UNITED STATES OF AMERICA

FOOD AND DRUG ADMINISTRATION

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CENTER FOR DEVICES AND RADIOLOGICAL HEALTH

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MICROBIOLOGY DEVICES PANEL OF THE MEDICAL DEVICES ADVISORY COMMITTEE (MDAC)

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September 8, 2023

9:00 a.m. EST

Via Web Conference

Transcript Produced By:


Translation Excellence

3300 South Parker Road, Aurora, CO 80014

https://translationexcellence.com/

**Participants**

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| | Nicolas A.H. Wentzensen, M.D. | Head, Clinical Epidemiology Unit Deputy Director, Clinical Genetics Branch, Division of Cancer Epidemiology and Genetics |
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| Consumer Representative | Roblena E. Walker, Ph.D. | Chief Executive Officer, EMAGAHA, INC. |
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| Designated Federal Officer | Candace Nalls | Designated Federal Officer, FDA |

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## Call to Order and Introductions

Dr. Van Der Pol: Hello. I'd like to call this meeting of the Microbiology Devices Panel to order. I'm Dr. Barbara Van Der Pol, and I'm the chairperson of this panel. I'm a professor of medicine and public health at the University of Alabama at Birmingham, and I have a focus on evaluation of diagnostic products for detection of STIs and other infectious diseases. I note for the record that voting members present constitute a quorum as required by 21 CFR Part 14. I would also like to add that the panel members participating in today's meeting have received training in FDA device law and regulations.

For today's agenda, the panel will discuss and provide recommendations to the FDA regarding topics related to in vitro diagnostic devices, used in pandemic preparedness and response consistent with the requirements under Section 3302 of FDORA. Before we begin, I would like to remind the public and the panelists that this is a non-voting meeting and ask our distinguished committee members and the FDA attending virtually to introduce themselves. Committee members, please turn on your video monitors, if you've not already done so, and unmute yourself as you're called on. I will call your name and then please state your area of expertise, your position, and affiliation. This morning we're going to start with Dr. Ricardo La Hoz.

Dr. La Hoz: Hi, good morning. This is Ricardo La Hoz. I'm a director of Solid Organ Transplant Infectious Diseases at the University of Texas Southwestern. I'm also an associate professor of medicine and my area of expertise is adult transplant ID.

Dr. Van Der Pol: Thank you. Dr. Thomas Moore.

Dr. Moore: Good morning. My name is Tom Moore. I'm an infectious disease physician in Wichita, Kansas, clinical professor at the University of Kansas in Wichita.

Dr. Van Der Pol: Thank you. Dr. Cathy Petti.

Dr. Petti: Cathy Petti, CEO of HealthSpring Global, board-certified infectious diseases and medical microbiologist. Areas of expertise are diagnostics and digital health.

Dr. Van Der Pol: Dr. Emily Blumberg.

Dr. Blumberg: Good morning. Emily Blumberg, professor of medicine, Director of Transplant Infectious Disease in the Infectious Disease Fellowship at the University of Pennsylvania, and my expertise is transplant infectious disease.

Dr. Van Der Pol: Dr. Camille Kotton.

Dr. Kotton: Good morning. Camille Kotton, I'm the Clinical Director of Transplanting Immunocompromised Host Infectious Diseases at Massachusetts General Hospital, and my area is within adult infectious disease. Nice to be here again. Thank you.

Dr. Van Der Pol: Dr. Angie Caliendo.

Dr. Caliendo: Good morning. I'm Angie Caliendo. I'm a professor of medicine at Brown, an adult infectious disease physician, and my expertise is in molecular diagnostics.

Dr. Van Der Pol: Dr. Marcus Pereira.

Dr. Pereira: Good morning. Marcus Pereira, associate professor of medicine at Columbia University Medical Center and medical director of the Transplant Infectious Disease Program.

Dr. Van Der Pol: Dr. Valerie Ng.

Dr. Ng: Good morning. I'm Valerie Ng. I'm a professor emeritus of the University of California, San Francisco. I am the lab director of the clinical laboratories at Alameda Health System, and my area of expertise, I'm a lab generalist. Thank you.

Dr. Van Der Pol: Dr. Peggy Honein.

Dr. Honein: Yeah, good morning. This is Peggy. I'm the Director of CDC's Division of Infectious Disease Readiness and Innovation in the National Center for Emerging and Zoonotic

Infectious Diseases. I'm an epidemiologist by training and my expertise is in public health emergency response.

Dr. Van Der Pol: Dr. Nicolas Wentzensen.

Dr. Wentzensen: Good morning. I'm a senior investigator at the National Cancer Institute. I'm a clinical epidemiologist with a focus on infectious diseases and cancer associations and gynecologic cancers.

Dr. Van Der Pol: Thank you. Mr. Brad Spring.

Mr. Spring: Yes, hi, Brad Spring. I'm with Roche Diagnostics and I head up our global regulatory policy and intelligence team, and I am the industry rep.

Dr. Van Der Pol: Dr. Roblena Walker.

Dr. Walker: Good morning. I'm Dr. Roblena Walker, CEO and research scientist for EMAGAHA Inc. Areas of expertise are microbiology and infectious diseases, and I also serve as a consumer representative.

Dr. Van Der Pol: Ms. Jennifer Schwartzott.

Ms. Schwartzott: Hi, I'm Jennifer Schwartzott. I'm the patient representative. I also serve with the NIH and the NCI on the SeroNet task force and have specialties in Covid.

Dr. Van Der Pol: Dr. Tim Stenzel.

Dr. Stenzel: Thank you. And good morning and welcome to everyone, particularly patients and other members of the public who are present on the panel or tuning in today. I am Dr. Tim Stenzel, and I direct the Office of In Vitro Diagnostics at the FDA. I'm board certified in molecular pathology. My expertise is in infectious disease, cancer, and genetics. Thank you.

Dr. Van Der Pol: Thank you. Dr. Kris Roth.

Dr. Roth: Morning. I'm Kris Roth. I'm a Deputy Director in the Division of Microbiology.

Dr. Van Der Pol: Thank you. Dr. Uwe Scherf.

Dr. Scherf: Yeah, good morning. My name is Uwe Scherf. I'm the Director of the Division of Microbiology Devices and have been in this position for almost 10 years. And it's a pleasure to take care of pandemics since 2009. Thank you.

Dr. Van Der Pol: Thank you. And now, Candace Nalls is our Designated Federal Officer for today's Microbiology Devices Panel, and she will make some introductory remarks.

**Conflict of Interest Statement**

Ms. Nalls: Good morning. I will now read the conflict-of-interest statement. The Food and Drug Administration, FDA, is convening today's meeting of the Microbiology Devices Panel of the Medical Devices Advisory Committee, under the authority of the Federal Advisory Committee Act, FACA, of 1972. With the exception of the industry representative, all members and consultants of the panel are special government employees or regular federal employees from other agencies and are subject to federal and conflict of interest laws and regulations. The following information on the status of this panel's compliance with federal ethics and conflict of interest laws covered by, but not limited to, those found at 18 USC Section 208, are being provided to participants in today's meeting and to the public. FDA has determined that members and consultants of this panel are in compliance with federal ethics and conflict of interest laws. Under 18 USC Section 208, Congress has authorized FDA to grant waivers to special government employees and regular federal employees who have financial conflicts, when it is determined that the agency's need for a particular individual's services outweighs his or her potential financial conflict of interest.

Related to the discussions of today's meeting, members and consultants of this panel who are special government employees or regular federal employees have been screened for potential financial conflicts of interest of their own, as well as those imputed to them, including

those of their spouses or minor children, and for purposes of 18 USC Section 208, their employers. These interests may include investments, consulting, expert witness testimony, contracts, grants, credits, teaching, speaking, writing, patents and royalties, and primary employment. For today's agenda, the panel will discuss and provide recommendations to FDA regarding topics related to in vitro diagnostic devices used in pandemic preparedness and response, consistent with the requirements under 3302 of the Food and Drug Omnibus Reform Act of 2022.

Based on the agenda for today's meeting and all financial interest reported by the panel members and consultants, a conflict-of-interest waiver has been issued in accordance with 18 USC Section 208 B3 to Dr. Angela Caliendo. Dr. Caliendo's waiver addresses her stock holdings and affected firms. The combined holdings are currently valued between $500,001 and $725,000. The waiver allows this individual to participate fully in the panel deliberations. FDA's reasons for issuing the waiver are described in the waiver documents, which are posted on FDA's website at http://www.fda.gov/advisorycommitties/default.htm**.** Copies of the waiver may also be obtained by submitting a written request to the agency's Division of Freedom of Information, at 5630 Fishers Lane, room 1035, Rockville, Maryland, 20857.

Dr. Bradford Spring is serving as the industry representative, acting on behalf of all related industry. Dr. Spring is employed by Roche Diagnostics Corporation. We would like to remind members and consultants that if the discussions involve any other products or firms not already on the agenda for which an FDA participant has a personal or imputed financial interest, the participants need to exclude themselves from such involvement and their exclusion will be noted for the record. FDA encourages all other participants to advise the panel of any financial relationships they may have with any firms at issue. A copy of this statement will be available for review and will be included as part of the official transcript. Thank you.

For the duration of the Microbiology Devices Panel Meeting on September 8th, 2023, Dr. Roblena Walker and Ms. Jennifer Schwartzott have been appointed to serve as temporary non-voting members. For the record, Dr. Walker serves as consumer representative to the Antimicrobial Drugs Advisory Committee at the Center for Drug Evaluation and Research, CDER. Ms. Schwartzott serves as a patient representative consultant to the Cellular Tissue and Gene Therapies Advisory Committee at the Center for Biologics Evaluation and Research, CBER. These individuals are special government employees who have undergone the customary conflict-of-interest review and have reviewed the materials to be considered at this meeting. The appointments were authorized by Russell Forney, director of the advisory committee oversight and management staff, on 7/25/2023.

Before I turn the meeting back over to Dr. Van Der Pol, I'd like to make a few general announcements. In order to help transcribe or identify who is speaking, please be sure to identify yourself each and every time that you speak. The press contact for today's meeting is James McKinney. Thank you very much. Dr. Van Der Pol.

Dr. Van Der Pol: I would like to invite the FDA to start the presentation. I would like to remind the public observers that this meeting is open for public observation. Public attendees may not participate, except at the specific request of the panel chair. FDA, you may now begin your presentation.

**FDA Presentation: IVDs Used in Pandemic Preparedness and Response Overview — Dr. Timothy Stenzel & Dr. Kristian Roth**

Dr. Stenzel: Hello, I am Tim Stenzel, Director of the Office of In Vitro Diagnostics at the FDA. Welcome to our meeting today, into this presentation. My colleague, Kris Roth, will be assisting. I will start the presentation and turn it over about halfway through. So, today the

presentation is on Microbiology Devices Panel of the Medical Devices Advisory Committee, to discuss IVD pandemic preparedness and response. Here is our agenda for this talk. Explain the purpose, the background, and finally end up with the panel questions for discussion during the panel meeting. So, I wanted to talk about preparing for pandemics, and the lessons learned. The lessons learned by CDRH from the Covid-19 pandemic, as well as the impacts, emergency and outbreak, can be applied to prepare for, and respond, to future pandemics involving in vitro diagnostic, or IVD, devices. Actual or potential emergencies for infectious diseases, in which FDA exercised EUA authority to authorize IVDs, include the following: influenza in 2009, avian influenza in 2013, MERS influenza in 2013, in 2014 we have an Ebola emergency, then an Enterovirus D68 emergency, and finally Zika, Covid, and Mpox. The objectives today are to further improve CDRH's ability to prepare for, and respond to, IVD testing needs in future pandemics and emergencies or potential emergencies.

To cover a Covid-19 background, briefly, on January 31st, 2020, a public health emergency was declared under section 319 of the Public Health Service Act. And then on February 4th, 2020, HHS issues the Emergency Use Authorization declaration under section 564 of the Food, Drug, and Cosmetic Act. And this allowed CDRH to use EUA authorities for IVDs. That same day, on February 4th, 2020, CDRH issued the first EUA authorization for a Covid diagnostic test. To briefly cover the emergency use authorization authorities, these are in statute, and the criteria for issuance include, there must be an agent that causes serious or life-threatening disease or condition. The bars are lower than the usual full authorization bars for medical products. And so, they may be effective, it is important to realize, to diagnose, prevent, or treat the condition. And also, the benefits are now known, and potential benefits outweigh known potential risks. And finally, there is no adequate approved, cleared or otherwise

available alternative. Unavailable also does include insufficient supplies of the approved alternative.

Next, I'll cover FDA's Covid-19 test policy. It was first published on CDRH's website on February 29th, 2020. This first authorization allowed laboratories who develop LDT's to launch their test, once validated, and once they had notified the FDA. And then they had 15 business days to submit their data, all of which time, tests could remain on the market and tests could be performed until FDA finished its review, and then can stay there as long as there were no issues in the final decision. This guidance and test policy was updated throughout the pandemic as the situation evolved. CDRH's EUA request review priorities and enforcement priorities for the Covid-19 tests did change throughout the pandemic, as new needs emerged, and as previous needs may have been covered well enough. By February 28, 2021, CDRH had received over 730 EUA requests related to Covid-19 tests. This figure shows up to last month, August 3rd, 2023, the number of EUA tests authorized.

Next, I wanted to cover the approaches we use during Covid-19 pandemic and emergency. Early versions of the Covid-19 test policy guidance provided a policy for certain developers and tests to market their tests without first obtaining EUA authorization. This was a notification policy. Independent evaluation of tests to enable laboratory-based evaluation and provide reasonable estimates and confidence intervals for test performance, given limited sample availability. So, this was a policy where we relied on others to perform evaluations of tests, independent of the developer, to ensure that the tests did function and were accurate. This occurred both at NCI for serology tests and at the NIH with the RADx and ITAP program. The Independent Test Assessment Program, or ITAP, was conceived and developed in order to accelerate regulatory review and availability of high quality, accurate, and reliable over the counter Covid-19 tests, to provide them to laboratories and to the public. This program was a

collaboration between NIH and FDA and resulted in a number of authorizations that were highly important, provided a significant number of the over time, the tests that were available to the public. Because of the close interaction between NIH and FDA, and alignment on the studies performed, and the data submissions, review of this material submitted by NIH to the FDA happened as rapidly as any other time during the pandemic. The FDA also pioneered the use of umbrella EUAs, which allowed a streamlined approach to the authorization of tests that meet specified criteria. And finally, the collaboration between UMass, NIH and FDA, on the study of serial testing. It showed that antigen tests benefit from serial testing, both for symptomatic and asymptomatic patients. This study, performed under FDA supervision, was of high quality and allowed the regulatory decisions based on it to be applied to all antigen tests without each antigen test having to perform the same step. So, these are just a small number of the key advances and approaches that the CDRH used during the pandemic.

At this point, I want to hand the presentation over to my colleague, Kris Roth. Kris, please take it from here.

Dr. Roth: Okay, thank you, Tim. My name is Kris Roth. I'm the Deputy Director of the Division of Microbiological Devices in the Office of In Vitro Diagnostics in OPEC, CDRH, FDA. Picking up where we left off, with our additional Covid-19 activities, we did have a monitoring of the shortage situation, and mitigation of any shortages for certain diagnostic supplies, such as swabs and VTM. We developed EUA requested templates for developers. We developed external communications for SARS-CoV-2 FAQs on CDRH's website, held virtual town halls, dedicated Covid-19 test inbox for questions, and developed safety communications related to various topics of Covid-19. We did monitor variant impacts, in collaboration with the Variant Task Force, at NIH and with Emory University. And FDA supported the collaboration

with the NIH RADx and ITAP programs. And you can see here on the right-hand side, just a sample safety communication related to variants that was published on January 8th, 2021.

This slide is a summation of our various engagements with both public health officials, clinicians, and the public directly. We put out 373 frequently asked questions, here covering a large variety of topics. And this was not just a one-time effort. We did revisit these questions as the pandemic evolved, and adjusted language as needed, and as additional information became available. We issued 24 letters to health care providers and safety communications. These were related to diagnostic tests, antibody tests, personal protective equipment, or PPE, and ventilators. We also received and responded to 445,000 emails throughout 17 mailboxes and 2 phone lines. Typical response times to this email box was 24 to 48 hours. And, in some cases, we had folks working in two shifts throughout the day in order to handle the volume of email on any particular day. We hosted 127 webinars and virtual town halls. 106 of these were related to diagnostic tests. So, these were hour-long town halls that were presented on Wednesday, typically at lunchtime. And we fielded emailed-in questions along with live questions from the callers that were on the line. 19 of these webinars really were related to PPE and to other topics. We issued 13 templates, 10 for diagnostic tests and three for other tests. These templates guided test developers in the validation of their Covid-19 tests, whether it be molecular, antigen, serology, home-use, or home-collection. And again, these templates were updated as new information came to light and new needs were identified in response to the outbreak. Finally, we participated in weekly calls with NIH's RADx and ITAP programs. These were to give early feedback on proposals and regulatory strategy for some of the tests that are going through these programs. We also held weekly calls with the testing coordination group, the TCG group. We had weekly, sometimes bi-weekly, calls with

international regulatory agencies. And frequent ad hoc calls as issues arise with our other government partners.

This slide is intended to highlight a new activity that we undertook during this pandemic, where we monitored for the impact of variance on test performance. So, there are a number of global databases that house genetic information. Perhaps some folks are familiar with Global Initiative on Sharing All Influenza Data (GISAID). And we do monitor these databases and have staff that are trained to look for genetic variation in a very large set of sequences. And since we do have the proprietary information from the test developer, we can kind of cross check emerging mutations for potential performance impacts on tests that have EUA. However, we do require that test developers conduct their own surveillance and analysis. And this is part of their condition of authorization. When we conduct our in-silico analyses, we use the target sequences, for all authorized molecular tests. And again, we can query the database against, you know, looking for mismatches between the target sequences and emerging variants. FDA provides information on specific tests, for which FDA has identified potential impacts on performance due to genetic mutations. So, we have reached out to test developers, and in some cases, we have provided safety communications on the FDA website, noting if there were performance issues with tests, related to mutations. This is provided as recommendations to clinical lab staff and healthcare providers, which are using these tests. And this is a resource that the public can use to maintain awareness of test performance in relation to emerging variants. We also collaborate with NIH's RADx Variant Task Force Program. This organization is studying performance of Covid tests, with variants, most recently, of course the Omicron variant.

Participated in assessments of Covid-19 test response. These are three assessments that CDRH participated in. One was from the Office of the Inspector General, titled FDA

Repeatedly Adapted Emergency Use Authorization Policies to Address the Need for Covid tests. The U. S. Government Accountability Office, the GIO, issued a report titled FDA Took Steps to Make Tests Available for Future Public Health Emergencies Needed. And also an assessment from Booz Allen Hamilton titled Emergency Use Authorization Assessment Final Report. And here, these links are available to you, and you can go and take a look at those reports. I think CDRH's own experiences learned through Covid pandemic can be summarized in kind of two bullet points. One is the value of regulatory flexibility. As the pandemic evolved and the virus evolved, different approaches to regulating tests were needed. We issued a number of umbrella EUAs, Immediately In Effect guidances, which were issued very, very quickly. We changed policy as needed, very quickly. And participated in research programs that were intended to inform regulatory decisions and then change regulatory policy based on those research outcomes. These are just a couple of examples of regulatory flexibility, but it was kind of a hallmark of our response, to maintain awareness of the current situation and the current science, and make sure that the decisions we were making were being informed by the best science possible at the time.

And also the power of engagement. The previous slide kind of highlights some of our engagement activities through email, phone calls, issuing templates, immediately in effect guidances. So, we've found a lot of value in collaborating with both partners inside the government and outside the government, to maintain awareness. Of the needs, the testing community, and also the clinical situation of the virus, as the pandemic went on.

So, here's some key lessons learned from those interactions. So, the importance of review of test before clinical use, and consideration of potential alternative approaches, such as prior certification of developers. But this is the kind of, you know, during the pandemic, we were aware of a lot of really good tests, and some tests that were potentially lacking. And so, there

were quite a bit of insight and data that we needed on all tests, to make sure that we were making the right decision. This potentially could be streamlined in the future, if there is a way to certify certain developers, to kind of pre-qualify, I wouldn't say pre-qualify, but to kind of certify that a set of developers is capable of developing a test and validating a test. The agile organization, you know, we've maintained the ability to quickly respond and adapt to changes, pivoting to focus on immediate needs and challenges as they rise, and this became kind of our day-to-day business. The only kind of constant in this pandemic response was change, to a certain degree. Again, the value of prepositioned commercial developers may be helpful in the future. If we establish contracts to preposition a handful of commercial developers to be ready for an outbreak response, that may lower the barrier to validation in the future. Also, de-risking test development through guarantees of minimum purchases. Reimbursement and product production funding support. This was evident from the large USG effort to distribute at-home tests. A centralized performance validation may be helpful, if we establish a clinical validation program to support test development and validation. Something that is a public private partnership, such as the ITAP, where there's additional insight into test performance. When folks for tests are kind of validated using kind of a master protocol approach, where everyone kind of follows the same protocol for analytical and clinical validation. That can really streamline the FDA review process and also help better understand test performance.

Sample sharing was a big issue during the pandemic. It seems that there were some private sample banks and some academic institutions sharing samples, but there was no real kind of coordinated effort to ensure, or help ensure, that samples were being shared appropriately. So therefore, establishing more effective mechanisms for sample sharing in outbreaks would facilitate test development and validation. Investment in novel technologies. A continued investment in novel test development, particularly point of care at home to

technologies, is something that we believe was helpful. And regulatory flexibility. And really, you can only have flexibility if you understand kind of what's going on with test developers, in the clinical community, with patients. And so, you can only do that if you have extensive engagement with developers and other folks.

So that leads us to the questions for the panel discussion. And I'll just read the questions here. The first question is, how can test developers, including both commercial manufacturers and laboratory test developers, best interact with CDRH when preparing for a future pandemic? What steps can CDRH take to strengthen its communication strategies in future pandemics, with test developers, laboratories performing tests, and other stakeholders such as patients and clinicians? Were any methods of communication, such as town halls, telephone hotline, website, FAQs, email boxes for stakeholders, or EUA templates, more advantageous than others? And what might CDRH consider doing differently in future pandemics?

Moving on to question number two, what types of educational resources, or communications, from CDRH, would be most valuable to aid test developers with respect to test development in preparation for a future pandemic?

Question three. Are there certain types of instrument manufacturers, or test component manufacturers, with whom CDRH should collaborate in preparation for a future pandemic response, to ensure test availability in a future pandemic. For example, would earlier engagement from CRDH, to work with manufacturers of high throughput systems, help ensure that well-designed high throughput tests can be made available at an appropriate volume to meet the needs of any future outbreak?

Question four. Are there certain types of tests or developers that should be prioritized for review in the early stages of a future pandemic? Examples include certain test types. For

example, diagnostic and high throughput, test protocol development for sharing with any laboratory, manufacturing capacity, or experienced test developers.

Question five. What are key features of tests, or are there certain test designs that would be helpful in a future pandemic?

Question six. What other lessons from the recent Covid-19 pandemic and Mpox emergencies might CDRH take into consideration in preparing for future pandemics? And with that, I will thank you for your attention, and we will go on to the next step of the presentation. Thank you.

**Clarifying Questions for FDA**

Dr. Van Der Pol: Thank you for those presentations. At this time, the FDA has received no requests to speak during the open public hearing portion of today's meeting. Therefore, we will continue with the agenda. Before I ask for clarifying questions, again, I'm going to take Chairs prerogative and just say, as someone who works in a laboratory, I converted my laboratory to Covid response, and we were evaluating new diagnostics. I sit on one of the RADx clinical review committees, and I have to say the FDA's efforts were greatly appreciated, and everybody could clearly see how much energy and how much activity was going in, to the FDA, really trying to help the public health response to this situation. And you guys did a fantastic job. So, I just want to take a second and throw that out there. So, with that, does anyone on the panel have any clarifying questions they'd like to ask the FDA about today's questions for discussion? Dr. Caliendo.

Dr. Caliendo: I have two. One is, how does this all end, this EUA? So that is one question. It clearly didn't end when the national emergency ended. So, that’s something interesting. And then, are you required, or are you permitted, by regulation, to treat some companies differently

than others? Like, with this pre-authorization. Is that within your purview or is that considered anti-competitive, or… Because that's a very interesting idea, but I don't have a sense for whether, how realistic that is for you.

Dr. Van Der Pol: Dr. Stenzel.

Dr. Stenzel: Yeah, I'll start with the second question first. So, certainly, there can be within the U.S. government an effort to sign up manufacturers and preposition them, you know, and, and plan out response, that would likely be of course, of competitive nature. And we are looking for the input from the panel today about, maybe what things to consider in looking at that. What are needed in different phases of an emergency response, what is needed first, you know, and so that would be welcome. Some of these lessons learned, we don't have authorities for, right now. So, it would potentially take additional authorities to be able to perform this function. But we do think that this type of creative, out of the box, regulatory thinking is going to be important to prepare for the next response, well in advance of the next response. Regarding your first question, and that is, how do the EUA authorities end? So, just to clarify, there are two main statutes dealing with public health emergencies. One is the declaration of the public health emergency. And the second, it has to do with FDA authorities around EUAs, and those EUAs can apply to devices, to drugs, biologics, therapies. And so, they are disconnected. So, the public health emergency can end, but the EUA authorities can persist. For example, the EUA authorities for Mpox or Ebola, for Zika, continue. And we were very grateful that we had EUA authorities that we could deploy for Ebola, because there were recent occurrences worldwide, Ireland, Africa, where we needed to prepare, in case something might happen. So, we continue to use EUA authorities for Covid, and are currently accepting additional EUA tests. In particular, multi-analyte tests, that test not just for Covid, but also for flu and RSV. And we're actively involved in those activities now, and hope to have some

additional authorizations prior to the peak of the respiratory season. How do these EUA authorities end? They end when the secretary says they can end. It's highly dependent on any continued needs. For example, Mpox, there's almost thankfully, there's almost no Mpox circulating right now. There's still a very, very low level, but we still want to keep focus on taking that to zero in the United States, and frankly, worldwide. But since there are almost no cases, it would be very difficult to get a full authorization for any of the Mpox tests that have EUAs. So, the continued availability of these Mpox tests under the EUA authorities, that laboratories can use, is highly important.

We've also been working very closely with the CDC, both obviously, and for Covid, but also for Mpox, and have given authorities to the CDC, to update and augment their Mpox activities. So, it may be that the need for Mpox EUA authorities will persist for a very long time. With Covid, it's perhaps a little bit different. We have so many tests authorized, and we also have a number of full authorizations of tests right now. We examine that on a regular basis. And, for right now, we have perhaps sufficient full authorizations for central lab tests, some for point-of-care, but very few for over-the-counter. I forget, maybe just one. So, we really would like to see more over –the-counter and point-of-care tests authorized. We would like to see more multi-analyte tests authorized fully. But there are final guidances out, for the transition from Covid EUAs to full authorization. And so, there is a pathway and a plan, carefully laid out. Once it is announced that the EUA authorities will come to an end, anyone who wants to have an IVD that can persist on the market after the transition period, which is 180 days, they do need to come in with a full authorization submission. And as long as that's in by the deadline, they can continue to market their EUA test while we review that test. And presumably, hopefully, that will be a positive decision, and then they're on, you know, they'll get De Novo granted, or a 510(k), you can stay in the market. So, the end of the EUA

authorities, in any situation, always looks at the long-term availability of tests. And so, once we have enough fully authorized tests across all categories, we'll feel comfortable to be able to bring an emergency authority to the end. Hopefully that answers both those questions. I see there's some other questions. Thank you.

Dr. Van Der Pol: Dr. Petti.

Dr. Petti: Cathy Petti, HealthSpring Global. Another clarifying question for Dr. Stenzel. As we all know, very challenging times in developing diagnostic tests during this pandemic. And I think all of us on this committee also are very aware of the different purviews of where EUA sits and where CLIA laboratory developed tests sit. I can't help but think that that guidance in November 2021, that the FDA issued, for me, living through this and advising many moderate to high complexity laboratories, as well as test manufacturers, it was sort of a landmark document, because not only did it address EUAs, but it also gave great guidance for those laboratories that were moderate to high complexity CLIA. And the FDA in that document dipped its toes in providing some policy recommendations for those laboratories, and in particular, brought clarity for the home-collection piece of this whole paradigm. So, us as a committee, would the FDA like us to stay firmly rooted in the EUA guard rails, or will there be some discussion and overlap with test developers of high throughput, high volume, laboratories that put together LDTs.

Dr. Stenzel: So, I think, you know, any needs of the LDT community as well as any needs perceived of any test developer, is open for discussion, today. Home-collection for Covid, and, which also included some that were multi-analyte some that were anterior nares, some that were saliva, which was very novel. We had never, prior to Covid, although we were open, authorized home-collection for respiratory disease. And, I forget the exact number, but I think it's over 80 authorizations of home-collection over, well over 30, home-tests, OTC tests. So,

this was groundbreaking in a number of ways. We had been open to home-tests for respiratory diseases, and welcomed them before Covid, and now it's very clear that the FDA is wide open to these tests. So, yes, you know, please bring any concerns to the FDA today. Thank you.

Dr. Van Der Pol: Thank you. Dr. Pereira.

Dr. Pereira: Hi, good morning. Marcus Pereira, Columbia University. I guess just as an initial statement, you know, as a clinician in infectious diseases living through Covid, like we all did, you know, I certainly am not an expert on FDA legal authorities and the legal framework that sort of operated throughout, before Covid and through Covid. So, my question, you know, and I listened intently to the slide presentation, which was very great, and read the documents that were given to us prior to this meeting. And, you know, I guess my question is sort of just understanding overall, sort of the legal framework that's going to dictate, I think, some of these questions that you ask, and we'll be trying to answer together today. You know, I don't fully understand sort of the nuances between, sort of, when EUA is authorized, or EUA is issued, or the sort of PHE is issued, I suppose, and how that changes your authorities. Obviously, I imagine that it gives you some flexibility and greater authority. But, in reading your questions, it seems that, you know, there's sort of, at least a consideration to pivot the agency from sort of a more passive framework and waiting for laboratories to issue or to submit tests, to sort of engaging the industry and academics and sort of, you know, getting these tests done more quickly and then sort of in terms of high-throughput. So, I guess my questions for you would be sort of, has the legal framework already changed since, sort of, the Covid pandemic, and how has it changed? And if not, I suppose, you know, where do you see some of the legal framework changing around the FDA? And, yeah. And it's just understanding sort of where we stand with those authorities. And also, you know, it seems also that some of what you were asking is almost sort of pre any emergency declaration, right? So how are you going to

position yourself and attain the authority, for example, to engage industry for some of these pre, sort of, you know, pandemic tests, without sort of some emergency authorization. Maybe this is a broad question, but I'm just trying to understand how it would operate.

Dr. Stenzel: Yeah, you've touched on so many different points, so I hope I can address most of them, or if not, all of them. So, the EUA authorities allow the FDA to lower the bar for test developers. So, we don't have to expect, or recommend, the same amount of evidence that we would for a 510(k), or a PMA. We have great flexibility to adapt to the needs of the current situation. So, for example, early in the pandemic, it was in Covid, it was very clear that there weren't going to be many samples, many actual patient samples, available in the U.S. And, some had tried to get samples, including the FDA, from other countries. And some were partially successful; others were not. So, it became very clear that asking for, you know, validations with actual patient samples, was not going to allow test developers to validate and submit their data to the FDA. So, we allowed contrived samples. We ask that negative patient matrix be used. And that, you know, that the whole virus RNA or long sequences of vitro transcribed RNA could be diluted into negative patient matrix. And ultimately arrived at, you know, 30 positives and 30 negatives. And, rather than our usual recommendations and expectations, that many more positives and many more negatives, and actual patient negatives and positive, meaning, you know, the same thing occurred for Mpox. Mpox, while there was, you know, there was an outbreak. It wasn't in anywhere near the same numbers of positives as for Covid, so we allowed banked samples, from the very beginning, even contrived. The first policy was going to involve completely contrived samples. It ended up that most developers could access banked samples for their validation. But, you know, very few, you know, if any initially, use prospective collection of patient samples to validate. As the Covid pandemic went on, we switched to ask them, for actual patient samples, to be used for validation, when they

were relevant. So, this kind of changing authority is allowed under EUAs. And this is in statute. And otherwise, it would be much longer before commercial manufacturers could develop and validate and get authorized and test. So, we absolutely need those statutory authorities to have that kind of flexibility. Is the FDA being more active versus passive? I would say we've certainly been very active since I joined the FDA in 2018. You know, by the end of February of 2020, we had actively engaged with 100 test developers for Covid. These were traditional kit manufacturers. These were academic labs. These were reference labs. We had a template of recommendations available by mid-January. It was just an adaption of the template that we used for all prior EUA emergencies. All 7 prior EUA emergencies, including Zika and Ebola. So, and, we immediately made that available, not to inquiries and, you know, and engaged with more than 20 developers of all types in January of 2020. So, the FDA has had our ear to the ground continually. When we heard that certain laboratories didn't know that they could submit an EUA, we then updated the, we made the policy decision of February 29th, 2020, to very clearly state that, you know, LDT developers, go ahead. You're very welcome. And we just didn't know that they were aware because we already had, you know, interacted with many LDT developers prior to the end of February. But within days of realizing that we, we came out with a policy that we did on February 29th. I'm not sure if I've addressed all your questions. It was quite broad.

Dr. Pereira: No, that was very good. Thank you. It sounds like you're already engaging, even before any declarations were issued in the United States, you're already engaging with the industry.

Dr. Stenzel: Absolutely. Absolutely. That's our long-standing trend. We actively engage with developers. Whenever a need's met, it doesn't always, you know, we don't announce it from the mountaintop, necessarily. Many of these conversations are confidential. I would say our federal

partners, also were very, were engaged very early at BARDA. So, BARDA very quickly, generated the list of potential companies that could assist early on. Those companies could apply for money. We shared that list. We contributed the FDA to that list. And we were made aware of activities around that. We're very aware with BEI's activities, trying to make virus stocks available to developers. You know, FDA became engaged in being able to, you know, make sure that key developers got those important samples as early as possible. So, yeah, a lot of, tons of activity on a daily basis, from the very earliest days. And continued throughout.

Dr. Van Der Pol: Thank you. We have one more question from Dr. Wentzensen.

Dr. Wentzensen: Thank you. Yes, so first, I wanted to echo our chair's comments. It was really amazing to see how FDA reacted to the pandemic, both on the diagnostic and the vaccine side. I think that that was very impressive. So, we were engaged early on with test evaluation, and we try to validate a number of the EUA tests, and some of them were really bad in the beginning. So, I mean, there were a lot of tests that we would never want to use in a clinical setting. But, then over time, it got very stable, very solid, I mean, and it was a great selection. So, maybe can you clarify like the EUA process, does it allow for a staged approach, where you can… We need a very low bar in the beginning to get tests on the market and in use, but can we keep asking for additional updates to keep this EUA authorization going for specific tests? As I understood, you said that the EUA rules changed over time, and so there were higher demands probably later, for new tests coming along, but can the same be requested for something that entered the market with a very low bar and then, I think, as the pandemic expanded and there was no shortage of samples, there was a lot of real-life clinical data that could be used. So, can manufacturers be asked to update these performance criteria? Is that a way that EUA could be modeled?

Dr. Van Der Pol: And before you start answering that, can I just add, because I have a question that was really just right on the same topic, but that was like, as we gather more data, can we rescind? Can you, do you have the authority to rescind an EUA given to a test that was fine in the beginning because we had nothing and anything was better than nothing, but now is really not something people should be using. Can we get those off the market? Because I think that impacts how willing we are to use those different bars, if you will. But I think that's related to Nick's question. So, I thought I would just throw that in there at the same time.

Dr. Stenzel: Yes, that's a great question. Yes, the EUA authorities allow us to rescind authorizations. Which we did, at times. And then, there's also been voluntary requests for rescinding EUA authorizations, you know, those that don't want to maintain the test. And those are at the request of the developer. Those were more frequent than the actual, fortunately we didn't have to rescind too many. Yes, the EUA authorities allow us to shift and start with a lower bar. We learned in Covid that this was very important, and we applied it to Mpox. So, in the beginning of Mpox, even though we might have allowed authorization based on contrived samples, we put into the conditions of authorization of the Mpox test from the very beginning that they would need to repeat with actual patient samples. And that's something we can do in all EUA authorizations. And we can put very specific conditions, even conditions specific for a task. We can require post-market work. We required, you know, test developers to monitor permutations. Kris mentioned what we did for molecular tests. We do something very, very similar for antigen tests as well. And the VTF team has been very helpful to the FDA in assuring that there isn't complete loss of single for antigen tests. So, yes, we can build in progressive improvement or progressive additional evidence needed. It's always, though, a careful balancing act, in such a situation, when everybody is working so hard. You know, how much is the right amount to ask at a given time? And how much is too little? How much is just

right? How much is too much? So, we have lots of discussions within the FDA, but also with key partners, internal and external to the government, to try to balance our approach at all times, to ensure that, I'm sure the nation that the tests that are performed are accurate, and are truly helpful to the situation. Hopefully I answered all those questions.

Dr. Van Der Pol: Thanks. Dr. Moore.

Dr. Moore: Thank you. Tom Moore, infectious disease at University of Kansas. So, I think it's striking that we're discussing this topic actually today, which is the anniversary of the removal of the handle for the broad street pump in London, that stopped the cholera epidemic. Anyway, I think it's rather fortuitous. I had a couple of questions, you know, I'm thinking about this from, about this problem, back relative to the anthrax attacks in 2001, when the pressure that was exerted on Bayer Pharmaceuticals to provide low-cost or no-cost large samples of Cipro, led to a lot of the innovation and research and drugs and treatments for biologic agents sort of dried up. And so, the government's been trying to walk that back. And you know, starting with, you know, BioShield and other defense authorizations in order to coax producers and pharmaceutical companies back into the field of looking at, and developing, drugs and other treatments for agents, which, you know, for which national emergency could be declared. I guess my question, I have a couple of questions. I mean, first of all, I want to say very clearly that for my perspective, in the middle of the United States, and from what we experienced, I think the FDA did a tremendous job. The government itself did a tremendous job and mobilizing resources and getting everyone involved and having excellent communications with people in the field. Would you be able to say, specifically, what the problems with sharing the data were. I mean, that to me, is one of the biggest problems. And I know that the FDA is has limited authority in mandating who can share with, I mean, making people share samples, but that's, I think that's an important problem. And I guess I'd like to know a little bit more about

what specific problems were encountered, because I suspect congressional action would be required to enforce some sort of sharing of the data. But also, one other thing that I was thinking about is, with the Covid pandemic, what were, and prior pandemics, that is the Influenza pandemic, were there, were there offers of… I'm more interested in the, the carrots that were offered to the developers. Were there discussions about extension of patents for these particular pathogens in order to coax people back to the development table?

Dr. Stenzel: Can I ask a clarifying question? And first of all, thanks. Thanks for your kind words about the FDA. Are you asking about sharing of data, and if data, what data? Versus sharing of samples.

Dr. Moore: Well, either or. I mean, I think, some people were very open about sharing data, it's my understanding. And I'm not privy to situations where they weren't sharing data, but you know, really both apply. I mean, there is open sourcing of open-source publication of some data. But in terms of, I guess, sharing samples, probably, I would imagine would be the more restrictive part. But, if the shoe fits, whichever, whichever you think would, you could inform.

Dr. Stenzel: Yeah, I can discuss both. So, first of all, any data related to test validation, anything, anytime a test was EUA authorized, the FDA posted our decision on the FDA website. It's everything that's still authorized. It's still on the FDA website, both for Covid and for Mpox. And it includes the package insert and instructions for use, it includes the authorization letter with all the stipulations laid out, the requirements and authorities. And, you know, essentially all the data that the FDA looked at to make their decision is in those documents. And we've heard that was very viable. We've now made sure that it's all information that's all available to those that have certain impediments, visual or otherwise. So, everything…

Dr. Moore: I'm sorry, Dr. Stenzel. Perhaps I misunderstood. I meant the people that were doing the research. Not FDA's communication with the public, but rather, you know, collaborators, people working together to try to develop these things.

Dr. Stenzel: Yeah, so the FDA has, I'm not sure we have any authorities in that area, as far as development goes, R&D research into Covid. We did, you know, within our authorities for OTC tests, we wanted all the developers to have a method of reporting the data, so that it can be used for helping public health purposes. Going to sharing samples. So, this is something we began in January, when we wanted to get access to actual viral samples at the FDA to study the virus, and to grow it up, and be able to produce a viral RNA. And we were very limited, and we ended up only being able to get sample or samples from within the U.S. There were so few samples in the beginning, there wasn't really much to share. If you're going to try to access samples outside the country, there were certainly plenty of samples within some countries. But some of those countries bar, legally, samples from being shared with anyone outside of that country. So, not only might we need national agreements to share samples with the right protections for patients, but also we would need international agreements to share samples. We explored this during Covid, particularly when we saw a variant of concern of Covid, that occurred in another country for which those variants hadn't yet been detected in the U.S. So, Kris mentioned that we had regular conversations with our regulatory partners around the world. We did, and other related governmental entities, and we very specifically asked if we could get samples for certain variants, so that they could go to NIH, RADx in the variant task force, to be able to make sure that they are entering tests in particular, where we couldn't use just bioinformatics to predict any loss of signal once we have a signal. But for the antigen test, we really needed life, actual sample, not any other independent samples, to do the testing. But we were unfortunately unable to do that, at the moment. It is something that is on our list to go

back to and try to figure out. It's, it's, it's an important topic. It's going to take a community, I don't know what authorities, or carrots or whatever will need to be used, but it is certainly something that's very important. And it's just too bad that we couldn't really deploy cooperation in that effort so far, on a broad scale, to be able to address the, not just in this country, but worldwide. We're very happy to try to share, you know, from the U.S. to other countries, where allowed, as well. So, it wasn't going to be a one-way street of somewhere else into the U.S. Some have discussed, you know, we could fund activities in collaboration with other countries, and have research posts that would allow tap collection and sharing, or even evaluation of tests in those countries with those samples. So, there's many different paths that we can potentially pursue to address the ability to share samples or share knowledge, and obviously we're very supportive of those, just don't have any firm answers yet. Thank you.

Dr. Moore: Thank you.

Dr. Van Der Pol: Dr. Kelly?

Dr. Kelly: Angie Caliendo and Brown. Tim, one thing that's not on these questions is anything related to FDA staffing. I suspect, in the beginning of this pandemic, you were totally overwhelmed with volume. Should we comment or make suggestions around how to allow some flexing in the staffing, for the FDA. Like, could you have pre-authorized reviewers that actually aren't employed by the FDA? Is this something you want us to address? Or is this out of scope?

Dr. Stenzel: Oh, no, that's perfectly okay to address. It was a challenge. To my knowledge, our office, we had one fully funded pandemic response person prior to Covid. We are dedicating more, now, and we'll dedicate more in the future, with or without specific funding for that. We did receive very generous funds to staff up, and we were able to add 65 reviewers with Covid funding. We are very grateful that. We use those authorities. We were able to

employ a third-party reviewer who has now reviewed over 100 Covid applications. That is the most IVD third-party reviews that I'm aware of. So, we were able to innovate in that area. We had some funds available for that, and that has been an exceedingly helpful and beneficial expansion of our abilities to respond. Of course, that's dependent on additional funding. You know, there was comment on vaccines and what was the carrots that can be used for tests. Well, there was specific funding for, early on, for vaccine development. There wasn't such funding available for test development. And obviously the lessons learned where we would like to spend those monies ahead of the next, to prepare, ahead of the next pandemic. This is something that South Korea did, following MERS and prior to Covid, where they invested, and there's an FDA white paper on this, and Jeff Shearn and I have an opinion piece describing what South Korea did, and the lessons learned, that we would like to, the overlap with what works for our system that we would like to use. But they did fund specific developers to be prepared, those developers met the need early on. They prepared, you know, how laboratories would respond, how they would select those laboratories, who would do the test evaluations, how that would be done, all those, they had priorities. And so, it wasn't an all-comers situation as it was in the U.S. They selected key developers early in the pandemic that met the South Korean needs. So, there were so many lessons learned as we looked at how other countries had prepared and responded. But South Korea, we think is one of the best. So, yes, so, just as far as staffing, just to sort of complete the response there. So, when we were at the beginning of the pandemic, we had 25 virology reviewers and no more in the office or the FDA for tests. So, we quickly expanded to the rest of the microbiology division, which is about a head count of about 50. And thereafter, we called in another 100 reviewers who were not experienced necessarily in microbiology reviews. So, all in all, we were able to staff up significantly, but not immediately, obviously. Still, in those early days, in the first two months, we actively engaged with 100

developers of Covid tests, and our response times were very short with the staffing we did have. We were very good.

Dr. Van Der Pol: Ms. Schwartzott.

Ms. Schwartzott: Just another comment back to the topic of sharing. I serve with SeroNet at the NIH and NCI, and, you know, they have very different groups. Throughout SeroNet, you know, lab work, epidemiology data, and I serve with the data. We created a database, which is now called ImmPort, that allowed sharing of data, which included slides, and I was absolutely amazed at the level of sharing there. I was wondering if the FDA tried doing something similar. That just seemed like a really great mechanism. And ImmPort's fairly new, but it was a great mechanism to get out the data sharing information.

Dr. Stenzel: Yes, we are aware of it. And you do remind me that there was an example of sample sharing, that was very valuable relatively early on in the pandemic, and it did involve NCI. So, the NCI, I will be forever grateful to NCI volunteering to help us to evaluate the serology tests that were so challenging in the beginning of the pandemic. You may remember that the FDA, early on, which we then reversed the decision, and first decision was a mistake. And I have admitted that publicly in writing, in the New England Journal. We allowed serology test developers to market their tests under certain stipulations. We quickly saw that those stipulations were not followed and that many of those tests had not been either fully validated or were functioning. So, we found a ready and willing partner at NCI, and some funding for them to evaluate the serology tests. The FDA, in collaboration with others, did reach out to a number of academic institutions, and other institutions, to identify, and the CDC played an important role here. NCI and FDA. In identifying convalescent serum, as well as pre-pandemic serum and plasma, for Covid that could be used. This was an enormous effort, though, to acquire those samples according to local state and federal rules and laws. To evaluate the

samples, we needed to pull those samples and test them at every step of the way. So, we had an entire huge team, interagency, huge team, including our academic partners, to be able to stand up that effort. But, sample exchange, sample sharing, was very critical to that effort. So, thank you for the reminder of that. And yes, that is one program that we're aware of and that could be used. Thanks.

Dr. Van Der Pol: Thank you. I think we've heard from most people, but just want to verify that everyone has had a chance to ask any clarifying questions before we start to try to respond to the FDA's questions. Okay, and seeing nothing further at this time, let's focus our discussion on the FDA questions.

**FDA Questions**

Dr. Van Der Pol: Panel members, copies of the questions are in your packets. I would ask that each panel member identify him or herself each time they speak, to facilitate transcription. Please don't forget to use the raised hand feature in Zoom. So, with that, if we can see question one on the screen.

**Question One**

Dr. Van Der Pol: Question one is long and has many subparts, so this can take us as long as we need. We're ahead of schedule. The question is, how can test developers best interact with CDRH when preparing for future pandemics, and some of the sub questions include what steps can CDRH take to strengthen its communication strategies or any methods of communication more advantageous than others? And then any other ideas. We will get to novel ideas for communication in one of the upcoming questions, but I think if everybody wants to just throw their opinions out there, I'll sort them into which question they probably go with. And when the

summary comes, we'll sort that out. There was a question from one of the panelists about the open public hearing. I will just remind you, I read a statement a few minutes ago that no one applied to make a statement during the open public hearing portion of this process. So, with that, you have the question in front of you. And I'm happy to start taking comments from the panelists again.

I think I'll take prerogative and start with saying that I think Dr. Stenzel already mentioned something that's, you know, one of the critical things. And that is, there was information up on the website. There is information available to people. Not everyone knows that information is there. Not everyone knows where to look for it. And so, how do we make sure that the information is not only posted, but actually everybody knows that it's posted, and where it's posted. And I don't know if that's something that, you know, is a mechanism that, while you've already got a lot of data posted on site, there needs to be easier search options. So, for example, I go in and I look all the time, at the molecular 510(k) and molecular genomics summaries, because I need to see what's going on in that field. But a lot of times when I'm working with developers, they have no idea that those even exist, or where they exist, or how to access them, until I send them a link. So, there's a lot of great data up on the FDA website, but I'm not sure that everyone knows how to access it, and maybe there needs to just be a button that's an accessing data tutorial. I have no idea, but you know, that's the kind of thing that I think that, from my perspective, if you guys have run down such a great job of getting the data online, now we just need to make sure people are A) aware that it's online, and B) have a comprehension of how to find it. So, because, somebody, a web person designs things and they think it's really super logical, but then for me, and I'm not a web person, it's not logical to me. So, that's my two cents worth. I'm just going to throw that out there. And then, I'll call on Dr. Blumberg to start us off with different opinions.

Dr. Blumberg: Emily Blumberg, University of Pennsylvania. First, I want to thank you for such an incredible presentation and for the answers to the questions. I actually learned a lot just in the past hour from everything that you've said, and I, well, you're asking partly about test developers. I want to speak about the community, both the physician community and the larger community. I think the FDA needs to find communication that actually is more easily accessible to practitioners in the moment. I know FDA members were periodically on the IDSA sponsored calls. But I think that it wasn't really a fully effective outreach for the larger community and definitely for the lay public. I mean, the rapidity with which you provided resources and, for us practicing, and the tremendous amount of work that went into this in such a short period of time, I think is extraordinary. And I don't think was fully appreciated by people. I mean, I learned so much about how things went, to actually bring testing to fruition and to the public, and I think there has to be some outreach that includes lay media, lay, you know, like, you need to do something that really showcases, because I think that would restore public trust to a large extent. I think during Covid public trust has been hard to maintain for a variety of reasons. But I think the work that really has happened is impressive and there needs to be, in addition to the fact that the website's very challenging, I mean, I find it challenging. There needs to be other mechanisms, social media, things that actually showcase what's going on in a way that people can really learn what's been going on. And that's both accessible to practitioners, whether that's every single medical professional society needs to have some sort of interface as well as, you know, major media markets. But I mean, I'm really impressed at what's been accomplished, and I'm sad that the public is unaware of how much and how quickly it happened.

Dr. Van Der Pol: Thank you, Dr. Blumberg. Mr. Spring.

Mr. Spring: Yes, thank you. Brad Spring with Roche Diagnostics. So, I'm just going to focus on the first question, but just make a statement that, because I represent all test developers, manufacturers, I won't be commenting on some of the questions where you're asked who to prioritize. But, having worked for my current company and prior companies dealing with the pandemic, I want to echo the comments earlier, Tim, and your team, just what a great job you did do, kind of plowing through a lot of the issues with pandemic and, you know, I think you always did keep the public health in the forefront in the activities you did. You'll always get criticism, you'll always be challenged, but I do think, in the end, I think you should be congratulated on a job well done, but we'll look at some of these lessons learned and try to make some improvements. I want to comment, though, on more specifics in this question. I personally, and I've received comments from other manufacturers that continue the town halls, I know you were doing it weekly. I think you went to what every other week and then less frequent, which made sense. Those were very valuable, especially for new manufacturers, new developers. I'm assuming some clinicians were involved, those developing LDTs, very valuable. Telephone hotline, the website, while it might need to be redesigned and re-tweaked, also very helpful. But I think as Dr. Van Der Pol said, there's a lot of information out there that manufacturers just can’t find. So, maybe there is kind of this, so called button you can press, or if there is an FAQ that has just a listing of all the resources, that might be helpful. The EUA templates are extremely helpful. I will say there's been some criticism from other manufacturers on them being overly prescriptive. So, I think the advice is just to provide a little bit more flexibility. But, again, very helpful. A lot of foresight went into those. And a lot of that's around the communication side. As we look ahead to prepare for whatever's next, I reflect back on, and I think Tim, you and I were there, and maybe other colleagues were there. There was an MDIC, the medical device innovation consortium, convened a discussion during the Ebola Emergency

Use Authorization period, or the emergency. And we were talking about, kind of the lessons learned with Ebola. How do we get specimens? So, a lot of these questions that were being discussed, here, I think we were, we were having those discussions at that meeting. So, my recommendation is to work with public private partnerships, other clinicians, in that planning for whatever is coming next, and taking, say the lessons learned you have here with Covid, trying to apply it to a future pandemic. But in that type of setting, where you get engagement from everyone. So, I'll end my comments there. You know, Tim, I could probably go on about this, but just wanted to give you that feedback. And I'll yield to Jennifer.

Dr. Van Der Pol: Dr. Stenzel, did you want to add anything? You unmuted for a second.

Dr. Stenzel: Oh, I was just saying thank you and you're welcome. Appreciate the input. I didn't have anything specifically to say.

Dr. Van Der Pol: Okay. Ms. Schwartzott.

Ms. Schwartzott: Jennifer Schwartzott, patient representative. I wanted to follow up on what Dr. Blumberg said. I mean, just the amount of information that we've learned in the past hour is valuable. And I'm thinking like, just plain old informational webinars. Whether it be to the test developers, whether it be to practitioners, on very specific topics, like, to the test developers, you know, what's the process, that kind of thing. And to establish what the need is. And then you can invite them to the town halls, show them where the information is on the website, that kind of thing, but it gets them to say, oh, wait a minute, this is something different, you know, and move forward. And, I mean, they're very excited. People are very excited to talk about epidemic preparedness. They don't want to see what happened with Covid. So, that was just my thought. That just, simple. Start simple and, you know, that's the way to get the conversation moving.

Dr. Van Der Pol: Thank you. Dr. Petti.

Dr. Petti: Thank you. Cathy Petti, HealthSpring Global. As we've all learned in this world, we all communicate differently. So, town halls, which is oral discourse, obviously the website. Unfortunately, the FDA website has a lot of text, and I think we would benefit more from charts and figures, particularly when you're trying to go through the steps of an EUA authorization. Colors and boxes, I think would do very, very well. An index, I mean, I, like Dr. Van Der Pol, go to that website frequently. And sometimes I forget how I got to this gem of a document, and then I get frustrated. It's like, I saw this just last week. How can I not find it again? And we're frequent users of your website. So, that is mission critical, because there are just amazing nuggets of information there. I also would encourage the FDA, and I'm not sure if you have the authority or charge to do so, but perhaps have a standing advisory committee, from, not only representatives from the community, patients, different backgrounds and industry, academia. In order to understand how to communicate out, you probably would benefit greatly from troops on the ground. And this is what we're hearing. These are the resources and tools we need. Wouldn't it be great, if Dr. Stenzel's Twitter feed would have various different ways of pushing information out. So, you may already have those committees, but I would strongly encourage FDA to have that, in a standing way, because we all know there's a huge vetting process to even have people advise the FDA. So, perhaps do that well before pandemic hits. So, again, communicating in various different channels will benefit all, because we all learn and receive information differently.

Dr. Van Der Pol: Thank you. And I'm going to add a tag on to that, that I have an organization that I work with that uses what they call digital champions. And basically, it's not about creating content as much as it's just about forwarding content within their networks. And so, by having, you know, about 200 digital champions, they reach millions of people. Because each of those people, and again, not creating content, but just retweeting, or just, you know,

moving things along in whatever platform it is that you use. I'm not good with digital media, but that's why I learned about this process, because I have to have help. I can't do it. But this is a process that requires pretty little effort. And wouldn't require a ton of vetting necessarily, because these people would not be speaking on behalf of the agency, but would just be passing messages along to really improve that outreach effort. So, I think that that's something, the digital champions, something to consider as well. Yes, Dr. Stenzel.

Dr. Stenzel: Yeah, I just wanted to make special note that this particular pandemic preparedness panel, this advisory committee, under statute now, we will be meeting at least annually going forward. So, this is, you know, a standing function. This is the first, of many, and it's primarily, almost entirely focused on IVDs. Future ones will likely be involved in other pandemic preparedness topics, other than IVDs, but IVDs are obviously the first one here and we're happy to kick it off. The other thing is, you know, there's been a lot of mention of communication. The FDA does social media. Facebook, Twitter, LinkedIn. We use email blasts, so we, you know, you can sign up for the email blast. So, and these email blasts and these social media postings, do hit tens, if not hundreds of thousands directly. And those folks can amplify that as they wish. You know, we do communicate regularly with the media. We got almost daily inquiries from the media recently. One of the most recent things that was picked up by the media was expiration dating updates for OTC tests. That was that was picked up by many media outlets and, you know, in fact, I shared that with a friend who didn't know how to determine whether there, I shared one of the new stories with a friend, because that was the easiest way for them to understand how the updates occurred to the expiration dating, and the link to the FDA website where they could look up their specific test. Look up the lot numbers, and determine if the expiration dating had been updated, and if their current tests were still therefore in date, even though the printed date had passed. So, but, we always are looking to be

more effective. So, I do appreciate all of this input. And the other thing on the website is, we've added some charts, color, and the video is a little bit harder to do potentially. But we have added search functions within, on certain, so if you get to the right location where the tests are listed, then you can search, there's search boxes for trying to find the test you're looking for, the features of the test you're looking along. Is there a home test or is there a home collection? Those features, those keywords can be searched. And we did constantly look at the website and try to update it to make it the right size and as easy to access as possible. We understand there are still challenges, and we appreciate the input.

Dr. Van Der Pol: Dr. Pereira.

Dr. Pereira: Hi, Marcus Pereira, Columbia University. I want to echo what Dr. Blumberg said, in terms of how incredible this last hour and a half have been in terms of learning more about everything that the FDA did during those initial months and thereafter. Really quite impressive. You know, in terms of sort of the communication aspect, I do think that sort of, you know, a greater effort in particularly having sort of communication champions within the agency, who are tasked with sort of providing information to several components, right, of the health care system, in terms of industry, but also to providers and to patients, I think would be enormously helpful, in particular sort of people who can be very engaging and answering questions. I mean, I have to say, one of the strengths of the FDA is the documents that it produces. You know, and sort of when Dr. Cotton mentioned previously about the package inserts, you know, for the EUAs in particular, I found myself constantly reading those documents, whether it was for therapeutic agents or more importantly, actually, for the therapeutic agents and sort of what they were supposed to be used for, and what they were not supposed to be used for. And actually, I did use a lot of those documents for my lectures, to fellow providers and even to patient groups who wanted to know more information. So those

documents were actually a great source of information and authoritative information, but certainly they had to be distilled to the public at large, you know.

The serological tests documents were a little bit less helpful. We did find ourselves sort of very confused by sort of, when to use all of those serology tests, as you alluded to, and there's enormous debate, for example, in the transplant community in terms of, you know, how to use them, whether to assess whether someone had responded to the vaccine or not, people were becoming very creative with sort of new tests that were coming. And there was sort of, I felt at that moment there was a little bit of lack of information from the FDA in terms of whether you should or should not, or under what circumstances those tests could be used, and could have led to a little bit less confusion. And that's where I think sort of, some communication officers would have been helpful. The last point I wanted to make, in answering your question, obviously, I'm not a developer, not a person from the lab. But one of the things to think about, in preparing for future pandemics, because obviously, they're never going to be like what the past pandemics. And I think that we can obviously learn a lot from Mpox and Covid-19 and everything, but sort of maintaining a certain sense of creativity, so to speak, and what may come next. I think it's obviously paramount here, right? You want to sort of figure out what could have been done better and what went well with these past ones, but also prepare for the things that you cannot even imagine at this point. So, to that effect, I don't, this might be a question. Is there, does the FDA, or sort of the public health sort of authorities, ever, sort of, undergo simulation games? Like, you know, preparing sort of a certain type of pandemic that comes, and are the agencies prepared, and are they, sort of, have the communications and relations with industry prepared?

Dr. Stenzel: Yes, yes, we do prepare. In fact, prior to Covid, we had assigned an interagency, MOU, a tri-agency, CMS, CDC, and FDA, and had met, started to meet, on a regular basis to

prepare prior to the pandemic. When the pandemic hit, we met weekly with that group. And we addressed anything of need. And we still meet regularly with that group. Now we're more focused on preparations for the next potential pandemic. We also have expanded a lab group led by the CDC, as well. So, the FDA is now an active member of that. And yes, I also wanted to comment that the FDA did what it could as far as how to use tests, and for, you know, which depended on the validation of the test and how well it worked for certain groups. And then provided that information in the instructions for use package insert, in the intended use statements. We also try to do some additional things, but it was always in collaboration with the CDC, which is the entity that does take lead for communicating to clinicians, laboratories, and public about how to use, in this case, how to use tests, whether they be diagnostic or serology. So, the CDC does take the lead on providing that kind of input and recommendations and information. And we collaborate and coordinate very closely with the CDC. And most of the time, anything critical is, you know, the FDA puts out, is that involves CDC, also gets to review and vice versa. So, lots of communication there and collaboration and alignment on our messaging. Thank you.

Dr. Van Der Pol: Thank you. Dr. Walker?

Dr. Walker: Hi, Dr. Walker, a consumer representative. And I echo the sentiments expressed, and I want to say, you know, excellent job on what has already been done and communicated thus far. However, I would be remiss if I don't say something from the consumer side. And the world we live in now is a digital world. I don't know about you, but I take my cell phone with me everywhere I go, from the restroom to the grocery store, so when I'm outside walking. And when we're talking about communicating and reaching other stakeholders, such as patients, such as individuals who look like me, there has to be, and I think somebody said it, a creative way. I went and looked on Instagram at the FDA's page, and there was nothing that attracted

me, to want to, you know, browse through the communications that are put there. I went on the website, and so, I'm saying all this to say that all of the communication that has already been put out, we understand it. We understand it because we work, and we live and we breathe in this field. But when we're trying to really execute and communicate to individuals who may not understand, there has to be other methods that we can employ that will be creative, creating reels on the Instagram page. If you want to, get something out quickly, post it on social media, and it will spread like wildfire, but it's all in how it's presented. I have individuals in my community who may hear something on the news that the FDA said, and they may not quite understand it. So, they call me because they trust me. to interpret it, but then to break it down so they understand it, in a language in which they get. So, hopefully I'm making sense of what I'm trying to communicate, as it relates to the consumer side of things, and being very creative to make sure that, you know, whatever measures and critiques are put out there, that individuals, especially low-income individuals, African Americans, Hispanics, and Latinos, fully understand and can take action to protect themselves and their community. Thank you.

Dr. Van Der Pol: And while I understand Dr. Stenzel's perspective that the CDC does a lot of the communication for, you know, patients as well as health care providers, but I think that, the world changed, and I think that the lay public actually has more of an interest in what the FDA does than they ever did before. And so, even though CDC is the primary communication mechanism for these things, people now, you know, it's so funny for me as a laboratorian to hear somebody saying, oh did you use the antigen test or the PCR test? It just slays me because, you know, two years ago I could have said, oh I'm going to use an antigen test for you, and they would have gone, what are you talking about? So, the world has changed, but that means that we need to keep that in the back of our minds. So, I think Dr. Walker's perspective is exactly right. Even though that's not your primary focus, and even in this question where we're really

supposed to be focusing on how the FDA interacts with developers and manufacturers, I still think that that lay user piece, especially once things are approved and people, as you just said, you know, you were helping a friend understand what the extension and expiration date mean. It's things like that, that people would like information, not from the CDC. But actually from the FDA. And so, I do think it's worth reinforcing that how important it is to communicate with all sectors, even though it's quite difficult. And I recognize that. I'm not good at it myself. So, Dr. Stenzel, did you have some feedback for Dr. Walker?

Dr. Stenzel: I did, just a little bit, and thanks for the input. It's all very valuable to us, and I would love to be able to do more, more quickly and, no excuses, and just to add, though, that, the clearance process for any communication and the official communication is quite thorough within the FDA, and within the government. So, it's very you know, we try to do that as quickly as possible, and we have timelines dependent on the need. But we have our process, so, thank you.

Dr. Van Der Pol: Dr. Caliendo.

Dr. Caliendo: Angie Caliendo, Brown. I just want to say that what Dr. Walker is saying is very important, in trying to fight misinformation, right? And if you can get information to lay public in a way that they can understand, that could be extraordinarily helpful. I just want to comment on, coordinating with the CDC with your communications. I'm sure you were doing it; it just didn't look like you were doing it. And I just think it would have been so helpful to physicians, other providers, the public, if there was just more alignment. With, because you do have different roles, I very much appreciate that, but to find a way to coordinate, I think would have been helpful. I'm really glad you guys are now involved with their laboratory system, because I think we'll get to that later. About things you could have done to help get us some information across tests, that the CDC could have helped with. So that's just one thing, is that that the

messages were so scattered at times, that better coordination, I think, would have helped everybody.

Dr. Van Der Pol: Thank you, Dr. Caliendo. And Dr. Honein.

Dr. Honein: Yeah, Peggy Honein, from CDC. Thank you. And I really wanted to congratulate FDA on this extraordinary communication and really setting up all these town halls, the volume of email that went through, keeping response times really short is incredibly impressive. I would recommend, in addition to all those things, which I think are great to keep doing, is to consider communication channels to reach people who aren't part of that community already going to those town halls. So, thinking about, national scientific meetings that may be relevant where something from FDA could help highlight it to people who aren't already plugged in to the FDA system. You know, building on the comment by the last person, I think there are some opportunities for coordinating with CDC, such as the clinician outreach communication calls, or the COCA calls that go on, could be a good time for CDC and FDA to co-present and reach the clinician community. There's a lot of existing calls with public health officials that go on every week, which could be another audience to reach state and local public health officials who can then amplify those messages in their communities. So, just encourage adding channels to the extent it's feasible, so that you broaden the audience, and more people have the opportunity to then directly access some of the ongoing things like the town hall meetings. Thank you.

Dr. Van Der Pol: Thank you. Dr. Stenzel, your hand’s up. I don't know if you want to respond to that or if your hand’s still up.

Dr. Stenzel: I just wanted to comment, you know, basically on the communication with CDC and others, and the coordination, it can always be better, we know. But the testing coordination group, which Kris mentioned in his talk, is ongoing. We meet approximately every other week,

and the CDC is represented there, high levels of CDC, I'm not sure if I should mention names, but often the White House is on the call, and then many agencies, including BARDA, and ASPR, CMS, FDA, of course, and NIH. And we're, you know, and this has been going on for a very long time. It's in addition to the tri-agency calls that I mentioned between the CDC, CMS, and FDA. And then in addition, I do meet with significant and publicly known leaders at the CDC. It's a meeting between me and my office, and key laboratory personnel at the CDC, and that is on a monthly basis. That started prior to the pandemic, and stepped up, and has included visits to the FDA as well, by the CDC. So, we can always do more. We need to do more. Thank you for the input. And oh, the other thing was, I was a frequent, if not weekly visitor on the CDC lab calls, and addressed open questions as well as pre-submitted questions there. And on the American Public Health Lab weekly calls, then moved to bi-weekly and then monthly. And still, I'm invited back to those meetings on occasion. Also, the state epidemiologists' calls, I was a key visitor and speaker there, and addressing questions. And have accepted numerous invites to various meetings. I can't accept all of them, but if it's an important meeting, I have somebody else on our team participate in those calls. So, but always can do more. So, thank you.

Dr. Van Der Pol: Dr. Ng.

Dr. Ng: Thank you. I'd like to present the perspective from the clinical laboratory. I want to commend the FDA. Your website, constantly updated with the EUAs, was the beacon of truth and the lighthouse for us, to identify tests that we wanted to bring in, at a time when there was no way to actually verify the performance outside of the submitted data. So, for me, your website was perfect. You can push me all the stuff you want, but I want to go pull it when I have time to pull it, and your website worked well. I want to add on to the communication to the laboratory network. The CDC brought up that locks laboratory outreach communication

system early on. We met weekly, the chat line was a pure tsunami of comments, questions from anyone. It was overwhelming. I want to also comment about, when I think about communication from a laboratory perspective, the key stakeholders for me are my users, which are the providers, the epidemiologists, which is public health, and then underlying that is the community, where the demand is. CLIAC happens to be a committee that brings together the 3 governmental entities, CDC, CMS, and FDA. We met through this pandemic. The agencies were well informed of what was happening at the ground level. I do recall early on, one of these meetings, our public representatives were Jennifer and Roblena, very passionately argued for free home-testing. And this was early in the epidemic, and shortly thereafter it became available. So, the role of the public consumer is critical and key in these committees, in case we all are running down some rabbit hole that is not aligned with what the demand is. And then finally, I would challenge this group. What is your role in the communication? My role is everybody comes to me and says, what test are you offering, and why are you offering it? And how does it perform? And you all know we're offering a test. We're basically flying the airplane while we are building it. But more importantly, as part of a public health system, I work with my county public health department, through the community organizations that stood up all the pop-up testing sites, and through all the faith-based organizations that are intimately engaged with our public health department to bring the message in an intelligible, clear to understand and factual message to our community members. That's not something I can do. It's very clear. I don't speak anybody's language. But it's through these partnerships that we can make that message heard, and I would encourage everyone on this list to figure out what your partnerships are and take ownership of that. That's what we have to do, sitting at the intersection of science, and providing a service that everyone needs. Thank you.

Dr. Van Der Pol: Thank you Dr. Ng. Are there any other comments? I'm going to just remind you exactly what the components of question one are: How can test developers best interact with CDRH when preparing for a future pandemic? So, I think we've focused a lot on users of product, and once products have an EUA, so if there's any comments that people want to take a step back, before that. If you're a test developer and thinking about how to get information about what information you need to provide to the FDA, is there a mechanism that would be helpful? What communication strategies should be strengthened, and how do we include other stakeholders such as patients and clinicians? That is part of it. And were any methods of communication particularly useful, or are there things that you have novel ideas about how the agency should approach communication? And I think we've got things in each of those categories, but I just wanted to throw those reminders back out there in case anybody had an epiphany and they wanted to share yet one more idea with us before I summarize.

Okay, seeing none, I'm going to give it my best shot. It is a complicated question. And I tried to sort of sort the different responses people had. So, the interaction mechanism, particularly as it applies to developers, I think, is really to think about how to improve the mapping of the website, so that people can find those documents, those guidance documents, those other people's already approved documents, so that people can model after what has been successful for other developers. So, I think that that interaction mechanism could be improved on the website. In terms of strategies for strengthening communication overall, make sure that you're including data specific for providers, healthcare providers, but also make sure that you're including methods of providing data to the public. And make sure that you're working with the lay media whenever possible, and also including digital outreach strategies. So those are some things that you have going on, but that could potentially be strengthened. One of the other things in the communication strategy that came up, was using more graphics and alternate

learning mechanisms as opposed to text. Infographics are something like, for example, CDC has really gone to. I would urge you not to lose the text. For example, CDC's STD annual surveillance reports are now all infographics, and there's no text. So, for those of us who want to read the details, that's a disadvantage. So, don't throw out the baby with the bath water, but again, try to make sure that you're offering a variety of different ways to present those data. Also, in the communication strengthening process, consider standing advisory committees, which I think maybe you've just indicated. This is one of those standard advisory committees, for pandemic preparedness. One of the things that we've heard sort of repeatedly in terms of mechanisms that are really useful, is the town halls were very well received. Webinars, providing basic information, exactly like the information that was presented to this committee, to this panel today, about the activities that are ongoing and how much it requires in terms of resources to present those activities. The telephone hotline was also very useful, particularly mentioned by our industry representative as well. And the EUA templates were also very useful, although it was suggested that maybe they be a little less prescriptive and a little bit more broad in their content. Also, in terms of mechanisms that were most useful, do include things like the basic information about how people should be accessing more information, or how people should be going to start their process of developing studies and documentations. But do start simple and include processes. I think that goes for not only manufacturers, but also the lay public.

My husband asks me all the time, why does it take so long? This has already been approved by the panel, but it's not approved yet. Because my husband's watching this Covid stuff with a fascination that for a lawyer, I find odd, but he wants his vaccine booster and the vaccine booster has been reviewed by the panel, but it's not approved yet. What's the holdup? I'm like, I don't know. But apparently it's a burning question for some people. So, people like to

understand process and that transparency and process is helpful, just to say, oh I get it now, and I'll just wait until, you know, it's available.

And then the novel ideas were, I think, probably the most important one, but communicating clearly with all the public through a variety of different digital mechanisms, as well as the email burst that you're already using, as well as, as the public. But also broadening your reach by working more with national scientific meetings, and not to say that you're not already doing that, but just continue that. That sort of outreach effort in places where people may be not looking for the FDA, but the FDA is there, and they're usually very… Those sessions, where the FDA is at meetings that are national society meetings, are always so well attended. People really are so eager to hear what's behind the curtain. So, working with those societies. And then that leads us in the novel interaction idea, and it's not novel per se, but working with these public-private collaborations and building these networks. And it may require multiple networks because when anything gets too big it's non-functional but maybe task force or, you know, networks that include societies, academic institutions, a ton of public health agencies, obviously. Many of them were mentioned today, including CDC, NIH, BARDA, DOD wasn't mentioned, but probably should be included. CMS, APHL. So, these public health agencies, academic institutions, large commercial laboratories, and manufacturers. And so, if there are subsets of those groups of people that could be in a task force to talk about emergency preparedness and strategies going forward that could perhaps meet quarterly or on some basis, just to build those relationships, so that when something hits, everybody is quick to mobilize and you start having weekly meetings instead of quarterly meetings, something along those lines. Cathy Petti has a comment at this.

Dr. Petti: Yeah, I apologize. This is just a very quick comment, circling back to that very first question. Since promoting development of new technologies is cornerstone in responding

to a pandemic, Mr. Spring, would you be able to speak to, when the EUA templates may not have been sufficient for small startup test manufacturer, did you find that there are sufficient resources, a hotline, where they could immediately engage with the FDA, such that they could start the test development process?

Mr. Spring: Yeah, thank you. Brad spring with Roche Diagnostics. And I think Tim, you'll probably have some comments here too. So, the answer is yes. I mean, very early on the pandemic I think we were all scrambling for answers on how to validate such tests and bring them through the EUA process. And I know, from my experience, now, I don't work for a small company, but FDA did make themselves available to, you know, they're rushing to get the right resources on this. So, I don't know if a hotline existed early on. But, you know, you just have to know who to call. I think that's probably the first challenge, who to call about this. Sometimes you're calling Tim himself, or you're calling one of the reviewers, or Uwe or someone on the staff there, but they did make themselves available. But I think too, the challenge with that is getting inundated with multiple manufacturers all at once, and the ability to provide consistent information is a challenge. So that first call comes in, you know, you're trying to give some advice. Then the tenth call comes in. Are you giving the same advice? And that's why the templates, I think, and other advice were very helpful, along with the town halls. And Tim, maybe you can comment on when those town halls came into play, because I thought those were helpful as well.

Dr. Stenzel: Sure. Tim Stenzel, FDA. So, the email was available very early, may have been January, that you could request Covid template recommendations. And that was staffed, as Kris mentioned, from early days, and we even went to two shifts. And we received submissions of pre-EUAs, which was asking us questions, and we also received the EUA submissions, via that email, and any inquiries about, you know, we got inquiries from labs about, you know, I can't

get this item. I can't get the swab. Could we substitute? Those email questions often, based on frequency, would show up then as frequently asked questions on the FDA website.

Dr. Van Der Pol: And the town halls started when?

Dr. Stenzel: Yeah. The webinar town halls started in early March. First Monday in March was the first, of 2020, was the first webinar. And we provided the access to the components of the commercial access to components of the CDC test, on that first webinar, with lot numbers that had been QC-ed by the CDC. And then, obviously we discussed the February 29th policy on that on webinar, and then webinars and town halls were regular from then on. We also, in addition to emails through the hotline, we also had calls. Everybody in the office that was handling Covid inquiries would be on calls, including me. I mean, I noted the peak day, when I had 22 scheduled meetings, during the pandemic. I don't know how I made it through that day. And we took calls from test developers, labs, states, cities, Congress, and so, it was all hands on deck 24/7 sometimes. So, much of this, obviously not visible to the public.

Dr. Van Der Pol: And I think that, one of the comments from the panel is that maybe it should be made visible to the public, because we all many, of us worked with the FDA very closely through this period. But also, many people did not. And so, I think you heard consistently and with really high levels of appreciation, for the volume of effort put in by the FDA and the rapidity of the response. I mean, if you think about January of 2020 already having EUA templates. I mean, that's really incredible because not everybody in the public health community was even taking Covid seriously at that point. They were thinking about whether they should take it seriously, but you guys had already taken action, you know, with a work product that was useful to the community. And I think that that response on the part of the FDA cannot be overstated. And I don't really think the agency always, and it's not that you're seeking glory, as much as, I think it would be really useful for the public to understand that

their tax dollars went into this, and that there was just this absolutely enormous, rapid, and really high-quality response. And so, I think that the panel, I'm seeing a lot of nodding, and I think the panel in general agrees with the statement, and it needs to be part of the record. And I think that, when you think about novel mechanisms for interacting, I think getting this out into the lay media is just another way to make sure that we rebuild that public trust, not only in science in general, but in medical technologies as well. Because, you know, we kind of constantly fight with that.

Dr. Stenzel: Sorry.

Dr. Van Der Pol: Oh, go ahead.

Dr. Stenzel: I was going to say that some of those conversations, many of those conversations, were treated by the FDA as strictly confidential.

Dr. Van Der Pol: Sure.

Dr. Stenzel: Needed to be. But, you know, and we can always improve, but when repetitive information or repetitive queries came in, we put out frequently asked questions on the FDA website. We mentioned the town halls. We do safety communications. So, we would take that information and those interactions and try to do something. But I hear your point that, committee panel's points here, and we will redouble our efforts to make it more transparent. Thank you.

Dr. Van Der Pol: Dr. Wentzensen.

Dr. Wentzensen: Yeah, thank you. I just wanted to just ask, and I'm not sure if you can address that, but I, so, Covid-19 was an extraordinary event that hopefully happens very infrequently. But for each of these, there are things rising somewhere and we read about them in the news, and there is… That's probably like, things being initiated that prepare a response, but then it's not needed. So, I wonder if you could comment on like, how many, and like, how

early these alerts happen, and when do you get engaged? Or is it at the stage when we're all aware and is it kind of like when we are deep in this already, or how early can you react, and how often does that happen?

Dr. Stenzel: So, the FDA typically, if not always, engages very early with CDC and other public health authorities and other agencies. So, for Mpox it was the earliest days. For the recent Ebola outbreak in Africa, the earliest days. And, you know, things pop up that don't ever make it public, that the U.S. government agencies prepare for, and hope that we don't have to do anything. You know, I would say that avian influenza is something that's been, you know, top of mind for a very long time, for those not aware. You know, avian influenza has been very problematic for, at least among birds, in the United States and around the world. And we have been monitoring it very closely. We, we've looked at available flu tests, and whether or not they can detect avian influenza, and have reassured within US government agencies that yes, we have the needed tests, if and when it might be needed, to respond to a flu pandemic involving avian influenza. But, you know, that's an ongoing, all the time activity, but when we don't need to broadcast that, we realize that, you know, when we say something, even if it's to say don't worry, it can you know, raise attention that isn't necessarily helpful. So, it's a balance. Always a balancing act, you know, when and how to communicate on something.

I wish there were more ways to show how much, and how effective, both the FDA and the U.S. government working together, is. I mean, this role that I play and within the FDA, this is the most professional organization of any that I've been in, and I've been in academics, I've been in industry, now the FDA. And it's really, you know, truly amazing how the U.S. government works together, most of the time, behind the scenes, to anticipate and prepare and to respond. And a lot of it goes unsung. We're not looking for kudos. It's just, it's our job, you know.

Dr. Wentzensen: And I think it's an important message to put out, even if you can do it at a very high level, and maybe you have it somewhere, but it's like buried in layers of FDA homepages. But I think like, just a general statement about that there is an alert system, that functions all the time and that's the reason why the response was so fast. Because otherwise, if you had started in March, when everybody now was aware, I mean, this would have been much later. So, I think I think that's a very important message, and people now actually understand after having gone through one, how important that is. Because before you get all these scares left and right, and it never comes here, and so it's yet another of those. But I think that that's an important, like, positive message to put out there.

Dr. Stenzel: Thank you.

Dr. Van Der Pol: Dr. Moore?

Dr. Moore: Yeah, just to echo that, I, you know, having worked in the government myself when I was at the NIH, and, you know, the government is in fact staffed with many, many professionals who take their jobs seriously and, and functionary, despite what you see on the headlines with the politicians and political yin yang, but, it's very clear that it, you know, that it works well when, especially when it needs to. My question is, yesterday it was announced that the Biden administration stopped, had to stop funding for the deep VZN, the research into zoonotic viruses. I'm not sure the reasons behind that. But the reason I bring this up, because in terms of anticipating the next pandemic, do program changes like that require the FDA, or is that something the FDA is involved with the CDC in terms of, as you mentioned, looking at, something may not be public, that is looking at emerging viruses early on. And you mentioned that you were doing that, that the FDA was involved, the CDC, and obviously avian influenza and Ebola. But I don't know if there are other viruses, or other pathogens of interest, with which you're engaging with, outside international authorities.

Dr. Stenzel: So, our surveillance system you know, for looking at potential threats, I don't think is affected by that. But you know, I really can't speak to that. It's above my pay grade, on all of that. But we're going to stay vigilant at potential threats. This focus today is primarily on IVDs, and our authorities and systems are in place. Fortunately, you know, in today's world, test developers may only need a sequence of a new virus to develop the test. That's typically all they need. They need a good sequence. The more sequence they have, the better they can design the test. And so, the world is very open in many ways. Some places are not so open, you know. But even those not so open places, we got an early sequence out of, that was used for the Covid response, and that was incredibly valuable and needed, and helped us get a start, before even, you know, spread to potentially other countries. So, all I can say is that we're doing the best we can with the tools we have, and we'll continue to work on, every day.

Dr. Van Der Pol: Thank you, Dr. Stenzel. I think that people have raised their concerns, as well as the things that they think are going well and right. Do you feel, Dr. Stenzel, that you've gotten everything that you need related to this first question?

Dr. Stenzel: Yes. Sorry, I was on mute. Yes, I think this was a lot of input, a lot of very valuable input, and we'll be examining this and redoubling our efforts, so thank you.

Dr. Van Der Pol: I was going to say, this is one of the ones where you're going to have to go back through the transcripts and really, really read it and take some time with it.

Dr. Stenzel: And we have talented communication experts within the FDA, and they will be with us looking through these transcripts and seeing what they can do. It's not members. I mean, certainly content-wise, members of our office provide content for the FDA website, but we're not website designers. We're not we're not coders for the website, but we work with them closely and communicate with them on a daily basis.

Dr. Van Der Pol: Dr. Kotton.

Dr. Kotton: Thanks, Camille Kotton, Mass General. So, for the past three years, I've been a member of the CDC Advisory Committee on Immunization Practice, and one thing I've learned is just how easy it is, as an ACIP, member to access so much at the CDC, and then for my institution and for colleagues, including many colleagues on this call, I've been a point of access. And I feel like I'm sort of an ambassador between the CDC and then the largely academic, medical world. But I guess I would think about whether, you know, even a call like this, I think many of us on this call we've said great things about the talk this morning, and the work that's been done, and the amazing work by the FDA. I think that we could almost serve as ambassadors to the FDA, in that, if you had more people like us in the community saying like, oh yeah, you know, there's a great FDA website on that, or let me show you how to answer that question, or actually I know someone at the FDA who would be interested in talking to you about that. I do think that we can serve an important role, kind of as ambassadors or liaisons, or it whatever it might be. And for many of us, we felt, at least the way I was brought up, is sort of the FDA and CDC were like federal agencies that were hard to penetrate and might even be unfriendly or not interested in what we have to say. And it turns out it's actually quite the opposite. And, I mean, I had amazing conversations with different, largely vaccine people at the FDA, when things were especially challenging. But I will remember the nighttime calls, like, being available anytime, just to basically save lives during this horrible time. So, I would just think about us as ambassadors.

And then, I keep thinking about this as well, but both the CDC and FDA could probably use a little bit more marketing, which is something that we don't really think about much in academic medical circles. But now we are being encouraged to do so. And I mean, honestly, the FDA is amazing. Amazing. Amazing. Amazing. So is the CDC, right? And it's been horrible to watch, especially the CDC, kind of get beaten up during this time. And so maybe just, I don't

know what marketing looks like there, but if I were in charge, I guess I'd try to do a little bit more positive public information. Not that I know how to do that, and not that I know anything about marketing, but I think we all probably know what I'm talking about, because really the work you do is the best in the world. So many countries follow what you do, what the FDA does. And so, I would think, both about more ambassadors and more marketing. Thanks.

Dr. Van Der Pol: And I think, I would add on to that, if you feel that your role can be to be an ambassador for the FDA, and if you're involved with a society that has annual meetings and/or you see, when they say, do you want to submit an idea for a symposium? Speak with the person at the FDA that would be related to that topic. Speak to the person at CDC, whatever, but invite them. I have found that to be a super successful strategy for making it really clear. I think there was a perception, in my particular field, that the FDA was just the stumbling block we all had to get over, right? And I think that making people have a better understanding of the process, the rationale, and the willingness, as you said, of the FDA to actively work with industry to really meet common goals and needs. I think it's on those of us who are involved in those national meetings to make sure that the FDA is invited. They can't invite themselves to give a talk, you know? We have to actively reach out and say, is this something about which you can talk? And then are you interested in doing that? So, I think that all of us on this panel, you know, probably have access to people that plan meetings. And we should just be thoughtful about that. That's a novel strategy as well for getting information out there. And I think that we can be involved in that. Dr. Stenzel.

Dr. Stenzel: Yeah, CRH has a speaker liaison, and our office gets daily invites to speak at all levels of our staff, and we want to meet those needs whenever we can. And we do have travel funds. We can't accept outside funding to travel, but we do have sufficient travel funds to go to

meetings. And sometimes our staff are incredibly busy, so, virtual participation is always greatly appreciated when schedules are tight. Thank you.

**Question Two**

Dr. Van Der Pol: So, I think I'm going to wrap up question one, unless there's anything else that people, I think we're going to move to question two, because we have time still before lunch is scheduled. So, if we could see question two up on the monitors. I'm wondering if we've already answered some of these, the components in here, with what types of educational resources or communications from CDRH would be most valuable, again, from the perspective of aiding test developers. So, we're trying to think about what can the agency do to make it easier for test developers to get data and products onto the market, so that in the future when it comes to pandemic preparedness, we're moving quickly. Are there items that people would like to discuss that we didn't discuss during that first question, because they are somewhat interrelated? But any educational resources or communication strategies that would be part of reaching out to developers. I see Dr. Ng has her hand up.

Dr. Ng: Thank you. I am curious. I kind of view this as a pyramid. The ground level is there's many, many, many people who are interested in developing a test, but sort of getting from that and having it available, that middle section, is how adequately can they scale up and what is the plan for scaling? And are they aware of what are they planning for? Whatever type of demand there might be.

Dr. Van Der Pol: Can we drop the slide presentation?

Dr. Ng: And perhaps question number three might relate, might be the bridge to talk to the developer, and then which manufacturers they can work with, who can scale up, right?

Dr. Van Der Pol: I think that that's going to be the key in three. So right now, but educational materials about, or just documents about, what scaling might be useful.

Dr. Ng: Yeah, the FDA to say this might be a possibility, right? And then how would you respond?

Dr. Stenzel: We were making inquiries of test developers early on in the pandemic about, you know, throughput manufacturing, and was monitoring that, early on a daily, weekly, if not daily, basis. A test availability, volume of tests that were produced, and providing that information within the U.S. government. And then as we moved ahead with prioritization, we were asking for the volume numbers and for kit manufacturers that we wanted high-throughput, high-volume test manufacturers when we had plenty of manual low-volume tests already. We were prioritizing those. Some of the lessons learned, part of, you know, and I think we'll get to this in other questions. How do I identify which manufacturers, what types of tests, what kinds of manufacturers to identify, to work most closely, perhaps, with them, to make sure that they're ready. Then, within the U.S. government, there did become financial resources available to invest in scaling up, so that, in the RADx program or one, ASPR also, BARDA. So, there were eventually funds to help with scale up. If the manufacturers that had tests that we needed, didn't yet have the manufacturing scale to meet the needs. And those efforts were really amazingly successful. So, those are clear lessons learned.

Dr. Van Der Pol: I think we'll come back to that as well. So, keep that in the back of your mind, and be thinking about different types and priorities. But I'm going to… Dr. Petti.

Dr. Petti: Cathy Petti, HealthSpring Global. I think, in addition to those EUA templates that we could issue to emerging test developers, about, if there were a pandemic, this is what it would look like. I think importantly though, it is an important communication to relay. And should you develop a test, these could be prioritization strategies the FDA will use to accelerate EUA review. And obviously it's a fluid process, but I feel like many, particularly startups were caught off guard when the prioritization strategies were released, and especially as we all know,

in this world, people have very short-term memories. Will people remember? Oh yeah, I either have to be a high-throughput, high-volume test, or really cost-effective, easy to use home-based test, where I could also scale up a supply chain. And even if we were to foreshadow that, I think that would be important communication pre-pandemic. I also think an important communication would be, a potential expectation is, a proficiency panel with an artificial matrix that you may be expected to use, to see how you perform against other potential manufacturers. Because I think some manufacturers were caught off guard when those kinds of, I won't say roadblocks, but…

Dr. Van Der Pol: Requests.

Dr. Petti: There were expectations that were placed on new test developers. And I think they're important, but those new in the business, as we all know, analytical validation is not a simple process. And matrices are very different for different kinds of tests and different sample collections. So, almost educating new test developers. This is what we might expect.

Dr. Van Der Pol: Dr. Stenzel.

Dr. Stenzel: Yeah, we engaged with over 1000 test developers during the Covid test. And many of them were new. And the town halls and the webinars and the templates were all in the frequently asked questions. Were all efforts to assist and educate. We do, if there is new guidance, we have rules against making foreshadowing, that public before it's issued. The many new test developers were really not familiar with how the U.S. FDA operates. They gained an education. I think there's a need to think about ways to educate all the, you know, so these, a lot of these new developers got EUAs. Now, they're probably thinking about how do they convert to a full authorization because, it is different. So, I will say we've been having that discussion. And we have the q-sub/pre-sub process, which I don't even think most, you know, new developers know about that process. It's a free submission to ask questions of the FDA. The

other thing to keep in mind is, even though there are EUA authorities during the pandemic, there is also the full authorization pathway that's always open, even when the prioritization happens, and by necessity, and in need, we needed to focus on the need of the day, and it switched from central lab tests that weren't necessarily high-throughput or high-volume, to point-of-care and over-the-counter. And now it's switched to multi-analyte. So, I understand that lots of people are interested and have plans. I would also say that the pre-EUA process… If we agree to something, just like through the pre-sub and the q-sub process, if we agree to review something, or if we state something, we'd like to hold to that. We reserve the right to change, you know, certain things if new information comes to light, but developers can always use pre-EUAs. In fact, it may not be known. We're open to receiving pre-EUAs about any potential outbreak at any time. It doesn't, you know, you're concerned about, X disease that might come to the U.S., and you're thinking about developing a test. You can come in through either the q-sub/pre-sub process or the pre-EUA process. Both are free. Both are always open, and an avenue to explore. So, but I understand that it's really challenging, especially as a new developer, and wanting to help out, and not knowing all the ins and outs that so many other developers who've have FDA experience know, and aren't necessarily in neon lights out there about how to do this or how to do that. But we were very open to helping everyone, in the beginning, and we did open it up to everyone, which, you know, it'd be nice to get the panel's input on whether that was the best decision to open up to everyone, because we ended up having the opportunity to help a lot of new developers, and say about learning, and it, you know… Is that the most efficient, effective way to respond in an emergency situation? So, but we're looking to panel input on that.

Dr. Van Der Pol: Cathy did you have a follow-up?

Dr. Petti: I did. So, I hear loud and clear how the FDA may not be able to foreshadow, then perhaps we can have a little button on the FDA website. This is your how to Covid-19 packet, that test developers could, it could be their guide for when we have our next pandemic. And in that how to Covid test development packet, it would say, this is the evolution of prioritization. First, it was the high-throughput, and then all the way to the multi-analyte, just to get their wheels turning, because I believe knowledge is best when it's distributed, not centralized, as does the FDA. I don't want to lose these precious lessons that we learned, and wouldn't it be great if it could just be in a little button on the FDA website, because as we all know, the FDA sometimes can't issue things as quickly as they would like. There's a process. But perhaps manufacturers can then look to well, this is what was working with Covid. It may not be the same, but at least I can get an idea.

Dr. Stenzel: Yes, thank you for that recommendation. I will point out that in the three reports, following investigations or inquiries and other activities around the FDA response on IVDs, that Kris noted in his presentation. There are recommendations around preparation, and we take those recommendations seriously, and they do include the recommendations that you just made. So, and we would be, you know, not doing our duty, if we weren't working on those things. I'll just say that.

Dr. Van Der Pol: And, I have a comment. I'm not sure if it belongs really on this question, or maybe on the next one or two, but I'm going to throw it out here when we're talking about education. And one of the things that I learned during Covid and, you know, it used to be that diagnostic assays for infectious diseases were developed by microbiologists, and they had an understanding of the bug, or they were developed by, you know, closely working with clinicians who had a good understanding of the disease. That's not the case anymore. We're really working more with engineers, you know, bioengineers and people who do biosensing and

all kinds of people come up with this really fantastic technology for us, but don't have nearly as much understanding of the pathogens, of the realities of clinical outcomes. I don't know if it's quite within the FDA's purview, but when we're thinking about educating manufacturers, if there could be some sort of document that teaches people something about use case scenarios, because I think that in different use cases, we have different requirements for sensitivity and specificity, for example. I mean, I know we'd always like them all to be as high as they can be, but you know that there's a tradeoff. And the thing that kept coming, and I'm not exaggerating this, I kept getting calls about how are we going to get people into Alabama football games? We need to screen 100,000 people very quickly because the game must go on. And I mean, this is, I am not making this up. This is my reality.

But so, when people were talking about a volatile organic compound detection method that had terrible specificity, but excellent sensitivity, so they could just block people from coming into the game, whether or not they had Covid, they had anything going on. Versus, really trying to say, okay you have Covid so you can't come in for this elective procedure, which is a very different use case. But these manufacturers had no concept of that at all, and so they don't think, oh maybe I can get an approval for this because it will fit that one use case. But that means that they need to think about that when they're creating an intended use, right? Because those intended use statements drive, and the limitations of with whom or for whom these products can be useful. I think that that lack of understanding of use case was one of the most stark lessons that I learned during this whole developmental process. And I think that anything the FDA could do to say, okay, during the early stages, our use cases, we need some sensitivity and we're not going to care about specificity because we just have to find people who are infected, until we get down to the next stage. And then we get to the next stage, and we get to the next stage. And I think that that would be a really helpful, useful educational tool for

developers. And that's my two cents worth. But again, it may be outside the FDA's purview because it may be something that people have to figure out on their own. I don't know.

Dr. Stenzel: No. No, no, that's well within, you know, the guardrails of this, of this panel and the recommendations to make, you know, that we consider all those different use cases and prepare for it and be ready to help develop.

Dr. Van Der Pol: Make sure we don't interrupt Alabama football.

Dr. Stenzel: Well, you know, but, you know, the same technologies that could screen 100, 000 people quickly can be used to screen visitors to the hospital.

Dr. Van Der Pol: Or airports.

Dr. Stenzel: Or airports, or other borders. So, you know, there are lots of connections to other things as well. And we authorized the first breath test for respiratory virus, you know. Quite novel. So, in support of those, and help, with developers of those novel tests are, you know, or any device, is important. We have our breakthrough program at CDRH. The office I am fortunate to lead leads the way in the number of breakthrough requests, and the number so far of granted breakthroughs, for the center. So, lots of innovation in the test development field. And that program allows some more attention to those novel developers, through our normal processes.

Dr. Van Der Pol: Brad?

Mr. Spring: Yes, thank you. Brad Spring with Roche Diagnostics. Just a follow up to your comment, Dr. Van Der Pol, is, first of all, I agree. I think it's not just in this environment of the EUA and Covid. I think diagnostic manufacturers and developers have this challenge just almost every day, as we think of developing new tests and what are the use cases, and what would an intended use look like, but also what are the clinical guidelines that are currently used? So, I think an educational resource that would be developed, and Tim may be already

thinking about this, not just with the FDA, but FDA outreach to experts in certain fields. Not just the microbiologist, virologist, whoever we're working with, but maybe also experts in certain technologies. So, obviously, you may not find that if the technology is brand new, and I think that's some of the challenge too, that we face is, how do you even validate a new technology when no one's ever seen that before? But I think convening kind of these, like, maybe small expert panels, that would help. It would certainly help us as manufacturers because we get a lot of the upfront challenges out of the way, and not learn the hard way after we submit to you, what we should have thought of. And I think that's just a general comment overall, but that would be a helpful approach.

Dr. Stenzel: Yeah, thank you, Brad. Not that we can't improve, but I do want to note some of the activities around education that we already do. So, twice a year, the FDA hosts the IVD round table for manufacturers, and I think that's open to all manufacturers. It's very well attended. There's a didactic portion and then there's open question portion, and we have restarted that. There was a little bit of a pause during the pandemic as we were having so much focus on Covid test development. We interact with the medical device innovation consortium, which is also open to manufacturers. We have, it's at least once a year, it might be twice a year, with AMDM manufacturer association, a two-day didactic meeting that the FDA are the educators, are the lecturers, to reach out to manufacturers. And then there is the collaborative community program, where the FDA can recognize collaborative communities and participate in those that the FDA recognizes. And there are at least four that are IVD related. One, for example, you know, is a very hot topic these days, is on liquid biopsies. And so, these are just, you know, as we're discussing, and there's just so many activities that we're already involved with that are known to those communities, but aren't necessarily widely known. So I'd like to mention them here. Thank you.

Dr. Van Der Pol: And maybe that speaks to, you know, increased diffusion of that information, just so that people are more aware that those are out there. Whether or not it's appropriate for them to all participate is a different question. So, do people have other comments on this particular question, which was types of educational resources or communications from CDRH that would be valuable for test developers responding to pandemics?

Seeing none, I'm going to try to summarize. In general, I think that the panel has expressed appreciation for the fact that there are templates like the EUA templates. And we find that it would probably be useful to make sure that examples from the Covid process are made available to people. And there was some mention that it would be useful to describe processes for prioritization, so that it's transparent and so that developers know in advance what those prioritizations, or as soon as they're available, let’s put it that way. What those prioritizations are going to be, so that they can know if they fit into that scheme. And I know that later in this panel meeting, we'll start talking more about how to prioritize, and which types of tests and et cetera. The other thing is that documents describing the requirements for scaling, and requirements for proving LoD or LoQ against pre-created panels of pathogens would probably be useful for developers to have in the back of their heads. And finally, some educational materials around how to think about use case scenarios, so that people have a little bit better understanding of that before they come to the FDA. And they would understand where their assay might fit in a prioritization scale because of those use case options. Have I, is the panel in agreement that I've captured most of what we've discussed? Okay, Dr. Stenzel, were there other topics that you would like the panel to discuss on this particular question?

Dr. Stenzel: No, and really appreciate the abundance of feedback. We can always use it.

Dr. Van Der Pol: Great. So we're about 10 minutes early, but I think we'll go ahead and break for lunch, and let everybody catch up on their emails and do other things, but we'll come back one hour from now. So, it will be 20 minutes after the hour, depending on your time zone. You should be able to work that out. Okay. Thanks.

**Question Three**

Dr. Van Der Pol: Welcome back, everybody. We're going to start up with question number three that's in your packet. We have four remaining questions to review, and I would like to remind you to please identify yourself each time you speak to facilitate transcription. So, question number three is related to types of instrument manufacturers or test component manufacturers with whom CDRH should collaborate in preparation for a future pandemic response. Please remember that this is types of instruments and types of manufacturers, not specific brand names per se. For an example, would earlier engagement from CDRH to work with manufacturers high-throughput systems help ensure that well designed high-throughput tests can meet be made available at an appropriate volume to meet the needs of any future outbreaks?

And I think I might start just by saying that I think from my perspective, the types of instrument manufacturers and test components that are likely to be critical since most of these outbreaks are infectious diseases, we are likely going to always need collection devices, whether that's for blood collection, or whether it's swab collection, and probably some sort of universal transport media. And I think I bring this up because the stock outs on those supplies actually were a bottleneck, even once we started having testing reagents available. So that's sort of my two cents worth about test components. But types of instruments become then a sort of different question. So, I'll open the floor up to get others' opinions on these topics and we can take the slide down. Dr Caliendo?

Dr. Caliendo: Angie Caliendo, Brown. You know, when I thought about this question, what kind of came to mind is the diversity of types of tests that we needed and that prioritizing one type of instrument, or one type of platform is probably not a good idea. We talked a little bit about it this morning about the ebb and flow of the needs of during the pandemic. And so, I guess my thought is a broader range of manufacturers or different types of platforms that we could use. The other thing that I have to say is I was still thinking, how is it possible that the FDA interacted with a thousand different companies? And was that actually good use of their resources? How many of those tests actually were used in any significant volume? And should there be different types of systems? But do you really need a thousand companies coming to you with a test? So, I don't know. But I'm afraid if we just prioritize one certain type of platform that you'll leave people behind because one thing we really understood was the value of being able to test in our own institution and not send it out, as far as turnaround time and the impact on care. And so, I think we're going to need diversity. I don't think people would have predicted the supply chain. I don't think any of us would have could have predicted that.

So, that's a whole other thing that Bobby just brought up that I think we really have to be prepared for and that's in some ways easier to prepare for than you having to make a new test because, as you said, Bobby, we're all going to need collection devices and we shouldn't be going through that again. So, just some thoughts.

Dr. Van Der Pol: Dr. Stenzel.

Dr. Stenzel: Sort a follow up question for Angie or anybody else, Dr. Caliendo or anybody else. Does it matter when in the pandemic, if you look at its phases, early, middle, late and you look at the technologies and the lead time to develop them and manufacture them, for example, molecular tests are probably the easiest to develop and deploy, what do we need early on from molecular tests? And then, serology tests, what role do serology tests play and how much

importance should there be on them? And then antigen tests, obviously, can play a role, but they take longer to develop, typically, if you don't already have antibodies. And in the beginning, some developers used antibodies developed to SARS, the emergency that happened in early 2000s and it worked. It worked pretty well. It was amazing. But if you don't have antibodies, you've got to develop antibodies and not just ones that that weekly bind, but ones that bind to the right location and tightly. That can take a lot longer than we would wish to do so. And so, I just would add that there could be different need for different kinds of tests at different points. And then, are there any that are less important at certain points than others? So, just to sort of build out some of the past.

Dr. Caliendo: So, it's interesting because if you look at Zika, for instance, the antigen test really never came into practice. So, I do think you're right, molecular will often be the first out of the gate. I do think we have to step back and ask the interesting question of what value did serologic test ultimately bring to the table? And particularly early on. I remember when the first serology tests came, people thought it was going to be a game changer. And I was confused by that. Because how is this really going to help us decide who to immunize, who to treat, who to do anything with? So, I think we have to be prepared to do molecular up front. Particularly, if you look at the pathogens that you're worried about, I suspect molecular fits the bill for all of them and whether they should be preparing now for unusual flus. Because I agree with you about avian flu. So, it's interesting, but you're right, I do think you need molecular upfront for most of these things.

Dr. Van Der Pol: And I think if you want to talk about what instrumentation, as Dr. Caliendo mentioned, you need a broad coverage because it's not clear if you're going to do serology or if you're going to do some sort of antigen detection, even if it's an ELISA, not a point-of-care. But, if you're thinking about instrumentation that you might want to focus on,

having a preparedness plan, so not those that you necessarily do, because it will depend on the outbreak. But I wonder if, in a broad way, it makes sense to say those instruments or those manufacturers that make instruments that cover the spectrum, because there are large systems that will do molecular and will do serology, and not necessarily in the same instrument, but those instruments can communicate with one another. And I think that you will also want to make sure that you put a focus on those instruments that have a user-defined capacity because that's going to be supporting your lab developed tests, which is often your very first response to a pandemic, is the large reference and/or research labs that can quickly turn out a lab developed test. And if they can develop it on a standardized instrument, then it might quickly be applicable in many, many lab settings. Sorry, took panel or chair's prerogative. Cathy Petti was next.

Dr. Stenzel: Well, I would like to riff off that. You're absolutely right. So open systems that, any developer, whether it be an LDT developer, another developer, we know what those types of common open systems are, might be the very first wave of tests, whether it's LDTs and/or kits. But if the need for high-throughput, as we saw with COVID, that labs that were doing manual setups on these open systems, they were limited in the number of tests that could perform per day. And we inquired of them on a regular basis. And then, clearly, when high-throughput systems became available and you could get the reagents, those were the workhorse. Those are the workhorses of the lab, but that might take a little bit longer to develop tests for those systems unless you pre-prepare for them, you sign up. The lessons we learned, especially from South Korea, and as we thought about this, is if you can pre-prepare certain types of manufacturers. You want those, common open systems that a lot of labs have to be used, perhaps very early on, but you don't want to delay getting really high-throughput automated systems deployed to fight the emergency is as well. So that's the kind of input that we really look forward to getting today. Thank you.

Dr. Van Der Pol: But I think what I'm thinking of is not exactly what you're thinking of. And that takes us back to definitions probably. But when I think about open systems, I'm not talking about me having a thermal cycler. I'm talking about me having a Roche Cobas or an Abbott Alinity or a Hologic Fusion that I can put my own primers and probes on, but that system as a whole is a high-throughput system. So, if I get my system to work, then I can put the high-throughput on that. So, I'm not talking about these small, with manual DNA extractions. I'm talking about the automated systems, but that have an open channel, because I think that's going to be one of our first wave responses.

Dr. Stenzel: That's excellent feedback.

Dr. Van Der Pol: And I'm not calling up those companies per se. I was trying to distribute that over a lot of different manufacturing.

Dr. Stenzel: Those are and perhaps others are very high-throughput systems and to focus on those that also have the so-called open channel or open modules that you can put your own tests on. And they can be high-throughput early on. Um, but then when you get. When you get out of the reagent business yourself, you can go to commercial reagents. So that makes sense. And it's still a high-throughput. Okay, thank you for that clarification.

Dr. Van Der Pol: Yeah. All right. Cathy, sorry, I'd left you out for a long time.

Dr. Petti: Cathy Petti, HealthSpring Global. I think there are two questions within that first question. Uh, first question is, which I think Dr. Caliendo and Van Der Pol articulated extremely well is with what we know. And with what we know with these high-throughput systems, such as the manufacturers that Dr Van Per Pol mentioned, very appropriate to have early guidance from the FDA, where we could rapidly deploy an LDT on an instrument that is very well known by the FDA and following that process all the way through on the supply chain from soup collection to nuts, which is result reporting. But I think what's embedded in that question is, well, where

were our failure points and one of the greatest failure points wasn't just lack of supplies and reagents all the way through, it was our technologists and the inability to have enough staff to process specimens to keep up with demand, and that's in a large reference laboratory. So, I'm going to speak from a very, very, very small community-based hospital where we did not have that luxury and early in any pandemic response, we're not going to necessarily have those closer-to-the-point-of-need instruments. So, I think I would charge the FDA to start having pandemic planning with BARDA on what would be the more novel instrument requirements that would help distribute, as Dr. Caliendo said, for having results tested on-site, no matter where you are.

I mean, there are technologies that use NMR. Could we use MRI instruments that exist in almost every hospital in the United States? Like, I think we need to start exploring, if we're trying to scale up a true pandemic response, let's not always focus on where the high-complexity laboratories are for the early phase of the pandemic, but how could we distribute high-throughput with instrumentation that truly already exists for technologies or platforms that aren't necessarily even the laboratory setting? They could be in the radiology suite. And that starts very early on with RFAs, RFPs, with BARDA now.

Dr. Van Der Pol: Mr. Spring.

Mr. Spring: Yeah, thank you. A couple of comments here, and obviously I won't comment on the types because I represent all types out here, but maybe follow on what you were saying, Dr. Van Der Pol, I think we have to do a landscape analysis first off and just saying what is out there. You won't know specifically because it is business-confidential information, who has what, but at least a landscape of all the systems out there, what are their capabilities and so forth. But I do think allowing manufacturers, developers who put out these open systems, right now, we are restricted from working directly with laboratories to develop tests. I think in an EUA

environment, we should be able to open up that and maybe address that challenge just because of the urgency, and maybe carve out an opportunity there. That's one suggestion.

Maybe it's more of a question of the panel is, I don't think you can answer the question today about a future pandemic, around who to work with first, where you should prioritize first, but if you were to look back at, let's say, December, January, that time frame when we first started to see it here, at least the United States, or maybe even earlier in other countries, would we have been able to foresee? Because Dr. Caliendo, right, you're questioning the value of serology, although serology seemed to have a bit of a prioritization at one point. Would we know that high-volume tests would be a priority, in-home tests would be a priority, point-of-care and so forth? Or is it something where you convene, and maybe the recommendation is, you convene these expert groups, representatives of the public health sector, maybe reference laboratories, the community hospitals, I think the moderately complex labs, around what are the needs there and where should the focus be? And then we, as developers, or even up-and-coming developers can prioritize our funding towards those initiatives. And maybe there is a type of scenario analysis that can be conducted that would look at what a future pandemic could look like. Just some suggestions there.

Dr. Van Der Pol: Thank you. Dr. Honein.

Dr. Honein: Yes, Peggy Honein from CDC. Just want to mention that early on in a response, the public health laboratories are an important network to utilize. So, in thinking about which instruments should be prioritized for preparedness, it would be good to look at what the public health laboratories have and make sure that that selection of repertoire, which is not a single thing, but which ones are the most common are also being prioritized early on and for preparedness, so that the public health laboratories are able to play that initial role and really make sure that testing is facilitated, can be expedited, can be prioritized for the greatest need and

can be a bit of a safety net system. Also, to emphasize, while I agree with a previous commenter that it's probably not efficient to think of thousands of different devices, but it is important to have some redundancies and not rely on too small a number of devices that are going to be more impacted by supply chain issues so that having enough of a repertoire that when one is knocked out from being a key player, there are others that we can turn to. And I know that the Laboratory Response Network has collected a lot of that information on public health laboratories. Of course, it's always changing, but that's something that CDC could make sure FDA has access to so that that can help with their planning. Thank you.

Dr. Van Der Pol: Dr Stenzel.

Dr. Stenzel: Yeah, thanks for those comments as well. And the CDC works closely with the laboratory research network to make sure that their needs are met. We have heard from those groups and others that we certainly don't want to put all our eggs in one basket and have options. We know that a virus like COVID mutates, every single base virus seems to have mutated. Fortunately, tests have been relative. The ones that are authorized at least have been relatively well designed, targeting conservation, we have encouraged two or more targets, for COVID, especially being that it's an RNA virus. So, the redundancy, yes, is something that makes a lot of sense, but I did want to say that public health labs, they’re one of the first lines of defense and preparation. It's definitely on the minds of FDA and we're interacting with them more than ever before on an ongoing basis. And they're initiating efforts and they engage with us, too. So, we appreciate that. Thank you.

Dr. Van Der Pol: Dr. Caliendo.

Dr. Caliendo: Dr. Angie Caliendo, Brown. Tim, one of the things that you brought up in your presentation was this pre-authorization of labs, which I think is a really good idea. It could be a broad spectrum that covers different platforms. And what Peggy said is really important. If now's

the time to do the inventory and what platforms are in our public health labs and our LRN labs, and then if there's common themes, preauthorize some of those companies so that you can get them out of the blocks. And again, it's not just one type, right? It wouldn't just be high-throughput companies. You want a diverse array of platforms. But I think your idea for pre-authorization is really, really smart because they will then be prepared, just like our LRNs are prepared, right? These companies would be prepared to quickly shift and hopefully they'll be doing internally what they would need to rapidly create a test. So, this is the way to link what the LRN labs need and getting them to them quickly. And I was on a working group to advise the CDC and one of the pieces of advice that we gave them was to make sure that the CDC tests that come out that are usually the first tests out are on more than one extraction platform or more than one amplification instrument so that they can be more widely deployed. But I do think there's real value to that pre-authorization idea.

Dr. Van Der Pol: And I'm just going to jump on that bandwagon by saying the pre-authorization kind of ties back into what I had brought up earlier with the open channel and what Angie finished with, CDC, if they develop primers and probes and amplifying conditions that are optimized. If I have an open channel on any of my high-throughput instruments, I can instantly put that assay on all of my instruments, right? And so, if you're thinking about pre-authorizing, I'm not even sure whether it's sort of a company or it's more to say it's the instrument because you know that this instrument A) can do high-throughput, B) has an open channel, but maybe C) has multiple components or modules. And so maybe it does molecular, but it also does serology, or it also does whatever else we can think of that might be a requirement. Part of what we're doing with this is where we might be doing like some sort of liver toxicities as an indicator that this particular thing is really causing disease in certain people. And so maybe we need to hook in with chemistry or maybe we need to hook in with hematology. And I'm not saying that we have

to have only platforms that have all of those components, but maybe those are somewhat prioritized, but at the same time trying to recognize that we don't want to close the door to people who have more point-of-care options instead of these huge monster options, but more point-of-care options, but they still have quick flexibility because they internally have an open channel thing. A great example of that is Cepheid with the cartridges, but they have a generic mix that you can put primers and probes into that cartridge. So, if I just needed something at a point-of-care and I got the primers and probes from CDC, I might be able to put it on the Cepheid, even though that's not a high-throughput thing, my need might not be high-throughput.

And again, I'm not endorsing any particular company. I'm just trying to provide examples of some of these different platforms and their structure so that we can think about maybe what makes sense in terms of, especially if we're thinking about preauthorizing. But I think we need to focus probably on the instrumentation. Dr, Ng.

Dr. Ng: Thank you. Valerie Ng, Alameda Health System. When we talk about high-throughput, I like to split the hair into centralized versus distributed models of how testing is performed. So, I'll start with centralized, and I'll focus on the large reference labs that have miles of automated instruments that are put together. So, they can scale up pretty quickly if there's something that's out there, but the blocks we uncovered were the front end, getting a sample from an individual lab to the reference labs, that's FedEx, that’s couriers, and then in the central lab, the front-end accession, not the specimen prep, but just moving a sheer number through. And then finally on the back end, how to get the result back to the submitting lab. This all points to the need for an informatics backbone. So that's the central lab.

We've talked about if there could be a landscape of how moderate small community laboratories, what their instrumentation is. And could we deploy in a distributed fashion of preauthorized test? I can tell you, I would be very loath to use an open system and use a

preauthorized method, mainly because I don't have the intellectual expertise in my staff or myself to verify or even validate that that thing is working the way it should be working. So, what I would want is a preauthorized thing, maybe you have a whole row of primer bottles on the wall, you send me a primer bottle and you send me an IFU for an EUA and I will implement that. I would need the informatics underlay to in the instrument. How to program it. What are the tolerance limits? You know, auto verification, all that other business. And then finally, I want to comment around our beloved, truly beloved public health laboratory system. But what we encountered in this pandemic, they have the same severe staffing shortage we do, ours works Monday through Friday, no weekends, no holidays. They work one shift. At one point when we were pushing through our COVID testing, we learned the critical point was to move the 96-well plate manually from the sample processor to the thermal cycling. That happened at 11p.m. at night. There's no one there to do that. My results would not come out until noon the next day when the staff came in at 8a.m. in the morning to move that plate.

So, I asked, can I have permission to come into your lab and move the plate and I just ran into a lot of bureaucratic stuff. Because that particular public health lab is housed in the same building as the share. And so, there's all kinds of security restrictions and it took us forever. So, what we ultimately had to do is ask our public health department to authorize overtime and hiring additional staff, and that's what we went through. So, I just wanted to bring those points out and to emphasize the importance of courier's transfer system transport, especially the informatics backbone that is so critical to getting to the results. And as we also learn, we could do the testing, but our state epidemiology systems could not receive this deluge of reporting. So, we have to fix that on the back end.

Dr. Van Der Pol: Yeah, and I think that like in my lab, we would have told you no, because from a CLIA perspective, you're not a qualified technician to move a plate from hither to yon,

and so do I turn a blind eye? Not in front of the FDA, no, of course I don't, wink wink, but you're right. It ends up being a staffing issue, ultimately, and I think I agree with you about the informatics support and lots of things.

Dr. Ng: The moving the plate is not a technical thing.

Dr. Van Der Pol: But it is.

Dr. Ng: So that's trained incompetency.

Dr. Van Der Pol: But it is. From a CLIA perspective, it is. It is part of running the test. Yes.

Dr. Ng: So, we can sidebar on that.

Dr. Van Der Pol: Well, regardless, I think maybe that's part of the other thing is that when the FDA is working with other agencies and when they're communicating strategies for preparedness, maybe they need to communicate where we can turn a blind eye from a CLIA perspective, right? So not patient safety or quality of results, but little things like this that really are meaningless, but under normal circumstances, we would be restricted from doing. Dr. Stenzel.

Dr. Stenzel: Yeah, I just wanted to comment that, yeah, always can improve, but we did have a great working relationship with CMS and there were definitely allowances by CMS to help deal with the pandemic. Remote sign out, was one obviously, but also when we needed to start testing folks who were without symptom, and there wasn't necessarily validation and authorization for asymptomatic people. So, expanding the sites that could do testing. So, CMS was a great partner during the pandemic, but obviously, from the FDA perspective, we can always get— (cuts out due to muting).

Dr. Van Der Pol: Dr. Caliendo.

Dr. Caliendo: Angie Caliendo Brown. I think Valerie's point is really interesting for LDT wouldn't have helped her or an open channel. There were many other labs that would clamor for

the same thing. Would have absolutely wanted that and couldn't get it fast enough. And I just want to reiterate the diversity of what has to be out there to meet everybody's needs. And to prepare for that ahead of time, I think, and, you know, the CDC probably should be part of this conversation because most people that do LDTs that are not their own commercial companies are going to use the primer pairs and the package that the CDC puts out. So, knowing that, what platform should we tell the CDC this would be really good if you validated on these three extraction instruments and four amplification instruments or something like that? Just thinking of that stuff ahead of time, I think would allow people to burst out a little faster.

Dr. Van Der Pol: Thank you. Dr. Pereira?

Dr. Pereira: Marcus Pereira, Columbia University. I know that we're in the middle of a very lab technical discussion here, and obviously I'm not part of that, but just a sort of a statement, just to step back a little bit. I know we're talking a lot about molecular testing, but there's nothing to say that in different pandemics, other forms of tests, and I know that we've talked about serologies and antigen testing, but certainly those might prove to be more useful, not necessarily from a diagnostic perspective, understanding that antigen test can be more complicated, but certainly understanding which populations might be immune and non-immune, which may have huge repercussions in how these pandemics are handled. So, as you sort of plan on pre-authorization of certain labs, certainly focusing on the ability to rapidly develop those tests as well might be important.

Dr. Van Der Pol: Great. Dr Kotton

Dr. Kotton: Camille Kotton, Mass General. In considering various test types, I guess I would just request a somewhat of a focus on testing equity, in that some of the testing we do is very expensive. Some of it necessitates expensive platforms, transport, all kinds of things. And, the kind of work I do, I do transplant infectious disease. So, I take care of many people very far

away from academic institutions, northern Maine, northern Vermont, rural populations. And especially during the pandemic, the access to diagnostics was often really highlighted where if you lived close to Mass, generally, just pop by for a CR test and it was all good. But for many people who live far away, there really was testing inequity. There were a lot of inequities highlighted during the pandemic, but I would just argue for, testing equity and also financial, looking at the cost of testing and thinking about equity there. Thank you.

Dr. Van Der Pol: Dr. Stenzel?

Dr. Stenzel: Thank you, Dr. Kotton. I wanted to respond. Equity is very important and equity across sites and populations and locations and geography, whether it be at-home or in-clinic, and cost is, is a big driver of that. And there isn't anything less expensive to the end user than a rapid antigen test, although there's potentially tradeoffs, obviously on sensitivity. Though, specificity can remain very hard. And it's probably important as well. So, part of, say, readiness or preparedness can be focused on having this one form of preauthorized is a fully authorized test that are say, pan disease. So, pan influenza and SARS. If we had such tests right now, authorized as such, they could be stockpiled, or they could be ready to be produced in large numbers and distributed very widely. And the other thing is there are technologies that could allow even today, and distributed tests today, that are sort of universal pathogen on tests. And the ability to have those in place or ready to be deployed to any site that needs to be testing, it could certainly address some of the issues that we discussed and others we've discussed. Thank you.

Dr. Van Der Pol: Thank you. Ms. Schwartzott.

Ms. Schwartzott: Jennifer Schwartzott, Patient Representative. When I'm thinking about the components of the tests, I'm also thinking about the packaging, the labeling, the instructions that go with it. A lot of the problems that I encountered when I had Covid and with all the at-home test kits and everything, that was one of the biggest problems. When I first got it in March of

2020, of course that's early on, but I went to the local urgent care, very, very, very sick. And the young girl doing the test had absolutely no clue how to use it and she brought the other people in, and they didn't either. And there was nothing to show them what to do. And Advent Health, I'm sure some of you have heard about this, ended up throwing away tens of thousands of their results because they were not properly done or whatever the other issues were with them. And also, just like the at-home test kits. I mean, the ones I have here in my house that came from the post office were wonderful. I did one at my brother's house and he and I both have master's degrees, and we were confused. So, that's a big issue. So maybe, coming out with suggested guidelines for how to use, like bring in a layperson on how to make these labeling decisions. And it should be done ahead of time because if you wait till then they're so worried about getting the actual specific disease covered, they're not thinking as much about those labeling issues.

Dr. Van Der Pol: Dr. Stenzel, I see you want to respond.

Dr. Stenzel: Those comments are really well received and important, and we've done our best. We can always improve. So, when we put out the recommendations for home-tests in the summer of 2020, one of those recommendations to developers was they needed usability testing of their over-the-counter test their home-tests, which means they take inexperienced users, give them simply the instructions and can the users follow them? So, that worked to a large degree, but we learned later on, and this gets back to equity as well, that there were certain subgroup who were, say, visually impaired or physically impaired, dexterity potential issues, comprehension issues and we partnered again with NIH ITAP to address some of those needs. One such test, it's the pen test. If you're familiar with it, was very, very easy to use, the simplest of all the tests. But we did ask developers and reviewed it in our UA reviews. How did novice users in the home, through usability studies, how were they able to do it? And then we also evaluated prospectively, the accuracy of those users of performing the test.

But again, we didn't state this, but for an EUA authorization, whether it's an over-the-counter test, the point-of-care test or a central lab test, we only asked for 30 positives and 30 negatives, so we're not collecting a lot of information. The numbers, the end, as we've decided yesterday, we discussed the end or the number of patients in the study, is very small. And so, we certainly didn't have the luxury of making sure that all sorts of types of users could do this. We were focused on quick development of invalidation to a certain level of tasks that could assure reasonable accuracy and expectations of accuracy. Thank you.

Dr. Van Der Pol: I think one of the issues that comes up with this, because I think Ms. Schwartzott is completely correct that these things have to be evaluated by end users, because what happens is when we do usability studies, often we do that in a clinical setting, but at a research institution where our patients are not naive because they have participated in other research projects, or they've done this, or they've done that. But then, even if it's their first research project, they did self-select to be a research project. And so, they are at a level of understanding that may be different from the average user. And so, I wonder if you know what Ms. Schwartzott has sort of suggested was that if you had a panel of people recruited off the street, as it were, we can do a Jay Leno session of interviews on the street. Can you use this COVID test? But I think that it would actually be relatively informative. I don't know how we would continue to recruit people because after a while people become educated. And so, you can't have the same people giving you feedback all the time. But I think her point is really spot on. And I would really encourage the FDA to think through a process where they could maybe independently get a review of those instructions.

Dr. Stenzel: Right, and when we focused on folks who had certain physical impairments, we reached out to those communities, it was primarily NIH, and had listening sessions. They already had what was available at the time, so they could say what was good about these tests and what

was not good about these tests and what we really need. So, that was that was very helpful in designing the next types of tests that could be more widely, more easily used. But the point is excellent. Thank you.

Dr. Van Der Pol: Dr. Hoz.

Dr. La Hoz: Yes. Hi, Ricardo La Hoz from UT Southwestern, with a big caveat that my expertise is not in laboratory medicine. But as I think through the last outbreaks and pandemics, I think I've always been humbled on how all these pathogens may wreak havoc. But there's been the respiratory infections that we've had, but at the same time, we've also had outbreaks with diarrheal illnesses like cholera. And I wonder if we need to start thinking, they may all be diagnosed in different ways. And for example, what are the nuances of testing on a respiratory sample with a molecular assay, versus testing in stool, versus testing in tissue where a biopsy needs to be taken from the skin and run molecular testing. And again, I am not a laboratory person, but I think we may have to be prepared to test in different types of samples on what are the nuances to testing stool versus respiratory versus tissue and so forth. And also, it brings us to the idea of this diversity of testing for certain diseases. Maybe serology may be the test to go because there's no compartment where molecular tests can be done, like a respiratory sample. But also want to think about who were the most affected by the COVID pandemic and certainly, those with comorbid illness, but currently a fair amount of the patients that we have in our hospital with COVID are those immunocompromised, in which either a natural or vaccine-induced immunity is waning. So, if the only diagnostic tests that we have is serology, we need to be mindful that that may underperform in the immunocompromised patients, and we have to keep that in mind that test may have to be developed for those at risk for complications that may not mount a serologic response.

Dr. Van Der Pol: Thank you. Dr. Ng?

Dr. Ng: Valerie Ng, Alameda Health System. I wanted to respond to Ricardo, Marcus and Jennifer because you triggered some things for me. Antibody testing, right? The antibody tests do not inform on immunity, right? That was an assumption that was made. There are neutralization tests out there, but what's the correlation of the *in-vitro* result to *in-vivo*, right? We don't know that answer. So, in terms of antibody testing, there is some magical thinking about the value of it and that magical thinking carried over into blood banking, that whole thing around convalescent plasma. Right? Which was ultimately not shown to be effective, and it was rationed so that created a lot of anxiety.

And then the second thing, there was a brief period, I think it was a companion drug? It was either a companion drug monoclonal antibody, or it was a drug that was out there, but was so heavily rationed that we were asked to bring up an antibody test overnight to identify who would be eligible for that treatment. They had to be antibody negative. And so, some of those things just rolling around about the antibody. For Jennifer, I wanted to tell you, my colleague of 20 years did one of those home tests and couldn't figure out how to interpret it. He FaceTimed me and said, what does this mean? So, I will say, the only thing I can follow is if it's in pictures. And the test ID, which I got through the postal service, the back of the box says one, two and three and I can follow one, two and three.

And then my final comment is around both social and structural determinants of health. The communities that COVID disproportionately impacted, the unhoused, the undocumented residents, they can't access any of this. So, I mean, they don't have smartphones, they don't have phones, etc. So, it's really us engaging with our community outreach to try to take care of that population. I want to highlight one population in particular, the Hmong. We have a large group of them in the Central Valley. They have no written language. So, it's got to be pictures, or it's got to be people talking to me. Thank you.

Dr. Van Der Pol: Great points. Dr. Pereira?

Dr. Pereira: Sorry. Yeah, Marcus Pereira, just point of clarification. I didn't mean sort of serology testing for SARS-CoV-2. I think we all lived through that period of uncertainty and me and my colleagues certainly fought very hard against that understanding that an antibody meant immunity and so forth. But, you know, this is more about future pathogens that it may play a role, right? I think we need to keep our mind open for what may come next and not necessarily look back at the models that we've seen before. And I think this is where we need to sort of have an open mind for the future pandemics.

Dr. Van Der Pol: Dr. Blumberg.

Dr. Blumberg: Emily Blumberg, University of Pennsylvania. I just wanted to say that I think COVID really taught us the importance of bringing testing to the community in a real diverse set of ways. And as sort of thinking forward about what kinds of tests and how to hazard resources, I think we've unleashed something very powerful in offering the community the ability to perform tests that would be helpful to maintain their health and protect their own local communities. And so, the whole community outreach piece and the equity piece, I think, are especially important to emphasize because we sort of made the laboratory outside of the actual clinical laboratory now. And I just think we have to be cognizant of this is going to expand the diversity of the type testing we're going to need to bring on.

Dr. Van Der Pol: Yeah, I think that's a really strong point. And one of the things that you could take away from that is that when you're prioritizing the types of instruments, or the components that support that instrument. The component may be those platforms that already have a self-collected device approved for a different assay that they could roll that device for self-collected samples over to a new assay. That's not always going to work, but if you're talking about prioritization, that may be a scheme for helping to do that. Dr. Kotton.

Dr. Kotton: I have a question that kind of relates to this general topic, but does the FDA ever give, I think the answer is no, but who gives guidance on pricing? Because I think Valerie's point is really well taken about access. And you know, when I, in CVS, I'll sometimes see two test kits for 25 bucks. And even I think, I'm not spending 25 bucks on that. So, I'm just wondering who sets pricing and I've increasingly felt that there's kind of predatory behaviors out there. Is there any, because that, that to me has an impact on overall ability to test people and whatnot. Does the FDA ever give commentary there?

Dr. Van Der Pol: Dr. Stenzel.

Dr. Stenzel: Tim Stenzel, FDA. So, certainly it's not our role to have anything to do with pricing or reimbursement. Those are not in our guidance. But what we can do is make sure that we prioritize technologies that are lower cost and include them and in our in our plans, like antigen tests. So, yes, even though antigen tests are probably the least expensive of something that can be deployed, many, such as yourself, didn't think that they were inexpensive enough. We hear in other countries, in Europe, where the test is one euro or two euros. It should be pointed out that it's our understanding that those tests were heavily subsidized, that those governments in those countries spent money to make it really cheap and that if it was left up to the free market as sometimes it was in the United States, the pricing would be very similar to the U. S. But there was funding for the home test from the federal government, which was free, it wasn't free to the government, or to taxpayers in the country, but that was an effort and I recognize that those that don't have homes or live in homes couldn't get those tests. But there were other programs that would reach out and provide tests to those other at-risk populations that wouldn't necessarily be able to have an address to receive tests. So, it's front of mind at the FDA to make sure that if the technology is good enough to be authorized, even though it might be less expensive, that we give priority to them as well, which we obviously did.

Dr. Van Der Pol: Thank you. Mr. Spring.

Mr. Spring: I think just some of the conversations, too, around equity, and by the way, I can't comment on pricing, I represent a number of manufacturers and I don't know how everyone comes up with the pricing, but I thought Tim provided a good answer. But I think just about equity and again, it's more advice that as you look at capabilities out there and the fact that some technologies might require certain platforms, cell phones, what have you, as long as you're also looking at that equity question where you might need simpler, lower cost tests that are easy to use without any sort of technologies. I think that's appropriate. When you look at prioritizing and who to work with is they may come up with the same result, but they may use two different approaches to get there at different cost points and just consider that. I think one thing on the sample collection devices, an example I want to raise to the panel that I thought would work very well with FDA is there are some products that are available outside of the country. And I think there's an example I can think of, there may be more, where you had a similar collection device outside the United States, didn't have FDA clearance, but it went through the EUA process just to get it into the United States to help fill that gap. And I think as long as you can continue to follow that type of approach, encourage manufacturers that have similar products out there to take those through the EUA process, especially when it comes to specimen collection, I think that'll help fill the gap in the future.

Dr. Van Der Pol: Thank you. Dr. Pereira.

Dr. Pereira: Yes, Marcus Pereira. Sorry. The gears are turning now. You know, I realized that we haven't had any talk about pediatrics and children sort in terms of vulnerable populations. But one thing to keep in mind as you sort of pre-authorize tests for these platforms that can take in consideration sort of neonates and children, particularly when you think about molecular testing

and how much blood it requires and so forth. So, just sort of thinking about the populations that you would be particularly wanting to test.

Dr. Van Der Pol: Other comments people might have? Again, the specific question as written is, are there certain types of instrument manufacturers or test component manufacturers with whom CDRH should be collaborating? I think we've gone a bit far afield from that specific question, but that's okay. Because they're the questions that come up next anyway. Dr. Roth?

Dr. Roth: Yeah, thanks. Yeah, I'm going to go stick with the far afield kind of topic. I heard a little bit of feedback about usability and some of these home-tests, and I'm just wondering if there's any more kind of feedback. Like what part of the instructions were unclear? Was it the interpretation of the test? Was it the execution?

Dr. Van Der Pol: Can I tell you that my experience, I'm big into the equity and outreach things. So, we're working all over rural Alabama. We're working with community health workers. So, they're not necessarily trained and certainly not laboratory-trained, and we just send them the test. And as we get the test, because of supply issues, sometimes it's this test. And sometimes it's that test. And every time we change a test, we have to go through, even though there's a quick instruction reference sheet, we have to go through and create something with pictures. Not drawings and cartoons in our case, we have to take a picture of the device, we take a picture of the tube and the swab if it has a buffer, and we take a picture of results. And still for the first week, I will get questions from all over the state. Well, but this one didn't quite, or, well, this one did that, or what does it mean when this, so, Dr. Kotton needs to teach them a lesson in how to read the IFU because they have the IFUs, but they also have these laminated sheets that we send out in advance, and sometimes I still have to do a webinar, and these are all for CLIA waved tests, so, it seems like the instructions should be obvious, it looked okay to us, it didn't pass the sniff test of the average person and so these are people that have been testing. It's just

every time they change the platform and I'm talking about using, for example, of Visby test that you just squirt the stuff in, and it gives you a lateral flow sort of output versus something that gives you a plus or a minus versus something that says COVID positive doesn't matter. That every single time, it's new, it's starting from zero. Thank you.

And other people can chime in on your experiences with that, but my experience is not how to run the test. It's not really how to extract it as much as there's so much on that quick information sheet. It's very tech-text dense. They don't want to read it. So that's why they want pictures, and they want to call somebody. So, they want Dr. Ng's step one, two, three, because they can do step one, two, three, and so if we give them that in picture format, they're fine, but you have to cut out all the verbiage, right? There's just a lot of extra words, and you have to say, stick the swab in the nose, spin it three times, stick it in the tube, break it off, squirt it in the machine, wait for the timer. I mean, you have to just use bullet points, no full sentences. So anyway, other people that have had experience with that, maybe Jennifer, you could weigh in on your experience.

Ms. Schwartzott: Yeah, the ones that come in the post office are wonderful, but this other one that my brother and I had, I think it was missing total directions. It made absolutely no sense, and it kept saying to look at the app and you had to download an app, which we couldn't get to work, and we finally just ended up going and getting another one, a totally different kind. But it's not just the people though, the layperson doing the tests on themselves. I mean, this was an urgent care place with staff that didn't know what they were doing. And yes, it was at the beginning, but with that shipment should have come directions on what they were supposed to do. And they didn't seem to have that; an error on their part for sure, because I'm sure that there was at some point, but the fact that the nurse didn't know that was the to-the-brain one. I mean, she didn't know how far to put it in, how many times, how long, I mean, that was a huge issue

and all the tests that they did, you can go back and look it up March of 2020, Advent Health in Florida, they were all thrown out. All of them. So, all those people got false positives, false negatives, who knows what from all those tests. And what damage did that do? And again, it was at the beginning, but this is what we need to prepare for if there's another pandemic, that this doesn't happen again, because it wasn't just one or two, it was a huge amount. And when I read that article I said, I know exactly why, it was unbelievable how they were not prepared. And I'm sitting there with a 105°F fever, and they don't know how to treat you, how to even test. So that was a big issue.

Also, for people with disabilities, I'm visually impaired, but I have good acuity, but there are a lot of people in my community that don't. And others that have learning disabilities and autism and that's why the pictures are important. Bigger font size is important and clarity. And then why you're doing this, there was so much misinformation out there, and it got to the point where nobody knew what to believe, and why should we do this, this isn't worth it, it's government control, whatever, all those different things. It's important to have it simplified to where they get it and understand why, because they'll gripe to me about, oh, we don't need this. And I'll say, no, you do. You really, really do. And then they start listening, because they're hearing it from somebody that they trust, that's at their level and not from a pamphlet or whatever. So, my suggestion is work with the big organizations that serve the people, serve people with disabilities, serve the communities with disparities and find out what is needed. And then have those recommendations, those guidelines to the companies so they can act on what you've learned. That's my two cents.

Dr. Van Der Pol: Thank you, Dr. Stenzel.

Dr. Stenzel: I wanted to make sure before I speak that Kris got some of the feedback that he wanted. What I was Pictorials, or even actual pictures, really simplified visual instructions without needing to read.

Dr. Van Der Pol: Angry birds.

Dr. Stenzel: I'm sure there's branding that has to be licensed. Kris, did you get what you needed there?

Dr. Roth: Yeah, I heard one key piece was I think some of the directions do have kind of a stylized look to them, right? It's not the picture of the actual swab or the picture of the actual test. It's more of a drawing or a rendering or something like that. So, maybe that's something that we can consider actually having realistic images of gosh, here's what's in the package and here's what to do with him.

Dr. Stenzel: Yeah, thanks. That was a lot of really great input. I want to give a shout out to NIH RADx funded an effort to try to create universal videos for how to do a home-test and they involved the FDA. And one of the challenges was every test seemed to be just a little bit different. You know, there were some tests where you put the swab in the card, and then you added the drops to it and you had to have not two, not four, but three drops. And other tests, the liquid that the swab would go in was not pre-aliquoted into the vial. And so, the users had to pre-aliquot. Part of it was all comers. It was, we didn't want to delay the access to the test just because the workflow wasn't optimized. But one of the things, if you preset who the types of technologies you're going to use, and the specific manufacturers you're going to use of, say, rapid antigen tests. If you have those contracts in place, as South Korea did prior to Covid, you can specify, it needs to be this workflow, which is made easy for visually impaired or autistic individuals, folks with learning disabilities, or physical dexterity issues. We can make those in positions onto the designs in the workflow. But if we're on our heels and not fully prepared as a

country, then it's a little bit more challenging to make sure that at least some of them are really easy to use. The other thing that we potentially could do, although manufacturers wouldn't like this, is there could be some independent usability measurement, you know, this test gets an A, this one gets an F. I would hate for the FDA to have to decide on this, but certainly independent organizations can do what they want and can make these assessments and make recommendations to certain groups. You can use this test, because it's super simple, works great. So, the FDA by law has to play fair with all developers, of course.

Dr. Van Der Pol: But one of the things that I know is that you do some types of research at the FDA, and maybe one of the things that would be super useful is you take all of the over-the-counter assays and even all of the point-of-care assays because I find that point-of-care people are not trained laboratorians either. And so, there's still some problems there. So, if you take anything that has a CLIA waiver or an over-the-counter claim, collect all of those instructions for use, the quick reference guide, the one pager, and get together a panel of like a hundred people that agree to do this and you just send it out to them and have them rank. This was the easiest for me to use, one through a hundred. And it's not that you're going to do that so that you can give feedback to manufacturers as much as so that you could say, okay, the common elements in the ones that were liked are these five features and the things that seemed universally disliked were those components. And then maybe you could put together guidance that would say: "For over-the-counter or point-of-care tests, this is the way your quick instruction sheet needs to look." Right? I mean, so I think you could do that with what we have from Covid right now and make a really great study out of it at fairly little cost. Brad, hang on one minute while I go to Jennifer.

Dr. Stenzel: Yeah, a good suggestion. I like that suggestion. We'll see if we can actually do it.

Dr. Van Der Pol: Let me cut the line and go to Jennifer.

Ms. Schwartzott: I just want to comment on what you're speaking of. You have the whole patient representative program right there for your testers. We all have disabilities and illnesses and represent communities. And there's an entire program of people that would be perfectly willing to do that kind of thing. Any kind of testing.

Dr. Van Der Pol: Great. Dr. Wentzensen, sorry.

Dr. Wentzensen: Yeah. (unintelligible) I agree with you. It would be great to use that experience to really to have some user testing and give some guidance. At the same time, I think it would be again important to consider doing this in a staged approach. In the beginning of a response, you have virtually no barriers, like a test should work somehow, but you want to get it on the market. And then over time, you raise the stakes and say, okay, now, please make this more uniform. I mean, there were some tests that even differed by a lot, whether it was pre-aliquot or not. And then sometimes you realize, oh, it's in a separate tube. So, I think that there's a lot that could be improved over time. But in the beginning, you don't want to hold anybody back, putting their test out. And so, I think it could go in parallel with more performance metrics. There could also be more usability assessment, but in a staged way.

Dr. Van Der Pol: Brad.

Mr. Spring: Brad spring, Roche diagnostics, lots of good discussion. I don't disagree with the fact that, I mean, we want our tests to be used appropriately. We want to have accurate results, and no result is an inaccurate result, delays treatment potentially. So, anything we can do as an industry to improve that, we're willing to do. I know FDA does have human factors programs, so there is a capability there to at least look at what kind of human factor studies were done. But I think Dr. Wentzensen's point, we were in a mode where we had to just so rapidly develop these tests. I think his point is correct that we probably had to then say, we're going to make it this way for now, but commit to improve it over time. And all these suggestions are very good

suggestions. The one other thing we do, I know this is a U.S. focused conversation though, but we do make these tests for global use too, which actually lends itself to a more, you know, image-based approach. And I think a lot of us try to do that to avoid worrying about translations, but, but a small comment here is, remember, some countries also read right to left versus left to right. So, we have to consider, we've seen these faux pas, as we call them, where countries will look at a picture, but they're starting where we might start at the end and go backwards. So, we have to take all those things into account. Because we don't want to just make one test for one country, then we're making 100 different types of tests. So, just things to consider, but definitely would align with the comments here that we got to make these tests as easy as possible. For all types of patients, if we're talking to the home-use, point-of-care use, all types of users and patients that will use that test.

Dr. Van Der Pol: Are there any other points? And again, I think we've strayed a bit, but it's fine. Are there any other points that you want to bring up about types of instruments or types of test components that the agency should be prioritizing, building relationships with in advance? Okay, I'm going to try to sum this one up, but it was a very robust conversation, which was a good thing, I think. Let’s see what I hit. Okay. So, I think the first point that we need to remind you, the agency, of is that the panel all agreed that we would hope that you can find some mechanism for prioritizing so that you are not having to deal with reviewing a thousand applications for new tests. And then, not all of them actually being super useful on the market, but we do need redundancy so that nobody's depending on any one specific manufacturer or even any one specific type of test. So, we need broad coverage and diversity in the types of mechanisms.

There was mentioned that it would be nice to utilize high-throughput systems that had an open channel so that LDTs, because LDTs are often the first responders, if you will. So, it would

be nice to be able to use those. And so, if you were going to prioritize types of manufacture or types of instruments, those instruments that have high-throughput, but also have open channel access, you may need to consider during an emergency situation, relaxing some of the restrictions on manufacturers, helping individual labs develop or optimize those tests on that system so that everybody can be optimized as quickly as possible. And consider taking CDC into this conversation so that CDC is validating or optimizing their first line of primers and probes on a variety of platforms, and especially focusing on those platforms that public health laboratories have in their settings, since public health laboratories are also going to be first responders. So, if they can put these lab developed assays onto those systems, that will help the whole country at once.

Also think about, those systems that are commonly widely used in commercial or large reference labs and central labs, but think also beyond just instruments, but think about those manufacturers that could help you with the informatics to ease up the problems with accessioning, but also with resulting so that we're not bottlenecked. And that running the test is the part that takes the time, but not receiving the test or getting results back out. But then also remember that fast followers to lab developed tests have to be things that have full and complete instructions because smaller laboratories don't have the capacity to do the validation and verification work that's required of LDTs. That may be that some of those LDTs could come under one of those umbrella approvals that you were mentioning earlier, so that public health labs in particular, or large reference labs weren't having to do a lot of independent validation. If it's already been shown to work on this instrument with these primers and probes, then each lab shouldn't be having to redo that validation. They should only be doing verification, which is much less expensive and time consuming.

Don't forget the equity concerns. So, when you're prioritizing manufacturers or platforms, you need to prioritize at least some that are going to be in that more affordable range and/or have more stable transport conditions that allow specimens to come in from further afield if that's what's happening. But we do need solutions that can be closer to the point of care. So, we don't want everything to be focused on reference labs. That may be the first responder, but then the second responder needs to be things that can get out into smaller settings. There was mentioned that it might be useful to try and prioritize work with someone who manufactures something that has a more broad target. Like the pan-SARS example was a good example, whether that's a molecular target or whether it's an antibody target, you could envision that going multiple ways. And you'd have to see where that would fit best. You also do need to consider a diversity of sample types. So, if you're looking at platforms, especially platforms that are molecular platforms, maybe you should prioritize those platforms that can use things like stool and tissue and respiratory samples, and so on and so forth.

So, you do need to consider solutions for immunocompromised people, particularly if you're working with antibody-based testing or immunological markers. It wasn't said exactly this way, but I think one of the things that came out was you need to keep biological plausibility in mind. And so, if somebody comes up with some scheme that this is the next best thing, make sure you think that through and then really decide “maybe it is the next best thing”, or “maybe we've got some concerns about it.” And so, in your prioritization, you take biological plausibility into consideration. I think that it's important to prioritize those components of testing. If somebody already has claims for a self-collection device and/or for a self-testing device, those people are most likely to be able to roll over and put new pathogens on those same types of devices and maybe the safety of the device or the safety of the transport buffer has already been

assessed and we don't have to start at ground zero, we can start somewhere further down the road.

And then finally, and I left it for last because I think it's actually quite important and I want to make sure it's on top of our mind. I think for anything that's at the point-of-care or that's over-the-counter, we need to really work to create user-friendly instructions. There should be a review process that includes actual end users. Possibly you should consider analyzing current Covid instructions for use and making sure that you find the commonalities that end users find useful and those commonalities of things that they did not find useful and you have to take equity and diversity and inclusion considerations into account when thinking about those instructions and if you could create some sort of template, to say: describe how to collect the sample, describe in one sentence how to handle the sample, show a picture of what the result looks like. Something like that that you give people a template that's not specific to any pathogen that would help them in their developmental process once something new emerges and we're trying to respond to it. Does anybody have anything to add that I forgot to cover? Dr. Caliendo.

Dr. Caliendo: Angie Caliendo, Brown. I just didn't quite hear it, Bobby, but the whole pre-authorization idea. Right?

Dr. Van Der Pol: I kind of thought this was all going into a pre-authorization idea.

Dr. Caliendo: You just didn't use those words and I just wanted to make sure that that they understand that we think that's a great idea.

Dr. Van Der Pol: Yeah. And so that was mentioned, and I'll make sure that I say it in a full sentence, but that the agency should consider pre-authorizing certain manufacturers or certain types of tests by working with those manufacturers to understand how they can quickly mobilize to meet the needs of what's out there. But again, in the context, probably of those systems that

are already in use in large reference labs and in public health labs, I think. Anything else that I forgot or didn't explain well? Okay, Dr. Stenzel, anything else that you needed on this topic?

Dr. Stenzel: Well, first of all, wow, that was a long list and excellent job. Another very robust discussion and many things to the panel. A couple of things to mention. One is there was mention of sort of an umbrella authorization that we hadn't discussed, the saliva direct test. We've been staying away from specific tests, but they weren't the only one that got, I think University of Illinois also got an authorization, that we authorize their protocol. There are protocols specified, order these primers, use these reagents, use these instruments, and Yale SalivaDirect was very active in working with the FDA and getting updates to that and scores of labs asked to be signed up and we authorized Yale SalivaDirect to actually select the lab, so there would be a checklist, "Are you going to follow the instructions? Are you going to use the components that are authorized? Okay, then you can use this test," but it was a very effective way to get essentially a lab developed test out and used. And really, it seemed appreciated by many, many, many users. I don't know if all labs can necessarily do that as we heard today, but for those labs who have certain capabilities, that certainly leveraged, with one central, original application, the ability to distribute a test protocol that was EUA authorized by the FDA, and that was great. There are certain things we can we can do in advance but there's others that we don't yet have authorities for, and there's discussions about how to obtain those authorities that the FDA can, through text or sort of programs and things like that, being able to give authorization to labs to develop tests and there are different ways of doing that. But some of that we don't clearly don't currently have authorization to do. It's not in our authorities to be able to do that. So, by and large, for the time being we're restricted to sometimes using enforcement discretion which we have done quite liberally, but we've also been criticized for that because some of the tests launched were not necessarily prior to FDA review or were not necessarily the best test, so we said. So, we'll do as

much as we can under our current authority, so that's my promise. But no other comments or questions and thanks again to this distinguished panel, appreciate all of it.

Dr. Van Der Pol: And I want to say, thank you for reminding us about that, for anybody who doesn't know, because it is kind of a lab-y thing. Yale had created a process for testing saliva for Covid, and they sent it to the agency for review. But then it was a protocol. And so, any laboratory that that met their criteria could apply that protocol. So, it was the same as, -ish, not legally necessarily, but similar to having a lab developed test, but without each lab having to go through the whole validation process, even though each lab would source their own primers and probes, but they would source them through these companies that Yale had already sort of evaluated and so it was a great mechanism that a lot of people were able to adopt this that might not otherwise have been able to go through the validation process. I wonder and I, again, don't understand the authorities at all and so I wonder if this is something that when a situation like Covid emerges, does the agency have the capacity to solicit someone to submit something like that or are you not allowed to ask for submissions?

Dr. Stenzel: I think we can encourage it. It was a creative solution.

Dr. Van Der Pol: It worked really well.

Dr. Stenzel: One that we were very open to. And there was comment about how proactive or active versus passive the agency has been. And, you know, when we heard it, we said, “Yes, let's do this.” And I was pleasantly surprised at how well received it was. And I think it's in our toolbox going forward.

Dr. Van Der Pol: Great.

Dr Stenzel: And there's, there's no reason, I'm sure there's other FDA people on the line, but I see no reasons why we can't fully authorize. Not just EUA authorize some of these kinds of concepts. So, we look forward to potentially doing that.

**Question Four**

Dr. Van Der Pol: Great. All right. So, with that, we're going to move on to question four. So, we have four, five, and six to go, but before you all take a heavy sigh, I'd like to put four up on the screen and see if we've actually answered it already because I don't think we restricted ourselves to instruments in the last hour of our conversation. So, the question is, are there certain types of tests or types of developers that should be prioritized for review in the early stages of the pandemic? I think that we covered that. I don't think we restricted ourselves to instruments, but does anybody on the panel have anything that they'd like to specifically say about types of tests and types of developers? Mr. Spring?

Mr. Spring: Yeah, I'm not going to comment on the types necessarily, but I know there were, and Brad spring, Roche Diagnostics, there were comments around the agency and having to deal with a thousand manufacturers and that there were challenges with the quality of the documentation that was coming in, the data that was coming in. So, is there a way to address because you want to be fair, right? So, there's this kind of first in first out, so to speak approach, which is fair, but is it really the best use of your time? And maybe I'm saying something here that you're already doing. But this refused-to-file type of approach that we have with current submissions, I think you were doing some of that, but is there a way to be much more efficient and focus on those submissions that are coming in that A) meet your priority list, but also give you that early sense that this is a quality submission upon first review, and that we're not going to be spending a lot of time haggling and whatever else you need to do there. So just a statement or comment on that. And I guess maybe Tim, I think I see your hand up to respond to that.

Dr. Van Der Pol: Dr. Stenzel.

Dr. Stenzel: Yes, Tim Stenzel. Okay, so we have tremendous authority and flexibility to tailor the EUA process for a particular need. And, with Covid, that changed with updated guidance.

That went through review and was very targeted and specific in what we were trying to do with that. So, we did move, when we were continuing to get a lot of me-too tests that weren't immediately going to really add to the response in a meaningful way when we really wanted to focus on, say, high-throughput tests or over-the-counter tests, or point-of-care test. Also, we had realized that that there were, at some point, and I don't remember the exact dates where this happened, where we really wanted to focus on well-experienced manufacturers, and we define that experience rather broadly. Basically, if you had gotten an EUA for Covid already, or you had a full authorization saying, for a respiratory virus, those were the kind of companies then we began to gain more priority to. And then we applied that all at the beginning of Mpox with our first and still to date the only guidance we've done on Mpox, where we really more closely imitated what was done in South Korea, where they had an open solicitation for developers and we use the pre-EUA process to come in and there was a window of time, I think it was around 30 days, he said, if you're really interested in developing an Mpox test, let us know through the pre-EUA process. We'll review your EUA, and we'll make selections and we outline the priorities and the guidance which said we were going to give preference to test developers that had demonstrated success with the FDA that included, say, an EUA for Covid or full authorization for something applicable to Mpox. So, we got those requests, and we made selections and we let the developers know who had been selected and that was an incredibly efficient process. So, we kind of want to know from the panel, is that supported by this panel? Is that something that we should be doing? Is that a good thing to do? It certainly allowed us more quickly to get to the test for Mpox and focus our attention on Mpox. And it vastly reduced the need for head count for Mpox at the time when we were still, this is more than a year ago that Mpox hit, we were still very busy with many Covid EUA applications. So, our busy team was further divided, but because of those mechanisms we use through the authorities, we're able to more limit the head

count within our office that was needed to properly and adequately respond to Mpox. And I think the feedback in Mpox to-date is good, but we're always open to hearing feedback that helps us to improve. So, thank you.

Dr. Van Der Pol: Dr. Petti?

Dr. Petti: Kathy Petti, HealthSpring Global. I think we've all witnessed the tremendous gap with home-based testing and the lack of chain of custody of data and reporting back to either agencies or to health care providers. There are some test manufacturers that have developed some solutions, be it external apps or use of QR codes, so perhaps in the prioritization list, those manufacturers that have made a commitment to closing that gap with home-based tests and having those results somehow reported back to the health care system or to the public health at large is pretty much mission-critical for us. As we respond to a pandemic, we've been shooting blind, not really knowing the numbers.

Dr. Van Der Pol: That's a really great point. To go along with that point, I would also suggest that the agency really work with CDC. One of our problems with older diseases that we report is that each jurisdiction has its own reporting mechanism. Their variables are not in the same structures and it's not consistent. So, from a manufacturer's perspective, it's quite hard to make a product that can seamlessly upload into something that can be communicated to local and national health agencies. With Covid, CDC developed a new reporting process for Covid that was the same across all jurisdictions, which supported development of connectivity solutions. So, I would strongly encourage CDC to also be part of this sort of emergency-preparedness-thinking process about making sure that future reportability is more streamlined so that that supports manufacturers who want to help us. Help them help us, I guess. So, other thoughts about the types of tests?

Dr. Stenzel: I could add some thoughts about Dr. Petti's comments on data. The FDA did ask and require, not necessarily pre-market, but post-market for over-the-counter tests, which were not required under certain Covid bills to be reported. So, home-tests didn't have the same requirement that labs did to report data. We did put into the conditions of authorization of every over-the-counter test to develop a data reporting system. And many did and some of them are now, or were connected, I assume they're still connected. I haven't gotten a recent update on that, but certainly not across the board. And NIH, we've been in discussion with the CDC, obviously, and NIH played a large role and also making a reporting option available and others as well as the FDA. One of the challenges that some have expressed with collection of home-based testing data is the reliability of that data and of those results. I think others are very open to the idea and if you start collecting it and recording it, you can get geolocation data, not to a neighborhood, but to a zip code, and you could be reporting back to that zip code. And so, everybody in that zip code can go to an online chart that says, “Well, you know what, Covid is very low right now. So, the risks are lower, not that they're zero.” But in other times, the risk may be very high in a certain community, and people can take that into account as they go about their lives.

But then there is an open question of the reliability of the data, especially if the reporting isn't automated. We've been talking about low-cost tests. So, to have an automated upload of a home-based result, there has to be some sort of instrumentation, whether it's even just a smartphone or other device versus manually an app, even, or manually going to a website and putting in your lot number, your test and reporting your result, whether positive or negative, and it's their bias. Are people more likely to report positive results rather than negative results? So, these are all great open questions, but I still believe that you could at least monitor trends, and even monitor performance in a zip code, say, between different home-tests is suddenly one of those tests is yielding a lot more positives, or maybe a lot fewer positives than the rest of the tests

in a geography. You might discover that there might be a test that's out of spec, that's not performing well, but if they're all performing about the same, which we might expect, and they're trending up, that tells you one thing, or they're trending down on positivity, that tells you another thing. So, can you have the same granularity and assurance of quality that you have with, say, a central lab test performed by high-complexity personnel and reported through existing reporting systems? No, probably, unless you have these automated systems that report every result, but then those are more expensive and harder to deploy and have equity issues, et cetera. But an excellent point that obviously we've been putting a lot of thought to. There are also some funded efforts at the FDA and other agencies to address the reporting issue and many grants have already been awarded in this area to develop and seek ways, not just for reporting, but the use of real-world evidence or data for regulatory purposes, whether pre-market or post-market. So, thank you.

Dr. Van Der Pol: So, question number four is: Are there types of tests or types of developers that the agency should be prioritizing in their approach to planning? I think that we've covered that mostly, again through the previous conversation. And then if there's any other things people want to say on this topic? Okay. So, what we've heard from the things that were added to the previous conversation are that some of the ways to prioritize may be based on the type of test. Once it's clear what that type of test is, that's ideal. But again, based on our previous conversation, we haven't picked a specific type of test that we know we can focus exclusively on to consider the quality of the submission, which is part of what Dr Stenzel said was an evaluation component in prioritizing during Covid or during Mpox on those manufacturers who already had experience in submitting a successful product for the EUA process for Covid or for something similar to Mpox. And then the last thing was to consider as a prioritization criterion, whether or not the assay has connectivity, but, as Dr. Stenzel mentioned, that's going to have to be taken into

the context of the other factors that you're considering when prioritizing. So, I think that the general summation is that the panel doesn't feel like there's any one type of test or any one type of developer that we could say you would be better off to focus on because the future is too uncertain for that, but based on past track records and the things we talked about previously about public lab support and central and reference lab support, I think that you sort of have your answer there that we want it all. And we want you to be ready to supply it all. It's an easy answer. Isn't it? Dr. Stenzel, do you have any more things that you'd like us to dig into more deeply on this particular topic?

Dr. Stenzel: No, thanks again for the input. We'll continue to do our best.

**Question Five**

Dr. Van Der Pol: Okay, so question five. Question five is: what are the key features of tests or certain test designs that would be helpful in a future pandemic? Again, we discussed a great deal of this when we discussed the earlier questions. And some of those features that we've already mentioned include things that can be high-throughput. There are things that can be run in laboratories that already have existing instrumentation, things that are very user-friendly, and that can address equity concerns and inclusivity and diversity concerns. And perhaps getting feedback from people about the usability, both in the laboratory and in the home of different Covid options that came out. Some of the options that came out were adopted by labs because we were in a hurry, and we would take anything. And then as soon as the next thing came, we dropped them. Might be worth the FDA's time to ask why we dropped the ones we dropped. What were the features that ultimately, like my lab right now is only running one Covid test. So, why was I running five Covid tests a year ago and now I'm only running one. So, there are things out there that laboratorians might be able to tell you if there was a survey process or something to ask that would help you learn a little bit more about the features that really made a difference.

I will tell you, one feature that I think is important that we've not talked about today that I recall is either using a dry sample or an unadulterated sample and say if it's a urine or a stool. So, something not in transport buffer is what I'm getting at, or using something that's in a universal transport buffer, because then that allows me what I did, during the beginning days of code was I took every platform that I have. I have five in my lab. I was able to use all of them. And so, anytime I had a supply out, I could move everything over to a different instrument. Or if I got so many samples, I couldn't run them on one instrument, I had multiple instruments, but that was because I was running everything mostly out of UTM. And so, it was very easy for me then to aliquot that into the manufacturer's tube and run it on the system. And I'm not saying I want to spend my days aliquoting, because that's not ideal. But then when it got to the point where people had, "Okay, that's fine, you can put the tube in UTM directly on the instrument." Well, then it becomes easier for me, right? But in the early days, something that I can run on anything because it's in a universal process, or it's unadulterated, if you will, really helps early response. So that's something that manufacturers that have those options available for other types of tests, may be those manufacturers that you want to focus on for sort of that prioritization. I see Dr. Caliendo has her hand up.

Dr. Caliendo: Angie Caliendo, Brown. I think one opportunity that was lost during all this was to assess agreement across different tests. By December of '20, there was an international standard for Covid. For SARS too. And while the FDA tried earlier in the pandemic to send out material that manufacturers would run in their tests, it was a lost opportunity to require everybody who had an EUA to get that material and report back to the FDA in the same units. What, in those international units, what their LoD was because you were looking at $TCID_{50}$s, you were looking at molecules, you were looking at copies, you were looking at who knows what. And when we did have a choice, we didn't know, really, how these tests performed. And I mean,

people were desperate. We were running anything we could, no idea how they compared to one another. And that standard sat out there and was never required, and that could have been a "You want your EUA to stay on the market, give us your LoD and then publish it, put it out on your website." This is what everybody's international units. And like I said, I know you tried to do that, but the material you sent out wasn't compatible with the last season. So, it was somewhat uninterpretable. But, moving forward, that's an opportunity we don't want to miss. I was so impressed that the WHO had a standard out that fast.

Van Der Pol: Great point. Brad?

Dr. Stenzel: If I could comment on the international standards. So, we did interact early and often with the WHO and the group, and they simply didn't have the ability to distribute that material to any lab it wanted in the U. S. So, secondary standard would need to be made. We would love to hear more feedback on the reference material that the FDA did send out and what was good about that or what it was not so good about that. We did link the FDA reference material to the international standard. So, we have the linkage between the primary standard and in our reference material. And we're going to take another run for Covid with reference material. So hopefully this one is successful. We've done this to some degree for flu for many years now, where the antigen test developers are required to obtain annual material and make sure that they have reactivity. Most of the molecular, not all molecular manufacturers, voluntarily also test that material. We needed to switch producers of that material. So, we didn't skip, I think we might have skipped one year, but it's coming back. So, this kind of effort for reference material and to be able to look at reactivity and potentially go further and determine comparable LoDs is something that the FDA does feel strongly about and feels like is important. But feedback on what we did for Covid here or other places would be greatly appreciated.

Dr. Caliendo: So, the feedback you're going to have to get from the companies. The feedback I got was from talking to manufacturers saying, why does your test look so bad? And so, we weren't the ones testing with that material, they were. So, I think the companies are where you're going to have to get that feedback for and then reaching out to a company that makes secondary standards and engaging them ahead of time so that the next pandemic, you have material that can be made. I mean, the manufacturers could go to WHO and get it. It's what they do now, right? And then make their own secondary standards. So, there's a way. This is another proactive engage ahead of time because, you know you're going to need it. H-5, H-7, whatever, people should be thinking about this already, to have a secondary standard somewhere so that the CDC or you could send out this panel.

Dr. Stenzel: Thank you for that input. Uwe may have some additional information to add.

Dr. Scherf: Yes, that's fine. Uwe Scherf, FDA. So, Angie, we totally agree with what you said, but I think one nuance that might not be known by everybody that the standard from WHO was not available in the amount they needed to be obtained to really do the LoD studies and for the assessment of the performance. Of course, they could have developed a secondary standard, but also it took a lot of resources and time, and this really didn't fit the purpose. And the material that we made available early on, which was, not perfect either, but that gave a certain assessment early on. Really was used to come up with these numbers. But as you said, there is space for improvement. But I have to say, from our perspective, we were head on, early on we provided material that allows us to make a good assessment that actually helped us later on to establish evaluation criteria and approaches for the antigen tests that otherwise wouldn't had allowed us to make the antigen tests available so quickly with the appropriate information about their performance.

Dr. Caliendo: And, Uwe, moving forward when you do that, requiring that to be in the package insert will be very helpful. Right?

Dr. Scherf: It is. Yeah, I mean, what is in there, you might have seen it, is in the authorization letter, it is proactively included as a condition of authorization. If we find the material that people believe helps to make this assessment, the sponsor need to test it. That's one of the conditions that they have to fulfill.

Dr. Stenzel: But Angie, I think you brought up one of the challenges that the FDA faced that some didn't like how we did it. And we are a responsive agency, and we have the opportunity to work with a lot of different people. So, you, you alluded to some challenges and that existed. Thanks.

Dr. Van Der Pol: Dr. Pereira.

Dr. Pereira: Marcus Pereira, Columbia University. So, thinking about sort of test features that I think will be important as you begin to understand whatever pandemic may come your way, obviously good diagnostic sort of sensitivity and specificity, not only among the general population, but also in particular populations. Again, I'm going to mention pediatric population that may have sort of different testing characteristics. And you do want to from the very early onset be able to characterize that. But I'm also thinking about immunocompromised patients who generally might have a different burden of disease and perhaps either lower or different testing sensitivities and specificity. So, it would be important from the get-go to include some of these important vulnerable populations that in some ways may actually be sentinel populations, right, in terms of sort of the beginning of a pandemic and so forth. That's one important point, I think, in terms of diagnostic component, we've been talking a lot about that particular component, but also monitoring of disease. We haven't talked a little about that in terms of developing tests that could give us some sense, is this patient, is their infection resolving or is it progressing and are

they still infectious or not? I mean, one of the things that I think we struggled with during Covid was when could patients come off isolation, whether they were still contagious or not, and trying to characterize or develop tests that could give those answers from the get-go would also be an important feature as well.

Dr. Van Der Pol: So, before Dr. Stenzel comes in, I'm just going to respond to you quickly to add to your list of populations that need to be included in research is pregnant women. And I understand why we don't, but we really just must. And we need to do that in a safe way, but pregnant women are at risk, and they need to understand how different things work and pregnant women are somewhat immunocompromised as well, so they have different needs depending on what type of test it is. I will add very quickly is that I think one of the features that Dr. Pereira maybe doesn't necessarily know is out there but is maybe a feature we want to think about is if we're doing molecular tests, maybe we need viability assays. And so, people that have a viability assay as part of their molecular diagnostics, maybe they should be prioritized because they already know how to make that process work. Sorry, Marcus, if you want to go again.

Dr. Pereira: No, that's exactly it, sort of link those tests. So at least they have sort of surrogate markers, right? A certain, we use a lot of CT values, right? In terms of nasal pharyngeal PCRs, obviously completely off-label. And I think it's sort of described how we needed that data for clinical practice.

Dr. Van Der Pol: And I will remark that some companies who shall not go named, Mr. Spring, are stopping us from allowing having access to CT values in the future from their instruments because they don't have claims for a quantitative test. So, you had access to that during the EUA process, but you're not likely to have access to it going forward. So, recognize that’s a barrier as well. Dr. Stenzel.

Mr. Spring: I was going to say on that, Dr. Van Der Pol, my experience was we were told we were no longer allowed to.

Dr. Van Der Pol: Oh no, I'm sure that's where it came from. But just as an FYI, I mean, I use those all the time for a variety of different tests and analytes. So, I was just warning Dr. Pereira that things that you've used in the past, you may not have access to in the future. And that's something maybe for the agency to consider as well. All right, Dr. Stenzel, you've been waiting patiently.

Dr. Stenzel: No, I didn't want to respond. There's a number of topics that Dr. Pereira brought up. But first, I want to know, hopefully, Brad, it wasn't the FDA that said you couldn't report out CTs because that's not our policy. And we, in fact, had a frequently asked question that didn't object to reporting out on CTs even if we didn't necessarily, after reviewing the literature and reviewing professional guidelines this area, which almost universally said that CT views are not comparable between labs, in fact, we only authorize one truly quantitative Covid tests. But given the nature of the sample type, typically of a swap, it's not the same sort of thing as I was involved in earlier in my career, in quantitative HIV from blood samples or HCV or HPV from those same samples on one of the commonly used or older commonly used by platforms now, because I'm not as young as I used to be, but, with respiratory samples, and we're open to these ideas as long as science and data backs it up. But delving into infectiousness is challenging. Some of the literature we've seen says that even very high-CTs people can transmit Covid.

The various at-risk populations are very important to us. We talked yesterday about certain populations for those tests, and we take that into account here as well. I think the serology authorizations, probably for EUAs, my team can confirm this perhaps, stated that you had to take to account, the immune status of the patient when you're reviewing the serology results. But the immunocompromised, this is an important group. I don't know that enough research has been

done on them for how they express infection to respiratory diseases or Covid and you know are they as easy or as hard sometimes to detect with antigen tests versus molecular tests? How do we optimize testing for those groups, whether it be an immunocompromised or pregnant patients.

As far as the pediatric population goes, I did want to comment that if the developer wanted to have a pediatric claim and that we wanted to see data, even though the numbers are small in the positives, and then the FDA was involved with another Emory, NIH, FDA scientific study that, in a back to school effort, looked at the ability of kids at school, down to age five, to self-collect and enter nasal swab. A video, a short video was developed in that process. They watched that then they collected. They had observers in the study. That study was published, I forget where, and we were pleasantly surprised to see that even five-year-olds at school could adequately swab their interior areas and get a good result. Actually, some of the older kids showed a slightly decreased performance. Teenagers were a problem, I think. But anyways, these are all important points. And the last point to make is that you talked about monitoring disease and resolving and prognosis. The FDA is open to all of these types of test submissions, always. We're always open and always available through if it's an EOA type test through the pre-EUA process is the best way to talk to us about novel technologies or applications and figure out what would be the best way to validate that? And what is the best pathway to submit to the FDA or the q-sub/pre-sub process that we talked about yesterday? Thank you.

Dr. Van Der Pol: Dr. La Hoz

Dr. La Hoz: Hi, this is Ricardo La Hoz from UT Southwestern. Thank you, Dr. Stenzel. I think you've addressed the comment that I was going to make already. So, I don't want to go as deeper as I was thinking, but the immunocompromised host tends to be lumped in a in a single group when, in fact, is quite the heterogenous in in in itself. Some of the patients that are on monthly reduction map had very unusual presentations where they have persistent infections. Some of

them, although the vast majority of the population fall within the bell curve off of infectivity, and we can institute isolation practices based on that, I think there is a need to determine the effectivity for isolation, for example, in a bone marrow unit. That could be quite helpful, no matter what the pathogen may be during the pandemic. But in transplantation, a question that became quite relevant was when to proceed with transplantation after infection, and I think we had to balance the tangible risk of dying on the wait list for the solid organ transplant candidate versus relapse of the malignancy in the bone marrow transplant patients. A well-known fact that at least some respiratory infections have been associated with worse outcomes after transplantation. So that's another area where infectivity assays may be helpful. And last but not least, there was a point in the pandemic where a large proportion of donors were testing positive for Covid it at the time of donation. And although some ventured to use those donors, there was an understandable concern to use the organs from those donors. Eventually the non-lungs were used with some degree of safety, but there was a large drop in the number of lung transplants performed and as much as we've recovered it was still a challenging situation. So, the infectivity assays may serve multiple roles with the big caveat, like I said, that the immunocompromised host is really multiple different populations and they're not all the same.

Dr. Van Der Pol: Thank you for that. Well, are there other comments on the key features or test designs that people think are important to consider in preparedness? Seeing no hands raised, I'm going to summarize this. I will remind the people that read the transcript that we also discussed many key features and types of test designs in previous question responses, but the ones that came out of this particular conversation include the potential to consider universal transport or samples that were transported without any buffer to look at agreement across platforms, particularly using, well-standardized panels so that we can see LoDs and understand LoDs across platforms using assays that have good performance regarding sensitivity and

specificity that included in their study designs: pediatrics, immunocompromised people from a variety of different backgrounds because the variety and types of immunosuppression is large, and so they need to be taken into account, including pregnant women as well. It might be useful to have those tests that have potential for quantification or viability assessment so that we can monitor disease status as well as infection status. I think that pretty much sums up the features that the group thinks might be very useful in terms of assays for future pandemic response. Dr. Stenzel, did you need anything more on this topic?

Dr. Stenzel: No, and thanks again to you and the panel. Appreciate you guys.

**Question Six**

Dr. Van Der Pol: All right. This is our last question, question number six in your packet. I think we've covered some of these, but we may be able to discuss more in-depth this question about other lessons learned from the recent COVID-19 pandemic and Mpox emergencies that might help the agency to take into consideration when planning for future pandemics. We discussed several of these features in previous sessions. One thing that I'll reiterate is that we thought it was important to review the clarity of the quick information sheets for people who are running tests at the point-of-care or buying over-the-counter tests. We thought it would be important to use packets from the COVID EUA and the full approval process since we've gone into that phase as a template for future submissions. And we thought it would be important to remind people that they need to use the pre-EUA process to help get feedback very early on in their developmental and design process. I see hands up from people who want to tell us about other lessons learned from COVID. Let's start with Dr. Honein.

Dr. Honein: Yes, Peggy Honein from CDC. One lesson learned that is completely understandable, but with the great ramping up that Dr. Stenzel described of adding a lot of new reviewers to the process, there was a lot of variation and the familiarity of some of those reviewers

with the FDA processes. Some of the feedback we received was that it was a little more challenging than we would typically expect. I also had a similar issue at CDC, when trying to onboard and train people during a pandemic. It was a huge challenge for all of us and I'm highlighting it as this is something we may want to give some consideration to as we're preparing moving forward. Thank you.

Dr. Van Der Pol: I would say that when inclusive, extensive guidelines are very helpful because they help the reviewers stay consistent as well. Next was Dr. Blumberg.

Dr. Blumberg: Hi, Emily Blumberg, University of Pennsylvania. We've talked about this before. I think it is especially important, when you think about pandemic preparedness, to make sure that the testing access, so the test platforms are created with access to those most vulnerable populations, as they may be the ones most likely to sustain or perpetuate ongoing infection. Platforms have to be available to people who will be lower resource charter, to reach things that are going to be simple, not something that will require a lot of effort on the part of the individual or a cost.

Dr. Van Der Pol: Agreed. Dr. Petti.

Dr. Petti: Yes. I'm following up on something that Dr. Caliendo had said earlier and also following up on Dr. Honein's comments. Could there be legislation where the FDA, at the time of a pandemic, could be a resource to hire an "X" percent increase, to respond to a pandemic where that legislation would be preexisting in anticipation of the next pandemic? Then, you would not necessarily have to ask for a resource increase. Another thing is that in the military, we have the reserves in the physician world. We actually have our medical boards that know who's retired but still holds a medical license. During the pandemic, a lot of those resources were actually activated to help with the human capital. I don't know if the FDA has a repository of retired reviewers or people with experience that you could call upon when you have so many submissions to review. I

wouldn't say any of us truly had the full capacity, but many of us are here to serve if called upon to review a submission or two. I think there are just more resources than full hires that you could draw from.

Dr. Van Der Pol: I will add my two cents to that and wonder if there would be a possibility of considering an NIH study session situation where you had pre-vetted people and you knew what their conflicts were in advance. Obviously, you wouldn't assign them to something that they were conflicted on, and you might only be able to assign one to a person, but if you had 100 people in the country, then it might not work. They wouldn't be your exclusive reviewers and obviously, they wouldn't be as familiar with the statutory requirements, but they could certainly look at the data, at the science of the performance, at the instructions, and the usability questions. They wouldn't give you everything you need, but they might be able to help.

Dr. Petti: And often you're blinded on who the manufacturer is.

Dr. Van Der Pol: Dr. Ng.

Dr. Ng: From the left field, for the future, please do not require any dry ice transport. I cannot get dry ice.

Dr. Stenzel: I know what you're referring to and the FDA never made that requirement.

Dr. Van Der Pol: Dr. Caliendo?

Dr. Caliendo: Angie Caliendo, Brown. I'm going to bring it back to center field and it is related to what Kathy said. You said that you contracted out to a group that did 100 reviews for you. Having that in place ahead of time would also be helpful. Again, it's the same concept: you're screening people ahead of time, whether they're individual experts or a company, and you're ready to roll, if you need them.

Dr. Stenzel: The group we used had many former FDA years. But it required funding that's not in our…

Dr. Caliendo: And you can get us poor souls, for free.

Dr. Van Der Pol: I was going to say, they pay you.

Dr. Caliendo: Lunch would probably be all we would really need.

Dr. Van Der Pol: Yes, we're pretty, cheap, I must say!

Dr. Stenzel: We're open to that, but when we call after you've already been working 24/7, just remember that you volunteered to help.

Dr. Van Der Pol: It is really an interesting thing that people in the healthcare field do things because we feel it's our expectation; it's our job to respond. I'm not saying that it's easy for people, but people will find a way to make time to help because I think that we're all on the same team and we all want the same outcomes. If there's a little bit of suffering, we're willing to deal with it. I think that's just life. We're saying that we're there for you, so find a way to use us.

Dr. Caliendo: Tim, I'll just add that during the peak, many of us were writing guidelines and volunteering our time for various organizations. I want to reiterate with Bobby just said. I think people appreciate that they have expertise, and they want to help.

Dr. Stanzel: I think it's a great idea.

Dr. Van Der Pol: Both Kathy and Angie said it and that is really the key. Do it now! Create now a cadre of people that you have on your list and send them once a year, so that they stay in practice. When something like this comes up, they have the skill set. Just as with anything else, if you've ever sat in a study section or just done this panel, it's formulaic. I have a script that I'm reading. If you sit in the study section, there's a process and everybody knows exactly what it will be. So, if you get external reviewers, you can get them in the loop, so that they're doing it once or twice a year. They will understand the process and they will be ready for you if and when you need that level of support. I know that you can't legally say, "We'll do it for you for no charge.", but the

reality is that we'll come as close to that as you can statutorily let us because that's what we do. So, keep that in mind.

Dr. Stenzel: Yes, I do. Thank you. I do want to reiterate that we will take seriously every bit of input from yesterday and today and consider it. Thank you.

Dr. Spring: Yes, Brad Spring with Roche Diagnostics. I want to comment on what you just said, Bobby. Tim, I know that sometimes your FDA hands are tied with the third-party review program, as far as what can be reviewed. But I think there is a good point here of having that pool available and maybe even sending them 510(k)s or EUAs that have already been through a review, as a bit of a test and a refresher. Then you can coordinate back on what the FDA looked for in the submission, what kind of comments came up, and maybe use that as a check. Just as a suggestion.

Dr. Van Der Pol: That's a really great idea. Also, going forward in the future, maybe you end up deciding that this becomes a process that the FDA wants to use for everything. You have people who are experts in the field, helping you in the same way that NIH has people helping them. Maybe it's an affordable way for you not to have staff when you don't need them, or have those staff freed up to do the things that are legal, restricted, and confidential that we can't look at. I think there's a lot of possibility in that.

Dr. Stenzel: I think it’s a great idea. We’ll take that. Thank you.

Dr. Van Der Pol: Are there other thoughts? We're still on lessons learned. If there are other things that we should be recommending to the agency to really pay attention to based on what we learned during the response to COVID, now's your chance to share. It's Friday afternoon. Dr. Kotton.

Dr. Kotton: Camille Kotton, Massachusetts General. I was just curious to know if there are SOPs in place. If this happens again, is the wheel or the pathways greased? Do we know what will happen next time?

Dr. Stenzel: Yes, we can respond as needed and when needed. The Mpox responses are proof. Mpox is our 9th emergency response under the EUA authorities. So, we have more than a decade of experience in doing this. The scale impacts things tremendously. Fortunately, Mpox scale was small. I was worried it would get into other populations, early on and it didn't, although a lot of harm was done, and it impacted the populations. I don't mean to minimize that at all, but it was neither at the same scale as COVID nor was any of the prior emergencies. We have to be prepared, not just for anything that might come our way, but also for something that's very big and that requires all hands on deck. The reports that were done on our response, contained a lot of good recommendations, including, making sure that we're ready for the next one in various ways. We're working on it. It will always be a work in progress. When requested, we interact with entities inside and outside the U.S. government, all the time, in preparing for the next time.

Dr. Van Der Pol: Are there any other thoughts on lessons learned before I start to sum it up? As I mentioned with some of the previous questions, there will be responses that apply to this question, in other sections of today's conversation, which you'll be able to get from the transcript. Here are our additional thoughts that apply to this question. There should be SOPs and templates, in place, based on what was successful, what worked well with COVID applications related to this response, and the Mpox response, so that you can continue to build on those activities that were successful. There was some concern about the variability in the review process because new people had to be brought on board and trained remotely since nobody was working together. That was another aspect that probably made a difference. But, again, templates, SOPs, and guidance will help reduce that variation in the review process. We must consider assays and products to be prioritized that provide access to the populations that are the hardest hit by whatever the pandemic may be. But that often is going to mean people who are in lower socioeconomic classes and people who, for other reasons, are disadvantaged or marginalized. We need to consider whether or not

there could be legislation in advance that when a public health emergency is declared, triggers a funding mechanism to allow FDA to quickly hire more people with the anticipation that you might need additional staff. We also suggested that the agency consider a pool or a cadre of retired FDA employees who might be reactivated, to quickly help and need less training or people in other settings that have served as reviewers for the agency in the past. We also suggested that the agency consider an expert review process, somewhat similar to the NIH study sessions. To end our day on a happy note, I'll add that there was a request for nothing that involves dry ice.

And with that, you see everybody on the screen is smiling, so that's just a perfect way to end this. I would like to have an opportunity to speak to some of the people who are representatives from other sectors. We have Dr. Walker, who's our Consumer Representative, Mr. Spring, who is our Industry Representative, and Ms. Schwartzott, who is our Patient Representative. Dr. Walker, we'll start with you, if you have any extra comments that you'd like to add at closing.

**Closing Comments**

Dr. Walker: Hi, Dr. Walker, Consumer Representative. In all, I think the last two days have been well spent. Today has been the most exciting for me, just really understanding exactly what the FDA has done to ensure communication strategies. We've all engaged in that dialogue. I'm excited to see what will come from this meeting. Thank you for everything that you've done to support our communities. I don't have anything further to add.

Dr. Van Der Pol: Thank you. Mr. Spring.

Dr. Spring: Yes. Thank you. Brad Spring, Roche Diagnostics. I don't have anything else to add. This was a pretty intensive two days, but as always very informative. I've been through a few of these, and not to belittle what was done before, this was by far, one of the more rewarding

conversations because there were a lot of "what ifs?" and I appreciated that. There is nothing else to add from my end. Thank you.

Dr. Van Der Pol: Thank you. Ms. Schwartzott?

Ms. Schwartzott: It was a very interesting discussion. We learned a lot from COVID. It was a terrible thing but some good has come out of that. Thank you for considering people from different disparities, and comorbidities, and thank you for all your hard work. I wish everybody knew what went on behind closed doors because they'd be a lot more grateful. Transparency goes a long way. I try to tell people how great the FDA and these panels are because there is a large amount of work that nobody knows about. Thank you all very much.

Dr. Van Der Pol: Thank you. At this time, the panel will hear summations, comments, or clarifications from the FDA. Dr. Stenzel, you have 10 minutes.

Dr. Stenzel: I won't need that much. This has been a really wonderful and helpful two days. Every part of yesterday and today has been very valuable to the FDA. I also want to thank all those members of the public who have attended this meeting online for their kind attention yesterday and today. I want to thank you, Dr. Van Der Pol for your expert and excellent chairing yesterday and today. I want to thank all of our panel members, including the Patient, Consumer, and Industry Representatives, and all those at the FDA, who made this day happen. The input, comments, and recommendations are all welcomed, appreciated, and valued. It was a great day and the FDA received important input on questions of today. Thank you one and all. Thanks.

Dr. Van Der Pol: Thank you. At this time, the panel members are actually allowed 10 minutes. If we have any extra items that have not been covered. Dr. Moore?

Dr. Moore: Yes. The biggest unmet need in these types of situations is really not in the FDA's purview, it's really the CDC and the rest of the government. That's the messaging from the FDA we talk about, post-marketing or marketing, and trying to get information out. It's not really the

FDA's responsibility, but I think the single greatest unmet need is to convey information about the problem to various populations. I'm just stating the obvious.

## Adjournment

Dr. Can Der Pol: Any other comments? I'm not seeing any hands raised. I'd like to thank the panel, the FDA, and the open public hearing speakers for their contributions to today's panel meeting. This meeting of the microbiology devices panel is now adjourned and we're only two minutes late.