MEETING OF THE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES (ACIP)

NOVEMBER 19, 2021
SUMMARY MINUTES

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MEETING PURPOSE

The United States (US) Department of Health and Human Services (HHS) and the Centers for Disease Control and Prevention (CDC) convened a meeting of the Advisory Committee on Immunization Practices (ACIP) on November 19, 2021. The meeting took place remotely via Zoom, teleconference, and live webcast. This document provides a summary of the meeting, which focused on COVID-19 booster doses.

THURSDAY: NOVEMBER 19, 2021

WELCOME AND INTRODUCTIONS

Call to Order/Roll Call

Dr. Grace Lee (ACIP Chair) called to order and presided over the November 19, 2021 ACIP meeting. She pointed out that because this meeting was scheduled quickly, not all members could be in attendance due to responsibilities that could not be rescheduled at the last minute. She acknowledged and sincerely thanked all of the colleagues of the ACIP members who had often during the COVID-19 pandemic rescheduled their own days in order to provide coverage for many of the members, including caring for patients, so that they would be able to attend emergency ACIP meetings. ACIP recognizes that it is not only the ACIP members who are public servants, but also their colleagues, friends, and family members who enable them to serve in these roles. Dr. Lee conducted a roll call, which established that a quorum was present. Dr. Wilbur Chen reported the potential for a perception of a conflict of interest (COIs) in that his employer, the University of Maryland, receives a grant from Emergent BioSolutions, Inc. for the development of a shigella vaccine. No other COIs were declared. A list of Members, *Ex Officios*, and Liaison Representatives is included in the appendixes at the end of this summary document.

Announcements

Dr. Melinda Wharton (ACIP Executive Secretary, CDC) noted that copies of the slides for the day were available on the ACIP website and were made available through a ShareLink™ file for voting ACIP Voting Members, *Ex Officios*, and Liaisons. She indicated that there would be an oral public comment session prior to the vote at approximately 1:00 PM Eastern Time (ET). Given that more individuals registered to make oral public comments than could be accommodated, selection was made randomly via a lottery. Those individuals who were not selected and any other individuals wishing to make written public comments may submit them through https://www.regulations.gov using Docket Number CDC-2021-0125. Further information on the written public comment process can be found on the ACIP website.

As noted in the ACIP Policies and Procedures manual, ACIP members agree to forgo participation in certain activities related to vaccines during their tenure on the committee. For certain other interests that potentially enhance a member's expertise, CDC has issued limited COI waivers. Members who conduct vaccine clinical trials or serve on data safety monitoring boards (DSMBs) may present to the committee on matters related to those vaccines, but are prohibited from participating in committee votes. Regarding other vaccines of the concerned company, a member may participate in discussions with the provision that he/she abstains on

all votes related to that company. ACIP members state any COIs at the beginning of each meeting.

Welcoming Remarks

Dr. Sam Posner (Acting Director, CDC/NCIRD) thanked the ACIP members for coming together so rapidly to deliberate the question of expanding the groups who may receive a COVID-19 vaccine booster dose. CDC greatly appreciates all of the work that the ACIP has done and continues to do for this response. ACIP is unable to expand groups for vaccination until the Food and Drug Administration (FDA) authorizes those persons in the Emergency Use Authorization (EUA). Although the ability to mix and match doses has made parts of the implementation process easier, it is clearly understood that the prior FDA groups were complicated to implement. Importantly, simplification of the booster dose recommendations will reduce confusion and will allow healthcare providers and the public health workforce to focus on high priority groups for boosters and continue to implement pediatric and primary series vaccination. He also took this opportunity to remind people of the importance of ensuring that people get the influenza vaccine this season. There already is increased circulation of both COVID-19 and influenza and there are vaccines to protect everyone from both.

FDA Update

Dr. Doran Fink (FDA/CBER) indicated the FDA EUA approved earlier in the morning expanded the populations eligible for a single COVID-19 vaccine booster dose to include all individuals 18 years of age and older who have completed primary vaccination with an FDA-authorized or approved COVID-19 vaccine, regardless of the vaccine used for primary vaccination. These authorizations apply to homologous booster doses in which the same vaccine is used for both primary vaccination and booster doses, as well as heterologous booster doses in which one vaccine is used for primary vaccination and a different vaccine is used for the booster dose. The authorized interval between completion of primary vaccination and a booster dose remains tied to the vaccine used for primary vaccination, meaning that individuals who receive a primary series of Pfizer or Moderna COVID-19 vaccines are eligible for a booster dose beginning at 6 months after completion of their primary series and individuals who receive primary vaccinations with the Janssen COVID-19 vaccine are eligible for a booster dose beginning at 2 months after their primary vaccination.

FDA's assessment of benefits versus risks for expanding booster dose eligibility following primary vaccination with Pfizer and Moderna COVID-19 vaccine relied primarily on clinical trial data previously reviewed when booster doses for these vaccines were first authorized for use, and real-world evidence regarding effectiveness of the Pfizer and Moderna COVID-19 vaccine primary series, preliminary safety information from use of Pfizer and Moderna COVID-19 vaccine booster doses in the US, and relevant safety and effectiveness information from use of Pfizer mRNA COVID-19 vaccine booster doses in Israel. In considering the recently increasing incidence of COVID-19 in the US and abroad, including breakthrough cases in vaccinated individuals, and newer evidence providing reassuring information about the risks of myocarditis and pericarditis, following mRNA COVID vaccine booster doses, FDA determined that the known and potential benefits of expanding booster dose eligibility for these mRNA COVID-19 vaccines now clearly outweigh the known and potential risks.

It is important to note that even with evidence of waning vaccine effectiveness (VE) among vaccinated individuals, the predominance of serious COVID-19 outcomes remains among unvaccinated individuals. Thus, FDA acknowledges that while the impact of expanding booster dose eligibility is expected to be most clear on the individual level (e.g., providing additional protection to vaccinated individuals against breakthrough cases of COVID-19 and potential serious consequences), the greatest impact on a population level is still dependent on increasing vaccine uptake among those who are eligible for primary vaccination but still unvaccinated, as well as maintaining scientifically proven non-pharmacologic measures for reducing transmission of the SAR-CoV-2 virus heading into the winter months.

CORONAVIRUS DISEASE 2019 (COVID-19) VACCINES

Session Introduction

Dr. Matthew Daley (ACIP, WG Chair) provided the session introduction on behalf of the ACIP COVID-19 Vaccines Work Group (WG). There have been over 47 million cases of COVID-19 in the US since the start of the pandemic and there have been over 764,000 deaths from COVID-19 in the US. Given the availability of vaccines that have a high degree of safety and real-world effectiveness, deaths from COVID-19 is, for most people living in the US, vaccine-preventable. The most recent wave of COVID-19 peaked in early September nationally. Unfortunately, case counts have been rising again for approximately the last 3 weeks. In some parts of the country, there is rapid rise in case counts. Colorado, for example, recently reinstituted crisis standards of care.

In November 2021, the COVID-19 WG's activities have been focused primarily on booster doses. In that context, the WG has heard Pfizer-BioNTech clinical trial data for booster doses; received safety updates regarding booster doses; reviewed the Grading of Recommendation Assessment, Development and Evaluation (GRADE); reviewed and discussed updates to the Evidence to Recommendations (EtR) Framework regarding booster doses; and had a very informative discussion about booster policy options.

As Dr. Fink reported, the FDA expanded eligibility for COVID-19 vaccine boosters earlier in the day. As Dr. Fink described, this authorizes the use of a single booster dose for all individuals 18 years of age and over at least 6 months after completion of primary vaccination with any FDA-authorized or approved COVID-19 vaccine. The EUA allows for the use of each available COVID-19 vaccine as heterologous ("mix and match") booster dose in eligible individuals following completion of primary vaccination with a different COVID-19 vaccine. The dosing interval for the heterologous booster dose is the same as that authorized for a booster dose of the vaccine used for primary vaccination.[1]

To provide an update about COVID-19 vaccination among children 5-11 years of age, almost 2 million first doses have been administered to children in this age group through November 17, 2021. This represents 6.2% of all children 5-11 years of age in the US who have received a first dose of Pfizer-BioNTech COVID-19 vaccine. In addition, the vaccine safety monitoring system that has been put in place to monitor the safety of COVID-19 vaccines is the most intensive ever for any vaccine. These systems include the Vaccine Adverse Event Reporting System (VAERS), Vaccine Safety Datalink (VSD), the Vaccine Safety Technical Work Group (VaST)

[1] https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-expands-eligibility-covid-19-vaccine-boosters

VEST system, and other systems. These systems are all very closely monitoring the real-world safety of COVID-19 vaccines in children 5-11 years of age.

Though not the area of focus for this meeting, Dr. Daley went off script momentarily to say that he has been hearing from and talking to children about COVID-19 vaccination and has found that many children are very excited to get vaccinated—not about the poke, but about the promise. Their parents have been very worried about COVID infections and they think that getting vaccinated will allow them to return to some level of normalcy, both in school and outside of school. What has been striking to him is that children in this age range, especially the ones who are a little closer to 10 or 11 years old, also brought up their social responsibility. They have described wanting to protect their classmates, their parents, their grandparents, and their community. While acknowledging all of this, he also has heard from parents who have been offered but declined COVID-19 vaccination for their children. To those parents, he says that the door is always open and to please share their questions and/or concerns.

Turning to data that were not yet publicly available on the CDC website, Dr. Daley reported that over the last 16 days there was a marked increase in the number of doses administered per day. Currently, an average of over 200,000 doses per day were being given to children 5-11 years of age in the US. As background, CDC issued Emergency Use Instructions (EUI) on November 17, 2021 about use of the COVID-19 vaccine by Pfizer-BioNTech approved by the FDA to prevent COVID-19 in people ≥16 years of age. The EUI authority (e.g., 2013 Pandemic and All-Hazards Preparedness Reauthorization Act) allows CDC to create and issue EUI to permit emergency use of FDA-approved medical products. EUI are provided as fact sheets for healthcare providers and recipients that include information about such products' approved, licensed, or cleared conditions of use.

The EUI covers the use of Pfizer-BioNTech COVID-19 vaccine for those who have completed primary vaccination with a non-FDA-authorized or FDA-approved COVID-19 vaccine, such as certain people who are vaccinated outside of the US with a COVID-19 vaccine listed for emergency use by the World Health Organization (WHO). This also includes certain participants in COVID-19 vaccine clinical trials, either within or outside of the US. The EUI specifically provides information about use, including an additional primary dose in certain moderately or severely immunocompromised persons aged ≥12 years and a single booster dose among certain adults ≥18 years of age.[2] The EUI Fact Sheets for healthcare providers (HCP), recipients, and caregivers are available on the CDC website.[3]

On the agenda for this session were presentations on the efficacy and safety of the BNT162b2 booster dose, an update on boosters from the Moderna perspective, COVID-19 vaccine booster dose safety, a VaST summary and interpretation of the current evidence regarding booster dose safety, updates to the EtR Framework regarding Pfizer-BioNTech and Moderna COVID-19 vaccine booster doses, and a vote.

[2] Refer to CDC's Interim Clinical Considerations for additional information on moderately or severely immunocompromised persons recommended for an additional primary dose and populations recommended for a booster dosehttps://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html

[3] https://www.cdc.gov/vaccines/covid-19/eui/index.html

Efficacy and Safety of BNT162b2 Booster Dose

Dr. John Perez (Pfizer) presented on the safety and efficacy of a booster dose of BNT162b2 from Study C4591031, which has recruited 10,000 individuals ≥16 years of age and older who completed a 2-dose primary series of BNT162 in Study C4591001. These subjects were randomized at a 1:1 ratio to receive either BNT162 30µg or a placebo dose at least 6 months after the second dose. Randomization was stratified by age, such that approximately 60% of the participants enrolled would be at least 16 years of age to 55 years of age and approximately 40% would greater than 55 years of age. Assessments included safety evaluations of adverse events (AEs) and COVID-19 case surveillance for booster efficacy estimation after the booster dose. Reactogenicity data were not collected in this study, but booster reactogenicity was reported from Study C4591001 and was presented previous to ACIP.

In terms of demographics, there was equal participation by males and females between the vaccine and placebo groups. About 79% of the subjects were White, about 15% were Latino, and about 86% were from the US. Roughly 55%-56% were between 16-55 years of age and the rest were greater than 55 years of age, with a median age in the study of 53 years. About 5.4% were positive for SARS-CoV-2 at baseline. Looking at when the booster was given after completing the 2-dose series, the median time to get that booster dose was about 10.8 months after completing the 2-dose series. The majority of booster doses were administered 10-12 months after Dose 2. Recipients were followed for a median of 2.5 months after their booster dose.

To review reactogenicity, this analysis was requested by CDC and these data were from Study C4591001. In terms of reactogenicity of a booster dose with at least a Grade 3 or higher severity, about 6.6% overall had a Grade 3 event or higher. All of the local reactions at Grade 3 or higher were less than 1%. For systemic events, about 5.6% of participants reported a Grade 3 reaction. The majority of these included 4.5% fatigue, 11.4% muscle pain, and 1% headache. Overall, low grades of Grade 3 or higher reactogenicity was reported. In terms of AEs 1 month after a booster dose, a higher rate of AEs and related AEs were reported for the vaccine group compared to the placebo group. This was seen previously in COVID-19 clinical trials. There was a very low rate of related serious adverse events (SAEs), withdrawals due to SAEs, or deaths reported in this group.

Analyzing the AEs that are being reported at greater than 1% by System Organ Class (SOC) after the booster vaccination, a similar pattern is seen as what has been seen before. Namely, that AEs that are being reported in clinical trials are primarily AEs reflective of reactogenicity. The most common are general disorders and administration site conditions, which includes local injection site and systemic reactions of fever, fatigue, and chills. Next are in the musculoskeletal system, which includes myalgia and arthralgia. In the nervous system SOC are headache, blood and lymphatic system disorders, and lymphadenopathy. In this study, the rate of lymphadenopathy was 2.7%. And as reminder, that is comparative to 0.4% seen after the second dose in Study C4591001.

Subjects were followed through the cutoff date of October 5, 2021. The same pattern was observed as at 1 month after the booster dose, with more AEs reported in the vaccine versus the placebo group. There were more AEs related to reactogenicity in the SOCs that were previously examined, with no new AEs or safety signals with the follow-up data. In terms of SAEs by SOC after the booster vaccination through the cutoff date, the rate of SAEs was higher in the placebo group than in the vaccine group. Specifically, there were 16 (0.3%) SAEs in the

vaccine group compared to 24 (0.5%) events in the placebo group. There was no imbalance seen in any of the SOC categories.

There were 3 related SAEs from the booster vaccination in the vaccine group and two in the placebo group. Beginning with the vaccine group, the first was a young male with a past medical history of postural orthostatic tachycardia syndrome (POTS) and orthostatic hypotension, who developed tachycardia consistent with these medical diagnoses 8 days after booster vaccination that was moderate in nature and resolved 2 days later. The next case was an elderly female with Gilbert's syndrome, who developed moderate hepatic enzyme increase that occurred 5 days after the booster vaccination that resolved over a month later. Importantly, she was taking TYLENOL® for diverticulitis that started 2 days before the booster dose. The next case was a young female who developed mild hepatic enzyme increase that occurred 49 days after the booster vaccination that was ongoing at the time of the cutoff. She saw her primary care physician (PCP) who thought that this was due to atorvastatin. In the placebo group, there was an elderly female who had multiple risk factors for cardiovascular disease (CVD), who developed an acute myocardial infarction (MI) 9 days after the placebo dose. It was life-threatening, but resolved 4 days later. Finally, there was a young adult male with supraventricular tachycardia (SVT) who developed chest pain of unknown origin that occurred 6 days after placebo that was severe in nature and resolved without treatment 1 day later. The subject was evaluated and troponin and electrocardiograms (ECGs) were normal.

Looking at relative vaccine efficacy (VE) during the blinded follow-up period in subjects without evidence of infection prior to 7 days after Dose 2, subjects in the vaccine and in the placebo group both had 2 primary doses of vaccine roughly 21 days apart. They were randomized to receive either a booster dose or a saline injection. There were 6 cases in the vaccine group and 123 cases in the placebo group who developed symptomatic COVID-19, which calculates to a relative VE of 95.3%. Regarding relative VE in subjects with or without evidence of infection prior to 7 days after the second dose now including people with evidence of infection, there were 7 subjects randomized to a booster dose who developed symptomatic COVID-19 compared to 124 people in the placebo group. This calculates to a relative VE of 94.6%. In terms of the cumulative incidence curve with first COVID-19 occurrence after booster vaccination, the 2 curves diverge starting prior to 7 days after the booster dose, and then maintained separation with additional follow-up time. Looking at relative VE by subgroup with demographic characteristics, irrespective of age, sex, race, or ethnicity, relative VE was high, irrespective of demographic variable. When the data were further analyzed by country and by comorbidity, there were high rates of relative VE by country and also high rates of relative VE regardless of whether someone had a comorbidity.

In conclusion, there was high relative VE in the boosted group compared to the un-boosted group from 7 days after the boost in those without evidence of infection was 95.6%. None of the protocol-defined cases of COVID-19 in the un-boosted placebo group resulted in hospitalization. Two cases of severe COVID-19 occurred in the placebo group based only on SpO2 <93%. Multiple subgroup analyses showed that efficacy was consistent irrespective of age, sex, race, ethnicity, and comorbid conditions. The AEs observed were consistent with those seen in previous studies with no safety signal identified. No cases of myocarditis or pericarditis were observed. Lymphadenopathy was higher after a booster dose at 2.7% compared to 0.4% seen in previous studies. Overall, these data strongly support that a booster dose of BNT162b2 administered in individuals 18 years of age and older ≥6 months after the second dose improves protection against symptomatic COVID-19.

Update from Moderna

Dr. Rituparna Das (Moderna) provided an update on a 50 µg booster dose of Moderna COVID-19 vaccine in individuals ≥18 years of age. The EUA that was granted earlier in the day was for a booster dose of the Moderna COVID-19 vaccine was for 0.25 mL. A single Moderna COVID-19 vaccine booster dose of 0.25 mL may be administered intramuscularly (IM) at least 6 months after completing a primary series of the Moderna COVID-19 vaccine to individuals 18 years of age or older. A single booster dose of the Moderna COVID-19 vaccine of 0.25 mL may be administered as a heterologous booster dose following completion of primary vaccination with another authorized or approved COVID-19 vaccine. The dosing interval for the heterologous booster dose is the same as that authorized for a booster dose of the vaccine used for primary vaccination.

To review the data Moderna presented during the October 21, 2021 ACIP meeting, which was the data package was used for the original 50 µg booster dose under the EUA, an immunobridging approach was taken per the FDA guidelines for boosters and variant vaccines. In terms of safety, the rates of adverse reactions (ARs) following the 50 µg booster dose were comparable to that seen after Dose 2 of the primary series. The comparison was the primary series received in the pivotal study, Protocol 301 (COVE Efficacy Trial). Pain at the injection site was the most common solicited local AR. Headache, fatigue, and myalgia were the most common systemic ARs. The majority of ARs were mild to moderate in severity. Axillary swelling or tenderness was the only AR that was more frequently reported after the booster dose compared to Dose 2 in the primary series study. There were no vaccine-related SAEs or deaths in the booster study.

Regarding the immunogenicity endpoints and analyses, the pre-specified co-primary hypotheses, the geometric mean ratio (GMR) and seroresponse rate (SRR) difference post booster compared to post-Dose 2 of the primary series, were met on the pooled dataset. The 50 µg booster dose following the 100 µg primary series resulted in a higher antibody response to the original virus (D614G) than post-Dose 2 in Study 301 (GMR = 1.8) compared to post-Dose 2 in the pivotal efficacy study. There was a 13-fold rise of antibodies compared to pre-boosters against the original virus. There was a 17-fold rise from pre-booster titers for the Delta variant. There were consistently high antibody titers in both age groups: 18-64 and ≥ 65 years of age.

To summarize ongoing studies of the 50 µg booster dose, boosting began in Protocol 301 (COVE Efficacy Trial) in September. To date, over 15,000 participants have received a booster dose 6-14 months after completion of their primary series. The safety and immunogenicity data from that cohort are being compiled. No unexpected signals have been reported. The safety and immunogenicity data will be brought forward as soon as they are available. Immunogenicity data are expected on subset of subjects in early 2022. In addition, sera are currently being tested to assess 6-month persistence of antibody (Study P201B) in approximately 300 subjects who were boosted with 50 µg. Moderna will update the COVID-19 Vaccines WG and the ACIP as soon as those data become available.

Discussion Summary: Perez & Das

- Regarding an inquiry about the number of people in the group of adults 16-25 years of age in the Pfizer study, Dr. Perez indicated that there were 78 persons 16-17 years of age, 472 persons 16-25 years of age, 933 persons 26-30 years of age, 855 persons 18-30 years of age, 1414 persons 31-40 years of age, and 2347 overall from 16-40 years of age.

- Questions were posted regarding whether the lymphadenopathy cases in the Pfizer study were all axillary, what percentage occurred in women versus men, and about the painful swelling reported of the soft tissue rather than lymphadenopathy in younger individuals. Dr. Perez indicated that the lymphadenopathy was primarily ipsilateral to the injection site at about 8-9 days after the first dose and 3-4 days after the second dose. Sometimes lymphadenopathy occurs in the cervical regions. These were all palpable and soft lymph nodes could be easily noted on exam. There was no obvious sex difference in this analysis, although it appeared in a few analyses to be somewhat higher in females as opposed to males. Nevertheless, men also reported lymphadenopathy. There were a few reports of lymphadenitis.

- Regarding the AEs reported in the Pfizer study, an inquiry was posed regarding whether any crowding of effects was observed depending upon the timing of the booster post-primary series. Dr. Perez indicated that while they did not look at it from that perspective, nothing stood out in the review of all AEs in the vaccinated group compared to the placebo group, other reactogenicity and lymphadenopathy.

- In terms of whether there are any data on pregnancy and boosters in these cohorts, Dr. Perez indicated that none of the subjects who were boosted were pregnant. Dr. Das added that Moderna is following everybody for pregnancy. While she had not seen any reports come through on pregnancy at this point, Moderna will compile those data.

- Regarding whether clinical efficacy was involved in the Moderna trial, Dr. Das indicated that this is not a placebo-controlled boosting trial. At the time they started the trial, they thought that they could no longer conduct placebo-controlled boosting. Case monitoring continues in the same way it always has been. During the last presentation to ACIP, the breakthrough case data were shown for early vaccinees versus late vaccinees to illustrate how early vaccinees seemed to be having more breakthrough cases. Anytime somebody has symptoms, they present for PCR testing and are followed to resolution. Moderna is also doing sequencing for all of the cases, so they will have incidence rates over time.

- Asked to address thoughts about immunocompromised patients who received the J&J vaccine who are now recommended to receive a 50 µg booster dose of Moderna 2 or more months after their J&J vaccine and the fact that many clinicians want their immunocompromised patients to receive a full dose of Moderna vaccine after J&J, Dr. Das reported that Moderna has an immunocompromised study for those receiving a third dose. That study probably will be extended to a fourth dose as well. There is not a recommendation for a third dose for the J&J vaccine, so she did not have any data on this.

- To summarize, ACIP members are very appreciative of the continued information on VE and safety by prior infection status and hope that will continue to be helpful going forward. They also are appreciative of further assessments on the impact of dosing intervals on efficacy and safety, and a continued focus on the age- and gender-specific safety data. In addition,

continued vaccine clinical trials are needed that are inclusive of children and pregnant women. Questions continue to arise about children and pregnant, including for booster doses, but data are typically on the general adult population. ACIP also appreciates continued input on duration of immunity.

Public Comment

The floor was opened for public comment during the December 16, 2021 ACIP meeting at 1:23 PM ET. Given that many more individuals registered to make oral public comments than could be accommodated during this meeting, selection was made randomly via a lottery. The comments made during the meeting are included here. Members of the public also were invited to submit written public comments to ACIP through the Federal eRulemaking Portal under Docket No. CDC-2021-0125. Visit http://www.regulations.gov for access to the docket or to submit comments or read background documents and comments received.

Ms. Mary Mahoney
Concerned Individual

Good afternoon. My name is Mary Mahoney and I'm speaking on behalf of myself and my family. Thank you for this opportunity and for the hard work and commitment that the advisory committee has put forth during the pandemic. My family and I registered to received initial vaccines as soon as we were eligible to protect ourselves. We did this so to be able to resume important and meaningful aspects of our lives that had been on hold, such as going to school, attending church in person, and being around older adults that we love. It is important that we're able to continue to enjoy these everyday experiences, which we now treasurer more than ever, especially having not been able to participate in them for almost 2 years. The opportunity for all adults to receive booster shots provides a much needed layer of protection, not only to each person who gets one, but all of those people with whom they interact. Every measure that cuts off potential avenues for this virus to invade, every step that keeps it from having places to replicate and possibly mutate, is a victory. I urge the committee to recommend that the booster shot be made available to every adult so that we continue to preserve and maximize the progress we've made toward ending its catastrophic impact on our lives, our traditions, our economy and our country. Thank you for your time.

Mr. Edward Nirenberg
Science Communicator Focusing on Vaccines and COVID-19

Hi, and thanks for this time again today. Before beginning I do want to take a moment to thank the ACIP team and professional collaborators for their extraordinary labors during this time. I think that this is more meetings than anyone wants to have for anything. I'm grateful as a citizen of this country that we have expert advisory committees that have worked to rise to the challenges of this crisis. As the subject of today's discussion is boosters, I think it's important to note that we are increasingly seeing recommendations for booster doses for adults, but there has been relatively limited guidance for those aged 12 to 18. And I think it would be helpful to have that data regarding whether or not appreciable declining effectiveness of the vaccine is being observed in that age cohort, as currently there seems to be something of a data vacuum and an absence of guidance. I'm sure that this data does exist, but it should be made publicly available. Additionally, on the subject of framing as a booster dose, I think Dr. Stanley Plotkin was the first to raise the suggestion that booster doses should not be considered booster doses, and rather should be thought of as part of the primary series. And I think that given the position we currently face and the substantial benefits we're seeing with third doses that exceed the

protection allotted by second doses at their peak, he was likely correct. I think it would serve the US better to acknowledge this is intended as a 3-dose series for adults rather than 2 doses. Equity concerns surrounding the use of these vaccines are substantial, but each day we have doses going in the trash because they are expiring, and there's presently no way to get these doses to the people that so desperately need them. First and second doses are always going to be far more important than third doses and if uptake in the US were better, we might not have such a significant need of third doses. But this counterfactual does not help our situation. It will always be better that a vaccine go into someone's arm than into the trash, even if the owner of the arm has already received 2 doses. We are already seeing that there is a divergence in the Kaplan–Meier curve as was shown well before 7 days just in rapid recall kinetics and rapid onset of enhanced protection with Dose 3, as was seen with other vaccines. I also wish to make a gentle reminder regarding the importance of influenza vaccination, as underscored earlier in the meeting. Influenza has been a serious public health scare that we have adapted to with tools like vaccination. And while we've been extremely fortunate in the last year that NPI has managed to reduce incidence so dramatically, flu activity is rising throughout the US and the world. It's a serious respiratory disease and super infectious with COVID-19 even more. So please, get your flu vaccines as soon as possible if you have not done so already. Thank you so much.

Mrs. Melody Butler, RN, CIC
Nurses Who Vaccinate

Good afternoon. My name is Melody Butler. I am a mother, a Registered Nurse (RN), and the Founder of Nurses Who Vaccinate (NWV). I'm also a dog owner, in case you hear that in the background. We are an organization committed to ensuring our patients have access to the most accurate evidence-based information from credible sources to support their decisions to vaccinate. We know vaccines save lives and we are grateful for the work of this committee to ensuring that before any vaccine is made available to the public, it is first and foremost safe and effective. The COVID-19 pandemic has been detrimental to the health of so many people, and not just due to the virus itself. It has kept people from routine exams, preventative care, and necessary vaccines. Much of our work is centered around ensuring our patients, colleagues, and communities understand the importance of keeping up with their routine vaccines, and doing their part to not only protect themselves, but society as a whole. We are disheartened by the misinformation campaigns that continually spread about the COVID-19 vaccine and treatments. While we as nurses are certainly no stranger to this anti-vaccine movement, the damage this can cause for those Americans who are simply looking for educated guidance for themselves and their families is unacceptable. What concerns us at Nurses Who Vaccinate is that sharing misinformation creates immense confusion, false hope, and in many cases encourages individuals to avoid appropriate medical care. This is why the work of this committee is so critical. Americans should be relying on the science-based assessments and recommendations by both the FDA and the CDC to guide their decision-making. The incredible advancements that have made in preventing and treating COVID-19 are something we as a nation should be proud of. And we strongly support the recommendation of a booster dose for all eligible Americans. We think this recommendation will provide much needed clarity for Americans who may be wondering if they are eligible for the booster and for whom that extra level of protection is needed. Vaccines represent our best tool in preventing serious illness and in reducing the overall threat of this deadly virus. We at Nurses Who Vaccinate appreciate this committee's thoughtful consideration of a broader booster recommendation. We do ask that there's further clarification and data about mixing boosters, and we will continue to do our part in educating our communities following your decision. Thank you very much.

Ms. Lisa Randall, JD, MPH
Concerned Individual

Hi. Good afternoon. Thanks for giving me the opportunity to make a public comment. And I send my enthusiastic thanks to the members and staff of ACIP for their hard work and good judgment in what has been a really long, stressful slog with COVID-19. I think it's so valuable that these meetings are available for the public to watch and I wish more people would watch, because the fact of your transparency will help them understand that there's nothing to be afraid of with recommended vaccines. I did have the experience recently of arranging a booster dose of COVID vaccine for someone in my family and I noticed that it was a little bit complicated by the need to ascertain that the person was eligible. When I tried to schedule online with the person's primary provider, something had gone wrong with the logic of the questionnaire and it wouldn't let me schedule. I only mention this to say that if the recommendation were simpler, this kind of thing would be less likely to inadvertently create a barrier. I'm happy to tell you I was able to straighten things out. But of course, the most important thing is to get doses to those who haven't had any yet. And on that subject I'll pass along one more anecdote, which is a conversation that my mom passed along to me with somebody who is her friend and not a bad person, but has fallen victim to misinformation about COVID. This person thought she could trust what she called "independent media," whatever she thinks that is, that she distinguished them from what she called "corporate-owned media." And she was just sure that what her sources were recorded was real science with studies backing it. The whole phenomenon of there being people who live in an alternate reality is not new, but it's getting worse. And I can only encourage continued efforts and creative thinking about how to break through it, whether that's through non-traditional partnerships, or media, or what have you. I appreciate everyone's contribution to getting us through this experience. And thanks again for letting me comment.

Ms. Karen Isabella Halabura
Vaccine Advocate Who is Autistic

Hi. I really appreciate how you've worked so hard to get these vaccines out. Vaccine advocates who are autistic have been fighting misinformation for many years. I actually seek out those sources because I kept getting told that vaccines cause autism, which is not true. I'm also a mom of an autistic child and we both are already immunocompromised. My autistic daughter has a tumor around pancreas which was diagnosed in April of last year and she's fully vaccinated. We both had our flu shots this year. We're doing great and it's really nice that we have this option to be able to give her personal topics or personal information. It's really hard to get through proper information online. All you find is people who are telling you that vaccines are going to end up hurting us in the long run. All I've ever had has been good information and I've never had a problem even when I got flu shots, and I'm allergic to eggs. So, I really want to say that I appreciate all the work you've done. Thank you very much.

COVID-19 Vaccine Booster Dose Safety

Dr. Tom Shimabukuro (CDC/NCEZID) presented on COVID-19 vaccine booster dose safety, first pointing out that for the purpose of this surveillance review, Pfizer-BioNTech vaccination doses administered beginning September 22, 2021 and Moderna and Janssen vaccination doses administered beginning October 20, 2021 are assumed to be booster doses. Some doses might be additional doses administered to immunocompromised individuals and therefore misclassified as boosters, but using these anchor points provide the cleanest analysis. COVID-19 vaccines are being administered under the most intensive vaccine safety monitoring effort in US history. Strong, complementary systems are in place—both new and established. These

include v-safe[sm], VAERS, VSD, and the CISA Project. A full list of US COVID-19 vaccine safety monitoring systems is available on the CDC website.[4]

As a reminder, v-safe[sm] is a CDC smartphone-based monitoring program for COVID-19 vaccine safety in the US. It uses text messaging and web surveys to check in with vaccine recipients after vaccination. Patients can register at any time after the first, second, or third dose. However, questions can only be answered moving forward. It is not possible to go back in time after registration to answer questions about previous doses. Parents and guardians also can register on behalf of children. V-safe[sm] solicits participants' reports on how they feel after COVID-19 vaccination to include local injection site reactions (i.e., pain, redness, swelling), systemic reactions (i.e., fatigue, headache, muscle aches), and health impacts (unable to perform normal daily activities, missed school or work, or received medical care).

In terms of patterns of vaccination for the 725,917 v-safe[sm] participants who reported a booster dose as of November 14, 2021 looking at the primary series that an individual reported receiving and the booster dose that they reported receiving of Moderna, Pfizer, or Janssen, the take-home message was that for the mRNA vaccines, people overwhelmingly got boosted with the same vaccine they receive during the primary series. For Moderna or Pfizer, greater than 95% received a booster dose with the same vaccine for which they were vaccinated for the primary series. That was somewhat different for Janssen for which 16% received a Janssen booster, for which there could be multiple reasons.

Looking at v-safe[sm] data on reactions and health impact events reported at least once in the week after Pfizer BioNTech vaccination by dose, local reactogenicity, systemic reactogenicity, and health impact events were generally reported less following the booster dose compared to Dose 2. These were statistically significant, although the differences were not that great. These are large data and that can impact the ability to find statistically significant findings. There was slightly more medical care received after the booster dose compared to Dose 2, but the differences were very small. This general pattern held true for Moderna as well for injection site reactions, systemic reactions, and health impact events generally. There was less reported reactogenicity or health impacts following the booster dose when compared to Dose 2, although the differences were fairly small in some cases.

For heterologous versus homologous prime boost combinations, the general was that regardless of the primary series on received, there was more reported local reactogenicity if boosted with the Moderna compared to getting boosted with the Pfizer. The Janssen booster was the least reactogenic for individuals who received the Janssen primary series. The general trends persisted in reported systemic reactions at least once in the week after vaccination. Individuals who were boosted with Moderna, regardless of the primary series, reported more systemic reactions compared with Pfizer and with Janssen for those who received the Janssen primary series. The differences were fairly small in the case of the Moderna primary and the Janssen primary series. For health impact events, the trends generally persisted such that there were more self-reported health impact events the week after booster for individuals getting the Moderna boost compared to the Pfizer boost, regardless of the primary series that they received.

[4] https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety.html

In summary, after over 725,000 v-safe[sm] registrants reported a booster dose, most reported a primary mRNA vaccine series followed by booster dose from the same manufacturer. Consistent with findings on reactogenicity following a primary series, generally Moderna boosters appeared to be more reactogenic than the Pfizer-BioNTech booster, regardless of the primary series manufacturer. For Pfizer and Moderna, local and systemic reactions and health impacts were reported less frequently following a booster dose than Dose 2 of the primary series.

Now moving on to data from VAERS. As a reminder, VAERS is the national spontaneous reporting or passive surveillance system that is co-managed by the CDC and the FDA. VAERS accepts reports from anyone, regardless of the plausibility of the vaccine causing the event or the clinical seriousness of the event. The key strengths of VAERS are its ability to rapidly detect potential safety problems and to detect rare AEs. As a passive surveillance system, VAERS has inconsistent quality and completeness of information and it is subject to reporting biases. Because of these limitations, it generally cannot be determined whether a vaccine caused an AE based on VAERS data alone.

In terms of reports to VAERS following COVID-19 booster dose vaccination, regardless of manufacturer, ≥93% of reports were non-serious. This is consistent with what is seen for the primary series for these vaccines and consistent with what is observed for other vaccines in general. Looking at crude reporting rates to VAERS for COVID-19 booster dose vaccination per million doses administered, the number of reports is divided by the doses administered and then multiplied by 1 million to get the reporting rate per million doses administered. For Janssen, it was necessary to do some extrapolation because there were less than 1 million doses. Using this formula allows for a standardized comparison for the 3 vaccines. For all 3 vaccines, the reporting rates for all reports and serious reports were comparable and were fairly similar to what has been observed with the primary series for these vaccines.

With regard to the patient characteristics for these booster dose reports to VAERS, most of these reports are in individuals ≥50 years of age. The median age was 62 years. The interquartile range was 45-71 years of age. Two-thirds of the reports were in females. The male-to-female ratio for reporting was consistent with what has been seen for the primary series for these vaccines, and also was consistent with what has been observed for VAERS reporting in general. There were more reports in females compared to males. VAERS also captures reports on race and ethnicity. Most reports were in persons of white, non-Hispanic race and ethnicity or unknown race and ethnicity, meaning that section of the form was not completed.

The most frequently reported non-serious AEs reported to VAERS following a COVID-19 vaccination were headache, fever, fatigue, pain, and chills. The most frequently reported SAEs were dyspnoea, death, fever, chest pain, and asthenia. There have been 82 reports of deaths submitted to VAERS. To put that in context, that is after 26.3 million booster doses administered in the US. Among the 82 initial reports of deaths following booster doses, 60 received Pfizer and 22 received Moderna. There were no Janssen reports. The median age in these reports was 79 years and the interquartile range was 69-90 years.

In terms of the preliminary impression of the cause of death (COD), when sufficient information was available to make that determination, included: Acute Leukemia, Cardiomyopathy, Congestive Heart Failure, COVID-19 Disease, General Decompensation (end stage disease), Glioblastoma, Myocardial Infarction, Pneumonia and Sepsis, Pulmonary Embolism, Renal Failure (end stage renal disease), Respiratory and/or Cardiac Arrest, and Stroke. This is based on CDC physician review of initial VAERS report and available documentation, including death

certificates. Based on an analysis conducted by CDC,[5] it was estimated that 236.5 coincidental all-cause deaths would be expected in 10 million vaccinated people within 1 day of vaccination; 1,655.5 coincident all-cause deaths in 10 million people within 7 days of vaccination; and 9,932.8 coincident all-cause deaths in 10 million vaccinated people within 42 days of vaccination. The reports after booster doses, given the amount of booster doses administered so far, put that below the background that would be expected.

Myocarditis and myopericarditis cases have been reported following booster doses. There have been 54 preliminary reports of myocarditis and myopericarditis, all after Pfizer-BioNTech or Moderna vaccination. The median age in these cases was 51 years, with an interquartile range of 38-67 years. Median time to onset was 3 days, with an interquartile range of 1-7 days. These reports were in 29 males, 24 females, 1 person for whom sex was not reported. The crude unadjudicated reporting rate was 2.1 cases per million mRNA COVID-19 vaccine doses administered. The characteristics of reports appear to reflect the population for booster dose recommendations, mainly older adults. Of the 54 cases, 38 are still under review, 4 did not meet case definition, and 12 have met case definition. For some additional information on these 12 cases that were concluded to have met the CDC case definition, the median age was 46 years, the median symptom onset was 4 days, 9 were male and 3 were female, and most were non-Hispanic White. There were 8 Pfizer reports and 4 Moderna reports, with 10 of these 12 were known to have been hospitalized. All 10 were discharged home. The recovery status was known for 8 of those, 6 (75%) of whom were known to have recovered from symptoms at the time of the report.

To summarize the VAERS findings, during the period from September 22, 2021 through November 5, 2021, there were 25.9 million mRNA and 334,000 Janssen vaccine booster doses administered. Most reports, 93% or more, were non-serious. This is similar to what is observed for the primary series for these vaccines. Almost half of the reports were among persons 65 years of age and older and two-thirds were in females. The most frequently reported non-serious AEs were known and well-characterized AEs associated with COVID-19 vaccination. There were no unusual or unexpected patterns observed with respect to reports of deaths following COVID-19 booster vaccination. There were 54 preliminary reports of myocarditis and myopericarditis identified. Of these, 12 reports met the CDC case definition, while others are under review or have been ruled out. The characteristics of these reports appear to reflect the population for booster dose recommendations.

V-safe^{sm} is available for booster dose registration and for surveys. Those who are already registered can access their account, enter the vaccine information, and proceed. Those who are not registered will need to register as a new user and then proceed. CDC is aware that there have been some questions about registering dependents in v-safe^{sm}. Parents or caregivers need to register children 5-15 years of age, which must be done through a parent or caregiver account. If a parent or caregiver is already registered, they can simply access their current account. Once on the landing screen, they can click “Add a Dependent” to register one of their dependents. Those who do not have an account can create a new account and then register their dependent. This will allow parents and caregivers to respond on behalf of their minor children.

[5] Abra et al. Expected Rates of Select Adverse Events following Immunization for COVID-19 Vaccine Safety Monitoring. medRxiv. doi: https://doi.org/10.1101/2021.08.31.21262919

VaST Summary

Dr. Keipp Talbot (VaST Chair) provided a summary from the VaST WG. As a reminder, the objectives of the VaST WG are to: 1) review, evaluate, and interpret post-authorization/approval COVID-19 vaccination safety data; 2) serve as the central hub for technical subject matter expertise from federal agencies conducting post-authorization/approval safety monitoring; 3) advise on analyses, interpretation, and presentation of vaccine safety data; and 4) provide updates to the ACIP COVID-19 Vaccines WG and the entire ACIP on COVID-19 vaccine safety. VaST continues to review COVID-19 vaccination safety data from passive and active surveillance systems. US safety monitoring systems include VAERS, VSD, FDA's Biologics Effectiveness and Safety (BEST) System, Department of Veterans Affairs (VA), Indian Health Service (IHS), and Department of Defense (DoD). In addition, there are the Israeli and Canadian data and data from the Global Advisory Committee on Vaccine Safety (GACVS). Special evaluations are underway on myocarditis case follow-up.

VaST has presented assessments during ACIP meetings almost monthly at this point. From December 21, 2020 to the present, VaST has had 41 independent meetings to review vaccine safety data and 11 joint meetings with the COVID-19 Vaccines WG focused on safety. VaST previously reviewed US safety for the September 22, 2021 ACIP vote on boosters. At that time, the data available for third doses were mainly for those provided under recommendations for persons with immunocompromising conditions. Since that time, VaST has been able to accrue more safety data. The data that were reviewed include data from VAERS, v-safe[sm], and Israel Ministry of Health data.

The booster vaccination data that come from VAERS include information from almost 26 million doses of mRNA and 334,000 Janssen vaccine doses. Among the almost 12,000 VAERS reports, nearly 93% were non-serious and almost half were in persons 65 years of age and older. The most frequently reported non-serious AEs were similar to AEs reported after earlier doses of COVID-19 vaccine, similar to the reactogenicity previously seen. There are 54 preliminary reports of myocarditis following mRNA vaccination. Of these, 12 have been verified as meeting the CDC case definition and 38 are pending investigation. The age distribution reflects the booster dose recommendations.

Safety data after booster doses have been reported by over 700,000 v-safe[sm] participants. Most reported a primary mRNA vaccine series followed by a booster from the same manufacturer. For both mRNA vaccinations, local and systemic reactions and health impacts were reported less frequently following a booster dose than following Dose 2 of the primary series. The Moderna booster appears to be more reactogenic than the Pfizer-BioNTech booster, regardless of the type of mRNA vaccine given previously.

In addition, VaST has been shown data from Israel for a third dose.[6] In Israel, booster doses of Pfizer-BioNTech vaccine were phased in first for persons ≥60 years of age. Since the end of August, everyone ≥12 years of age has been eligible for a third dose. Approximately 4 million third doses have been administered to persons ≥12 years of age through November 15, 2021. Rates of reported systemic, local, neurologic, allergic, and other reactions were lower after Dose 3 than after either Dose 1 or Dose 2. The reported rates of myocarditis have been lower than after Dose 2.

[6] Updated from: https://www.fda.gov/media/153086/download

The VaST WG assessment of COVID-19 booster vaccination safety data is that data regarding booster doses to date are reassuring. Reactogenicity and adverse events of special interest (AESI) are similar to or lower than those seen after the primary series. Myocarditis risk after a Pfizer booster dose appears lower than after Dose 2. However, there are limited data available to assess myocarditis risk after Moderna booster. As a reminder, Moderna booster dose is a lower dose (50µg) than the primary series dose (100µg). Deaths reported to VAERS after a primary series or a booster dose do not suggest any concerning patterns and reported rates are below background rates. VaST will continue to review further safety regarding booster doses as data become available, collaborate with global vaccine safety colleagues on key issues, and provide updates to the ACIP COVID-19 Vaccines WG and ACIP during future meetings.

Discussion Summary: Shimabukuro & Talbot

- In response to an inquiry regarding the total number of people who died of COVID infection after receiving the booster and which primary series of vaccine they received, Dr. Shimabukuro indicated that he did not have that information on hand and would have to go back to the physician reviewers and the database to obtain it. He indicated that of the 82 individuals who died, some died of COVID-19. However, he emphasized that these are preliminary reports and that CDC is in the process of following up on these reports to obtain medical records, death certificates, and autopsy reports. That process can take a while. The conclusions were based on a physician review and an initial impression made based on the reports submitted, some of which had limited information. Therefore, additional follow-up must be done before any harder conclusions about the CODs can be made and whether these individuals actually had COVID-19 can be confirmed. Dr. Shimabukuro said that he would get this specific information to provide to ACIP.

- Regarding a request for further information about the size, scope, and relationship v-safe[sm] has to VAERS, Dr. Shimabukuro reminded everyone that v-safe[sm] is a voluntary self-enrollment program. Anyone who receives a vaccination can register and enroll in v-safe[sm] and start sending information to CDC. It is anticipated that a lot of people who got early booster doses probably were existing v-safe[sm] participants and essentially were early adopters. CDC was pleasantly surprised about the participation for the booster doses, and those numbers continue to grow by the day. VAERS is a spontaneous reporting system that receives reports that patients or HCP choose to submit. It is anticipated that the database on booster dose safety in VAERS will continue to grow as more doses are administered. If an individual reports that they received medical care during one of their health check-in surveys in v-safe[sm], that case is referred to a follow up group which contacts the person to take a VAERS report if appropriate, or helps facilitate the patient to report the AE to VAERS. The VSD also is monitoring booster dose safety, which is a very robust electronic health record-based system that has complete or near complete information on about 12 million persons per year. Booster dose information will accumulate over time. Dr. Shimabukuro said that they would be happy to present again to ACIP at a later date to provide an update on the safety findings from the VSD.

- In terms of a question regarding myocarditis being rarer after a booster than a second dose, Dr. Shimabukuro said he thought it was early to draw conclusions about a booster dose and myocarditis. There have been a relatively small number of reports of myocarditis and myopericarditis relative to the number of booster doses that have been given, but it is difficult to compare what is being observed with a booster dose compared to what is being seen with the primary series at this point. Because of the recommendations, most of the individuals getting booster doses tended to be older. The demographics of the reports

received so far after booster doses are representative of the population getting vaccinated, which is different than for the primary series where this risk has been seen primarily in adolescents and young adults.

- Asked whether the VaST WG had any insight on the data from Israel that included younger children, Dr. Talbot indicated that the WG did not receive an extensive briefing beyond what was given during the Vaccine and Related Blood Products Advisory Committee (VRBPAC) meeting. There was not much information specifically looking at the young adults. Israel has looked prospectively for myocarditis and did not observe any increasing rates. While they did have cases following booster doses, there were less than seen after second doses.

- Regarding a question about whether it is possible to ascertain if individuals reporting AEs to v-safe[sm] following booster doses experienced similar events with their primary series, Dr. Shimabukuro indicated that CDC is exploring how they may be able to address that question in v-safe[sm]. They do have individual level data and should be able to look at that. He cautioned that depending upon what happens with a second dose may impact people's decision regarding whether to get a booster dose, which could complicate any analyses.

Updates to the EtR Framework: Pfizer-BioNTech and Moderna COVID-19 Vaccine Booster Doses

Dr. Sara Oliver (CDC/NCIRD) provided updates to the EtR Framework on Pfizer and Moderna COVID-19 vaccine booster doses, first reminding everyone that a slightly modified EtR Framework was used to discuss recommendations pertaining to COVID-19 boosters. Previous presentations and discussions for booster doses of COVID-19 vaccines occurred on September 23, 2021 during which there was a benefit/risk discussion regarding COVID-19 vaccine booster doses and the EtR Framework was presented on booster doses of Pfizer-BioNTech COVID-19 vaccine. There was a vote at that time for Pfizer-BioNTech COVID-19 booster doses.[7] On October 21, 2021, there was a presentation on a National Institutes of Health (NIH) mix and match booster study and an EtR Framework presentation on booster doses of Moderna and Janssen COVID-19 vaccines. In addition, there was a vote for Moderna and Janssen COVID-19 booster doses, including heterologous boosting.[8]

The current recommendations for a COVID-19 vaccine booster dose in persons who received a Janssen COVID-19 vaccine primary series are, for which no updates were discussed during this session:

> *All persons ≥18 years should receive primary vaccination with Janssen COVID-19 vaccine should receive a single COVID-19 vaccine booster dose at least 2 months later.*
>
> *And any FDA-approved or authorized COVID-19 vaccine (Pfizer-BioNTech, Moderna, or Janssen) can be used for a booster dose, regardless of the vaccine received for the primary series.*

[7] https://www.cdc.gov/vaccines/acip/meetings/slides-2021-09-22-23.html
[8] https://www.cdc.gov/vaccines/acip/meetings/slides-2021-10-20-21.html

The current recommendations for a COVID-19 vaccine booster dose in those who completed an mRNA vaccine primary series are:

Persons who should receive a COVID-19 booster dose include those who are:
- *Aged ≥65 years*
- *Aged ≥18 years and reside in long-term care settings*
- *Aged 50-64 years with certain underlying medical conditions*

Persons who may receive a booster dose, based on individual benefit risk, include those who are:
- *Aged 18-49 years with certain underlying medical conditions (includes pregnant people)*
- *Aged 18-64 years at increased risk for SARS-CoV-2 exposure and transmission because of occupational or institutional setting*

The mRNA booster dose is recommended at least 6 months after completion of the primary series. Any FDA-authorized or approved vaccine may be used.

The focus of this session's discussion was on the "may" recommendations. The relevant policy question brought before the ACIP was, "Do the balance of benefits and risk and facilitation of implementation warrant an update to COVID vaccine policy?" The proposed update would clarify that all other persons ≥18 years of age may receive a COVID-19 booster dose ≥6 months after completion of the mRNA primary series under the current EUA.

Moving to the public health problem, over 47 million cases of COVID-19 had been reported to CDC as of November 16, 2021. In late October, the recent wave had declined to a point at which the 7-day moving average was just over 60,000 cases per day. There have been increases over recent weeks, with the 7-day moving average back up to over 80,000 cases per day. Trends in COVID hospitalization are being monitored closely as well. Hospitalizations can lag behind increases in COVID cases. While substantial increases have not been seen in hospitalizations to date, this will be watched closely moving into the next few weeks and months.[9] In a country as large as the US, it is known that the pandemic can evolve differently in various regions of the country. While parts of the country had an earlier Delta surge, many areas of the country are seeing higher case rates now than they had in recent weeks to months.[10] Over 195 million people are fully vaccinated in the US, representing 69% of the population 12 years of age and over.[11] As a reminder, As you know, early in the vaccine distribution, much of the older population was vaccinated. Vaccination moved into younger age groups as time progressed.[12]

In terms of VE data for the primary series, data from the Increasing Community Access to Testing (ICAT) platform gathers pharmacy testing data and assesses VE against symptomatic infection. Because the data set is so large, it provides the unique opportunity to look at waning both before and during Delta. Similar trends have been observed across age groups, with some waning during the pre-Delta period and additional waning in the Delta period. Looking at 4 studies[13] that assessed waning of Pfizer-BioNTech vaccine by time since second

[9] CDC: https://covid.cdc.gov/covid-data-tracker/#new-hospital-admissions Accessed November 17, 2021
[10] CDC: https://covid.cdc.gov/covid-data-tracker/#cases_casesper100klast7days Accessed November 18, 2021
[11] CDC. https://covid.cdc.gov/covid-data-tracker/#vaccinations_vacc-people-onedose-pop-12yr. Accessed November 18, 2021
[12] Source: Immunization Data Lake.
[13] Lin, North Carolina surveillance, Alpha & Delta, symptomatic disease, ≥12 years; Tartof, Kaiser Southern CA, Delta, any infection, ≥16 years and all variants, severe disease, ≥16 years; Lin, North Carolina surveillance, Alpha & Delta, ≥12 years; Tenforde, IVY, Alpha & Delta, hospitalization, ≥18 years (Feikin et al. in press at The Lancet and Tenforde et al in preparation)

dose, outcome, and age, 2 studies (Lin, Tartof) included estimates against both of these outcomes. Lin et al showed a steep decline in the VE between 2 and 7 months from the second dose against symptomatic disease, but saw much smaller declines against more severe endpoints. Tardiff et al showed similar warning against infection, but not against severe disease. Looking at similar data for Moderna, overall waning was slightly less pronounced. However, the pattern was similar with declines again shown for VE against infection and minimal declines against severe disease.

In summary, over 195 million people are fully vaccinated in the US. COVID-19 cases are increasing in some jurisdictions recently. VE after the primary series is waning for infection. Overall, protection remains high for severe disease and hospitalization, and waning appears to be less pronounced for the Moderna vaccine compared to the Pfizer vaccine.

Moving to the benefits and harms domain and the PICO questions, the population is persons aged ≥18 years who completed a COVID-19 vaccine primary series ≥6 months ago. The intervention varies by vaccine: Pfizer-BioNTech COVID-19 Vaccine booster dose (BNT162b2, 30 µg, IM) and Moderna COVID-19 Vaccine booster dose (mRNA-1273, 50 µg, IM). The comparison is no booster dose. The outcomes are symptomatic laboratory-confirmed COVID-19 (critical), hospitalization due to COVID-19 (critical), death due to COVID-19, transmission of SARS-CoV-2 infection, serious adverse events (critical), and reactogenicity. These have not changed from previous presentations.

They heard from Pfizer earlier in the day about the data from the Phase 3 trial of around 10,000 participants.[14] All received a 2-dose primary series of the Pfizer-BioNTech vaccine, and then were randomized to receive either a booster dose or placebo with median follow-up of around 2.5 months. For the outcome of symptomatic laboratory-confirmed SARS-CoV-2 infection, the primary outcome evaluated was symptomatic COVID among persons with no evidence of prior infections, with events counting from 7 days post-booster dose. The outcome showed a relative vaccine efficacy of 95.2%, with a confidence interval of 89.3%, 97.9%.

The secondary VE outcomes, including those with prior infection and the all-available efficacy group, showed similarly high relative VE efficacy results. For the other beneficial outcomes, no hospitalizations due to COVID-19 occurred in either the booster (3-dose) group or placebo (2-dose) group. No deaths due to COVID-19 occurred in the booster or placebo groups. There were no data to assess the outcome of transmission of a SARS-CoV-2 infection. SAEs occurred in 0.3% of the booster recipients compared to 2.5% of placebo recipients. There were 3 AEs deemed by the investigator to be potentially associated with the vaccine that were described earlier by Pfizer, including the tachycardia and some elevations in hepatic enzymes.

Looking more broadly at AEs of clinical interest, there were no cases of anaphylaxis, hypersensitivity, myocarditis, or pericarditis reported in the trial. However, given the rarity of these events, it would not necessarily be expected to capture them in a trial of this size. Lymphadenopathy was more common after the third dose (2.7%) than in the primary series (0.4%). Lymphadenopathy following a booster dose was typically mild to moderate and located in the axilla or cervical nodes. Most occurred 1 to 3 days post-booster and resolved within 1 to 3 days after onset. The frequency of lymphadenopathy was slightly higher in younger participants and female participants. There was no updated reactogenicity from the Phase 3 booster trial.

[14] Clinical trial data requested by CDC

Now to summarizes the GRADE assessment for the Pfizer BioNTech COVID-19 vaccine for persons 18 years of age and over who completed a COVID primary series ≥6 months after the primary series. In terms of benefits, the newly available data indicate that the Pfizer-BioNTech COVID-19 booster dose is effective in preventing symptomatic laboratory-confirmed COVID-19 with a high evidence of certainty. No new data were submitted for the outcomes of hospitalization due to COVID-19, death due to COVID-19, or transmission of SARS-CoV-2 infection. The GRADE assessments for these outcomes did not change. In terms of harms, the available data showed no increase in SAEs for the booster group. The evidence certainty was low, and no new evidence was available for the outcome of reactogenicity.

Looking at the data is from the Israeli Ministry of Health reported during the last VRBPAC meeting, myocarditis rates reported after the Pfizer-BioNTech COVID-19 vaccine booster dose in Israel suggests that the rates of myocarditis after a third dose fall between the rates seen after Dose 1 and Dose 2.[15] In terms of the benefit/risk assessment of booster doses previously presented to ACIP,[16] the risk of myocarditis is now equivalent to the risk after the first and second dose averaged, as indicated by the Israeli data. All other inputs remained the same. Over the next 6 months, per million booster doses given, many more hospitalizations would be prevented than myocarditis expected for all age groups, even when considering a differential myocarditis risk by sex.

In summary, the Phase 3 randomized controlled clinical trial (RCT) booster efficacy data demonstrate that this booster dose provides additional protection and is safe. There were no hospitalized cases of COVID-19 even after the 2-dose primary series and even in those who did not receive the booster. Based on data from Israel, the myocarditis risk after the booster dose of Pfizer appears to fall between the rates seen after Dose 1 and Dose 2.

No Moderna booster vaccine efficacy/effectiveness studies were identified. One Moderna booster study was previously presented to ACIP.[17] In this study, participants already had received a Moderna primary series and were recruited to receive a booster dose in the open label study. This was immunobridging with a pre-specified non-inferiority analysis comparing the immune response 28 days after a booster versus 28 days after Dose 2 of the primary series. For the outcome of symptomatic laboratory-confirmed COVID-19, the GMTs of the 149 booster recipients were compared to over 1,000 primary series recipients. The GMR was 1.76, which met the non-inferiority criteria. No SAEs occurred among the participants receiving the 50 ug booster dose in that open label study within 28 days. Severe reactogenicity occurred among 10% of participants receiving a booster dose in the open label study.

To summarize the GRADE assessment for the Moderna vaccine for persons 18 years of age and over who completed the COVID-19 vaccine primary series ≥6 months or more before receiving a booster dose, there were no updates to previous discussions. In terms of benefits, the available data indicate that the Moderna booster dose induced an immune response that was non-inferior to those following Dose 2. The evidence certainty was very low. No data were available for the outcomes of observational data that suggested a protective effect against any SARS-CoV-2 infection. The evidence Type 4. For hospitalization due to COVID-19, observational data suggested an increased protective effect against severe COVID-19. The evidence was Type 4. No data were available on important outcomes of deaths due to COVID-

[15] As reported by Israel at FDA's VRBPAC meeting. Slides here: https://www.fda.gov/media/153086/download
[16] Scobie et al., COVID-NET, VISION, IVY Network; COVID-NET hospitalization rates from the week of August 21, 2021; Myocarditis rates from VAERS data through August 18, 2021
[17] Unpublished data obtained from the study sponsor: https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-10-20-21/02-COVID-Miller-508.pdf

19 or transmission. In terms of harms, available data identified no SAEs attributable to the booster dose, and this was Type 4. Grade 3 reactogenicity was reported by 6% of booster dose participants, which also was Type 4. This was the same as presented previously for GRADE.

In summary, there were no Phase 3 RCT booster efficacy data available from Moderna, but the immunogenicity study demonstrated the ability to boost antibody levels. Effectiveness after a primary series appears to have waned less in Moderna than in Pfizer. Myocarditis risks after a booster dose are unknown. Accumulating evidence from multiple sources suggests a higher risk for myocarditis following the Moderna compared to the Pfizer primary series vaccination, but note that the Moderna booster dose is lower at 50 µg than in the primary series at 100 µg. Therefore, the ability to extrapolate what was seen after the primary series to the booster dose is unknown.

When considering the number needed to vaccinate (NNV) with a booster dose to prevent 1 hospitalization over 6 months, the fewest doses are needed in those 65 years of age and over. When considering the NNV with a booster dose to prevent 1 infection over 6 months, the numbers are substantially lower with fewer doses needed to prevent infection in the younger age groups.

To summarize the safety surveillance findings presented earlier by Dr. Shimabukuro, local and systemic reactions were less frequent overall following a booster dose than after Dose 2. The Moderna booster appeared to be more reactogenic than Pfizer. For VAERS, most reports were non-serious. Rare cases of myocarditis have been reported after a booster dose, and investigations are ongoing to review and confirm these cases.

To highlight what is known around the impact of booster dose on transmission,[18] after a primary mRNA COVID-19 vaccine series, protection against asymptomatic infection and presumably transmission was found for a time period[a,b]. The largest impact was seen in the first 2 months post-vaccination,[b] and likely an impact of very high antibody titers. There are limited data of the impact of boosters on asymptomatic infection or transmission. However, one study from Israel found lower viral loads in patients with breakthrough infections after booster doses, similar to the viral load seen within 2 months after the primary series.[b] Early VE against SARS-CoV-2 infection after a booster dose demonstrates an increase in VE, including asymptomatic infection.[c,d] While it is known that protection against asymptomatic infection may not be permanent, even temporary protection may factor into the benefit/risk balance, especially approaching the winter and holidays with increased traveling and indoor gatherings.

In summary, booster doses of the Pfizer vaccine were effective in preventing laboratory-confirmed symptomatic SARS-CoV-2. Data from the Moderna trial does not provide efficacy data but demonstrates the ability to boost the immune response. Individual benefit/risk balance for boosters varies by age, with the largest benefit seen in older adults. Among other ages, there is likely variation within the balance of benefits and risks given exposure, medical condition, and sex. However, the myocarditis data after booster doses is reassuring to date. It also was not possible account for other benefits, including the possible impact on rates of community transmission.

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[18] a) CDC Science Brief https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/fully-vaccinated-people.html; b) Levine-Tiefenbrun et al. Nature Medicine 2021 https://www.nature.com/articles/s41591-021-01575-4; c) Saciuk et al. Journal of Infectious Diseases https://academic.oup.com/jid/advance-article/doi/10.1093/infdis/jiab556/6415586; d) Andrews et al. Effectiveness of BNT162b2 (Comirnaty, Pfizer-BioNTech) COVID-19 booster vaccine against covid-19 related symptoms in England: test negative case-control study | medRxiv

Moving now to values and acceptability. A survey[19] was conducted recently that showed that there appears to be uncertainty among fully vaccinated adults around eligibility for a booster dose, with 4 in 10 fully vaccinated adults stating that they were unsure whether they were eligible for a booster dose. Among fully vaccinated adults 65 years of age and over, 21% said that they already received a booster dose and another 52% said they believed they were eligible. Young adults were more uncertain, with two-thirds of fully vaccinated adults 18-29 years of age saying that they were unsure if they were eligible for a vaccine. It is known overall that the booster dose discussion seems to have increased rather than decreased public confidence in COVID-19 vaccines, although the opposite may be true for those who remain unvaccinated. More than 6 in 10 adults overall said the news that some people might need boosters show that scientists are continuing to find ways to make vaccines more effective, while one-third say that the vaccines may not be working as well as promised.

Now to consider feasibility and implementation. It is known that in general, booster doses are feasible to implement overall. Over 31 million people have received a booster dose. For the mRNA vaccines, people have mostly received a homologous boost. There is more variation for those who have received a J&J primary dose.[20] In terms of the daily number of booster doses by vaccine type over time, doses of Pfizer increased after the initial recommendations and then that expanded to all authorized vaccines with the updated recommendations.[21] Overall, at least 31 million individuals in the US have received a booster dose. To date, about 17 million of those are individuals 65 years of age and over. Some states are currently broadening booster eligibility criteria. For considerations around implementation, vaccine recommendations that are based on risk or exposure are more difficult to implement than age-based recommendations. ACIP recommendations that are consistent with an FDA EUA are easier to communicate and implement. If recommendations for booster doses varied across the mRNA vaccines, meaning if they were different for Pfizer and Moderna, this would be quite difficult to communicate and implement.

For the equity domain, the percentage of people who received at least 1 dose of the COVID-19 vaccine was assessed by race and ethnicity over time. These data were shown to ACIP previously, and were updated with additional time and data. American Indian and Alaskan Native (AI/AN) populations have consistently had the highest percentage among those who have received at least 1 dose, and some equity gaps have improved over time.[22] Looking at initial booster data in those 18 years of age and over by race and ethnicity, the highest uptake of booster doses in this population was in the non-Hispanic white population.[23] To summarize the equity domain, some disparities in primary series delivery have improved over time. However, early data on the COVID-19 booster doses demonstrate disparities by race and ethnicity. Recommendations that are complex, difficult to communicate, or difficult to implement may worsen disparities in booster vaccination rates.

[19] KFF COVID-19 Vaccine Monitor (October 14-24, 2021) KFF COVID-19 Vaccine Monitor: October 2021 | KFF
[20] CDC. https://covid.cdc.gov/covid-data-tracker/#vaccinations_vacc-people-onedose-pop-12yr. Accessed November 18, 2021
[21] Source: Immunization Data Lake. Data as of November 16, 2021, 0600 AM.
[22] CDC. https://covid.cdc.gov/covid-data-tracker/#vaccination-demographics-trends as of November 16, 2021, and US Census Bureau National Population Estimates
[23] Source: Immunization Data Lake. Data as of November 16, 2021, 0600 AM.

To summarize the WG interpretation, the WG reviewed and discussed the data as well as the policy option. They continue to emphasize that the top priority and largest impact will come from vaccination of the primary series in the unvaccinated population. It is known that the balance of benefits and risks varies by age. Older adults have the clearest benefits and risks. The myocarditis data are reassuring to date and will continue to be monitored closely. Increases in COVID-19 cases may also impact this benefit/risk balance. Previously, the goals of the overall COVID vaccination program have been discussed. The primary goal remains prevention of severe disease. The WG has discussed the importance of the secondary goals of maintaining the workforce and healthcare capacity, as well as the goal to reduce infection and transmission. The impact of a COVID-19 vaccine booster dose on prevention of transmission remains unknown. However, even a reduction in transmission may be important around this winter and holidays.

As a reminder, the types of ACIP recommendations that can be made have been presented previously with these booster discussions, including:

- ❑ We do not recommend the intervention, which is used when the risks clearly outweigh the benefits.

- ❑ We recommend the intervention for individuals based on an assessment of benefits and risk, which is used when there is a diversity of the benefits and risks to allow flexibility across a population. (May receive a booster)

- ❑ We recommend the intervention, which is used when the benefits clearly outweigh the risks in a population. (Should receive a booster)

The language currently in the clinical considerations to illustrate the factors that may go into this benefit/risk discussion already exists and will continue to be in the clinical considerations.[24] These are as follows:

- ❑ Potential **benefits** of booster dose
  - Reduced risk of SARS-CoV-2 infection, severe disease
  - May reduce transmission of SARS-CoV-2 to others

- ❑ Potential **risks** of booster dose
  - Rare risks of serious adverse events (e.g., myocarditis, pericarditis, TTS, GBS, anaphylaxis)
  - Common risks of transient local and systemic symptoms

- ❑ **Individual risk factors** for SARS-CoV-2 infection
  - Risk of exposure (occupational and institutional settings, e.g., healthcare workers, long term care settings)
  - Risk for infection (time since completion of primary series)

- ❑ **Individual impacts** of SARS-CoV-2 infection
  - Risk for severe infection (related to underlying conditions)
  - Risk associated with a person's circumstances (living with/caring for at-risk individuals or consequences of inability to meet obligations due to infection)

[24] CDC https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html

In the future, the WG will present updates to ACIP on data from the Moderna booster dose; rates of myocarditis after a third dose; updated data for the overall safety profile of a booster dose; and continued evaluations for VE, including VE for the primary series and booster doses. Dr. Oliver shared a figure developed to represent the current recommendations and another that was adapted for the proposed updates, if the recommendation was expanded to reflect that those 18-49 years of age and 50-64 years of age with no risk factors would be eligible in the **may** category. The proposed policy question had no edits to the **should** population and would consolidate the **may** population to "all other persons aged ≥18 years."

ASTHO Statement

Dr. Nirav Shah (Director, State of Maine CDC; President, ASTHO; ACIP Liaison Representative for ASTHO) made the following statement: Thank you very much, Dr. Lee. Good afternoon, everyone. I'm Nirav Shah, the Director of the State of Maine CDC and I also have the privilege of serving as the President of ASTHO, the Association of State and Territorial Health Officials. Since I'm addressing the committee, I wanted to note that I have no conflicts. Dr. Lee, thank you for the opportunity to address the committee on this important issue. I would like to provide some context and perspective to the committee from the point of view of state health officials, specifically on the operational and implementational contours of the issue under discussion today. Last night, on our All-State Health Official Call, we actually discussed this precise topic in detail. States were strongly in support of expanding, clarifying and simplifying the eligibility guidance in the manner that's been discussed and proposed. Indeed, I'll take it a click further. There was not a single state that voiced opposition to this move. Our summary and rationale was that the current guidelines, so well-intentioned and thoughtful, generate an obstacle to uptake of boosters. In pursuit of precision, they create confusion. This is what we see happening in our jurisdictions. Individuals who right now are absolutely eligible for boosters are not able to parse the guidelines to come to that conclusion on their own. This is in part an inherent limitation of the approach that we've used here, wherein individuals make their own eligibility determination. But this is why states believe that a move of the sort under discussion today would remove confusion and replace it with clarity. Our concern is that eligible individuals are not receiving boosters right now because of this confusion, and as a result, not enjoying the various benefits that have been discussed today. We urge you to move in the direction of expanded, simplified eligibility. In that world, instead of wondering if individuals are eligible, anyone 18 and over simply needs to find a clinic and get a booster. Operationally, such a move has the benefit of easing pressure on state health department immunization program staff, who are now fielding a high volume of booster eligibility questions. Simplifying eligibility will allow staff across the states, territories, and local health departments to focus on making vaccination, primary vaccination series, as easy and accessible as possible. Thank you very much, Dr. Lee.

Discussion Summary: Oliver

- There was broad agreement that the recommendations need to be as clear as possible, particularly given the statement from ASTHO about states, practitioners, and individuals being unsure about eligibility for boosters. This is especially important with respect to equity.

- It is important to be clear about the meaning of "fully vaccinated." The current primary series has been shown to be effective in terms of preventing serious disease, hospitalization, and death.

- It seems reasonable at this time to facilitate individuals being able to make a decision themselves based on benefits/risks.

- Consideration needs to be given to what the criteria would be for moving from a "may" to "should" recommendation for younger age groups. It seems that the goalposts have been moved to some extent, but the recommendations need to be broadened for the sake of equity.

- It is important to remember that these are all interim recommendations that will need to be re-evaluated continuously, including for younger populations. This will be impacted by incidence and what is known about the safety of boosters, particularly in terms of the risk of myocarditis.

- There was support for expanding the "should" recommendation to "Aged ≥50 years" due to the substantial number of individuals 50-64 years of age with risk factors:

    - Concern was expressed that this could create a barrier inadvertently when no barrier was intended, given the long list of possible underlying medical conditions.

    - Referring to Slide 61 with the proposed recommendations and revised table, Dr. Oliver reviewed the pros and cons of a "should" recommendation for those ≥50 years of age. As mentioned previously, age-based recommendations are easier to communicate and it is known that easy-to-communicate recommendations can facilitate equitable distribution. There is a very inclusive list of underlying medical conditions, which means that about 75% of persons 50-64 years of age would be covered. The remaining persons in that age group who would not meet a criterion on that list is relatively small. Moreover, having to check this inclusive list of underlying medical conditions can be difficult for providers to identify those who are at risk each time. This age group has the lowest risk of myocarditis after mRNA vaccines in this age group, which would impact that balance of benefits and risk. Adults 50-64 years of age, even those without medical conditions, may be at increased risk of severe COVID just due to a slightly older age. In thinking through the potential cons, there are limited VE data to specifically compare this exact age group with/without underlying medical conditions. Therefore, it is not possible to have detailed waning data. There is a risk of rare AEs, but myocarditis is low in this age group. However, it is also known that the risk of Guillain-Barré Syndrome (GBS) is a concern. GBS risk after a J&J vaccine has been seen in this age group.

    - Concern was expressed that it seemed dangerous in the last five minutes for ACIP to make a substantial change move without having spent an hour reviewing hospitalizations and outcomes of persons 50-64. The NNV is quite large and it is unlikely that there would be harm, but it is important to remember that a "should" recommendation from ACIP is taken by others to be a mandate.

    - Dr. Oliver emphasized that there may not be substantially more data forthcoming specifically related to persons 50-64 years of age without medical conditions, even with additional time. This was one of the reasons for the proposed recommendations presented during this session.

- There continued to be support for the stronger recommendation of "should" for persons ≥50 years of age, particularly heading into the holiday season and winter and given the equity issues.

- It was noted that time and again, risk-based recommendations have not worked. Persons 50-64 years of age represent a subgroup of whom the vast majority meet the criteria.

- The observation was made that immunosenescence begins before 65 years of age, and would seem to become more relevant around 50 years of age and favoring the concept of a "should" recommendation for persons ≥50 years of age.

- Practicing physicians emphasized simplicity as a sound rationale for a "should" recommendation for persons ≥50 years of age.

Votes: COVID-19 Booster Doses

Dr. Sara Oliver (CDC/NCIRD) showed the proposed recommendations table for booster doses of COVID-19 vaccine, which reflected the following:

*Persons who **should** receive a COVID-19 booster dose include those who are:*
- *Aged ≥65 years*
- *Aged ≥18 years and reside in long-term care settings*
- *Aged ≥18 years who received the Janssen COVID-19 vaccine primary series*
- *Aged 50-64 years with certain underlying medical conditions*

*Persons who **may** receive a booster dose, based on individual benefit risk, include those who are:*
- *Aged 18-49 years with certain underlying medical conditions (includes pregnant people)*
- *Aged 18-64 years with no risk factors*

The proposed policy question had no edits to the ***should*** population and consolidated the ***may*** population to "all other persons aged ≥18 years."

Discussion Summary: Vote

- Based on the key discussion points following Dr. Oliver's presentation, Ms. Bahta made a motion for ACIP to recommend that "COVID-19 vaccine boosters ***may*** be given to all other persons ≥18 years of age and that COVID-19 boosters ***should*** be given to persons ≥50 years of age."

- Dr. Cohn suggested that given the discussion, perhaps taking two votes would be the best option.

- Ms. Bahta withdrew her previous motion. She then made a motion to for ACIP to approve an interim recommendation stating that "A single COVID-19 vaccine booster dose is recommended for all persons aged **≥18 years*** who received an mRNA vaccine primary series **based on individual benefit and risk**, at least 6 months after the primary series,

under the FDA's Emergency Use Authorization." *Individuals not otherwise recommended to receive a COVID-19 vaccine. Dr. Kotton seconded the motion.

- Dr. Loehr made a motion for ACIP to approve an interim recommendation that "A single COVID-19 vaccine booster dose is recommended for persons **≥50 years** who received an mRNA COVID-19 vaccine, at least 6 months after the primary series, under the FDA's Emergency Use Authorization." Dr. Poehling seconded the motion.

Motion/Vote #1: COVID-19 Vaccine Booster Doses in Persons ≥18 Years of Age

Ms. Bahta made a motion for ACIP to approve an interim recommendation stating that "A single COVID-19 vaccine booster dose is recommended for all persons aged **≥18 years*** who received an mRNA vaccine primary series **based on individual benefit and risk**, at least 6 months after the primary series, under the FDA's Emergency Use Authorization."
*Individuals not otherwise recommended to receive a COVID-19 vaccine.

Dr. Kotton seconded the motion. No COIs were declared. The motion carried with 11 affirmative votes, 0 negative votes, and 0 abstentions. The disposition of the vote was as follows:

11 Favored:	Ault, Bahta, Brooks, Chen, Cineas, Daley, Kotton, Lee, Loehr, Poehling, Sanchez
0 Opposed:	N/A
0 Abstained:	N/A
0 Absent:	N/A

Motion/Vote #2: COVID-19 Vaccine Booster Doses in Persons ≥50 Years of Age

Dr. Loehr made a motion for ACIP to approve an interim recommendation that "A single COVID-19 vaccine booster dose is recommended for persons **≥50 years** who received an mRNA COVID-19 vaccine, at least 6 months after the primary series, under the FDA's EUA." Dr. Poehling seconded the motion. No COIs were declared. The motion carried with 11 affirmative votes, 0 negative votes, and 0 abstentions. The disposition of the vote was as follows:

11 Favored:	Ault, Bahta, Brooks, Chen, Cineas, Daley, Kotton, Lee, Loehr, Poehling, Sanchez
0 Opposed:	N/A
0 Abstained:	N/A
0 Absent:	N/A

Discussion Points

Subsequent to the vote, Dr. Lee invited ACIP members to make a statement about the rationale for their vote and/or to share any additional general comments:
Dr. Kotton said that as a clinician deep in the clinical trenches, she was really glad that there was now clarity and streamlining of the recommendations so that all Americans can understand the vaccines that are recommended for them at this time. She said that she was proud of the work they had done during this meeting.

Dr. Loehr thanked Dr. Oliver for portraying all of the excellent reasons for having this recommendation. He thought it would be especially important going into the holiday season and the winter season. He looks forward to having more data in the future about whether this is actually a booster dose or whether it is a third dose in the primary series, recognizing that it would take months, if not years, to figure that out.

Dr. Lee thanked ACIP's colleagues for the discussions throughout the day. She felt that it was important for them to acknowledge the "elephant in the room" in that there are many voices the public hears regarding the best way to use vaccines to handle this pandemic. ACIP recognizes that this pandemic has created a situation where absolutely nothing is normal. Everything moves quickly, data are constantly evolving, and local context can drive differences and the urgency and the need for these boosters and vaccines in general. She emphasized that diverse opinions at every level are always valued. However, it does create communication challenges and can often lead to more confusion not only for the public, but also even amongst the provider community. ACIP has been in place since 1964 and became a federal advisory committee in 1972, nearly 50 years ago. A priority for the ACIP always has been to ensure that they apply a consistent process for reviewing data and that this is done in public view so that there is transparency regarding the rationale for ACIP recommendations. During a pandemic, both speed and process are incredibly important. Ensuring that the public can understand the rationale behind any recommendation is critical for ongoing public trust. Because of this, Dr. Lee took a moment to thank Dr. Rochelle Walensky for being consistent, unwavering, and ensuring that ACIP continues to have a process that allows the members to transparently review the data and the science that are available in these open public meetings. ACIP is often criticized for not being fast enough, but this is the 22nd open meeting that ACIP has convened dedicated to the topic of COVID-19 vaccines, not to mention the hundreds of meetings that are occurring before and after each of these open meetings. Their commitment as ACIP members is to the public. She expressed her hope that they would continue to rely on the ACIP process, because she believes that public deliberation is an important part the pandemic response.

CERTIFICATION

Upon reviewing the foregoing version of the November 19, 2021 ACIP meeting minutes, Dr. Grace Lee, ACIP Chair, certified that to the best of her knowledge, they are accurate and complete. Her original, signed certification is on file with the Management Analysis and Services Office (MASO) of CDC.

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ACRONYMS USED IN THIS DOCUMENT

AAFP	American Academy of Family Physicians
AAP	American Academy of Pediatrics
ACHA	American College Health Association
ACIP	Advisory Committee on Immunization Practices
ACOG	American College of Obstetricians and Gynecologists
ACP	American College of Physicians
AE	Adverse Event
AESI	Adverse Events of Special Interest
AHIP	America's Health Insurance Plans
AI/AN	American Indian/Alaskan Native
AIM	Association of Immunization Managers
AIRA	American Immunization Registry Association
AMA	American Medical Association
AOA	American Osteopathic Association
APhA	American Pharmacists Association
AR	Adverse Reaction
ASTHO	Association of State and Territorial Health Officers
BEST System	Biologics Effectiveness and Safety System
CBER	Center for Biologics Evaluation and Research
CDC	Centers for Disease Control and Prevention
CICP	Countermeasures Injury Compensation Program
CISA	Clinical Immunization Safety Assessment
CMS	Center for Medicare and Medicaid Services
COD	Cause of Death
COI	Conflict of Interest
COVID-NET	COVID-19-Associated Hospitalization Surveillance Network
CSTE	Council of State and Territorial Epidemiologists
CVD	Cardiovascular Disease
DFO	Designated Federal Official
DoD	Department of Defense
DSMB	Data Safety Monitoring Board
DVA	Department of Veterans Affairs
ECG	Electrocardiogram
EMR	Electronic Medical Record
ET	Eastern Time
EtR	Evidence to Recommendation
EU	European Union
EUA	Emergency Use Authorization
EUI	Emergency Use Instructions
FDA	Food and Drug Administration
FQHC	Federally Qualified Health Center
GACVS	Global Advisory Committee on Vaccine Safety
GBS	Guillain-Barré Syndrome
GMR	Geometric Mean Ratio
GMT	Geometric Mean Titers
GRADE	Grading of Recommendation Assessment, Development and Evaluation

HCP	Healthcare Personnel / Providers
HHS	(Department of) Health and Human Services
HRSA	Health Resources and Services Administration
IDSA	Infectious Disease Society of America
IHS	Indian Health Service
IM	Intramuscular
ISD	Immunization Services Division
ISO	Immunization Safety Office
J&J	Johnson & Johnson
LTCF	Long-Term Care Facilities
MASO	Management Analysis and Services Office
MMWR	*Morbidity and Mortality Weekly Report*
MI	Myocardial Infarction
NACCHO	National Association of County and City Health Officials
NACI	National Advisory Committee on Immunization Canada
NAPNAP	National Association of Pediatric Nurse Practitioners
NCEZID	National Center for Emerging and Zoonotic Infectious Diseases
NCHHSTP	National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention
NCHS	National Center of Health Statistics
NCIRD	National Center for Immunization and Respiratory Diseases
NEJM	*New England Journal of Medicine*
NFID	National Foundation for Infectious Diseases
NHSN	National Healthcare Safety Network
NIH	National Institutes of Health
NMA	National Medical Association
NNV	Number Needed to Vaccinate
NWV	Nurses Who Vaccinate
OID	Office of Infectious Disease
OIDP	Office of Infectious Disease Policy and HIV/AIDS
PCP	Primary Care Provider/Practitioner
PCR	Polymerase Chain Reaction
PHAC	Public Health Agency Canada
PICO	Population, Intervention, Comparison, Outcomes
PIDS	Pediatric Infectious Disease Society
POTS	Postural Orthostatic Tachycardia Syndrome
RCT	Randomized Controlled Trial
RN	Registered Nurse
RNA	Ribonucleic Acid
RR	Relative Risk
SAE	Serious Adverse Event
SAGE	Strategic Advisory Group of Experts on Immunization (WHO)
SAHM	Society for Adolescent Health and Medicine
SHEA	Society for Healthcare Epidemiology of America
SME	Subject Matter Expert
SOC	System Organ Class
SRR	Seroresponse Rate
SVT	Supraventricular Tachycardia
TTS	Thrombotic Thrombocytopenia Syndrome
UK	United Kingdom

US	United States
USG	United States Government
VA	(US Department of) Veteran's Affairs
VAERS	Vaccine Adverse Event Reporting System
VaST WG	Vaccine Safety Technical Work Group
VE	Vaccine Efficacy
VE	Vaccine Effectiveness
VRBPAC	Vaccine and Related Blood Products Advisory Committee
VSD	Vaccine Safety Datalink
WG	Work Group
WHO	World Health Organization