

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'd like to welcome you to today's COCA call, Recommendations for bivalent COVID-19 booster doses in people ages 12 years and older. All participants joining us today are in listen only mode. Free continuing education is offered for this webinar.

Instructions on how to earn the continuing education will be provided at the end of the call. In compliance with continuing education requirements, all planners and presenters must disclose all financial relationships in any amount with ineligible companies over the previous 24 months, as well as any use of unlabeled product or products under investigational use. CDC, our planners, and presenters, wish to disclose they have no financial relationships with ineligible companies whose primary business is producing, marketing, selling, reselling, or distributing healthcare products used by or on patients. Content will not include any discussion of the unlabeled use of the product or product under investigational use with the exception of Dr. Elisha Hall, Commander Sara Oliver, and Dr.

Evelyn Twentyman's discussion of vaccine use under emergency use authorization or emergency use instruction. CDC did not accept financial or in-kind support from ineligible companies for this continuing education activity. At the conclusion of this session, participants will be able to accomplish the following. Discuss new recommendations for bivalent COVID-19 vaccines for people ages 12 years and older, including those who are moderately or severely immunocompromised. List key points for healthcare providers to use when discussing bivalent COVID-19 vaccines with patients, and describe where to find online resources for clinicians about bivalent COVID-19 vaccinations.

After the 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 we often receive many more questions that we can answer during our live webinars. If you're a patient, please refer your questions to your healthcare provider.

If you're a member of the media, please contact CDC Media Relations at 404-639-3286 or send an email to [media@cdc.gov](mailto:media@cdc.gov). We have introduced self-knowledge checks through the presentation. We hope you enjoy these opportunities to assess your understanding of today's session. Please do not type your answers into the Q and A box, as this may disrupt the Q and A portion at the end of the session.

I would now like to welcome our presenters for today's COCA call. We're pleased to have with us Commander Sara Oliver who is the lead for the COVID-19 coordinating unit for CDC's COVID-19 response. Dr. Elisha Hall, who's the lead for the Clinical Guidelines Vaccine Policy Unit for CDC's COVID-19 response. Dr.

Evelyn Twentyman, the COVID-19 Vaccine Policy Unit Lead for CDC's COVID-19 response, and Dr. Anne Hause, who is the V Safe Team Lead for CDC's National Center for Emerging and

Zoonotic Infectious Diseases. It is now my pleasure to turn it over to Commander Oliver. Commander Oliver, please proceed.

Thanks so much. I'm happy to walk through some of the information that was discussed at the ACIP meeting for September 1st. Next slide. So, this is our evidence to recommendation framework. We've used this to walk through the data to inform the recommendations we had.

We had a full presentation of the data and discussions, again, at this all day ACIP meeting September 1st. We'll only be able to provide a summary of that on this call today. So, for additional questions, the slides, the recording of the meeting are all available on the ACIP website. But I do want to highlight the equity domain. And something that we did differently with this ACIP meeting.

Throughout the COVID pandemic and COVID vaccine recommendations, it's become clear that considerations of equity are integral to every aspect of production, study, authorization, and recommendations for the COVID-19 vaccines. The need for systematic, reliable, action-oriented review of evidence towards advancing equity is clear. Its structural problems require structural solutions. So, for the data presented at the ACIP meeting this last time, and then we've committed to doing this moving forward. We're adjusting the structure of the framework to allow for a meaningful change and a full presentation of data around equity.

Next slide. So, overall, to get into the discussions of the bivalent vaccines, the question asked at ACIP was if ACIP supports the use of an updated or bivalent COVID-19 vaccine booster dose for individuals and age groups that are currently recommended to receive a COVID-19 vaccine booster. So, currently, that is ages five and over. On the left, you can see the previous recommendations we had where the focus was really counting the dose numbers. Those five through 49 years were recommended for three doses.

Those 50 and over were recommended for four doses. On the right is really how we've kind of reframed the program a little bit. Individuals are now recommended for a primary series and a bivalent booster dose, regardless of previous booster doses that may have been given in the interim. The ages and vaccines for this will be as authorized by FDA and recommended by ACIP and CDC. Dr.

Hall will walk later through the details of the schedule, but I just wanted to orient for the overall broader discussion for where we are now. Next slide. This slide shows the weekly trend in COVID associated hospitalizations by age group from COVID-NET. The hospitalization rates peaked for all age groups during last winter's omicron wave and then since April hospitalization rates in the older age groups have increased relative to the other age groups. Next slide.

This slide shows COVID hospitalization by race and ethnicity. Again, it's a callback to the equity domain. We have specific equity components that were shown throughout the entire presentation. Like he had shown all the data. I did want to provide some aspects of the data.

So, when we look at hospitalizations, we can see that throughout the pandemic, hospitalizations have been more represented among racial and ethnic minority populations. Next slide. So, now,

we see age adjusted rates of COVID-associated hospitalizations by vaccination status among adults. In June, unvaccinated adults had 4.6 times higher of COVID-19 associated hospitalization rates compared to those who have been vaccinated with at least one booster dose.

The next slide. This slide shows the age adjusted rates of COVID-associated deaths by vaccination status. In June, unvaccinated people five and over had eight times higher COVID-associated death rates compared to those with at least one booster dose. Next slide. And if we zoom in and focus on the death rates by vaccination status among people 50 and over, we can see that in June of 2022, people with two booster doses had 14 times lower risk of dying from COVID compared to unvaccinated individuals and a three times lower risk of dying from COVID than people with one booster dose.

Next slide. So, in summary, when we think about the public health problem, what COVID looks like these days, as of August 2022, over 94 million COVID cases are reported in the U. S. Since April, hospitalization rates of older age groups have increased relative to other age groups. And in June, we know that unvaccinated individuals had a higher COVID-associated death rate compared to those who had at least one booster dose.

Vaccination rates, we didn't go into the detail on this call. But we know that vaccination rates are much higher among older adults relative to other age groups. And we know that people of racial and ethnic minority groups have been disproportionately burdened by COVID illness, hospitalization, and death. Next slide. So, again, we don't have time to review in detail the totality of evidence that was presented at the ACIP meeting, but I just wanted this slide to show the comprehensive review of the data that was conducted.

So, we'll briefly walk through the clinical trial data, both the Moderna and Pfizer. We'll do that on this call. In addition, at ACIP, we talked about myocarditis data, modeling data, and considerations around immune tolerance and imprinting, antigenic cartography, which is mapping out of the immune response, looking at the va1 versus va45 data, what we know about a vaccination in the setting of prior SARS-CoV-2 infection, and what we know about boosters provided with non-mRNA vaccines. Next slide. So, in summary, with the Moderna clinical trial data, people were given a 50-microgram bivalent boost which consisted of 20 micrograms each of the ancestral vaccine and an omicron va1 spike as a second booster, and they were compared to those who were given the ancestral booster or kind of the current, the monovalent vaccine as the second booster.

The trial participants were 18 and over, and there were over 400 that received bivalent booster and about 370 that received an ancestral booster. You can see that immunogenicity or the immune response was assessed by the antibody response on day 29 after the vaccine, and they looked at the geometric gene ratios comparing the antibody response in those that got the bivalent booster compared to those who got the monovalent ancestral vaccine. When you compared it that way, the bivalent vaccine met superiority criteria, meaning that it was statistically better. So, in the column on the far right, you can see that the ratios were all over one for both, when they looked at both omicron and ancestral SARS-CoV-2 antibodies. Next slide.

When the superiority criteria, meaning that it was statistically better, were all met in participants with and without evidence of prior infection. But the highest titers that were observed in those who had had prior infection before on the far right. Next slide. This slide looks at the local and systemic reactions that were seen with the Moderna bivalent booster. When compared to this bivalent vaccine given as a fourth dose compared to what we know for the ancestral Moderna vaccine with the second and third doses, the reactions were similar or less reactions that were seen.

This graph shows the percentage of participants reporting any local or systemic reactions, and you can see the pain or fatigue is what was most commonly reported. Next slide. So now we turn to the Pfizer bivalent booster trial. Those individuals received a fourth dose of a 30-microgram bivalent vaccine, but again, was also comprised of the ancestral strain and the omicron va1 strain and was compared to those that received a fourth dose of a 30 microgram of the ancestral monovalent vaccine. It looked at safety and immunogenicity among participants 55, over 55 years.

There were about 300 participants that received the bivalent vaccine and around 300 participants that received the monovalent vaccine. Again, they looked at immunogenicity with the antibody responses one month after the study vaccine. And again, looking at ratios in the same way as we saw previously. Those that got the bivalent booster met the superiority criteria for the omicron antibodies, and the noninferiority criteria. Meaning it was the same.

Next slide. Then, again, this compares the participants over 55 that reported any local or systemic reaction following vaccination. And again, when we compare this to what we see with the monovalent vaccine, overall, the reactions were similar. Next slide. So, in summary, the bivalent booster doses for both Moderna and Pfizer increased the immune response in most who completed a primary series and a booster previously.

Compared with the ancestral booster dose, there was a superior immune response to omicron for both vaccines, and then when compared to the ancestral strain, Moderna was superior and Pfizer was noninferior. So, it was at least not inferior to the ancestral strain for both. There was a similar reactogenicity profile to the primary series and what we see with the ancestral booster doses. Although, we do know that the data from a clinical trial were limited somewhat in size, age, and bivalent booster type. Next slide.

Now, to discuss some of the other considerations. Again, at the meeting, we showed these data in detail, but just in summary, we know that the risk of myocarditis has been identified after COVID vaccines. The risk is rare and primarily observed in adolescent and young adult males. Then, looking at it across several vaccine safety platforms. In the VAERS data, the reporting rates of myocarditis were lower after a booster dose compared to what we see after the dose two of the primary series.

Among the VST data, which is another one of the safety surveillance platforms, the incidents of myocarditis following dose two of the primary series and the booster dose were similar, but the piece counts were very small. And we also looked at surveillance data from Canada that indicated the risk of myocarditis after the first booster dose in Canada was lower than the risk

following the second dose of the primary series. And they saw this from both Pfizer and Moderna. Most individuals with myocarditis have fully recovered at follow up, and we showed data from those previously presented to ACIP on a long term follow up study. We also know that the risk of adverse cardiac outcomes were 1.

8 to 5.6 times higher after SARS-CoV-2 infection than after COVID vaccines among males 12 to 17 years. We also know that an interval of eight weeks between vaccine doses may further lower that myocarditis risk. Next slide. So, now, I wanted to just quickly talk about omicron variant itself and what it means that we're talking about bivalent omicron vaccines and the differences between va1 and va45.

As people are aware, the clinical data from the bivalent vaccines are primarily obtained using a va1 variant. Here's what that means, and here's what the difference is. So, compared to the ancestral virus, what was circulating in early 2020, and what is currently in the monovalent vaccines, all omicron sublineages have shared mutations that shown here in the black box in the black arrow. Many of these mutations are in the receptor binding domain. That's what's in the black box.

The receptor binding domain, as the name implies, is the primary binding site for antibodies. And we know that these mutations contributed to a decreased neutralization and increased transmissibility that we see for all omicron sublineages. So, any vaccine that uses any omicron subvariant would include these mutations. Next slide. So, then, the differences between va1 and va45 specifically.

First, I also wanted to clarify why there are two numbers, why we say va4 slash va5. Va4 and va5 are two different omicron sublineages that the spike protein for each, which is the focus of the vaccine, is identical. So, when we're talking about the vaccine, it is the spike protein for both va4 and va5, but it is still just one single sequence, not two different ones. Then, when we come to compare va1 and va45, the bar on the top is for va1, and the bar on the bottom shows va45. The numbers and letters are areas where they differ from the main virus of comparison, that ancestral strain.

And the text on the right lists out the differences between va1 and va45. Without getting too technical, this figure just really highlights where several of these are in the red arrows comparing the differences between the two. So, you can see there are some differences, but they aren't fundamentally different or new virus, as they actually share nearly all of the same genetic code. Next slide. So, overall, the bivalent booster doses for both Moderna and Pfizer increase the immune response, and we know that the reactogenicity profile or the side effects we see after compared the primary series are similar to what we see with the primary series in the ancestral booster dose.

The myocarditis risk following the bivalent booster doses are known, but we anticipate a similar risk, similar to what was seen after the monovalent booster doses. But I didn't go into this in detail, but to summarize, the modeling projections said that more hospitalizations and deaths were averted when booster doses are recommended for a broader population. So, persons 18 and

over compared to limiting it to just 50 and over. And when the booster campaign begins in September compared to a later campaign in November. And the benefits and harms for the U.

S. population are always best assessed when the clinical trial and study populations are optimally representative of the U. S. population. Next slide.

So, let me briefly walk through who may be willing to get this booster dose. This slide shows survey data from an online survey conducted in partnership with CDC and the University of Iowa. For COVID, we've shown results from this partnership frequently. The survey was conducted only the month of August and showed that 72% of eligible respondents said they definitely or probably would get the updated booster that protects against omicron. Next slide.

Then, as we move into the fall, we know this booster program will overlap with the influenza vaccination season as well. We'll hear more data in a minute around coadministration of COVID and flu, but the survey recipients were also asked if they would be willing to get their flu shot and their COVID vaccine together, and 63% of individuals said that they were extremely or somewhat willing to receive them together. Next slide. Then, when we look at kind of the who has, who would be eligible and the timing for that, here you can see trends in completed primary series and first booster doses for persons five through 11 years in purple, 12 through 17 years in orange, and 18 to 49 years in blue. And as you can see highlighted here on the right, most individuals ages five to 49 years, it's been well since six months or more since their last vaccine dose.

Next slide. Now, this looks at the population 50 and over for those who've completed a primary series first or second booster. Fifty to 64 years in orange and persons 65 and older in blue. And while some have received the second booster in the past six months, comparatively fewer individuals have received those in the last eight weeks. Next slide.

So, then, this pulls all of those together. So, you can see around early September, the total number of persons eligible. So, that would those who have completed a primary series but not received a COVID vaccine dose in the last two months, is around 209 million individuals. While the number ineligible, which would only be, for this, would be those who have had a vaccine dose in the last two months, is less than five milligrams. Next slide.

So, we'll hear more about kind of the feasibility considerations and implementation from Dr. Hall, but we know that over 200 million people would be eligible for this vaccine. Nearly 22 million adults 50 and over have received a second booster, but most individuals five years and over are at least six months out from their last COVID-19 vaccine dose. CDC has provided an operational planning guide for jurisdictions to prepare for the fall campaign, and there will be a sufficient but finite supply of the bivalent vaccines. Some aspects of the vaccines will be easy to implement.

There's no changes to storage and handling, but we'll hear from Dr. Hall in a minute about the vials and labeling that maybe need some additional education. And again, we didn't show this data in detail, but significant racial and ethnic disparities persist in receipt of a booster dose, suggesting that the intervention or the vaccine may not be as equally feasible to implement

across all populations and needs to be closely monitored. Next slide. So, when we look at the summary of the data to inform these recommendations, we know we have experience using the COVID vaccine mRNA platform for nearly two years, and there were 600 million doses in the U.

S. alone. We have extensive vaccine effectiveness studies as well as robust post authorization safety data across multiple platforms. Then, we also have clinical, human data from bivalent COVID-19 vaccines that have been given in over 1700 persons. This includes bivalent vaccines with both beta and omicron variants, but from the manufacturers and from NIH studies.

Over 1400 individuals received a bivalent vaccine with an omicron component specifically. We know that there are subtle differences in the mutations between va1 and va45 spike protein sequences. We don't anticipate that those differences would have any meaningful impact in safety or reactogenicity of the vaccines based on the smaller mutations. And the overall composition of. The variants are up to antigenic cartography and antibody studies as well as modeling studies.

Next slide. So, here's what we know. COVID vaccines have a high degree of safety. There are rare events of myocarditis that have been seen after the mRNA vaccines and post authorization studies, and we do know that cases of myocarditis were apparent in the Novavax clinical trials. But overall, they have a high degree of safety.

COVID vaccines also provide a high level of protection against severe disease. Initially, the COVID vaccines provided high levels of protection against protection and transmission as well. However, as the virus evolved, we did see rapid waning of protection against asymptomatic or mild disease. We know that COVID booster doses further increased protection against severe disease and that the bivalent vaccines expand that immune response after vaccination. Vaccines that contain omicron will improve the antibody response to omicron.

And the bivalent vaccine, so I didn't show this data. But we did show that the bivalent vaccines, when you looked at how it responded to what it did to the antibody titers to other variants of concern, they actually increased those responses as well, compared to the monovalent vaccine. So, these bivalent vaccines provide more diverse responses overall which will likely improve the response to future variants as well. Next slide. Then, we do have to acknowledge what we don't know.

We don't know the rate of myocarditis after the bivalent vaccines. It's unlikely that the inclusion of an omicron component specifically would increase the myocarditis rate. We know that overall, it's likely age and sex of the individual that are likely contributing factors to the development of myocarditis after the vaccine. The interval since the previous dose, and the total dose may also be related. We don't know the incremental increase in vaccine effectiveness.

The antibody titers to currently circulating variant were higher after a bivalent booster than the current monovalent boosters. And most of the data to inform the recommendations were again from a va1 bivalent vaccine. The incremental benefit for the va45 vaccine is unknown. And we

don't know the duration of protection. Antibody titers after a bivalent vaccine and prior SARS-CoV-2 infection were robust.

This is encouraging, as it may prolong the duration of protection and decrease the need for frequent boosters. And as with all vaccines, the duration of protection may vary by age and immune styles. Next slide. So, in summary, next slide. I know this looks a little bit like a lot, but I'm just walking through the composition of the updated or bivalent vaccines on the right compared to the previous or monovalent vaccines on the left.

You can look for Moderna first at the top. For the previous monovalent vaccines, there was 50 micrograms in the ancestral strain, and for the previous Pfizer vaccine, there was 30 micrograms of the ancestral strain. But on the right, for the updated or bivalent vaccines, for Moderna, it contains 25 micrograms of the ancestral strain and 25 micrograms of va45. Then, for Pfizer, it's 15 micrograms of ancestral and 15 micrograms of va45. But the summary is that overall, the bivalent vaccines have the exact same total antigen amount as the previous monovalent vaccines, just a slightly different composition.

Next slide. So, we know that the monovalent vaccines have dramatically reduced COVID hospitalizations and death. As the virus is evolved, declines in neutralizing antibodies and vaccine effectiveness as well as more rapid waning of the vaccine were noted. Inclusion of this second variant, the vaccine broadens the antibody response. We know that the omicron specific bivalent vaccines were studied in over 1400 individuals and that these resulted in higher titers for omicron, higher titers for other variants, and titers that were as high or higher for the ancestral SARS-CoV-2.

Broad uptake of these vaccines in early fall could prevent over 100,000 hospitalizations compared to a later or more limited rollout, and billions of direct medical costs could be saved. Next slide. So, the work group and the ACIP is about discussed broad policy discussions around the use of the updated vaccines for all age groups currently recommended for booster doses. The current authorizations and recommendations are for a Pfizer vaccine in those 12 and over and a bivalent Moderna vaccine in those 18 and over. And additional authorizations for other ages and vaccines may follow.

Next slide. We know that the current population recommended for these boosters is very heterogeneous. Many individuals in the U. S. have had omicron over the last nine months.

And individuals recommended for this booster dose may have previously received a primary series, one booster doses, or for the population 50 and over, two booster doses. The balance of benefits and risks for individuals may vary by age, by previous receipt of a booster, or by recent SARS-CoV-2 infection. And there are uncertainties around the incremental benefits for some individuals, including those who have had recent infection or a recent vaccine received. Next slide. We know that COVID vaccines are recommended, even for those with prior infection, and we know that the rates of reinfection increase during the omicron period.

The bivalent vaccines in the setting of prior SARS-CoV-2 infections, what we call hybrid immunity, resulted in the highest antibody titers. And again, these high and diverse titers may



result in a longer duration of protection and a decreased need for frequent vaccine booster doses. We also know that studies have shown that an increased time between infection and vaccination may result in an improved immune response. So, those with recent SARS-CoV-2 infection may consider delaying a vaccine dose by three months from symptom onset to positive test. Next slide.

And time since the most recent vaccine may be more important than the cumulative number of doses. We acknowledge that this is a time of transition as the recommendations are moving from counting dose number to the optimal timing of the vaccination campaign. We know the vaccinations that are simple and easy to communicate are important, and if SARS-CoV-2 becomes a seasonal virus, an annual COVID vaccine program could be an effective strategy for the future. Next slide. So, the ACIP votes more than a single dose of the bivalent vaccine Pfizer vaccine for those 12 and over at least two months after receipt of the primary series of prior monovalent booster.

And single dose of the bivalent Moderna vaccine for those 18 and older, at least two months after receipt of the prior dose. Because the EUAs were revoked for the monovalent vaccine. ACIP followed and replaced the recommendations for the monovalent boosters with those for the bivalent boosters. And again, emphasizing what Dr. Hall had said that the bivalent booster recommendations are without regard to the previous number of monovalent booster doses.

Next slide. So, the self-knowledge check. In this section is under the EUA as issued by the FDA. The bivalent vaccines are recommended to be administered at least how many months after receipt of a primary series of prior dose? Next slide. That is two.

Two months. Alright. Next slide. At that, I will turn it over, I think one more slide and I'll turn it over to Dr. Hall.

Thanks so much.

Thank you, Dr. Oliver. I'll go ahead and discuss the interim clinical considerations for COVID-19 vaccines, considerations for bivalent boosters. Next slide. So, as Dr.

Oliver covered, on August 31st, Moderna COVID-19 vaccine bivalent was authorized for use in people ages 18 years and older, and Pfizer BioNTech COVID-19 vaccine bivalent was authorized for use by people ages 12 years and older. It was authorized as a single booster dose administered at least two months after either completion of primary vaccination with any authorized or approved monovalent COVID-19 vaccine or receipt of the most recent booster dose with any authorized or approved monovalent vaccine. Next slide. Everyone ages 12 years and older is recommended, then, to receive one age appropriate bivalent mRNA booster dose after completion of any FDA approved or authorized monovalent primary series or last booster dose. This means people cannot get a bivalent booster without first completing a primary series, and the booster can be homologous, meaning the same manufacturer as the primary series, or heterologous, meaning a different manufacturer than the primary series.

As long as the dose is age appropriate. So, in other words, the Pfizer bivalent can be given to people 12 through 17 only because Moderna is not authorized in this age group. But either Moderna or Pfizer bivalent can be given to people ages 18 years and older, regardless of which primary series the person received. There is no preference for one or the other based on the primary series. And there are no changes to schedules for children ages six months through 11 years.

Next slide. So, the bivalent booster recommendation replaces previous booster recommendations for people ages 12 years and older. Monovalent mRNA COVID-19 vaccines are no longer authorized as booster doses, and therefore cannot be given as a booster dose to individuals ages 12 years and older, even if that person had not previously received a monovalent booster dose. And later in this presentation, I'll go over errors if such dosing does occur. And this means that everyone ages five years and older who are eligible for a booster dose will only be eligible for one.

So, for people ages five through 11 years who received Pfizer as their primary series, they are eligible for one monovalent booster dose and then people 12 years and older one bivalent booster dose. Next slide. So, shown on this slide is just a visual of what the revised schedule looks like, and this is for people who are not moderately or severely immunocompromised. The schedule looks quite a bit different, as it's been significantly simplified and, again, just looking at those 12 years and older right now. So, starting with that top row, people 12 years and older are recommended to receive a primary series, either Moderna, Novavax, or Pfizer is recommended followed by an age-appropriate booster at least two months or eight weeks after completion of the primary series or after the most recent previous monovalent booster dose.

And again, the bivalent is the new recommendation, regardless of how many previous monovalent booster doses were received. In certain limited situations, Janssen can be used followed by a bivalent booster dose at least two months later. Next slide. So, now, looking at the schedule for people who are moderately or severely immunocompromised, the primary series is not changing. This remains the same for those who have not yet received one.

Moderna, Novavax, and Pfizer are recommended. For Moderna and Pfizer, this is three doses, and for Novavax, this is two doses. And also, again, the bivalent booster recommendation is the same for people who are immunocompromised. Just one bivalent booster dose at least two months after completion of the primary series or most recent previous monovalent booster dose. Again, Janssen is only used in limited situations.

Those with a Janssen primary dose get an additional mRNA dose followed by a bivalent booster. Next slide. So, if you perceive this as a big change to dose counting, you're certainly right. Our recommendations are simplified, and we're thinking of this as sort of a reset. We're changing the way we're thinking about these vaccines from dose counting, the monovalent booster doses to one bivalent booster dose for everyone eligible.

So, this table just reinforces that regardless of whether a person has received zero, one, or two monovalent boosters, one bivalent booster is recommended. Since some people may have already received three, four, or even five total doses for some immunocompromised groups, they

were up to five. We want to emphasize that we're no longer looking at that total number, and if someone is eligible, meaning they basically meet three criteria. They're 12 and older, they have completed at least a primary series, and they're two months out from the last dose. A bivalent booster should not be denied based on the number of total doses the person has received.

So, I've seen this question pop up. So, our current timing guidance for vaccination in persons with current or prior SARS-CoV-2 infection also applies to bivalent boosters. So, if a person has current or prior SARS-CoV-2 infection, at a minimum, vaccination should be deferred at least until recovery from acute illness and criteria to discontinue isolation have been met. So, that's the minimum. Then, additionally, these people may consider delaying vaccination longer by three months from symptom onset or positive test if infection was asymptomatic.

Individual factors such as risk for COVID-19 severe disease, community level, or characteristics of the predominant strain should be taken into account when determining whether to delay getting a COVID-19 vaccination after infection. Next slide. So, with new bivalent vaccines, coadministration guidance has not changed. We continue to recommend routine administration of all age-appropriate doses of vaccines simultaneously as best practice for people for whom no specific contraindications exist at the time of the healthcare visit. Extensive experience with non-covid vaccines have demonstrated that immunogenicity and adverse event profiles are generally similar when vaccines are administered simultaneously as when they are administered alone.

And on the next couple slides, I'll talk specifically about data on influenza and COVID vaccines. So, we recommend that providers should offer all vaccines for which a person is eligible. And I'll note one exception is orthopox virus vaccine. This does not follow the same routine guidance, and further information on this very specific situation can be found in CDC's interim clinical considerations, and at the end of this presentation, I have links to get to the interim clinical considerations. Next slide.

So, with both influenza and COVID-19 vaccine campaigns, we've received a lot of questions about coadministration of these vaccines specifically. So, again, providers should offer influenza and COVID-19 vaccines at the same time if eligible. This does include adjuvanted or high dose influenza vaccines. In those cases, we would recommend to administer in separate limbs. With both influenza and SARS-CoV-2 circulating, getting both vaccines is important for prevention of severe disease, hospitalization, and death.

And getting the vaccines at the same visit increases the chance that a person will be up to date with their vaccinations. Next slide. So, studies looking at coadministration have shown that immunogenicity is similar between those who receive coadministered COVID-19 vaccine and seasonal influenza vaccine and those who receive these vaccines separately. We also know that many people received simultaneous vaccination with influenza vaccine last season. Approximately 92,000 Be Safe participants reported simultaneous vaccination with an mRNA COVID-19 vaccine and seasonal influenza vaccine.

And approximately 454,000 people enrolled in the vaccine safety data link or VSD received simultaneous vaccination with a COVID-19 booster and influenza vaccine during the '21-'22 influenza season. Additionally, studies have shown COVID-19 vaccines administered with

seasonal influenza vaccine show similar or slightly higher reactogenicity. However, no specific safety concerns have been identified. Next slide. So, in terms of best practices for multiple injections, we recommend labeling each syringe with the name, dosage, lot number, initials, and exact beyond use time of the vaccine, if applicable.

Administer each vaccine in a different injection site and separate injection sites by one inch or more if possible. And finally, I mentioned this a little earlier. Administer the COVID-19 vaccine and vaccines that may be more likely to cause a local reaction, in different limbs. So, again, example being the adjuvanted or high dose influenza vaccine and COVID-19 vaccine. Next slide.

So, now, I'll take a look at the bivalent vaccine products in comparison to the current monovalent products. Starting with Pfizer, the monovalent and bivalent cap and border label colors are identical. Both are grey. Most of the characteristics are the same. They're both authorized for people 12 years and older.

They're 30 micrograms. The injection volume is 0.3 milliliters. Dilution of this formulation is not required, although other Pfizer formulations do require dilution. And they have the same beyond use date time and storage.

The only differences here are the dose it is authorized for, the monovalent being primary series, and the bivalent being booster dose. Next slide. So, shown here are the labels for the monovalent and bivalent. The monovalent on the left and the bivalent on the right. As you can see, these labels are very similar.

The main difference I've outlined in a red box on the label on the right. And that is in the name of the vaccine. It specifies bivalent original and omicron, va4, va5. So, it will be critical to pay attention to what is on the very top there. Since we can't really use the cap color and the label border color to differentiate the two.

Next slide. For Moderna, I'll highlight two different files in comparison to the bivalent. The one for the older age group and the one with a similar appearance. Next slide. So, first, the monovalent product authorized for ages 12 years and older is much more visually distinct from the bivalent product authorized for ages 18 years and older.

The monovalent product is in a red capped vial with a light blue label border color and of course is only authorized for primary doses now. And comparatively, the bivalent has a dark blue cap and a grey label border. Next slide. And here, you can see the labels are much more visually distinct. There's a different font size, font type.

You can, it's similar to Pfizer. The bivalent has bivalent original and omicron in the name. It very clearly has in all caps "booster doses only," which of course is not on the monovalent label. So, there are several differences in these two labels that are easier to spot immediately. Next slide.

So, the vial that actually looks the most similar is the monovalent product authorized for primary doses in people ages six through 11 years. This also has a dark blue cap and a similar label. The

visual distinction is a purple label border. Next slide. So, here's a picture comparing the vials and labels.

As I mentioned, these are more similar. Again, the bivalent does say in the name of the vaccine, bivalent original and omicron. However, they both have all caps booster doses only. And in will note that that monovalent on the left for primary series in ages six through 11 is only primary series. It is no longer authorized for booster doses.

It was previously in adults. However, that is still printed on the label. So, really, the name distinction here is the name and then the color of the border and the shade behind the booster doses only. Next slide. So, with these lookalike vaccines, there is a lot more opportunity for vaccine administration errors.

So, I'll cover some strategies to put in place to prevent errors. Next slide. So, the first group is staff training practices, integrating vaccine administration training into orientation and other appropriate education requirements. Additionally, providing education when new products are added to inventory or recommendations are updated. Next slide.

Some storage practices that can help to prevent vaccine administration errors include circling important information on the packaging to emphasize the difference between the vaccines. Separating those vaccines into bins or other containers according to type and formulation. Using color coded identification labels on vaccine storage containers for one of those lookalikes. Storing lookalike vaccines in different areas of the storage unit. And consider using name alert or lookalike stickers on the packaging and areas where these vaccines are stored.

Next slide. And then, for preparation and administration practices, this includes establishing do not disturb or no interruption areas or times when vaccines are being prepared or administered. Preparing vaccine for one patient at a time, and once prepared, labeling that syringe with a vaccine name. And finally, never administering vaccines prepared by someone else. Next slide.

And then, one big rule of thumb, and we also emphasize this with routine vaccines. It's always important to check your work, so triple checking work before administering a vaccine, and if possible, asking another staff member to check. Next slide. So, if a vaccine administration error does occur, this slide lists the recommended actions based on the type of error. So, if a bivalent vaccine is incorrectly administered for the primary series, and of course, that should have been a monovalent, this, the recommended action depends on the vaccine administered.

So, if it was Pfizer bivalent, we recommend do not repeat the dose. Just count that dose. And if it is Moderna, we do recommend to administer one monovalent dose immediately, no minimum interval, as the repeat dose, because administration of the booster dose results in a lower than authorized dose for the primary series. And I'll note there, there's a footnote at the bottom. That interval can be extended, particularly for groups at increased risk for myocarditis or pericarditis.

And then, the second type here, if a monovalent vaccine is correctly administered for the booster dose, if the bivalent is indicated. So, for those 12 and older. In general, we recommend not to

repeat the dose. But providers may administer a bivalent booster dose as a repeat dose based on clinical judgment. Next slide.

So, for all vaccine administration errors, we recommend informing the recipient, consulting with the state program, reporting the error to VAERS. That is required. Determining how the error occurred and implementing strategies to prevent it from happening again. And following the revaccination guidance we have in our interim clinical considerations. Next slide.

Finally, CDC continues to encourage people to stay up to date with our COVID-19 vaccines. This keeps people current with COVID-19 vaccine recommendations. And with these new recommendations, people are up to date if they have completed a primary series and received the most recent booster dose recommended for them by CDC. Next slide. And finally, I'll just quickly go through some resources.

You'll have all these links in the slide deck available on the website. Next slide. So, this website that the link listed here on the slide is essentially the one stop shop for clinical and professional resources. You can get job aids here. Reach our most updated clinical guidance.

Stay up to date with requirements and find tools to help educate vaccine recipients. Next slide. This slide shows the main landing page and provides the link for vaccine specific job aids for each vaccine. As you can see here, you can choose the vaccine you are looking for and find job aids specifically on that one. Next slide.

I just want to highlight once you click on one of those vaccines, there are a lot of resources for each one. Some examples include storage labels, schedule, preparation and administration summary, standing orders. Next slide. Then, this web page shows the interim clinical considerations. It's a lengthy document, so each time we update it, we have a summary.

I would encourage you to navigate here and sign up for email updates, and we'll send an email each time we update the guidance. So, you'll be notified as soon as new guidance is available, and you don't have to refresh it or wait to see if guidance is updated. Next slide. This slide navigates you directly to the resources for vaccine recipient education, including things like FAQs, posters, social media, graphics, and more. Next slide.

And finally, each manufacturer of the currently available bivalent vaccines have a formulation of presentation guide that can be printed and hung up in, for example, a vaccine preparation area. So, I've linked both of those. Next slide. And then, I'll just wrap up with the self-knowledge check. So, true or false, eligibility for the bivalent booster dose depends on how many monovalent booster doses were previously received.

True or false. Next slide. So, the correct answer is false. People ages 12 years and older who completed a primary series are recommended to receive a bivalent booster dose, regardless of previous monovalent booster doses, as long as it's been two months and they've received that primary series. Next slide.

And now, I'll hand it over to Dr. Twentyman.

Thanks so much, Dr. Hall. We just wanted to take a moment in this nice simplification of vaccine recommendations to consider the full complement of resources that we have to protect people with moderate to severe immunocompromise. I'll be briefly talking about preexposure prophylaxis to this end. And preexposure prophylaxis refers to a medication that is given before exposure to an infectious disease, like COVID-19, to protect an individual against that disease.

Next slide, please. The preexposure prophylaxis Evusheld is recommended for those ages 12 years and up who weigh at least 40 kilograms with moderate to severe immunocompromise due to a medical condition or receipt of certain immunosuppressing treatments. Evusheld is also recommended to be given to those who are unable to receive available COVID-19 vaccines due to history of severe adverse reaction or allergy to a vaccine or one of its components. Next slide, please. Tixagevimab and Cilgavimab or Evusheld is a combination of two long-acting human monoclonal antibodies derived from B cells donated by convalescent plasma patients after SARS-CoV-2 infection.

And in the interest of time, I'll just point out on this slide and for this audience, including clinicians, that there is a new ordering pathway for Evusheld available through the HHS health partner order portal, such that in addition to the large orders available through HPOP distribution process, providers not participating in this large-scale process can now order up to three doses through the small orders portal link here at the bottom of the slide. Next slide, please. I know we've had some questions about efficacy, so I'll briefly say that use of Evusheld is evidence based. In a randomized clinical trial, Evusheld had efficacy for the prevention of COVID-19, and in multiple other studies, including real world data, Evusheld was also shown to have efficacy against severe COVID-19 outcomes including during the period of omicron variant predominance. Next slide, please.

And unfortunately, despite the protection that Evusheld can provide, most people with immunocompromised in the U. S. have not actually received Evusheld. As you can see on the left-hand side, just about 5.3% of qualifying individuals have thus far received it.

On the right side of the slide, you'll see that this is not a supply issue. Supply far exceeds administration to patients. It's probably not a cost issue in that Evusheld is distributed by the U. S. government at no cost to recipients.

Next slide, please. Here we're just illustrating how use of monoclonal antibodies for preexposure prophylaxis can complement receipt of COVID-19 vaccines for optimal protection for those with immunocompromised, specifically after any dose of COVID-19 vaccine, individuals should wait two weeks before receiving Evusheld. But after Evusheld, there is no minimum interval to the next COVID-19 vaccine. Either within a primary series or if receiving a booster dose. Evusheld is recommended to be administered every six months, and individuals can consult with their physician for a prescription.

Next slide, please. I'll briefly say we've updated multiple webpages to make this information about Evusheld more widely available, so please come check out our interim clinical considerations, and other website content including specifically for providers like those on this call. I'll stop there in the interest of time and turn it over to, you, Dr. Hause. Thanks.

Thank you. See if I get my slides up.

Sorry. This was our knowledge check, and I was just going to say we just wanted to emphasize no minimum interval between Evusheld dose and subsequent vaccine. There is a two-week minimum interval between COVID-19 vaccine dose and a subsequent Evusheld dose. And on the next slide, you'll see that we have this nice graphic also on our interim clinical considerations page. And hopefully, that serves as a handy reference.

Now, over to you for real, Dr. Hause.

Thank you. Alright. So, I just wanted to briefly touch on safety monitoring for COVID-19 vaccine booster doses in Be Safe and VAERS. Next slide. So, just to remind everybody, Be Safe is a voluntary smartphone-based safety surveillance system that allows anyone to register after any dose of COVID-19 vaccine.

So, Be Safe allows existing participants to report receiving a booster dose and new participants to enter information about all doses received and then complete health surveys on their most recent dose. Next slide. So, Be Safe health surveys are sent daily during the week following each dose of vaccine, and they include questions about local injection site and systemic reactions as well as health impacts. Surveys also include questions to identify participants who might be interested in and eligible for a pregnancy registry. Be Safe is available in five different languages.

Next slide. So, Be Safe does rely on vaccine providers to promote registration of Be Safe, and there are a few ways to promote Be Safe to parents and to patients. You can verbally direct them to go to [besafe.cdc.gov](https://besafe.cdc.gov) or provide a Be Safe information sheet.

We also have informational Be Safe posters that can be displayed. And these print outs and additional information are available at the link listed at the bottom of this slide. Next slide. So, just to briefly touch on VAERS or the Vaccine Adverse Event Reporting System, VAERS is a national passive surveillance system, and it serves as an early warning system for vaccine safety. Anyone can submit a VAERS report, regardless of the plausibility of the vaccine causing the event or the clinical seriousness of.

Next slide. This is just a screenshot of the VAERS website. Highlighted in this red box is the link to the VAERS form. Next slide. And this is just a screenshot of the VAERS form.

Next slide. That concludes my presentation. I'll hand it back to our moderator.

Presenters, thank you for providing this timely information to our audience. We will now go into our Q and A session. Joining our presenters for the Q and A session are Mr. Chris Dugger, who is the lead for the COVID Vaccine Unit for CDC's COVID-19 response. Dr.

Pragna Patel, Acting Chief Medical Officer for CDC's Coronavirus and Other Respiratory Viruses Division, and Dr. Emily Coolmans, Acting Clinical Team Lead for CDC's Epidemiology Branch, Coronavirus, and Other Respiratory Viruses Division. We really have time for just one



question, and the question asks if someone has not received their primary vaccine dose yet, do they still need to go with the primary formulation that you shared earlier or the new bivalent formulation as their primary series.

Sorry. I don't think I had my mic quite there, but I can answer that one. So, if they have not yet received their primary series, they do need to receive the monovalent formulation and complete that primary series first before they can receive the bivalent formulation for their booster dose. It is specifically authorized that way.

Thank you very much, and as we approach the hour, I want to thank all our presenters and our Q and A SMEs for joining us and sharing their expertise with us today. Please note that all continuing education for COCA calls is issued online through the CDC training and continuing education online system at [tceols.cdc.gov](https://tceols.cdc.gov). Those who participate in today's live COCA call and wish to receive continuing education, please complete the online evaluation and posttest before October 17, 2022, with the course code WC4520-091322.

The access code is COCA091322. Those who will participate in the on-demand activity and wish to receive continuing education should complete the online evaluation and posttest between October 18, 2022, and October 18, 2024. And use course code WD4520-091322. Again, that access code is COCA091322. Continuing education certificates can be printed immediately upon completing your online evaluation.

A cumulative transcript of all CDC ATSDR continuing education obtained through the CDC training and continuing education online system are maintained for each user. Today's COCA call will be available to view on demand a few hours after the live call at [emergency.cdc.gov/coca](https://emergency.cdc.gov/coca). A transcript and closed caption video will be available on demand on the COCA call's webpage later this week.

We invite you to join us this Thursday, September 15th at 2:00 P. M. Eastern for our next COCA call. The topic will be 2022 to 2023 Recommendations for Influenza Prevention and Treatment in Children: An Update for Pediatric Providers. Continue to visit [emergency.cdc.gov/coca](https://emergency.cdc.gov/coca) to get more details about upcoming COCA calls.

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