Good afternoon. I'm Commander Ibad Khan and I'm representing the Clinician Outreach and Communication Activity, COCA, with the Emergency Risk Communication Branch at the Centers for Disease Control and Prevention. I would like to welcome you to today's COCA Call, Additional mRNA COVID-19 Vaccines for Moderately to Severely Immunocompromised People. All participants joining us today are in listen only mode. Continuing Education is not offered for this COCA Call.

After this presentation, there will be a Q and A session. You may submit questions at any time during today's presentation. To ask a question using Zoom, click the Q and A button at the bottom of your screen then type your question in the Q and A box. Please note that today's COCA call is about additional doses in moderately to severely immunocompromised people. Questions regarding boosters will not be addressed. Questions should focus on additional doses for immunocompromised people only.

A video recording of this COCA Call will be posted on COCA's web page and available to view on demand a few hours after the call ends. If you're a patient, please refer your questions to your healthcare provider. For those who may have media questions, please contact CDC Media Relations at 404-639-3286 or send an email to media@cdc.gov.

Due to inclement weather in the metro Atlanta area, we may experience technical difficulties. Please be patient if we are disconnected. Please note that COCA Calls are archived at the COCA web page at emergency.cdc.gov/COCA shortly after webinars. If we are unable to reconnect, we will do our best to reschedule. Thank you for your patience.

I would now like to welcome our presenters for today's COCA Call. We are pleased to have with us Dr. Kathleen Dooling, who is the ACIP Workgroup Team Lead on the Vaccine Task force as part of CDC's COVID-19 Response. Dr. Neela Goswami, who's the Clinical Guidelines Team Lead on the Vaccine Task Force as part of CDC's COVID-19 Response. Captain Tom Shimabukuro, who's part of CDC's COVID-19 Response Vaccine Taskforce. And Ms. Katherine Shealy, who's the Vaccine Clinical Inquiry Management Team Lead on the Vaccine Task Force as part of CDC's COVID-19 Response.

It is my pleasure to now turn it over to Dr. Dooling. Dr. Dooling, please proceed.

Thank you very much, Commander Khan. So as stated, my name is Dr. Kathleen Dooling. I'm a co-lead of the ACIP COVID-19 Team Vaccine Workgroup and today I'll be focusing on the discussion that led to the new recommendation for an additional dose of mRNA COVID-19 vaccine for immunocompromised people. Next slide.

Before getting into the evidence that supported the recommendation for an additional dose of mRNA in immunocompromised people, I'd like to reference the regulatory allowance upon which the ACIP proceeded. On August 12th, the FDA, or Food and Drug Administration, authorized a conditional dose for certain immunocompromised individuals. It should be noted that the amendment only applies to immunocompromised people. Other fully vaccinated individuals do not need an additional dose right now. The amendment applies to Pfizer-

BioNTech COVID-19 vaccine, ages 12 and older, and Moderna COVID-19 vaccine, ages 18 and older.

Due to insufficient data, the Emergency Use Authorization amendment for the additional dose does not apply to Janssen COVID-19 vaccine or to individuals who received a Janssen COVID-19 vaccine as their primary series. CDC and FDA are actively engaged to ensure that immunocompromised recipients of Janssen COVID-19 vaccine have optimal vaccine protection. Next slide.

At the evidence to recommend patient framework is the framework ACIP has adopted in order to systematically and transparently assess scientific evidence for vaccine recommendations. I'll now highlight two of those domains that were considered; first, the public health problem and then the potential benefits and harms associated with an additional dose. Next slide, please.

So, the conversation that will ensue that I'll lay out here, the discussion will be focused on the immunocompromised population. The list that follows here outlines who this is. I will not go over this in detail because Dr. Neela Goswami in the next presentation will do so in detail. Next slide.

The intervention that we're focused on is an additional dose of mRNA COVID-19 vaccine, an additional dose of Pfizer vaccine or Moderna vaccine after an initial two-dose primary series of an mRNA vaccine in immunocompromised people. Consistent with the previously existing emergency use authorization or EUA, age limits that's 12 and older for Pfizer, and 18 and older form a Moderna. Attempts should be made to match the additional dose type to mRNA primary series that was received. However, if that's not feasible, a heterologous additional dose is permitted.

The additional dose of mRNA COVID-19 vaccine should be administered at least 28 days after completion of the primary mRNA series. Next slide.

First, a description of the public health problem. Next slide.

COVID-19 cases have been increasing since early July. As of August 9th, there have been over 35 million cases reported to CDC, with the most recent seven-day average as of the end of last week of over 100,000 cases per day. Next slide.

According to one -- in terms of immunocompromised people and SARS-CoV-2 infection according to one national survey, immunocompromised people comprise approximately 2.7% of the US population. That's about 7 million adults.

Immunocompromised people are more likely to get severely ill from COVID-19. They are at higher risk for prolonged SARS-CoV-2 infection and shedding, and viral evolution during their infection and treatment phase, certainly for hospitalized patients. They have a lower antibody neutralization titers to SARS-CoV-2 variants compared to non-immunocompromised people, and they're more likely to transmit SARS-CoV-2 to their household contacts. Next slide.

In terms of immunocompromised people, and breakthrough infections, so those who are vaccinated and get an infection following their vaccination, in small studies of hospitalized breakthrough cases, 40 to 44% were found to be immunocompromised.

Several observational studies have shown lower vaccine effectiveness with VE estimates ranging from 59 to 72% among immunocompromised, where their non-immunocompromised comparators in those studies ranged from 90 to 94% vaccine effectiveness after a second dose. Next slide.

So, this figure shows the percent antibody response after two mRNA vaccine doses by different types of immunocompromising conditions. Studies among people with cancer are shown in blue, with hematologic cancers shown in darker blue, the proportion of an antibody response range from 45% and 95%, with lower response seen among people with hematologic cancers. Studies of people on hemodialysis are shown in green and ranged from 71 to 98% response following two doses.

Studies of people with solid organ transplants had the largest deficits in antibody response ranging from 0% to 79%. Studies of people treated for autoimmune or inflammatory disorders was quite broad and ranged from 40 to 94% response to an mRNA primary series. By comparison, healthy controls, where they were included in studies, ranged from 95% to 100% response. Almost all studies that assess antibody response after one -- after the first dose, separate from the second dose, demonstrated less robust response after only one dose. Next slide.

Moving on to the benefits and the harms of an additional dose. Next slide.

Last week the first randomized control trial of third dose of mRNA vaccine in transplant recipients was published. This study randomized 120 vaccinated people to either a third dose of Moderna vaccine or to a placebo dose. The primary outcome was a receptor binding domain antibody level of at least 100 units per mil at one month post dose three.

As you can see from the figures, panels A and B, antibodies for higher in recipients of the third dose of Modern vaccine with 55% of the vaccine group achieving the endpoint versus only 18% in the placebo group. And knowing, of course, that the placebo group had already received their two dose primary series, encouraging improvements in immune response were also observed for neutralizing antibodies and T cell function in the study. Next slide, please.

So, this slide shows five observational studies, two in recipients of solid organ transplants and three of patients on hemodialysis. This -- these studies looked at the seropositivity after a second dose of mRNA, which ranged from 20% to 89%, then a third dose of mRNA is administered. Among those who had no detectable antibody response to the initial mRNA vaccine primary series, 33 to 50% developed an antibody response following the third dose. Next slide.

To go into more detail about some of those studies in the Kamar et al. study in solid organ transplant patients, the proportion of the group who were seropositive increased after each dose, 40% post dose two and then 68% one month post dose three. In addition, as you can see in panel B, the average antibody titer increased after each dose.

So, even those who were seropositive experienced increases in their antibody levels. In this study of 99 transplant patients, no serious adverse events reported after administration of a third dose, and no acute rejection episodes occurred. Next slide, please.

Here we highlight the findings of Epsi et al. study, which showed that the reactogenicity of a third mRNA vaccine dose in a cohort of patients on hemodialysis. No patients develop side effects that required hospitalization, and symptoms reported were consistent with previous doses, and the intensity of the symptoms was mostly mild and yellow or moderate in orange. Next slide.

So, to summarize, the available evidence regarding possible benefits, emerging experimental and observational data in adults suggests that an additional mRNA COVID-19 vaccine dose in immunocompromised people enhances antibody response and increases the proportion who respond to the vaccine. No efficacy or effectiveness studies of COVID-19 prevention following a third dose were available for evaluation. With respect to potential harms in small studies of an additional dose of mRNA vaccine, no serious adverse events were observed, and the reactogenicity of the third dose was similar to that of prior doses.

It should be noted that mRNA COVID-19 vaccines are associated with rare but serious adverse events, including anaphylaxis as well as myocarditis and pericarditis in young adults. The impact of immunocompromising conditions on these rare events is unknown. There are no safety studies of an additional mRNA dose in immunocompromised adolescents. Next slide.

In summary, next.

This slide highlights all of the work group judgments for each of the evidence to recommendation domains, not all of which are covered in this presentation, but to summarize, the work group concluded that COVID-19 in immunocompromised people is an important public health problem. They anticipated that the desirable effects from an additional dose of mRNA are large and that the undesirable effects are expected to be minimal, thus favoring the intervention. The certainty of the evidence was not formally debated. The work group felt the target population valued the intervention and that the intervention was acceptable to stakeholders, feasible to implement, and a reasonable use of resources. The work group thought an additional dose of mRNA vaccine for immunocompromised people would probably not impact health equity. Next slide.

Overall, most work group members felt that the desirable consequences clearly outweighed any undesirable consequences in most settings. Next slide.

In addition, after reviewing the totality of information presented in evidence to recommendations framework, the work group discussed the type of recommendation to propose to the ACIP, the options being we do not recommend the intervention, we recommend intervention for individuals based on shared clinical decision making or we recommend intervention. Most work group members supported we recommend the intervention. Next slide.

And last Friday, the ACIP voted unanimously in favor of an additional dose of Pfizer BioNTech COVID-19 vaccine for people who've already received their primary series 12 and older or

Moderna COVID-19 vaccine for people who have already received the primary series 18 and older in immunocompromised people under the FDA's emergency use authorization. Next slide.

I'd like to acknowledge all the people who helped make this presentation possible, and I would like to turn the presentation over to my colleague, Dr. Neela Goswami.

Thank you, Dr. Dooling. My name is Neela Goswami and I'm currently serving as clinical guidelines team for the CDC COVID-19 Response Vaccine Task Force, and today I'll be sharing with you clinical considerations for you seven additional mRNA COVID-19 vaccine dose following a COVID-19 primary mRNA series for immunocompromised people. Next slide.

Before we launch into the discussion about the additional vaccine doses, I'd like to outline the process for the consideration of an additional dose of COVID-19 vaccine in immunocompromised people, which is being discussed today.

The first step is of course data review to assess the safety, immunogenicity, and implementation features related to use of an additional dose of COVID-19 vaccine in this population, which Dr. Dooling just presented. Then there's regulatory allowance by FDA. FDA has issued at this point an emergency use authorization, or EUA amendment, for both Pfizer and Moderna COVID-19 vaccines that allows ACIP to make recommendations under an EUA. Once there's regulatory allowance, CDC or ACIP can have a clinical update with clinical considerations or recommendations for use. This presentation will review the updated interim clinical considerations for use of an additional dose of mRNA COVID-19 vaccine in immunocompromised people. Next slide.

To continue making sure we're all on the same page, it's important to keep in mind that there are two distinct potential ways an additional vaccine dose can be used. The first way an additional dose can be used is after but in association with a primary vaccine series. Administration of this additional dose is needed when the initial immune response following a primary vaccine series is likely to be insufficient.

Now, contrast that with using an additional dose as a booster dose. This is a dose of vaccine administered when the initial sufficient immune response to a primary vaccine series is likely to have waned over time. We do want to clarify right away that the need for and timing of a COVID-19 booster dose has not been established and the focus of today's conversation is on the first category. Next slide. Next slide.

The focus of these clinical considerations then are essentially as follows. For people with moderate to severe immune compromised due to a medical condition or immunosuppressive treatment, the potential to increase immune response coupled with an acceptable safety profile support consideration for an additional dose of mRNA COVID-19 vaccine following an initial two-dose primary mRNA COVID-19 vaccine series in this population. Next slide.

Here are the categories of moderately and severely immunocompromised people we list in our considerations document. As was alluded to in Dr. Dooling's talk, this list was developed from a combination of resources, including the ACIP general best practice guidelines for immunization,

CDC, Yellow Book, and the 2013 IDSA clinical practice guideline for vaccination of immunocompromised host.

Candidates for the additional mRNA vaccine dose following or associated with their primary COVID-19 vaccine series, therefore include patients undergoing active treatment for solid tumor and hematologic malignancies; patients who received a solid organ transplant and are taking immunosuppressive therapy; patients who received chimeric antigen receptor T-cell or hematopoietic stem cells transplant within two years of transplantation or currently taking immunosuppression therapy; moderate or severe primary immunodeficiency; advanced or untreated HIV infection, defined as people with CD4 cell count less than 200, history of an AIDS-defining illness without immune reconstitution or clinical manifestations of symptomatic HIV; active treatment with high dose care to corticosteroids, that is 20 milligrams or more of prednisone or equivalent per day; alkylating agents, antimetabolites, transplant related immunosuppressive drugs, cancer chemotherapeutic agents classified as severely immunosuppressive, tumor necrosis factor blockers, and other biologic agents that are immunosuppressive or immunomodulatory.

I will pause here for a moment to highlight some of the conditions you don't see. You don't see as an independent category here all comers with diabetes, all comers who are pregnant, all people over 65, all dialysis patients, and many more groups. At this point, we don't have evidence to suggest that these groups do not mount a sufficient response to the primary vaccine series.

It's important to recognize the current guidance is meant for patients who have a greater level of immune deficit. So certainly, if you have a patient one of these other categories, who has additional characteristics that place him or her at moderate to severe immune compromised, that patient might be a candidate for a third dose to supplement their primary vaccine series. At this point, a third additional dose meant to supplement a primary vaccine series response is not being recommended for all people, because the clinical benefit, that is the added protection from infection, hospitalization, and death is not known. Next slide.

Some additional considerations in line with general vaccine principles, when feasible that mRNA COVID-19 vaccination primary series, as well as the additional dose, should be administered before initiation of chemotherapy, before treatment with other immunosuppressive drugs, and before radiation.

But we are of course, cognizant that, especially in this population are unique circumstances for some individuals, such as ablative therapy prior to stem cell transplant and other very specific scenarios. So, a patient's clinical team is best situated to determine the degree of immune compromised and appropriate timing of vaccination. Both the nature of immunosuppression and optimization of the patient's medical condition and response to vaccine should be considered. Factors to consider and assessing the general level of new competence of patients include disease severity, duration, clinical stability, complications, comorbidities, and any potentially immune suppressing treatment. We do very much emphasize in our recommendations that utility of serologic testing or cellular immune testing to assess immune response to vaccination and guide

clinical care, that is, such in determining the need for an additional dose has not been established and is not recommended at this time. Next slide.

Implementation considerations that needs to be thought about. The additional dose should be the same mRNA vaccine as the primary series. An alternate mRNA product can be used if the primary series product is not available. Until more data are available, the additional dose should be administered at least 28 days after completion of the initial primary series.

Currently, there are not data to support the use of an additional mRNA COVID-19 vaccine dose after a primary Janssen COVID-19 vaccine in immunocompromised people. FDA and CDC are actively working to provide guidance on this very important issue. These clinical considerations for use of an additional dose of an mRNA COVID-19 vaccine apply only to people who are moderately or severely immunocompromised. Next slide.

Now, I'll finish with the importance of infection prevention measures. Unfortunately, we can't be confident that the third dose is the magic bullet to definitively give our moderately to severely immunocompromised patients sufficient response to their primary vaccine series. So, it continues to be very important to provide these people with additional layers of protection.

Immunocompromised people, including those who receive an additional mRNA dose, should be counseled about the potential reduced immune response to COVID-19 vaccination and need to follow prevention measures. That is wearing a mask, which as a reminder is not unique to immunocompromised persons. Of course, CDC is currently recommending everyone wear a mask as the best protection, particularly amists the Delta variant. Stay six feet apart from others they don't live with, avoid crowds and poorly ventilated indoor spaces until advised otherwise by their healthcare provider, and close contacts of immunocompromised people should be strongly encouraged to be vaccinated against COVID-19 as an even further layer of protection. Next slide.

There are updates to CDC clinical resources regarding the administration of the additional dose associated with the primary vaccine series for immunocompromised patients that you'll be able to find at this web link. Next slide.

With that, I'd like to acknowledge colleagues on the COVID-19 Response Vaccine Task Force. And from here, I'll turn the mic over to Dr. Tom Shimabukuro. Thank you.

Thanks, and good afternoon. I'm going to be providing a brief update on CDC vaccine safety monitoring systems.

It's a general update on what systems we have in place to monitor vaccine safety, and I'm going to specifically focus on a couple systems that healthcare providers and patients and parents or caregivers can participate in. Next slide. Next slide.

I just want to remind you of some of the timelines and some key recent recommendations. So, back in May, ACIP recommended the use of the Pfizer BioNTech COVID-19 vaccine and adolescents aged 12 to 15 years.

There is the capability -- and one of our systems which I'll get into later called V-Safe, that allows parents to register children on their behalf and to participate in the V-Safe program. And then, more recently, there's the recommendations for the additional dose in immunocompromised people, and this essentially involves a third dose which we have either -- that capability was existed in our systems already, or we implemented the capability to monitor third dose in our systems. Next slide.

So, I'm with the Immunization Safety Office at CDC. That's the safety that that's the office that does postauthorization or postlicensure in the case of a licensed product, safety monitoring of vaccines.

So. that's when the vaccine is out there and being used in the community. The preauthorization or prelicensure work is the responsibility of the FDA. So, we basically have three core programs, the Vaccine Adverse Event Reporting System, or VAERS, the Clinical Immunization Safety Assessment Project, or CISA, and the Vaccine Safety Datalink, or VSD, plus a new system called V-Safe. Next slide.

I'm going to start off with VAERS, the system with which probably most of you are familiar with. VAERS is a long-standing spontaneous reporting or passive surveillance system. It's a national system that's co-managed by CDC and FDA, and as a spontaneous reporting system, we depend on individuals to send reports to the VAERS system. Next slide.

So, anyone can report to VAERS, healthcare providers, patients, parents, caregivers, other members of the public, and then vaccine manufacturers are required to report adverse events that come to their attention to VAERS. And VAERS accepts all reports from everyone regardless of the plausibility of the vaccine causing the event or the clinical seriousness of the event. Basically, a report to VAERS gets into the system and gets analyzed, again, regardless of seriousness, or regardless of whether we or anyone else thinks the vaccine caused the event. The key strengths of VAERS is because it is a national system and essentially anyone who gets a vaccine is eligible to participate either directly or indirectly, we can rapidly detect potential safety problems in VAERS and we can detect rare adverse events that might not have been detected in the clinical trials which are relatively small.

The key limitations to VAERS are those of passive surveillance or spontaneous reporting or passive surveillance in general. There can be inconsistent quality and completeness of information in the reports.

There can be reporting biases such as underreporting, stimulated reporting, which is often due to media attention or public awareness of adverse events, and other types of reporting biases. And because of the limitations, generally we cannot determine cause and effect from VAERS data alone. There are some limited exceptions to that. But generally, we cannot determine if a vaccine caused an adverse event just based on the VAERS reports. Next slide.

So, this is a slide that just shows how to report an adverse event to VAERS. It's a fairly simple process. You can go to the website at vaers.hhs.gov. If you Google VAERS, that'll probably be the first thing that comes up or if it does take you to a CDC website, you can easily navigate to

the VAERS website. Then right on the landing page, there is that box up there that says "report an adverse event". You simply click on that link and it takes you to the portal to report an adverse event. There's two ways to report. One is using it using an online -- basically an online questionnaire or web survey, which is an HTML-type survey where you can directly enter in information.

The other way is to download a fillable PDF, which you then upload to the portal. If you have questions on how to report, there's a 1-800 number, there's also an email, and there's video instructions there on YouTube. The VAERS 1-800 number and the info email is basically to facilitate or assist in reporting. If there if there are specific questions about vaccine safety or adverse events, you can contact CDC or the VAERS program will refer you to CDC for those types of questions. Next slide.

This is a screenshot of one of the sections of online reporting, of the reporting form on VAERS, and so if you go in and you report, it may not look exactly like this, but it'll probably look pretty similar to this. And I'm just highlighting the dose number and series. So, for the third dose of COVID vaccines in individuals where it's recommended, you would simply go in there and enter the dose number and series, which would be three if you're using the PDF form. It's a drop down, you simply click on the drop down and select dose number three. And I mean, obviously, if it's the first dose, it's one, second dose, third dose, three. If there's -- in the future, if there's a variant booster or some other dose, you would simply add the dose number there. Next slide.

So, now I'm going to talk about the V-Safe after vaccination health checker, which is a smartphone based active safety monitoring program. Next slide.

So, V-safe, again, it's a CDC smartphone-based monitoring program that was developed for COVID-19 vaccine safety monitoring. It uses text messaging and web surveys, so the text messages have links embedded in them to check in with vaccine recipients after vaccination. It's a voluntary self-reporting system.

So, patients have to register after they get vaccinated or at the time of vaccination, and that kicks off the text messaging process. Participants can report side effects or health problems after vaccination, and reports are accepted after dose one, two, or three. That is built into the system, and you all basically specify that when you register or when you -- after you've registered you and you get a second dose or a third dose you go in and you basically will select your dose.

It also includes active telephone follow up by CDC for reports of a medically attended health impact event and identifies women who are pregnant when vaccinated or become pregnant shortly after vaccination. Next slide.

So, V-safe conducts these electronic health check-ins with the recipients. It's daily for the first week post vaccination, then it's weekly thereafter until six weeks, and then there are additional health checks at three, six and 12 months and when you get a second dose, this timeline resets and then for individuals getting a third dose, it resets again. So basically, we follow people 12 months after their last dose, and enrollment in the V-safe Pregnancy Registry occurs through a separate process. Next slide.

So, this is a schematic of how the process works. You see the vaccine recipients up there in the right hand corner, and again, participants need to voluntarily self-enroll at the time of vaccination, and this kicks off this text messaging process that I just described. And then you see a basically a schematic there of how the surveys look on a smartphone. If someone does report a clinically important health impact, and that is defined for the purpose of follow up as they received medical care, that information is transmitted to a call center, and then the V-safe call center reaches out conducts active telephone follow up and takes the VAERS report if appropriate. And again, there is a separate pregnancy registry team that runs the V-safe pregnancy registry. Next slide.

I just want to mention now another one of our programs, the Clinical Immunization Safety Assessment Project, and healthcare providers can participate in this program, mainly through requesting clinical case consults for complex vaccine adverse events in their individual patients. CISA also does clinical research. Next slide.

Our Vaccine Safety Datalink is an electronic health record safety monitoring system and research program. There really isn't any patient or provider active participation. This is basically -- this information is gathered through normal -- through the provision of health care just in general and, and EHR and administrative data collection. Next slide.

So as far as your role, and this is really separated into the general public, and for healthcare providers, I will say that healthcare providers can be patients as well.

So, in a sense, you're also the general public, and we encourage your participation. That includes participating in V-safe as a patient when you get vaccinated, and also reporting adverse events to VAERS. And then for healthcare providers specifically with respect to their patients, we encourage -- we ask that you encourage patients to participate and V-safe in the 15 minute waiting period after vaccination is a great time for patients to enroll in V-safe and kick off the process. And we also ask that you continue to report clinically important adverse events to VAERS. We really do value healthcare provider reports to VAERS, because it's important to us when a healthcare provider has gone through the process of determining that they think that an adverse event might be associated with a vaccine and takes the time to report that event to VAERS and to document what happened. And for certain events of special interest or serious adverse events, we may reach out to you and request medical records, and that is permitted under HIPAA. That is also part of the participation process in VAERS. Next slide. Next slide.

And with that, I will turn it over to my colleague, Katherine Shealy, for the next presentation.

Thank you very much, Tom, and the next slide.

So, hello, everybody. My name is Katherine Shelley, and I wanted to share with you just a tiny bit of information about one of the variety of ways that we make sure that clinicians and other partners of ours are able to get their complicated questions answered effectively and efficiently and with the information that they need. So, by way of introduction, management of complex response related inquiries is a standard element of CDC's Incident Management System, which is the system that CDC relies on when activated in response to any type of public health

emergency. And the structure that we have in place today is one that we have refined and improved over the past almost 10 years now. And it works. It's been quite helpful.

So, on December 11th of this past year, CDC stood up the Vaccine Clinical Inquiries Management Team, or VCIMT, in anticipation of the large number of complex COVID-19 vaccine questions from clinical and public health partners that we expected along with the rollout of COVID-19 vaccinations. As a team, VCIMT is responsible for both systematically addressing complex COVID-19 vaccine inquiries and also for effectively coordinating the escalation and management of these inquiries across all the task forces and units of CDC's entire COVID-19 response structure. The majority of the inquiries that VCIMT manages were escalated to us from CDC's national contact center known as CDC-INFO, and this is probably the most important part of this slide.

The nice thing is you can Google CDC-INFO and you will get this information. So, many people are already familiar with them. They have now managed 1.3 million inquiries to CDC about COVID-19 alone, on top of everything else that they manage. So, if you're not, you can join the party.

So, CDC-INFO is staffed with agents that really become experts in answering all kinds of questions related to CDC's work overall, and in COVID-19 in particular. They have a whole variety of tools that they can use to get to the information that people need quickly, and some templates and other kinds of tools that they use to make sure that questions that they need assistance with can go to the right place. So, we use an ABC mnemonic to help the CDC info agents and also other partners remember what types of inquiries they can send our way and we will make sure they get addressed, and that is inquiries that are about COVID-19 vaccine. They're beyond the scope of what the CC info agents are able to address on their own using the tools they have available to them and they are clinical in nature. As of today, BCIMT clinicians and inquiry management specialists have addressed more than 8000, we actually crossed 8000 this morning, kind of exciting for us, COVID-19 vaccine inquiries.

The clinicians on our team, we address these inquiries in a variety of ways. We reply directly to them by email, our team works only by email, to the inquiries that we receive from our clinical and public health partners. And then we also assist others across the response in addressing questions and inquiries they receive, both as internal and external facing technical assistance. Also, we work very closely with others across CDC and beyond to ensure that urgent requests for consultation on safety, adverse events, and other unique situations are adequately addressed. So, for example, we partner with IDSA, Infectious Disease Society of America, on inquiries from healthcare providers that are needing to talk through a complex decisions about their patient's unique situation related to COVID-19 vaccine.

So, through this partnership, we have a direct line to connect providers with IDSA clinician volunteers who can do peer to peer calls to really talk through these situations and figure out the best course forward. And another really important aspect of our team is identifying and addressing emerging and recurring issues that we are able to see in real time in the tracking that we do have our inquiries, so that we can feed that insight directly back into CDC's overall response activities and plans. And you know, a lot of these pieces you have seen. So, the one of

the best ways that we can get a good sense of what our clinical partners in particular are really needing help with clarifying or tools come to us through these inquiries. And they're incredibly helpful in making sure that we are as responsive as we can be in helping navigate this pandemic.

So, I wanted to make sure you knew that was available to you, and if you feel like you have questions that you need our assistance, you can contact CDC-INFO and they will get it to us as quickly as possible. And that's all and I will now pass back to Ibad. Thank you.

Thank you so much. Presenters, thank you for providing our audience with this timely information. We will now go into our Q and A session. Please remember to ask question using Zoom, click the Q and A button at the bottom of your screen, then type your question. Please note we receive many more questions than we can answer in the time during our webinars, and as a reminder questions should be about additional vaccine doses in moderately to severely immunocompromised people. We will not have time to answer questions other than that.

And as a reminder, again, due to inclement weather in the metro Atlanta area, you may experience technical difficulties. Please be patient if you're disconnected. Please note that COCA calls are archived at the COCA webpage at emergency.CDC.gov/coca shortly after the webinar, and if you are unable to reconnect, you will be able to find the archived video there shortly.

So, for our Q and A session for our presenters, one of our question inquires, what is the minimum amount of time we should wait for the additional dose after completing the full two-dose cycle? Does it depend on whether the third dose is going to be Moderna or Pfizer?

Hi, this is Neela Goswami. I'll take that question. At this point, we're recommending that the third dose occur at least 14 days after completion of the primary vaccine series, the first two doses. We recognize that that many folks have gotten their primary vaccine series several months ago now. So, it is understandable that that third dose would occur at a later time frame.

Thank you very much.

This is--.

Yes, please--.

Dr. Kathleen Dooling. I'd just like to clarify that the recommendation is for a minimal interval of 28 days following the second dose of the primary series, and that the exact timing -- we encourage it to be made with the patient's clinical care team to optimize both the likelihood of responding to a vaccine for a person who's immunocompromised, as well as optimizing the treatment that they're on.

Thank you very much for the clarification. Our next question asks, based on the medical condition of these patients, is the expectation that these patients should receive their additional dosed at a healthcare provider or can they get it anywhere the vaccines are available?

Hi, this is Dr. Kathleen Dooling. I'll take that question. A patient can get this additional dose anywhere vaccines are available, and I notice the number of questions in the chat asking specifically what type of -- is there any proof of immunocompromised that's required? What type of screening my pharmacy or vaccination location undertake? And those are great questions and I'd like to make it very clear that there should be no documentation in terms of proof of immunocompromised. There does not need to be a physician's prescription validating the immunocompromised status.

This will be self-attestation, where necessary, but in all cases, we encourage immunocompromised people to consult with their clinical care team about getting the third dose and the timing of the third dose.

Thank you very much. That is very helpful. We also have questions regarding VAERS and V-Safe. One of our question asks that does a local public health agency who initiated a VAERS form have the ability to edit or add more information later if needed?

This is Tom. I don't think you can go in and edit the original VAERS form, but you can certainly add to it, and that's mostly done by -- if there's additional, like medical records or additional documentation that the reporter feels would be important for the report. You do have to have the record, the ID number for the additional report, but there are ways to go in and add supplemental materials and I'm not familiar with the specifics of that. But certainly, the VAERS customer service folks could help with that.

Thank you very much. And a V-safe question along the same lines that we received is is there potential to use the V-safe system for the patient, that is, to receive either a reminder or recommendation to get their additional dose if they are a moderately to severely immunocompromised individual?

So, there are reminders for the standard series. There's like a reminder for second dose. I think the issue that complicates the third dose for immunocompromised persons is we don't know who those -- we don't know who those people are. There's really not a way in V-safe for them to identify who's immunocompromised and it's even kind of challenging just to define immunocompromised in general. So, I guess the answer for the third dose is, no, there's not really a mechanism because we don't really have good visibility on immunocompromised vaccinated persons who would need to come in just based on V-safe data alone.

Thank you very much for that. We have received multiple questions about specific medical conditions whether it's sarcoidosis, bone marrow transplant, asplenia, chronic kidney disease, etcetera. So, for the benefit of time to try and consolidate these, is there a guidance or a resource that you would direct our audience to that would list these medical conditions and help classify moderate to severe immunocompromised situation as per the recommendation from CDC and ACIP for additional doses of vaccination?

Hi, this is Neela Goswami. Yes, I'm seeing many of those questions in the chat. At this point, the definitions of our moderately and severely immunocompromised people are very much based in three resources, the ACIP General Best Practice Guideline for Immunization, the 2020 CDC

Yellow Book, and the 2013 IDSA Clinical Practice Guideline for Vaccination of the Immunocompromised Host. We do want to emphasize that particularly in this population, patients can be quite complex and nuanced, and it is very reasonable for an experienced physician to exercise a clinical judgment around some of those nuanced definitions.

Thank you very much. Another question we've seen is if a patient completes their first course of two doses of one mRNA vaccine product, do they have to stick to the same brand for their third additional dose or can they switch to another mRNA vaccine product?

Hi, this is Dr. Kathleen Dooling. I'll take that one. So, our original recommendation was to use the same vaccine for the first and second dose for all two-dose vaccines. Once again, our recommendation is to have an additional dose which is the same as the primary series vaccine type. But we recognize that that's not always going to be possible given vaccine availability. So, where it is not feasible to have an additional dose which is the same as the primary series, you can have the other mRNA vaccine as that third dose.

Thank you for that clarification. Very helpful. Another question we have is when discussing this new recommendation for additional doses of COVID-19 vaccines, are we to understand that this additional dose is specifically being recommended for moderately to severely immunocompromised patients 18 years and older or would the original UAE authorization, say for example, the Pfizer vaccine being authorized for 12 and older apply?

Hi, this is Dr. Kathleen Dooling again. So, yes, the ages are consistent with the emergency use authorization, so immunocompromised people who received Pfizer, who are 12 and older can get an additional dose. For Moderna, that is 18 and older.

Thank you very much. We have also seen a few questions asking to please reiterate your criteria for determination associated with HIV patients. If you don't mind, please, recapping that, that would be appreciated.

Absolutely. This is Dr. Neela Goswami, and right now this definition stems from, again, our immunocompromised definitions in the Yellow Book, including advanced or untreated HIV infection, which is people with CD4 cell count less than 200, history of an AIDS defining illness without immune reconstitution, or clinical manifestations of symptomatic HIV. As with other categories in these kinds of populations, we cannot emphasize enough how much we defer to the treating clinician at bedside who may have additional insight and perspective as to other aspects of a person's comorbidities in addition to HIV infection that might provide some nuance to application of that definition.

Thank you very much. Another question we have is can you please explain that if a fully vaccinated moderately to severely immunocompromised patient receives monoclonal antibodies, do they then need to wait 90 days to get the additional dose of COVID-19 mRNA vaccine?

Hi, this is Neela Goswami. I will provide a little clarity there. Currently, we don't have data on safety and efficacy of COVID-19 vaccines in people who received monoclonal antibodies or convalescent plasma as part of their COVID-19 treatment. Based on the estimated half-life of

such therapies and evidence suggesting that reinfection is uncommon within the 90 days after initial infection, we're recommending the vaccination be deferred for at least 90 days after receiving monoclonal antibodies or convalescent plasma. This is a precautionary measure until additional information becomes available to avoid potential interference of the antibody therapy with vaccine-induced immune response. And we are continually evaluating whether any of our guidance needs to change based on data that comes in.

Thank you for that. And in the remaining time we have, we'll take one last question. We talked about medical conditions. So, going back into the slides under the list of biologic agents, would you consider that to include medications for conditions like rheumatoid arthritis, ulcerative colitis, Crohn's disease, etcetera? And if so, you listed a few doses, for example, for prednisone; would duration also be a criteria for how long a person has been taking this medication?

Yes. So, again, recognizing that this CDC guidance and formed by ACIP recommendations is a starting point, the framework we very much used are bound in general vaccine principles. So, based on that we incorporate things such as the prednisone greater than 20 milligram dose for at least two or more weeks. And there are other kind of nuances around the different medications laid out in some of these other resources. But again, recognizing that individual patients may go on and off immunosuppressive therapy, that there may be additional medications or therapeutics on board, we do not want to be a replacement for that clinical decision maker at bedside.

Thank you very much. I really appreciate it. This concludes our Q and A session. I want to thank everyone for joining us today, with a special thanks to our presenters. As I mentioned earlier, today's COCA call will be available on demand a few hours after this live webinar.

You can find the video recording of today's webinar at emergency.cdc.gov/coca. Again, that's emergency.cdc.gov/coca. Please continue to visit emergency.cdc.gov/coca to get more details about upcoming COCA Calls as we intend to host more COCA Calls to keep you informed of the latest guidance and updates and COVID-19. Please share these call announcements with your clinical colleagues.

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