this is through a contract maintained by CDC with McKesson Corporation.

Every year, 80 million doses of vaccine are distributed through this technique, and the contract was developed with the ability to be able to greatly increase that capacity multiple-fold to be able to respond in the event of a pandemic, just what we're facing now.

When we talk about allocation of vaccine, we use that term in two ways, starting with the amount of vaccine that will go to each jurisdiction. Most likely, the allocation methodology will be pro rata based on the population of the jurisdiction.

Our modelers have looked at a number of different ways that the allocation could be based on differences in at-risk population, but at the end of the day, the similarities are greater than

the differences.

So, again, the decision making is ongoing, but at this point, I would anticipate probably we'll see a pro rata method of allocation.

One of the things that we don't know with certainty right now, but I think Dr. Corey projected a very good educated guess, is the number of doses of vaccine which will be available when.

And we do anticipate that the first doses of vaccines will be shipped and start being administered during the month of December, and I think it's very reasonable to anticipate tens of millions of doses being administered before the end of 2020.

The shipment and the planning of vaccine is being done with 64 jurisdictions. These are the 50 states, the District of Columbia, eight of the territories, and then five large urban health departments, New York City, Philadelphia, Chicago, Houston, and San Antonio.

The other parts of the distribution plan that I think are notable is that the vaccination sites will be in a wide variety of venues, in

providers' offices, and eventually, particularly as we move onto platforms that are more feasibly handled, also potentially at mass vaccination sites conducted by public health agencies, but then also in commercial pharmacies, and we anticipate that we will be getting vaccine as soon as possible to your neighborhood pharmacy.

Also, you may have heard that we are working with two of the large pharmaceutical chains, CVS and Walgreens, to be able to offer the opportunity to deliver vaccines at long term care facilities, and many states are pursuing that option as well.

Let's go to the next slide, please, Susan.

So, the overarching objectives for the COVID-19 vaccination program are listed here. The first and most obvious is to ensure the safety and effectiveness of COVID-19 vaccines as based on the clinical trials, as well as the work that Dr. Gruber described by FDA in going through the Emergency Use Authorization as well as licensure processes, with the goal of reducing mortality, morbidity, and the overall incidence of COVID-19 disease.

We need to minimize disruption to society

and the economy, as well as maintaining healthcare capacity, and I think we're all aware that this is more needed now than ever as we're now at a phase with the pandemic really spreading almost out of control in many jurisdictions, and in some areas, our hospitals really reaching maximum capacity, and then finally, to ensure equity in vaccine allocation and distribution.

As Dr. Hildreth described and I think said very well, you know, it was reasonable to anticipate that the pandemic would really shine a bright light on the health inequities in our country.

I heard someone early on say that we're all in the same boat together during the pandemic. I think, unfortunately, that's the wrong analogy.

We're all at sea in the storm together, but some of us are in very seaworthy vessels and others are much more challenged in boats that are not going to be able to hold up under the waves.

And that's why we see so many challenges with people who are at increased risk of exposure

and unable to take some of the steps that others of us can take such as teleworking, as I speak to you remotely, to be able to reduce our risk of exposure.

The approach going forward will be phased, and this is building on some of the work that was done through the National Academies in the ethical framework for allocation of COVID-19 vaccines.

Once we have the EUA, then the Advisory Committee on Immunization Practices at CDC will begin developing the recommendations, and we anticipate that to be a fast-tracked process with two questions being answered.

One is should COVID-19 vaccine, A, be recommended using the standard grade framework to make that recommendation, and second of all, who should be vaccinated first, which gets into some of those challenging ethical questions?

And the ACIP has decided to start that conversation, but not make final decisions because of the framework that's already been laid out and the foundation that they can build on through the

group that was hosted by the National Academies, as well as work by Johns Hopkins University, and the work at the WHO. Next slide, please.

So, when we think about who might be vaccinated first, this is purely hypothetical, but as we look at some of the groups that have been discussed by ACIP, and this is almost verbatim from the National Academies report, we can look at people who are at increased risk of exposure, people who are increased risk of severe disease, and also people whose livelihood is most tightly tied to societal function.

And, you know, based on that, we can certainly see that healthcare providers might be the first group to receive vaccine, followed very quickly by essential workers, persons with high-risk medical conditions, and persons at high risk of more severe disease such as those over age 65.

And this Venn diagram shows the populations of the U.S. for each of those, and it shows also the challenges in defining what we will do in the first month of vaccine availability.

Even based on the numbers that Dr. Corey

shared earlier, it's clear that we're not going to have enough vaccine in the first month or two to be able to vaccinate all of these individuals.

So, that process and prioritization will be a difficult job that has already started with a number of thoughtful analyses, and will be continued by the ACIP.

The next slide shows what that might look like, and again, let me just stress, as the slide says, this is illustrative for scenario planning, but we anticipate early on that the supply of vaccine will be much less than demand and that we'll be targeting those groups such as healthcare providers, as well as those at higher risk of bad outcomes.

And then as time goes on and also we're vaccinating essential workers, we will reach a time where the amount of the various platforms of the vaccines will equal demand and everyone who wants to be vaccinated will be able to receive a dose of the vaccine. Next slide, please.

We've already touched on some of the issues around vaccine competence and being able

to reassure the public that the vaccines are safe and effective. The data from Phase III trials will be analyzed very carefully.

Certainly the preliminary reports that we've seen in the media are very encouraging, but it's important to recognize that Phase III trials may not recognize, be able to identify all of the more rare adverse events, so we want to be able to make sure that we have Phase IV or post-marketing surveillance in place.

And so a number of the systems that do that are listed here on this slide. These already exist now and we can use this infrastructure immediately to be able to assess the safety of the vaccines, including the Vaccine Safety Datalink, the Clinical Immunization Safety Assessment Project, and also VAERS.

VAERS is a passive surveillance system that is collaboratively operated by both CDC and FDA. It's traditionally provided initial data from the safety profile of flu vaccines when they're introduced.

Of course, healthcare providers play

a key role in reporting those events, but we've also found a way to be able to enhance that that we're calling V-safe, which is a smartphone-based active surveillance system.

It is voluntary, but it's a possibility for when you receive a dose of the vaccine to be able to register for V-safe, to have the app on your phone. The next slide shows a little more of how that works.

It's that after vaccination, text messages, which are basically a check in from the CDC, would occur daily for the first week post-vaccination, and then weekly until six weeks later. There would also be follow up at three, six, and 12 months.

If there's any kind of clinically important event reported which might be missed work due to illness, or unable to do normal activity, or a need for medical care, that can then be submitted through the app.

That would generate a message to the VAERS call center and a VAERS customer service representative will circle back with the individual

to get additional information and determine if a VAERS report is appropriate.

So, I know there is a lot more information I could cover, but in ten minutes, that was it, and I hope that was complementary to what the other speakers have addressed and I really look forward to taking your questions.

DR. HAMBURG: Well, thank you so much, and if I could ask the other panelists to come back on video and turn off their mute so that we can have some discussion, and a lot of questions have come in, more than we're going to have time for in what remains for this session.

But I'd like to start out with a question that has been worrying me, and I did notice that this also came up in some of the questions from the audience, and I'd maybe start with Dr. Gruber on this one.

And that is, you know, how do we think about the next sort of set of vaccines that are going to be coming down the pike and what those future studies are going to look like once we have a couple of vaccines that have had authorization

and/or approval and are going out?

There's the first question, I guess, of what happens with these two studies that we focus so much, these two vaccines that we focus so much attention on in terms of when do they get stopped and does the placebo arm then get vaccine?

But what happens with other trials of different vaccine candidates in terms of structure of the trials, placebo controls, et cetera? It's a complicated challenge because we don't normally test this many vaccines for one disease at the same time.

DR. GRUBER: Yeah, absolutely, I think that's a very important question and something that we intensely debate, not only within the FDA, but also with our partners and stakeholders.

So, first of all, from a regulatory perspective and talking about the currently ongoing Phase III clinical studies that have been advanced and for which we have a final analysis for efficacy as was published today, it is likely and this was, you know, discussed that an Emergency Use Authorization request will be submitted by the

vaccine manufacturer, and if supported by the data, the FDA is likely to issue an EUA for this vaccine.

But we feel that an EUA issuance in and of itself should not automatically be a reason to stop the blinded follow up in the placebo arm in these ongoing Phase III clinical studies because we feel we need to make efforts to let them continue to get additional data on safety follow up, you know, more data on protection against severe disease, data on is there a potential risk for enhanced disease.

These are questions that can only be answered if you really try to keep these currently ongoing Phase III clinical trials going.

Now, there may be a situation where this is no longer feasible, but right now, with limited amounts of vaccine doses to even be available, we think we need to make efforts, and we have asked vaccine manufacturers actually for contingency plans on what to do and how this can be achieved keeping these trials going.

Now, there is, of course, an ethical debate that is ongoing here in parallel, and I think

we have to, you know, think about this very carefully.

In terms of follow-on vaccines, vaccines for which Phase III clinical studies have not been started even, and so what do we do if the first vaccines out of the gate become available or even approved or licensed?

There are mechanisms by which we can investigate these vaccine constructs which have not started Phase III clinical studies. For instance, we could design clinical studies to really compare the new still investigational vaccine to the COVID vaccine that has been licensed.

We can also think about, and there is a lot of research going on, can we identify a so-called immune marker that is predictive of protection, let's say an antibody response coming out of these currently ongoing Phase III studies to see if we can use an immune marker to predict protection? And then we could potentially do immunogenicity studies to look at vaccine effectiveness.

So, there are approaches to evaluate the safety and the efficacy of these follow-on vaccines, but again, we'll have to, you know, further

the discussions on this very important question. Thank you.

DR. HAMBURG: Thank you, and it looks -- Larry, do you want to make a comment too?

DR. COREY: Yeah, I guess I would nuance this like Marion, but maybe a little bit differently.

I think we have polled our investigators and I think the operant kind of thought process is that when the vaccine becomes available to a person who is eligible in that region, it really does become untenable to not allow that person to have access to the vaccine.

That is especially true when we have enrolled 30 percent of the trials with healthcare disparities, of people with healthcare disparities.

So, as we move through the period of time, and that's why I spent so much time on one of the slides looking at what is the amount of vaccine available and who will get it, because I think that what will happen is that by sort of February or March, it will be a reasonable number of people at the highest risk will have access to the vaccines, and that's going to be untenable to keep them on

placebo.

For the ongoing trials, the AZ and the Janssen trial, there's really a push to get those fully enrolled and get those quickly as done as we possibly can.

So, I think there are some ways of getting durability. There are crossover blinded studies. I think there is an enormous importance to look at durability of efficacy. It's easy to get durability of antibody.

It's not that easy to get a correlative protection when we have so few vaccine breakthroughs. Our statisticians can get up to 30. We might be able to learn something.

We might have a threshold effect, but I think this is an incredible, you know, an important issue that has some nuances with respect to being able to know all of what we want to know, and I guess I'll sort of stop there.

Comparative trials are another way, and I can say for some of them, we're planning to look at conducting the trials outside the United States.

I think, to be honest, our international sites don't look like mRNA is available to them and they recognize the importance of the other vaccines to them globally.

And actually, the rate of accrual now in these vaccines have been embraced with enthusiasm and I have every confidence that our international sites are capable of doing the same quality as our U.S. sites.

And we may have to look at data from those parts of the trial and/or if we use a combined trial, to use healthier people in the United States and try and get the high risk people in other countries, although that requires some ethical issues that have to be ironed out also. So, yes, a really great question and a complicated one.

DR. HAMBURG: Yes, well, this is a complicated area. The science is complicated and also the design, and of course the ethics of the trials are complicated as well.

A little bit in that regard, but an easier question, I think, there have been a number of inquiries about kids and how can we know whether

these vaccines will work in kids?

What's going to be happening with pediatric trials? I guess Pfizer has started enrolling younger ages in their studies down to 12, but they probably don't have very large numbers.

Would any of you like to comment on what is the thinking about pediatric trials, bridging trials, the approaches for ultimately making this vaccine available to that population as well?

DR. COREY: Well, we certainly agree with it and the bridging studies are starting and are being proposed. Certainly the NIH programs are really ready, have written up massive protocol, and I'll let Marion comment on that.

But getting the right dose is important, and getting the right safety profile, and bridging down to, you know, Pfizer has already done it to 12, and I think Moderna is starting to think about it. Marion will probably know more than I, but getting it down to five is sort of the standard norm, and trying to do it as quickly as possible, but not shortcutting the safety information that's required.

DR. HAMBURG: Thank you. There was also a great deal of information in the questions that have been coming, a great deal of interest in the questions that have been coming in about some of the work that Dr. Hildreth mentioned, both in terms of the importance of enrolling communities of color into these trials, but also how do you develop the content of your messaging to the communities that you are providing outreach to, both around getting people to participate in the clinical trials, but also with respect to the issues of how to engender greater trust and confidence in the vaccines that may soon be becoming available?

And a question was also asked specifically about could you say more about the work you've done with the faith community? So, it's sort of a two-part question, I guess.

DR. HILDRETH: Thank you. Well, we make use of focus groups to a great extent, groups of individuals who express their apprehension or mistrust, and we have conversations with them.

And what we have found is that there are a lot of legitimate questions that are posed

by these individuals who are interested in the science and biology of what we're doing, but there's also a lot of myth busting or, you know, getting rid of some myths that people have about certain things.

We leveraged the fact that I was here before at Meharry some years ago. We formed a partnership with a faith group. It was called the -- well, anyway, we have a group of ministers, a group of investigators, and a group of physicians, and we got together and had conversations about viruses and why viruses are not the same as sin, because that was one of the assumptions that we had back then. The stigma associated with HIV was one of the big challenges we had.

So, a lot of it was dispelling some of the myths and misconceptions about vaccines and viruses and what they are, but a lot of it comes down to conversations with the trusted messengers, having them understand what the challenges are, what the facts are, then allowing them to be the ones who answer the questions or engage the community, and that's proven to be quite effective.

And one of my colleagues who I believe

is doing this for the network is Reverend Ed Sanders. Reverend Sanders is one of our partners in this and he has been a great teacher and, you know, colleague in making sure we get this right, so that's one of the things that we're doing.

DR. HAMBURG: Thank you. Thank you. And now turning to Dr. Butler, obviously these issues around the distribution are very important.

You know, building on what we were just talking about with respect to making sure that we adequately reach out to and engage communities of concern, that would be both communities of color disproportionately burdened by COVID-19, and also elderly populations and others.

So, as we think about the complexities of the distribution process and the system of prioritization that is being developed as we speak, how do we ensure that we're really going to be able to adequately really track and provide the ongoing oversight necessary since some of this distribution is going to not be in accordance with the way that people have traditionally gotten their care because you're going to be prioritizing people in certain

settings as opposed to through, you know, their traditional healthcare providers or whatever, and will you be creating a whole new distribution tracking system?

How can we ensure that people get the second dose of the vaccine with the right timing? And how can we be sure that these systems for the ongoing pharmacovigilance really are fully integrated into the patterns of distribution?

DR. BUTLER: Great, well, I explained, yeah, I think there's about an hour presentation that could really address every component of your question, but I'll try and compact it and address each part as briefly as possible.

First of all, in terms of the equitable distribution, as well as really the data tracking also, it's one of the reasons why we come into this recognizing that there's not a one-size-fits-all, and that these 64 jurisdictions know their communities better than we are going to know at the federal national level.

So, working with the states, we have asked for vaccination plans, which have been

received. The executive summaries of those plans are posted on the CDC website now.

And in developing those plans, we also went through a planning process and actually went and worked with a number of states that are going through the process of what are some of the challenges that have to be addressed?

In terms of addressing the equity issue, I did want to highlight again something that Dr. Hildreth said about the importance of working with community spokespeople and trusted persons, and that's going to be different in different communities.

And one of the things that we've worked on at CDC is developing kind of the core messages, but helping the jurisdictions and community partners to be able to adapt that as appropriate.

In terms of the data tracking, that's a very crucial part of the vaccination program, and I think the pandemic, in addition to health inequities, also really shined a bright light on some of the bioinformatic shortcomings of the public health enterprise in the United States.

So, it had involved looking at our current tracking vaccine forecasting infrastructure, as well as developing some new tools to be able to make sure that we have visibility.

One of the things that's unusual about Operation Warp Speed is we have the Department of Defense working with the CDC. The expertise that comes together is logistics, people who know how to get stuff from point A to point B, with people who have experience in managing vaccine programs.

And as one of the generals has said, we need to be able to see ourselves and we need to be able to see the enemy, and we need to be able to see the terrain.

So, developing a system known as Tiberius has been one of the goals that's been achieved in trying to get states ready to be able to utilize that tool so that we all have the same visibility on where the vaccine is on the flow, where it is in terms of being administered, and being able to provide the appropriate reminders for those second doses so that we know how much vaccine is going to be administered and who is going to need reminders

for second dosing.

So, it really is quite an undertaking. I think a question that I ask myself every morning when I wake up is are we ready? And I think readiness and preparedness is a process, and we don't want perfect to be the enemy of the good. So, we're more ready this week than we were last week. We'll be more ready next week.

And when the vaccine is available, we have to go with what we have, and it may not be perfect, but every day, we're more prepared than we were the day before working with our state partners and trying to address all of these issues that you raised in that question.

DR. HAMBURG: Well, thank you. I apologize. I did try to put a whole bunch of other questions all into one action-packed question for you.

But as we're running out of time, I do want to come back to an issue that I think has surprised many people. Larry Corey touched on it in his presentation that first of all, it's going to take a while for vaccines to get out to all of the people

who need it.

But also, we don't yet know whether people can become infected and thus also transmit even with vaccination, and so for a whole lot of reasons, people can expect to still be wearing masks, still be being asked to follow those non-pharmaceutical public health measures that we've all come to know so well.

But perhaps there is interest in some greater clarification about what does it mean that you could still get infected after being vaccinated with a vaccine that has this level of efficacy? I don't know. Larry, do you want to take that one?

DR. COREY: Well, sure. So, the way the trials are done is that people are under surveillance and they're asked to come in to get cultured for the OWS studies.

They have to actually be seen by, the first culture, by someone medically or through themselves with someone medically. In the Pfizer study, if they called in, they could self-collect.

So, by definition, you're seeing people who are symptomatic, and they are generally

symptomatic for a little period of time, and then with this disease, we follow them intensively to find out if they get worse over time.

So, we know that it's the pre-symptomatic phase that is the most infectious. We know that. We know that from the White House. We know that from everything else that has occurred with these outbreaks.

So, the study actually doesn't ask that question and there's really no information on it at this point in time. We know that there's a high infectivity pre-infectious, but their immunity is good enough.

We know in the non-human primate, if you start sampling right away, that you could potentially decrease nasal carriage, but we don't know what's the level of nasal carriage that's required for forward infection, and the duration of that, and what the vaccine does on that.

I think it's an important question. You know, I think I'm typical of most people. I mean, I'm wearing a mask obviously, but it's not something I'd like, and I also know that when we

get vaccinated, we're likely to have what in HIV we called behavioral disinhibition.

We'll start eating in restaurants, starting to go to movie theaters, starting to go more out and shopping, and resume to work, and resume to world, and so what vaccine efficacy is in that situation is also important.

So, if we don't decrease infectivity, we need really high coverage because you would be asymptomatically shedding it and you wouldn't know, like a lot of infectious diseases, and you would spread it.

So, it's, I think, just a critical part of the puzzle that this agent has and I want people to start being aware of that, and I think there are some studies that we could rapidly do to resolve that.

I think it's better for us to do it now than to wait to do these epidemiological studies that may come in a year or year and a half because we're not going to have a huge amount of coverage, and I think mask wearing is really something that the people care about, and I think if we attack

it now, we'll all be better off.

DR. HAMBURG: Yeah, well, there's clearly still a lot more we need to learn even with all of this very promising initial data coming in from these vaccine studies. We are seeing a strong response in various subpopulations, including the elderly. We're seeing this unexpectedly high level of efficacy.

So far, we haven't seen any significant safety concerns, but we know that we may see some issues emerge over time, and of course, this is one class of vaccines and it's only two vaccines that we've been focused on now, and there will be more, and we certainly need to learn about the duration of protection as well.

So, all of you will be busy on many levels. We so appreciate the work that you're all immersed in, and even despite the many demands on your schedule, that you were willing to come and spend time with us for this COVID-19 conversation.

Sadly, we have come to the end of our time and there are lots more questions that people wanted to ask, but really, thank you so much for

your presentations, your insights, and your many, many contributions.

So, with that, I will conclude today's webinar. I know that if we had the audience, they would give you a rousing round of applause, but instead, just I will thank you once again, and just remind people that there will be more really interesting timely COVID-19 conversations.

The next webinar will take place Wednesday, December 2 at 5:00 Eastern Time. Everyone who has been registered for this session will get an invitation to the next webinar.

And this webinar has been recorded and the recording, and transcript, and slide presentations will be available on covid19conversations.org so you can go back and look at some of the information that was presented and hear some of the wise comments of our panelists.

So, thank you all again to our panelists, and to the APHA and the National Academy of Medicine for sponsoring this webinar series, and thanks to all of the listeners for joining us today. I apologize that I didn't get to all of your questions,

but there were a lot of them.

So, best wishes to you all, all best. Stay safe and stay healthy, and have a great evening. Thank you so much. Bye-bye.

(Whereupon, the above-entitled matter went off the record at 6:31 p.m.)