DEPARTMENT OF HEALTH AND HUMAN SERVICES
CENTERS FOR DISEASE CONTROL AND PREVENTION

Advisory Committee on Immunization Practices (ACIP)

Summary Report
December 11-12, 2020
Atlanta, Georgia

Final - December 11, 2020

MEETING OF THE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES (ACIP)
Centers for Disease Control and Prevention
Atlanta, Georgia 30329
December 11 and 12, 2020

	AGENDA ITEM	PRESIDER/PRESENTER(s)
Friday, December 11, 2020		
12:00	**Welcome & Introductions**	Dr. José Romero (ACIP Chair) Dr. Amanda Cohn (ACIP Executive Secretary, CDC)
12:30	**Agency Updates** CDC, CMS, FDA, HRSA, IHS, NIH, OIDP	
1:00	**Coronavirus Disease 2019 (COVID-19) Vaccines**	
	Introduction	Dr. Beth Bell (ACIP, WG Chair)
	BNT162b2 Development Program	Dr. William Gruber (Pfizer)
2:15	***Break***	
2:30	GRADE: Pfizer-BioNTech COVID-19 vaccine Work Group interpretation and next steps Discussion	Dr. Julia Gargano (CDC/NCIRD) Dr. Sara Oliver (CDC/NCIRD)
5:00	**Adjourn**	
Saturday, December 12, 2020		
11:00	**Welcome & Introductions**	Dr. José Romero (ACIP Chair) Dr. Amanda Cohn (ACIP Executive Secretary, CDC)
11:30	**Coronavirus Disease 2019 (COVID-19) Vaccines**	
	Introduction	Dr. Beth Bell (ACIP, WG Chair)
	Evidence to Recommendation Framework: Pfizer-BioNTech COVID-19 vaccine	Dr. Sara Oliver (CDC/NCIRD)
	Clinical Considerations	Dr. Sarah Mbaeyi (CDC/NCIRD)
1:15	***Break***	
1:30	**Public Comment**	
2:30	**VOTE**	
	Pfizer-BioNTech COVID-19 Vaccine	Dr. Sara Oliver (CDC/NCIRD)
	Amendment to 2021 Child and Adolescent Immunization Schedule	Dr. Sara Oliver (CDC/NCIRD)
	Amendment to 2021 Adult Immunization Schedule	Dr. Sara Oliver (CDC/NCIRD)
3:00	**Adjourn**	

Acronyms

CDC	Centers for Disease Control and Prevention
CMS	Centers for Medicare and Medicaid Services
COVID-19	Coronavirus disease 2019
EtR	Evidence to Recommendations Framework
FDA	Food and Drug Administration
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HRSA	Health Resources and Services Administration
IHS	Indian Health Service
NCHHSTP	National Center for HIV, Hepatitis, STD and TB Prevention [of CDC/OID]
NCIRD	National Center for Immunization & Respiratory Diseases [of CDC/OID]
NCEZID	National Center for Emerging and Zoonotic Diseases [of CDC/OID]
NIAID	National Institute of Allergy and Infectious Diseases
OIDP	Office of Infectious Disease and HIV/AIDS Policy
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
WG	Work Group
WHO	World Health Organization
VE	Vaccine Effectiveness

Acronyms

AAFP	American Academy of Family Physicians
AAP	American Academy of Pediatrics
AAPA	American Academy of Physician Assistants
ACA	Affordable Care Act
ACHA	American College Health Association
ACIP	Advisory Committee on Immunization Practices
ACNM	American College of Nurse Midwives
ACOG	American College of Obstetricians and Gynecologists
ACP	American College of Physicians
ACTT	Adaptive COVID-19 Treatment Trial
AE	Adverse Event
AESI	Adverse Events of Special Interest
AGS	American Geriatric Society
AHIP	America's Health Insurance Plans
AIM	Association of Immunization Managers
AMA	American Medical Association
AOA	American Osteopathic Association
APhA	American Pharmacists Association
ASTHO	Association of State and Territorial Health Officers
BCG	Bacille Calmette-Guerin
BLA	Biologics License Application
BMI	Body Mass Index
CARES Act	Coronavirus Aid, Relief, and Economic Security Act
CCI	Charlson Comorbidity Index
CDC	Centers for Disease Control and Prevention
CISA	Clinical Immunization Safety Assessment
CMS	Center for Medicare and Medicaid Services
COCA	Clinician Outreach and Communication Activity
COI	Conflict of Interest
COU	Clinical Operations Unit
COVID-19	Coronavirus Disease 2019
CoVPN	COVID-19 Prevention Network
CSTE	Council of State and Territorial Epidemiologists
DFO	Designated Federal Official
DMC	Data Monitoring Committee
DoD	Department of Defense
DSMB	Data Safety Monitoring Board
DSPC	1,2-distearoyl-sn-glycero-3-phosphocholine
ECMO	Extracorporeal Membrane Oxygenation
eDiary	Electronic Diary
EtR	Evidence to Recommendation
EUA	Emergency Use Authorization
FDA	Food and Drug Administration
FFCRA	Families First Coronavirus Response Act
GI	Gastrointestinal
GMT	Geometric Mean Titers
GRADE	Grading of Recommendation Assessment, Development and Evaluation

HBV	Hepatitis B Virus
HCoVs	Human Coronaviruses
HCP	Healthcare Personnel / Providers
HCS	Human Convalescent Serum
HCV	Hepatitis C Virus
HCW	Healthcare Workers
HHS	(Department of) Health and Human Services
HIV	Human Immunodeficiency Viruses
HRSA	Health Resources and Services Administration
ICU	Intensive Care Unit
IDCRC	Infectious Diseases Clinical Research Consortium
IDSA	Infectious Disease Society of America
IFN-γ	Interferon-gamma
IHS	Indian Health Service
IL	Interlukin
ISTM	International Society for Travel Medicine
ITT	Intention-To-Treat
LTC	Long-Term Care
LTCF	Long-Term Care Facilities
MMWR	*Morbidity and Mortality Weekly Report*
mRNA	Messenger Ribonucleic Acid
NAAT	Nucleic Acid Amplification Testing
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
NCIRD	National Center for Immunization and Respiratory Diseases
NEJM	*New England Journal of Medicine*
NFID	National Foundation for Infectious Diseases
NIAID	National Institute of Allergy and Infectious Disease
NIH	National Institutes of Health
NIVW	National Influenza Vaccination Week
NMA	National Medical Association
NPI	Non-Pharmaceutical Intervention
NSAID	Nonsteroidal Anti-Inflammatory Drug
NVAC	National Vaccine Advisory Committee
OIDP	Office of Infectious Disease Policy and HIV/AIDS
OWS	Operation Warp Speed
PCR	Polymerase Chain Reaction
PHAC	Public Health Agency Canada
PHE	Public Health England
PICO	Population, Intervention, Comparison, Outcomes
PIDS	Pediatric Infectious Disease Society
QC	Quality Control
QI	Quality Improvement
RCT	Randomized Controlled Trial
RNA	Ribonucleic Acid
rRT-PCR	Real-Time Reverse Transcription Polymerase Chain Reaction

RT-PCR	Reverse Transcriptase Polymerase Chain Reaction
SAE	Serious Adverse Event
SAHM	Society for Adolescent Health and Medicine
SARS	Severe Acute Respiratory Syndrome
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus-2
SHEA	Society for Healthcare Epidemiology of America
SLU	Saint Louis University
SME	Subject Matter Expert
SUDs	Substance Use disorders
TEC	Tribal Epidemiology Center
THB	Tribal Health Board
µg	Micrograms
UK	United Kingdom
US	United States
USG	US Government
VA	(US Department of) Veteran's Affairs
VAERS	Vaccine Adverse Event Reporting System
VaST	ACIP COVID-19 Vaccine Safety Technical Subgroup
VE	Vaccine Efficacy
VE	Vaccine Effectiveness
VFC	Vaccines for Children
VIS	Vaccine Information Statement
VRBPAC	Vaccines and Related Biological Products Advisory Committee Meeting
V-SAFE	Vaccine Safety Assessment for Essential Workers
VSD	Vaccine Safety Datalink
VTrckS	Vaccine Tracking System
WG	Work Group

December 11, 2020: Opening Session

José Romero, MD, FAAP
ACIP Chair

Amanda Cohn, MD
Executive Secretary, ACIP / CDC

Dr. Romero called to order and welcomed everyone to the first day of the December 11 and 13, 2020 emergency meeting of the Advisory Committee on Immunization Practices (ACIP) meeting, the focus of which was to review the evidence to support a recommendation for the Pfizer/BioNTech coronavirus disease 2019 (COVID-19) messenger ribonucleic acid (mRNA) vaccine BNT162b2.

Dr. Cohn explained that ACIP would meet for a second day immediately after the Food and Drug Administration (FDA) issued an authorization for this product. If FDA issued an authorization by 10 am on December 12th, the second day of the emergency ACIP meeting would be moved from December 13th to December 12th beginning at 10:00 AM Eastern Time (ET). Given that this could shift very rapidly, information would be posted on the ACIP website as soon as available.

She indicated that all of the meeting materials were available on the ACIP website, that this meeting was available by live webcast, and meeting participants had joined the meeting via Zoom. In addition, she indicated that the slides were made available through a ShareFile link for ACIP Voting, Liaison, and *Ex-Officio* members; videos of the live webcast would be posted on the ACIP website approximately 4 weeks after the meeting; and that meeting minutes also would be posted on the ACIP website, generally within 120 days of the meeting. She noted that slides to be presented during this meeting could be accessed by all participants via the ACIP website, but were not 508-compliant and would be taken down at the end of the meeting, made 508-compliant, and then reposted approximately 4 weeks following the meeting. She then reviewed meeting logistics, emphasizing that the goal was to stay on schedule per the meeting agenda even if the meeting was running early.

The next regular ACIP meeting will be convened on February 24-25, 2021 and will be virtual. In addition, emergency ACIP meetings are scheduled for Friday, December 18th and Sunday, December 20th to review considerations for the Moderna COVID-19 vaccine product. If the FDA issues Emergency Use Authorization (EUA) for the Moderna vaccine before 10 AM ET on Saturday, December 19th, the second day of that emergency meeting would be moved to December 19th beginning at 10 AM ET. Whether another emergency ACIP meeting is scheduled prior to the regular February 2021 meeting will depend upon applications for EUA of any additional COVID-19 vaccine products.

Dr. Cohn indicated that there would be a public comment period during the second day of this meeting on either December 12th or 13th, depending upon issuance of an EUA. Members of the public were requested to comment only on the question that ACIP was considering, a recommendation and vote on the COVID-19 vaccine product under consideration.

ACIP's oral and written public comment processes are designed to ensure that the public has an opportunity to inform ACIP's considerations for immunization recommendations. Efforts are being made to maximize opportunities for comments and make the public comment process more transparent and efficient. Those interested in making an oral comment were asked to submit a request online in advance of the meeting. Priority is given to these advance requests, and if more people request to speak than can be accommodated, a blind lottery is conducted to determine who the speakers will be. Speakers selected in the lottery for this meeting were notified in advance of the meeting. Written public comments may be made via regulations.gov using the Docket ID: CDC-2020-0122. Information on the written public comment process, including information about how to make a public comment, can be found on the ACIP website. The docket for this meeting would open upon publication of the *Federal Register* notice on December 13, 2020 and would remain open through midnight on December 14, 2020.

Members of the ACIP agree to forgo participation in certain activities related to vaccines during their tenure on the committee. The Centers for Disease Control and Prevention (CDC) has issued limited conflict of interest (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 these vaccines, but are prohibited from participating in committee votes on issues related to those vaccines. 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 the vaccines of that company. At the beginning of each meeting and prior to each vote, ACIP members will state any COIs. Members participating in National Institutes of Health (NIH)-sponsored clinical trials for COVID-19 vaccines would be asked to abstain from voting on product-specific recommendations.

Dr. Romero conducted a roll call of ACIP members during which the following COIs were identified:

- ❑ Dr. Robert Atmar is serving as the Co-Director of the Clinical Operations Unit (COU) of the NIH-funded Infectious Diseases Clinical Research Consortium (IDCRC) that is working within the COVID-19 Prevention Network (CoVPN) to evaluate Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) vaccine candidates in Phase 3 clinical trials, including those produced by Moderna, AstraZeneca, Janssen, Novavax, and Sanofi.

- ❑ Dr. Sharon Frey is employed by Saint Louis University (SLU), which has a Vaccine Treatment Evaluation Unit (VTU) that is part of the IDCRC. She is currently a Site PI for two Phase III COVID-19 vaccine clinical trials.

- ❑ Dr. Paul Hunter owns a small amount of stock in Pfizer and has received a small grant from Pfizer to conduct a quality improvement (QI) project on pneumococcal vaccines.

A list of Members, *Ex Officio* Members, and Liaison Representatives is included in the appendixes at the end of the full minutes for the December 11-12, 2020 ACIP emergency meeting.

Agency Updates

Centers for Disease Control and Prevention (CDC)

Dr. Messonnier provided a few updates on CDC activities related to COVID. There have been notable declines in pediatric immunization including vaccine ordering, outpatient visits, and routine childhood vaccines starting in March 2020. As a result, children and communities are at increased risk for preventable diseases and outbreaks. Even though in recent months some weeks are comparable to the same week last year, there is still a large cumulative deficit, indicating the need for substantial catch-up. For the Vaccines for Children's (VFC) program, there is a deficit of more than 9 million doses overall and 1.2 million doses of measles-containing vaccine. The data sources show a faster recovery on the private sector side. CDC is urging healthcare systems and healthcare providers to identify families whose children have missed doses and contact them to schedule appointments, prompt clinicians when these children are seen to deliver vaccines that are due or overdue, and let families know what precautions are in place for safe delivery of in-person services. It is National Influenza Vaccination Week (NIVW). Since influenza preparation has been so closely tied to COVID, it would be remiss not to mention this year's influenzas vaccine efforts. So far this year, 188 million doses of influenza vaccine have been distributed in the US. That is the highest number of doses distributed in the US in a single season. That is somewhat connected to COVID.

While there have been many conversations about preparing for, authorizing, and distributing a vaccine for COVID, Dr. Messonnier said she wanted to share a few highlights of CDC's other work in responding to COVID-19. To date, 1440 CDC deployers have conducted 2694 deployments in 233 cities across the US and abroad. A total of 7893 CDC personnel have supported the outbreak response. Currently, more than 450 CDC staff are supporting the work of CDC's Vaccine Task Force. The *Morbidity and Mortality Weekly Report* (*MMWR*), sometimes called "the voice of CDC," has published more than 160 COVID-19 articles since the beginning of the pandemic. One of the most recent was the publication of "The Advisory Committee on Immunization Practices' Interim Recommendation for Allocating Initial Supplies of COVID-19 Vaccine — United States, 2020" published on December 3, 2020 [*MMWR* / December 11, 2020 / Vol. 69 / No. 49].

CDC has awarded over $12 billion to states, localities, territories, and tribes. To date, the agency has provided $140 million to jurisdictions for influenza season support in addition to $200 million for COVID vaccine planning. CDC will provide the next COVID allocation of planning funding to jurisdictions late in December, with a total amount of $140 million. CDC has produced 4113 documents providing information and guidance for government agencies, businesses, and the public regarding COVID. In preparing to distribute and administer the COVID vaccine quickly and efficiently, CDC has worked with its many partners in state and local health departments and throughout the country. A total of 41,000 COVID-19 providers are enrolled in the Vaccine Tracking System (VTrckS). That includes more than 20,000 pharmacy providers. Many of those pharmacy providers will help CDC reach the 55,000 long-term care facilities (LTCF) covering more than 3.5 million persons that have been enrolled in CDC's Pharmacy Partnership for Long-Term Care (LTC) Program. Specific to vaccine activities, CDC has had more than 150 partner meetings in the last few months, reaching almost a billion participants. A Chief Health Equity Officer was added to the COVID response to engage national partners addressing health equity in the context of COVID-19. In August, the Chief Health Equity Officer released a Health Equity Strategy that continues to be the guide for the

agency's response efforts, including efforts around COVID vaccine, which is available on the CDC website at:
https://www.cdc.gov/coronavirus/2019-ncov/downloads/community/CDC-Strategy.pdf

Centers for Medicare and Medicaid Services (CMS)

Dr. Hance shared an update focusing on cost-sharing for COVID-19 vaccines. For most individuals enrolled in Medicare, Medicaid, and private health insurance. there are no out-of-pocket expenses related to COVID-19 vaccines. CMS issued both an Interim Final Rule and a series of toolkits on October 28, 2020 addressing this. The Interim Final Rule was effective on November 2, 2020 and was published in the *Federal Register* on November 6, 2020. Specifically for Medicare, the Coronavirus Aid, Relief, and Economic Security (CARES) Act included COVID-19 vaccines in Medicare Part B without cost-sharing for Medicare beneficiaries. For those beneficiaries enrolled in Medicare Advantage plans, for years 2020 and 2021 the administration fee will be paid through fee-for-service Medicare. For those in private insurance coverage, the CARES Act also required non-grandfathered group or individual health insurance coverage plans to cover COVID-19 preventive services, which includes any ACIP-recommended vaccine without cost-sharing. In addition, the Interim Final Rule requires that there is no cost-sharing for those individuals in non-grandfathered group or individual health insurance plans who receive COVID-19 vaccines from out-of-network providers. For Medicaid, the Families First Coronavirus Response Act (FFCRA) includes an increased federal matching rate for states, with a condition of receiving that matching rate being that states cover COVID-19 testing services and treatments, which includes vaccines without cost-sharing. There is a small exception for those enrolled in Medicaid limited benefit groups. The temporary matching rate increase is in effect until the end of the quarter in which the public health emergency ends. Currently, all states have opted to claim the temporary rate increase. The Medicaid toolkit also describes vaccine coverage outside of the public health emergency, with cost-sharing prohibited for many categories of Medicaid eligibility outside of the public health emergency. For uninsured individuals, providers will be able to be reimbursed for administering COVID-19 vaccine through the Provider Relief Fund administered by the Health Resources and Services Administration (HRSA). CMS intends for these toolkits to be living documents and therefore, they are being updated as needed. All of this information is available at: https://www.cms.gov/covidvax

Food and Drug Administration (FDA)

Dr. Fink reported that on December 10, 2020, FDA convened the Vaccines and Related Biological Products Advisory Committee Meeting (VRBPAC) to discuss the EUA request for the Pfizer/BioNTech COVID-19 vaccine. The agenda for that VRBPAC meeting included an introduction by himself, followed by 3 presentations from representatives of the CDC that included an update on COVID-19 epidemiology, discussion of plans for vaccine safety and effectiveness monitoring should the vaccine be authorized for use under an EUA, and a description of operational distribution plans for the vaccine under an EUA. There was then a presentation on considerations for placebo-controlled trial design if an unlicensed vaccine were to become available under an EUA. In addition, there was an open public hearing. Most of the afternoon was spent hearing the details of the clinical trial results presented by Pfizer, followed by a presentation of the results of FDA's own independent analysis to cover the clinical data submitted in support of Pfizer's EUA request. There was a committee discussion on two items following those presentations, neither of which VRBPAC was asked to vote on. The first of these items was the discussion of Pfizer's plan for continuation of blinded placebo-controlled follow-up in ongoing trials if the vaccine were made available under the EUA. Pfizer has proposed to make vaccine available to placebo recipients if and when the placebo recipient would otherwise

have access to the vaccine under the conditions of EUA recommendation from federal, state, and local prioritization for use of the vaccine and vaccine availability. In that situation, study participants requesting the vaccine would be unblinded to their treatment assignment. If they previously received placebo, they would be administered the vaccine in study visits with scheduled follow-up. The second discussion item was to ask the committee to discuss any gaps in plans described for further evaluation of vaccine safety and effectiveness in populations who received the vaccine under an EUA. In terms of the first question about continuation of blinded placebo-controlled follow-up, the committee discussed that preservation of placebo-controlled follow-up for as long as is feasible should be attempted, but they certainly acknowledged that placebo recipients should not be denied the opportunity to receive vaccine if they would be otherwise eligible for the vaccine under the conditions and availability of the vaccine under an EUA. In terms of the second question, the committee expressed the need for continued evaluation of the vaccine specifically to gather more information on safety and specific populations, including HIV-positive individuals, and data on SARS-CoV-2 shedding and transmission and any impact, if any, that the vaccine might have on those parameters.

Following these discussion items, the committee was asked to vote on the single question, "Based on the totality of the scientific evidence available, do the benefits of the Pfizer/BioNTech COVID-19 vaccine outweigh its risks for use in individuals 16 years of age and older." A large part of the discussion surrounding this question involved concerns raised by some of the committee members that available data in individuals ages 16 to 17 years were very limited. They thought, in their opinion, that an EUA should include only individuals ages 18 and over. However, other committee members thought it would be reasonable to extrapolate a favorable benefit-risk balance for individuals 16 and 17 years of age based on safety and effectiveness data available for younger adults ages 18 and above and also supported by the available safety data from the clinical setting in participants 16 and 17 years of age who are enrolled in the study. There also was further discussion about the small numbers of severe COVID-19 cases in the trial that provide direct evidence of vaccine effectiveness against severe COVID-19. However, as discussed by FDA and some other members of the committee, extensive experience with preventive vaccines has demonstrated that vaccines that are effective against mild to moderate disease are also effective against severe disease. There is no expectation that this would not be the case for this COVID-19 vaccine. Available data from the clinical trials support the likelihood that the vaccine would be effective against severe COVID-19. One committee member expressed concern that further follow-up in clinical trials is needed prior to issuing an EUA. Following this discussion, the committee voted on the question. The results of the vote were 14 committee members in favor, 4 committee members against, and 1 abstaining. Thus, the vote of the VRBPAC was in favor of a determination that the benefits of the Pfizer/BioNTech COVID-19 vaccine outweigh its risk for use in individual 16 years of age and older based on the totality of scientific evidence available. FDA is now taking the VRBPAC vote and discussion into consideration as they continue to work on finishing the FDA review of the EUA application.

Health Resources and Services Administration (HRSA)

Dr. Rubin indicated that the Division of Injury Compensation Programs (DICP) did not have any updates to report at this time.

Indian Health Service (IHS)

Dr. Weiser reported that the IHS and Operation Warp Speed (OWS) are prepared for COVID-19 vaccine distribution and administration. The IHS attended COVID-19 Vaccine Task Force meetings, engaged in training regarding new reporting systems, developed priority population estimates with direct input from federally-recognized tribes, and mapped out distribution pathways for the 330 clinical sites that will be receiving their vaccines through the direct IHS allocation. Tribal and urban programs were given the option to receive vaccine through IHS or their respective state allocations, and 150 tribal and urban programs opted to receive vaccines through their state immunization programs. IHS also has strengthened vaccine safety monitoring, including Vaccine Adverse Event Reporting System (VAERS) and the V-SAFE^{SM} program, in cooperation with CDC. A sentinel surveillance program for active surveillance of adverse events also has been established. Each IHS area is working closely with their federal IHS Tribal and Urban Indian Health programs, Tribal Epidemiology Centers (TECs), and representative of Tribal Health Boards (THBs) to coordinate all aspects of carrying out a successful COVID-19 vaccine program.

National Institutes of Health (NIH)

Dr. Beigel provided updates from the NIH. In terms of vaccines, the National Institute of Allergy and Infectious Disease (NIAID) and Moderna recently published a letter in the *New England Journal of Medicine* (*NEJM*) detailing the 3-month follow-up from the Phase I study. That is 3 months after Dose 2 on Day 119 of the study. That data point is important because it gives the first clear evidence of the longevity of that vaccine. The previous week, NIAID and Moderna also announced the interim results of their Phase III study. NIAID has been part of the design and implementation of that study, with many sites from across many programs at the NIH supporting that study. That study will be the focus of the next VRBPAC and CDC meetings. Regarding therapeutics, the Adaptive COVID-19 Treatment Trial 2 (ACTT) that conducted the Remdesivir study published the findings of the ACTT-2, which is the trial that supported the EUA of Remdesivir plus Baricitinib anti-inflammatory therapy. That was published in the *NEJM* earlier in the day.

Office of Infectious Disease Policy and HIV/AIDS (OIDP)

Dr. Kim expressed gratitude to all of the organizations represented on ACIP for the comments they provided during the public comment period on the latest draft of the National Vaccine Plan. All of the public comments are currently being adjudicated. The final report is expected to be released in January 2021. The Vaccine Safety Report that OIDP releases was last published in 2014. OIDP is in the process of updating this report, which also has gone through a public comment period and all of the public comments are currently being adjudicated. This report is expected to be released in March 2021. The National Vaccine Advisory Committee (NVAC) meeting that was convened on December 4, 2020 was opened by the Assistant Secretary for Health (ASH), Admiral Brett Giroir, and Dr. Stanley Plotkin. Their opening was followed by presentations/discussions on approaches to include pregnant women in COVID-19 clinical trials. There also were presentations and discussions on vaccine safety systems and COVID-19 and on co-pay coverage for COVID-19 vaccines by CMS. The meeting also included a report on vaccine confidence overview by the NVAC Chair, Dr. Robert Hoskins. A vote was taken to accept that report in its entirety for submission to the ASH.

December 11, 2020: Coronavirus Disease 2019 (COVID-19) Vaccines

Introduction

Beth Bell, MD, MPH
ACIP, COVID-19 Vaccine WG Chair
Clinical Professor, Department of Global Health
School of Public Health, University of Washington

Dr. Bell introduced the COVID-19 Vaccines session. She began by taking a moment to reflect on the fact that over the last week, there had been an average of over 200,000 cases of COVID-19 every day in the US and more people in the hospital suffering from this condition than at any point so far in the pandemic. When last they met 9 days previously, she offered the sobering statistic that there was 1 American dying of COVID-19 every minute. Sadly, she had to report that there are now 2 people dying every minute. On December 9, 2020, there were 3411 deaths in the US. There is a huge amount of suffering at the moment in the US. The fact that during this meeting they would review evidence about one of the vaccines that has an EUA application pending at FDA and discuss interim recommendations offered some hope for the future.

As a reminder, during the meeting on December 1, 2020, ACIP voted on and approved interim recommendations for allocating initial supplies of COVID-19 vaccine in Phase 1a to include: 1) healthcare personnel (HCP); and 2) residents of long-term care facilities (LTCFs). During the November 23, 2020 meeting, ACIP reviewed: 1) the Evidence to Recommendation (EtR) Framework for the domains of Public Health Problem, Resource Use, Equity, Values, Acceptability, and Feasibility; and 2) phased allocation of COVID-19 vaccines.

ACIP's COVID-19 Work Group (WG) meets 1 to 2 times weekly. Topics covered since the last ACIP meeting have included safety and efficacy of Pfizer-BioNTech COVID-19 vaccine, a presentation of the GRADE (Grading of Recommendation Assessment, Development, and Evaluation) of the Pfizer-BioNTech COVID-19 vaccine, a discussion of the balance of benefits and possible harms related to Pfizer-BioNTech COVID-19 vaccine, and additional discussions around Phase 1b and 1c populations.

Dr. Bell indicated that the agenda for the December 11, 2020 ACIP meeting would include presentations on the following topics:

- ❑ Pfizer-BioNTech (BNT162b2) COVID-19 Vaccine Development Program
- ❑ GRADE: Pfizer-BioNTech (BNT162b2) COVID-19 Vaccine
- ❑ WG Interpretation of Evidence and Next Steps

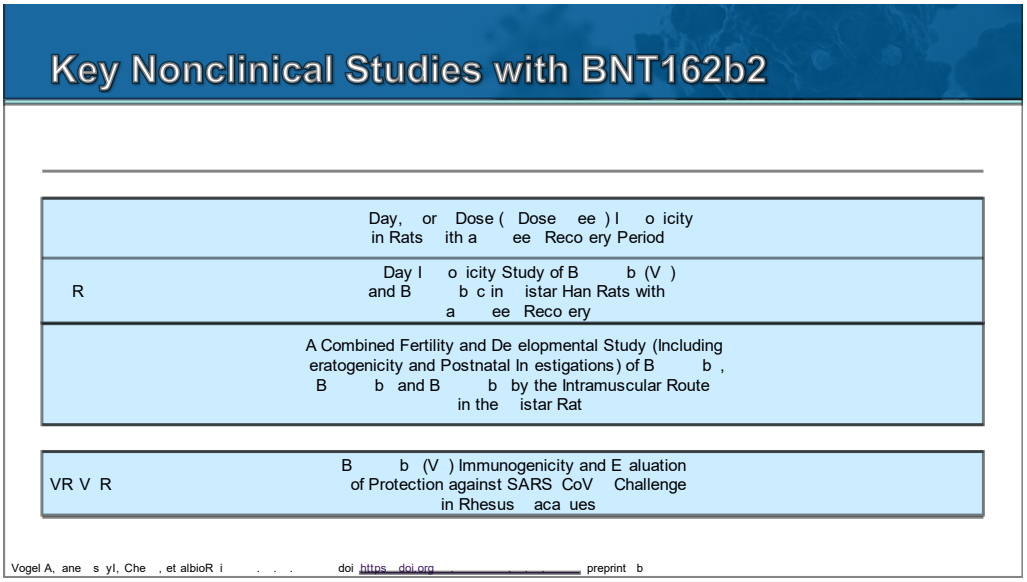
In terms of next steps, if by the second day of this ACIP meeting the FDA has issued an EUA for the Pfizer-BioNTech COVID-19 vaccine, ACIP would vote on recommendations for use in the US.

BNT162b2 Vaccine Candidate Against COVID-19

William Gruber, MD, FAAP, FIDSA
Senior Vice President
Vaccine Clinical R&D, Pfizer

Dr. Gruber described the development program for vaccine candidate BNT162b2, which is Pfizer's mRNA COVID-19 vaccine. BNT162b2 was developed for the indication of prevention of COVID-19 in individuals 16 years of age and older. The dose level is 30 micrograms (µg) with 2 doses given 21 days apart. The current vaccine presentation is a 5-dose multi-dose vial that is preservative-free and stored frozen between -80ºC to -60ºC until use.

Regarding the non-clinical data that encouraged Pfizer to move forward, Dr. Gruber described the following studies that are included in the briefing documents that are now publicly available based on them being provided for the VRBPAC presentation:



Two toxicity studies were conducted in rats, including the BNT162b2 vaccine construct. These were completed with no safety concerns. Development and reproductive toxicity studies are ongoing, with preliminary results available by mid-December. In a SARS-CoV-2 Rhesus challenge model, the BNT162b2 construct provided complete protection in the lungs as determined by nucleic acid amplification testing (NAAT) for SARS-CoV-2 and bronchoalveolar lavage (BAL) fluid. This information is now published. Importantly, there was no radiologic or histopathologic evidence of vaccine-elicited disease enhancement. Despite the recognized limitations of animal models, these findings anticipated results in our Phase III clinical trial in which there is no evidence of enhanced disease. The overall results of the toxicity as well as the challenge studies were encouraging. They satisfied FDA guidance criteria and permitted progression of human clinical trials into later phases.

In terms of the clinical safety, immunogenicity, and efficacy data on BNT162b2 from Pfizer's overall clinical development program, Dr. Gruber described safety and immunogenicity from the German and US studies and aspects of the Phase II/III global trial (e.g., study design, primary and secondary objectives, COVID-19 definitions, safety, and efficacy).

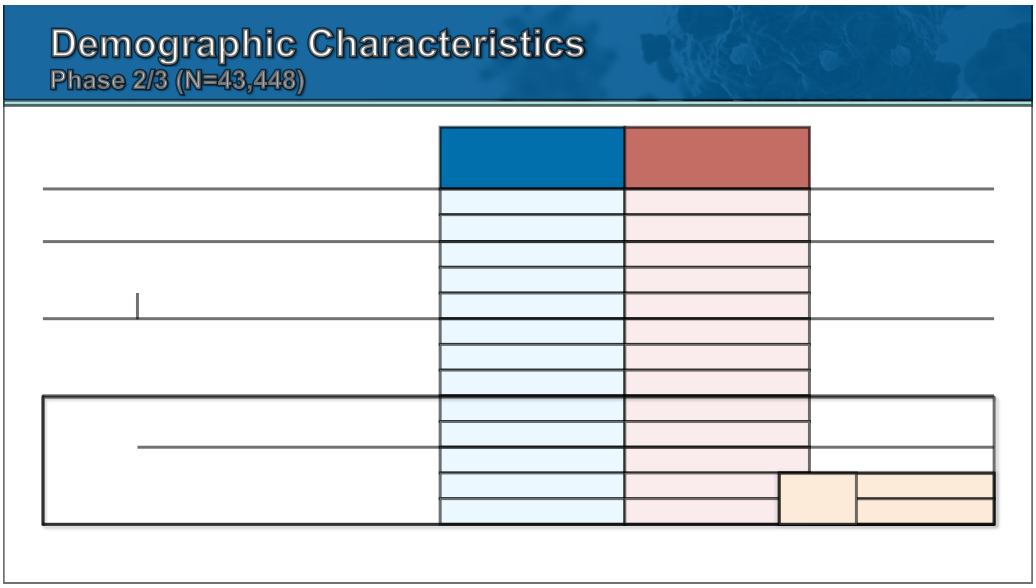
Beginning with the two Phase I studies, the German Phase I dose-ranging study was conducted in individuals 18 to 55 years of age in which 12 subjects received the active BNT162b2 vaccine for each dose level cohort. This study evaluated safety, binding and neutralizing antibody responses, and cell-mediated immune response to look at the potential for Th1-biased CD4 and CD8 T-cell responses. The US study is a seamless study which had Phase I portion that moved into Phase II and then Phase III. The Phase I dose-ranging portion included individuals 18 to 55 years of age and 65 to 85 years of age, among whom 12 received vaccine and 3 received placebo per dose level cohort. Safety and immunogenicity were assessed with both binding and neutralizing antibody responses, and reactogenicity was followed by electronic diary (eDiary). These individuals will continue to be followed for a full 2 years after the second dose. The results from the Phase I experience have now been published, with the details included in the briefing document.

To briefly summarize reactogenicity in Phase I, mild to moderate injection site pain was observed frequently and was consistent with local reactions observed with other commonly licensed and recommended adult vaccines. Fever and chills, along with other systemic manifestations, were observed. Reactogenicity was generally higher after Dose 1 than Dose 2. Reactogenicity events after each dose of the vaccine in older adults were milder and less frequent than those observed in younger adults [Sahin U, et al. *Nature*. 2020; Walsh EE, et al. *N Engl J Med*. 2020].

The antibody responses in Phase I to two 30 µg doses of the chosen BNT162b2 vaccine focusing on the neutralizing antibody titers from the US-based trial have been published in a peer-reviewed journal and are described in the briefing document. By Day 28, for 7 days after the second 30 µg dose, 50% neutralizing antibody responses are observed. Antibody responses are well maintained out to Day 52, approximately one month after Dose 2 in both the younger 18 to 55 years of age group and the older 65 to 85 years of age group. The geometric mean titers (GMTs) in the vaccinated participants ranged from 1.5- to 3.8-fold higher than the virus neutralizing GMTs of 94 observed in a panel of 38 human convalescent serum (HCS). These results were encouraging that a functional antibody response was being achieved that could be associated with protection [Walsh EE, et al. *N Engl J Med*. 2020].

It also was very important to examine cell-mediated immune response to be confident that there was a Th1-biased CD4 and strong CD8 T-cell response. Based on data from the German trial, a substantial increase has been seen in interferon-gamma (IFN-γ) that is very consistent with Th1 and at levels above responses following natural infection. There was a relatively higher proportion of S-specific CD4 cells expressing IFN-γ, IL-2, or both compared to a lower proportion expressing IL-4. One again, this emphasizes a Th1-bias that could be associated with protection. Likewise, not only was it important to demonstrate the CD4 responses and the concomitant potential for inducing memory, but also it was important to demonstrate CD8 T-cell response to indicate the potential for virus killing of infected cells. A robust CD8 T-cell response was seen that exceeds responses observed from natural infection. On the basis of promising neutralizing antibody response, Th1-biased CD4 response, and a robust CD8 immune response, Pfizer was encouraged to move into the Phase II/III portion of the clinical studies with the BNT162b2 vaccine construct [Sahin et al., manuscript in preparation].

In terms of the high-level fundamental elements of the trial, the goal is to enroll approximately 44,000 healthy subjects. Stable chronic disease was allowed because Pfizer found it important to make sure that those individuals with underlying diseases are included. They stand to have the greatest benefit from a vaccine because of their high morbidity associated with COVID-19. Individuals also have been included with stable human immunodeficiency viruses (HIV), hepatitis B virus (HBV), and hepatitis C virus (HCV) infections. At least 40% of participants are at least 56 years of age or older. Again, this is important because Pfizer recognizes that this population is also particularly vulnerable to severe disease. Pfizer also recognized the importance of conducting this study in people of color and has adopted an approach that ensures a diverse racial and ethnicity profile, including Black/African-American, Asian, and Hispanic/Latinx populations. Immunocompromised individuals were excluded because it is yet to be determined whether different dosing might be required in this population. Pfizer plans to evaluate those populations in future studies. Here are the demographic characteristics for the full population data cut on over 43,000 subjects on November 14, 2020:



There is good representation of gender, race, ethnicity, and age and even splits between vaccine and placebo recipients. The age breakdown is highlighted to show the different age groups above and below 55 years of age. In the older 65 and above groups, note that over 9000 (20.9%) of the 43,000 plus participants were over 65 years of age.

Turning to the safety data from the Phase II/III portion of the clinical trial, Pfizer has ongoing safety reviews by an independent Data Monitoring Committee (DMC) of unblinded safety data that occur weekly. This makes sense in the context of a rapidly enrolling trial with this new vaccine candidate. The DMC consists of 4 adults or pediatric infectious disease experts and 1 statistician, all with expertise in assessing vaccine safety, immune response, and efficacy. As recently as the past week, this DMC has identified no safety concerns during the duration of the clinical trial and has recommended that the study continue as planned at all of their safety reviews.

To summarize the safety data base population submitted to the FDA for this review. There are over 43,000 study participants with safety data collected in the trial as of the data cut off on November 14, 2020. Nearly 38,000 of these represent a subset with median safety follow-up time of 2 months post-Dose 2, meeting FDA guidance. This means that there are over 19,000 participants for whom safety follow-up data are available for at least 2 months post-Dose 2. Of the total safety population, there are over 8000 subjects for whom 7 days of solicited local and systemic reactions were obtained by eDiary.

In terms of how the safety of subjects was monitored, vaccination doses were given 21 days apart. The first dose of vaccine was followed by very intense active surveillance for potential COVID-19 symptoms that would trigger a telehealth or in-person visit and nasal swab. This was done both as a safety measure as well as to evaluate efficacy. Individuals either could be swabbed at the investigative site or obtain a self-swab. An eDiary was used to address common reactions seen after vaccine administration encompassing at least 6000 subjects and at least 500 in each of the countries that are included in the trial. Non-serious adverse events (AEs) also were captured 1 month post-Dose 2. Serious AEs (SAEs) also will be collected actively for at least 6 months post-Dose 2 and deaths and related SAEs out to the end of the trial at 2 years after the second dose.

Regarding the eDiary data related to local AEs and representing data that were captured over 7 days after Dose 1 and Dose 2 in participants 16 to 55 and 56 to 85 years of age, redness, swelling, and pain at the injection site are very consistent to those seen with commonly licensed and recommended vaccines. There was very little redness or swelling. Pain was largely mild to moderate in severity and no Grade 4 local reactions were observed. Again, this is a satisfactory safety profile as far as local reactions of concerned. The eDiary also was used to assess systemic events. In terms of events 7 days after Dose 1 in the vaccine and placebo groups in participants 16 to 55 and 56 to 85 years of age, the reactions fall within a tolerable range compared to other adult vaccines. Fever and chills appear to be the most discriminating in the vaccine compared to the placebo groups, but both were within an acceptable range.

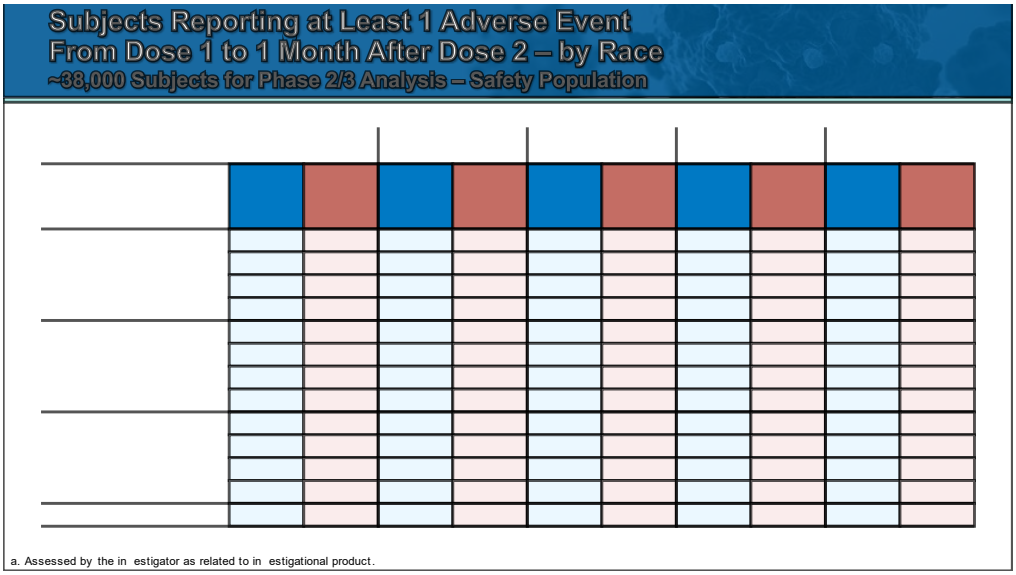
Looking at systemic events 7 days after Dose 2, there was a somewhat higher incidence of fever and chills as well as other systemic manifestations compared to placebo. The only Grade 3 or severe solicited AEs ≥2% in frequency after the first or second dose were fatigue at 3.8% and headache at 2% following Dose 2. One vaccine recipient reported a fever of 41.2°C only on Day 2 after Dose 2 and reported no fevers for all other reporting days. One vaccine recipient reported fever of 40.7°C Day 4 after Dose 1 with no fever at the end of the 7-day reporting period. Otherwise, no Grade 4 systemic reactions were observed. There was a difference between younger individuals and older individuals in that younger individuals tended to have more reactions. But in all age groups, the vaccine was well-tolerated and the reactions were within an acceptable range.

In considering how these events peak and decline over the 7-Day post-Dose 2 period in the vaccine group, the duration is short-lived. Participants are vaccinated on Day 1. Fever typically appears on the day after vaccination and lasts only a single day. Otherwise, systemic events peak at Day 2 and rapidly decline over the next 2 days in both age groups. In terms of severe or Grade 3 local reactions, after both Dose 1 and Dose 2, severe pain at the injection site occurred in less than 1% of vaccine recipients and the incidence of severe redness and swelling were even lower. Fever > ◦C after Dose 1 already was mentioned for one vaccine recipient. Two such fevers were reported in placebo recipients. Severe systemic reactions all occurred in less than 1% of vaccine recipients. For most findings, less than 0.5% of these participants had an incidence comparable or higher than placebo. Likewise after Dose 2, the one high fever already

mentioned was observed. Again, fatigue and headache were the only categories with Grade 3 systemic events with an incidence exceeding 2%, with severe chills at 1.6% and all other events with an observed incidence somewhat greater than placebo.

Spontaneously reported AEs were captured by the system organ class in the nearly 38,000 subject subset for which median safety follow-up was 2 months after Dose 2. AEs by system organ class occurred in 1% or more of the study population. More details are included in the briefing document. The most common AEs observed were general disorders in administration site conditions. The top four classes of unsolicited reactions in this nearly 38,000-participant dataset mirrored the common reactions captured by eDiary in the 8000-participant subset previously described. For example, general disorders and administration site conditions include reports of injection site pain and systemic reactions of fever and chills. Musculoskeletal and connective tissue disorders predominantly reflect myalgias and arthralgias as part of systemic events. For nervous system disorders, the highest proportion was headache. For gastrointestinal (GI) disorders, diarrhea and vomiting predominated. When terms reflecting local reactions and systemic events typically occurring within 7 days of vaccination, there is a more even split of AEs between the active vaccine and placebo groups apart from general disorders and administration site conditions, where the predominant remaining event is unspecified pain in the vaccine group at 2.4% vs. 0.2%. In general, AEs by system organ class are infrequent and within range of such reactions reported after other licensed vaccines.

This table depicts AEs from Dose 1 to 1 month after Dose 2 by race:



To summarize the key elements looking at subjects reporting at least one AE, the observed frequencies of any AE showed some variability across racial and ethnic groups but within a tolerable range. Little differences were observed when evaluating SAEs across these groups as shown in the middle row. Any AEs leading to withdraw are similarly infrequent across racial and ethnic groups. Deaths were infrequent at the time of the November 14, 2020 data cutoff and distributed among these groups with 2 in the vaccinated and 4 in the placebo recipients.

Rounding out this part of the safety review, SAEs by system of organ class are consistent with what is typically seen in populations that include not only 40% of individuals being older than 55 years of age, but also with over 50% of the population being obese and/or having at least one underlying morbidity. SAEs have been balanced between vaccine and placebo recipients. These include observed SAEs of special interest (AESIs) designated by the CDC, which are few in number and comparable between vaccine and placebo recipients. A total of 6 deaths have occurred in this population, with 4 of these in the placebo group, as of the data cutoff on November 14, 2020. None of these have been considered related by the investigator. Further description of the deaths and the full safety data available are included in the briefing packet. To summarize the safety conclusions, the tolerability and safety profile of the BNT162b2 vaccine at 30 µg administered as a 2-dose regimen 21 days apart is favorable. No clinically significant safety findings other than mostly mild or moderate reactogenicity were identified.

Moving to the efficacy evaluation, the vaccine doses were administered 21 days apart. To qualify for the first primary efficacy endpoint evaluation, individuals needed to have no evidence of prior or current infection before each dose. That was determined either by obtaining a swab at the time of each dose to identify evidence of SARS-CoV-2 by NAAT or by obtaining a blood specimen N-antigen antibodies test at the time of the first dose to indicate evidence of prior infection that may have preceded vaccinations by months. This offered confidence that the individuals for the purpose of this primary endpoint had no evidence of prior or current infection at the time of each dose. This is important because this is the group that would be anticipated to be most vulnerable to SARS-CoV-2 disease or COVID-19. As mentioned earlier, Pfizer has active surveillance for potential COVID-19 symptoms that trigger a telehealth or in-person visit and nasal swab. This will continue for up to 2 years after the second dose.

To summarize what constitutes the case definition for the first primary endpoint, individuals had to be baseline negative by serology and polymerase chain reaction (PCR) for prior infection. The illness was then characterized to be one or more of these symptoms: fever, new or increased cough, new or increased shortness of breath, chills, new or increased muscle pain, new loss of taste/smell, sore throat, diarrhea, or vomiting. These largely coincide with symptoms that are captured by the CDC case definition, but with somewhat more potential specificity. Comparable efficacy observed in the trial encompassing all of the CDC criteria are shown in the briefing document. Once an individual qualifies for the first two categories, they need to have a positive validated PCR, either in Pfizer's central laboratory or from a local laboratory that is approved as a type of testing that Pfizer agrees is valid. All tests were performed blinded to treatment effect. It is this combination that determines the case definition for the efficacy results that Dr. Gruber shared.

An interim analysis was performed in the 94 cases of individuals without prior infection and with observed efficacy of 95.7%. A final vaccine efficacy evaluation has also now been performed against COVID-19 occurrence from 7 days after Dose 2 in 170 cases without evidence of Prior infection. Observed efficacy is high at 95% with high confidence. There is 95% probability that efficacy falls in the interval 90.3 to 97.6, meaning over 97.5% likelihood that efficacy is greater than 90%. Likewise, the probability that vaccine efficacy is at least greater than 30% greatly exceeds the FDA COVID-19 vaccine guidance.

This efficacy trial was not powered to evaluate efficacy based on age stratum, gender, racial, or ethnic groups. Nonetheless, Pfizer thought it would be useful for the ACIP to see vaccine efficacy broken down by these parameters. Observed efficacy was high regardless of age and consistent with overall results. There were 15 cases seen in adults 65 to 74 years of age and only 1 case occurred in the vaccine group. There were 5 cases observed in participants ≥75 years of age, and all were in the placebo group. Likewise, efficacy was high in both males and females and across racial and ethnic groups. Comparable high observed efficacy was seen across White, Black/African American, and other racial groups and likewise across Hispanic and non-Hispanic ethnicity, with lower bounds of the confidence intervals above 80% across these ethnic groups. There are also comparable values of observed efficacy seen across geographies.

This efficacy trial also was not powered to evaluate efficacy based on risk groups. Nonetheless, Pfizer thought it would be useful for the ACIP to see vaccine efficacy broken down by these risk parameters. The risk groups, including individuals with body mass index (BMI) >30 kg/m^2 and/or those from the Charlson Comorbidity Index (CCI), included malignancies, chronic pulmonary disease, chronic cardiovascular disease, diabetes, renal disease, and many others. Observed efficacy was high regardless of whether the participants were at risk or not, consistent with overall results. Likewise, efficacy was high across age groups with and without risk as well as those with or without obesity. Breaking out comorbidity, regardless of category (e.g., past history of malignancy, cardiovascular disease, pulmonary disease, diabetes, obesity, or hypertension) point estimates of observed vaccine efficacy remain high and for some, the nominal lower bound of the confidence intervals are well above zero. Hence, there is confidence that the vaccine is likely to work well in older or debilitated individuals. Pfizer has now evaluated efficacy against COVID-19 from 7 days after Dose 2 in those with and without prior infection, the second of the 2 primary endpoints. Efficacy remains high at 94.6% (89.9, 97.3) with similarly high confidence.

It also was important for Pfizer to define severe cases for evaluation of safety and for determinations of efficacy. For this, a definition of “severe COVID-19” was used based on the FDA guidance, which includes any the following:

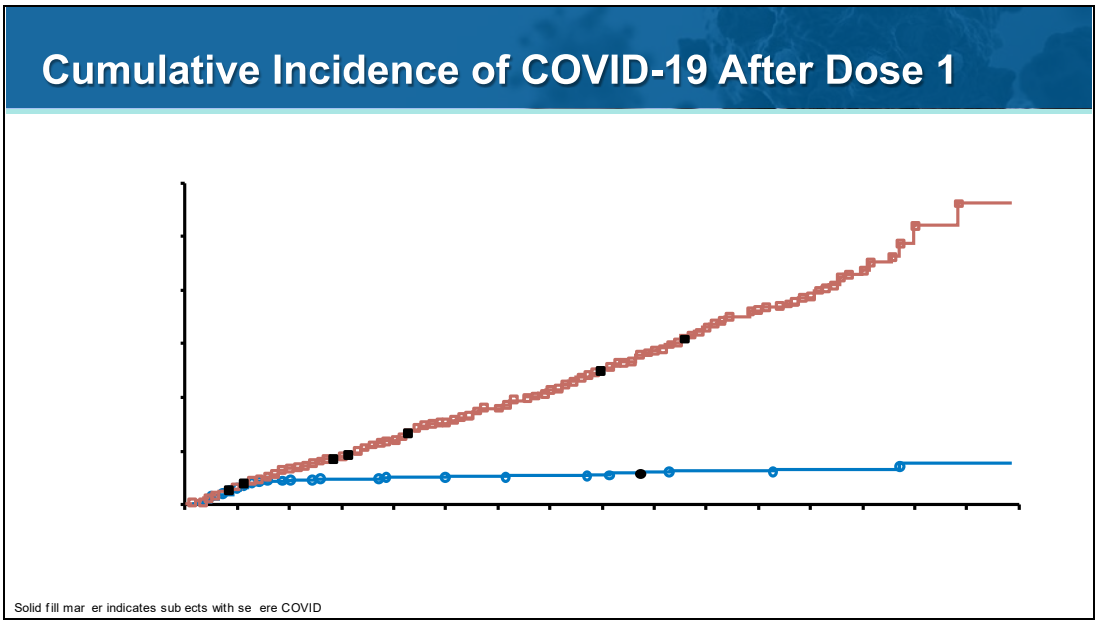
- ❑ Admission to an ICU
- ❑ Clinical signs at rest indicative of severe systemic illness (RR ≥ bre aths per minute, HR ≥ b eats per minute, SpO ≤ % on room air at sea level, or PaO2/FiO2 <300 mm Hg)
- ❑ Evidence of shock (SBP <90 mm Hg, DBP <60 mm Hg, or requiring vasopressors)
- ❑ Significant acute renal, hepatic, or neurologic dysfunction
- ❑ Respiratory failure (defined as needing high-flow oxygen, non-invasive ventilation, mechanical ventilation, or ECMO)
- ❑ Death

Using this FDA definition of severe disease, although not statistically significant due to a small number of cases, protection against the few cases of severe disease occurring at least 7 days after Dose 2 is consistent with the overall efficacy results, with 1 case in the vaccine group and 3 cases in the placebo group in those without prior infection. However, examining the “all available” population for persons with severe COVID-19 cases after Dose 1, only 1 case was seen in the vaccine group and nine 9 are observed in the placebo group for an observed vaccine efficacy of 88.9%. The vaccine recipient only met a single FDA criterion for severe disease of SpO ≤ % and was not hospitalized. In contrast, out of the 9 placebo recipients

with severe disease, 6 met 2 or more criteria, 6 were hospitalized, 3 were admitted to the intensive care unit (ICU), and 1 was intubated or mechanically ventilated. This is consistent with overall vaccine efficacy seen several more days after the second dose, and indicates that the BNT162b2 vaccine is likely to protect well against severe or serious disease.

The FDA definition does not include hospitalization as a specific criterion for severe disease. However, the CDC definition of severe disease includes hospitalization, admission to the ICU, intubation or mechanical ventilation, or death. Therefore, Pfizer thought it would be useful to perform a post hoc analysis of severe disease using the CDC definition to further assess the impact of vaccine on this outcome. Using this parameter, efficacy against severe disease ≥ days after Dose 2 was observed, with zero cases in the vaccine group and 5 cases in the placebo group with a conference interval of -9.9 to 100. Once again, protection also was observed for the first severe COVID-19 occurrence after Dose 1 of 92.9%, with 1 case in the vaccine group and 14 cases in the placebo group. The lower bound of the 95% confidence interval in this case was well above zero (53.2, 99.8). The 1 vaccine recipient was hospitalized 12 days after receiving the first dose of vaccine, but without additional CDC defined morbidity. Of the 14 placebo recipients hospitalized, 3 were admitted to the ICU and 1 was intubated or mechanically ventilated. This analysis provides evidence for vaccine protection against hospitalization and attendant morbidities.

This curve shows the cumulative incidence of all available COVID-19 cases beginning after Dose 1. Placebo cases are shown in red, vaccine cases in blue, and the darker dots represent severe cases using the FDA guidance definition. There were 9 severe cases in the placebo group and 1 in the vaccine group, with 2 instances where cases overlap graphically at Day 8 and Day 67 in the placebo group. One can see that by as early as 12 days and at least by 14 days, the curves begin to spread, indicating some efficacy after the first dose. Placebo cases continue to increase after 105 days at the time of this data cut, while the vaccine case curve remains relatively flat:



In fact, the all-available attack rate is so prominent and efficacy so high that it is possible to observe not only total efficacy after the first dose, but in each of the defined intervals. Efficacy measured beginning after Dose 1, including those who received a second dose, was 82% (75.6, 86.9). Efficacy after Dose 1 and before Dose 2 was 52.4% (29.5, 68.4), between Dose 2 and 7 days was 90.5% (61.0, 98.9), and ≥ day s after Dose was 94.8 (89.8, 97.6). The bottom line is that efficacy begins shortly after the first dose but maximum and important benefit is achieved after the second dose.

The efficacy conclusions are that both primary efficacy objectives met the success criteria. In individuals without prior SARS-CoV-2 infection, observed vaccine efficacy against COVID-19 occurring at least 7 days after Dose 2 was 95%, with high probability (97.5%) that the true vaccine efficacy is at least 90%. Again, this meets the pre-specified FDA criteria for EUA. Observed vaccine efficacy was greater than 93% for the first primary endpoint across age, race, ethnicity, and at-risk subgroups. Per the FDA definition, 9 severe COVID-19 cases were observed in the placebo group and 1 in the vaccine group as of the interim analysis cutoff dates, and 14 hospitalizations and associated morbidity were seen in placebo recipients versus 1 vaccine recipient hospitalization in a post hoc analysis. This provides evidence to support efficacy against severe disease consistent with that seen against all COVID-19. From the cumulative incidence curve, there is early onset of protection, with divergence of the placebo group from the BNT162b2 group as soon as 12 days and at least by 14 days, with steady accumulation of cases in the placebo group. Overall, the efficacy results show that BNT162b2 vaccine at 30 µg provides protection against COVID-19 in participants who had or did not have prior SARS-CoV-2 disease.

In terms of Pfizer's plans to meet FDA guidance for risk and benefit during use of the vaccine under EUA, Dr. Gruber briefly described pharmacovigilance and pharmacoepidemiology plans. Since this vaccine is likely to be administered to millions of people in the short time, Pfizer has expanded its capacities to process AE reports with an online AE reporting portal. Signal detection activities will occur on a more frequent cycle and there are plans for future clinical studies to expand the more vulnerable populations. Regarding proactive risk minimization, clear comprehensive labeling and educational material for vaccine providers will emphasize key messages about appropriate handling, storage, and preparation of the vaccine. For vaccinees, educational materials will emphasize the importance of following up for their second dose to maximize their protection. Product and cold-chain will be monitored in real-time. Pharmacoepidemiology studies are obviously important to describe. Several safety studies are planned to continue safety data collection. These will access healthcare information from millions of lives to monitor safety events, including AESI. Pfizer now has good evidence that its vaccine works in the clinical setting and plans to investigate its effectiveness in real-world use. Regarding collaboration with vaccine safety stakeholders, Pfizer's plans are intended to be complementary to FDA and CDC pharmacovigilance activities that include the Vaccine Adverse Event Reporting System (VAERS), the Clinical Immunization Safety Assessment (CISA), the Vaccine Safety Datalink (VSD), V-SAFE, et cetera.

Pfizer also intends to conduct a number of clinical studies recognizing that there are other populations that stand to benefit and that other things need to be learned about the vaccine. These include boostability stability, dose ranging studies in pediatrics, use in pregnancy, use in immunocompromised populations, a refrigerator-stable next generation formulation, and concomitant use with influenza vaccine. Pfizer looks forward to expanding the safety, immunogenicity, and efficacy profile demonstrated to date.

Discussion Points

Dr. Poehling observed that none of the roughly 283 participants 16 or 17 years of age had any evidence of COVID-19 disease, and asked whether any further health information could be provided about the 23 enrolled women who became pregnant and received vaccine, and noted that there did not appear to have been any episodes of anaphylaxis during the study.

Dr. Gruber indicate that 283 is the number enrolled within the safety database and a smaller number than that who have reactogenicity data as of the data cut on November 14th. His recollection was that none of the 283 had prior evidence of infection based on either NAAT or serostatus. However, 1 individual had evidence of prior infection in the placebo group. These data are still being collected and over 700 are enrolled at this point, but those are not part of this data. Regarding the 23 women who became pregnant and received the vaccine, all participants agreed to adhere to contraception during the course of the trial. The developmental and reproductive toxicology (DART) study will be completed by mid-December and the plan is to begin to evaluate vaccination prospectively in pregnant women in the first quarter. For this stage in capturing safety information, males and females in the study were cautioned to continue contraception. Nonetheless and not anticipated because this has been seen in other trials, individuals still became pregnant. As part of this data cut, 23 women became pregnant. There has not been enough time for any of them to go to term at this point. There have been no reported outcomes in terms of the rate of AEs associated with the vaccines for the pregnancies or the outcomes themselves to date. Anaphylaxis is highlighted by the experience that has been well-reported from the United Kingdom (UK), and that there have been no episodes related to the vaccine. He called upon Dr. Mather to speak to this issue further.

Dr. Mather added that no events of serious allergic reactions were seen in the clinical studies. They looked at the enrolled participants and searched for participants who had a medical history of allergic conditions, which could have ranged from pollen allergies, to food allergies, all the way up to anaphylaxis itself. Almost 6000 participants in each of the groups had a medical history of allergic conditions. When they then searched to see if any of them had allergic AEs reported during the study, 1 was found in each group. The vaccine participant who had a history of allergy to specific tree pollen had an AE of drug hypersensitivity and urticaria that was reported on the day he received Dose 1 of the vaccine. The AEs that he experienced were of moderate severity and lasted only one day. The placebo participant, who had an allergy to shellfish, reported an AE of allergy to vaccines. That is a description of the AEs that were consistent with allergic reaction that occurred in subjects with known histories of allergy.

Dr. Romero asked for further insight into the VE for the population from Brazil that was lower than the VE in Argentina and the US, noting that the confidence intervals were very wide.

Dr. Gruber said that the simplest explanation was to look at the dataset. There was a total of only 9 individuals, so the wider confidence interval was not surprising. This is in large part by virtue of the size of the dataset. They are reluctant to conclude that the efficacy for these individuals ultimately would prove to be 95% until they have more cases. This study continues and Pfizer will be engaged in discussion with the FDA about the appropriate timing for any additional data cuts that will help to inform the nature of persistence and protection, as well as further discriminate with more cases specifically from these areas is the attack rates remain high.

Dr. Bernstein recalled the demographics presented that 40% of the subjects are 56 years of age and older, 21% are 65 and older, and there is an almost 20% balanced population in terms of race and ethnicity. He wondered whether Pfizer had some a priori power calculations for those who are younger than 18 years of age.

Dr. Gruber said that in the context of the sample size, there is only 1 case in the 16 and 17 year olds. At this point, that sample size is too small within that narrow age band. He would argue that almost any 2-year age band might be too narrow. It certainly is true that fewer people get enrolled, which compromises the ability to have sample size. But for any 1 to 2 year age period, it might be difficult to demonstrate efficacy. There is no a priori reason to suspect that the efficacy would be any worse in that age group. He gained confidence from the review the previous day by the FDA and VRBPAC that concluded that the risk-benefit profile was satisfactory to include that age group. More information will be available over time.

Dr. Bernstein asked what the thought was behind including the 16 and 17 year olds in the EUA request if the sample size was too small at this point.

Dr. Gruber said he thought it was in part to begin to provide insight into what is considered to be a critical population. They do have obligations from the FDA to move into pediatric populations. This is a population that in a regulatory sense is more of an adult population than they are a pediatric population, so to broaden the potential application and indication to encompass as many individuals as they possibly could and being confident in the likely safety given the data they already had in 18 to 55 year olds, they included them to get that safety information with the expectation that they would have the same level of efficacy as the rest of the older individuals. Pfizer is actively looking at population of 12 to 15 year olds, of which there are about 100 for whom they already have submitted some safety information to the FDA that looks good to Pfizer in comparison to those 18 to 55 years of age. Pfizer's potential concern was that as they move further down into that age group, the reactogenicity would amplify. That does not seem to be the case, so they are expanding that population to 2000 children between 12 to 15 years of age to potentially seek a license in that group by safety and immunobinding to the older group and to serve as a springboard to move into a successfully younger pediatric population.

Dr. Ault asked whether people who were seropositive at baseline were excluded from being vaccinated.

Dr. Gruber clarified that there is a difference between what they chose to do in Phase I of the trial. Referring to Slide CC-31, he indicated that Pfizer recognized that from an efficacy and safety point of view, it was important to vaccine individuals who had no prior evidence of infection because they are the most vulnerable and for whom there is the most concern about protection. Many individuals do not know that they have been infected because they have been asymptomatic, so Pfizer wanted to capture information on safety and efficacy in that population. What actually happened in this Phase of the trial, which is somewhat different from what was done in Phase II/III, was that when an individual presented for their first vaccine dose, they had blood drawn to determine whether they had antibody to the N-protein because it is obviously distinctly different from the S-protein in the mRNA construct. In addition to obtaining that serology to help determine whether an individual was infected months before, they also wanted to know if the individual was infected at the time of immunization. Strikingly, even before being in the current pandemic state, a small proportion had virus identified by testing right at the time they were vaccinated. The nature of that was not to exclude them, but to know so that they could identify how many individuals were previously infected, those who were not, and what happens to them when followed up. The same thing happened at the second dose in that

testing was done to determine whether any participants had virus identified at that time. All of that information identifies evidence of prior or current infection at time of immunization. Those are treated as a separate group from those who are identified as being without infection. Individuals with prior evidence of infection were not excluded from this part of the trial because it is important to know what happens to them. In terms of assessing those with and without evidence of prior infection, no differences are observed in the reactogenicity or AE profiles for either group. He would not claim statistical significance for this. Some of the point estimates of what was observed for some of the systemic findings were actually lower, so they have some confidence that giving the vaccine to individuals who had prior evidence of infection by PCR or being seropositive did not differ from individuals who were naïve and this was their first exposure to the S-antigen.

Dr. Lee requested clarification about the range of timing for Dose 2. While she realized the intent was 21 days, she was interested in the range in the data. Secondly, she requested clarification about whether the day of vaccination is considered to be Day 0 or Day 1. In addition, she requested to look at this by proportion of individuals with any systemic symptoms that are mild, moderate, severe, and Grade 4 because when planning a vaccination program, it is important to understand what proportion might actually need to miss work regardless of symptoms. There is a focus on fever for sure, but understanding Day 2 post-vaccination what proportion of the workforce might be out is important. Finally, she asked whether there is a sense about the timing of anaphylaxis in terms of whether it occurs within 5 minutes, 15 minutes, or 30 minutes.

Dr. Gruber indicated that based on the protocol, a range of 21 to 42 days was allowed as being per protocol. In a well-controlled trial, most of the individuals were close to 21 days. However, some individuals did go out to 42 days and some went out even beyond that to 56 days. However, that was a small fraction. Most of them would be pretty sanguine about the prospect that the longer interval is unlikely to be associated with a diminished response. In fact, it is more likely to be associated with a better response to the second dose. That type of information is not yet available, because they have not done enough of the immunologic evaluation on the full cohort of individuals in the trial. He is hopeful that that might give them somewhat of a clue. The day of vaccination is considered to be Day 1. It is in the first 24 to 36 hours, particularly the day after vaccination, that people typically reported chills or fever. Dr. Gruber could not recall whether there were any slides in this set on the proportion of individuals anticipated to be out of work on Day 2 post-vaccination, but he recalled that the WG had requested information on this question. He called upon Drs. Perez and Snow to provide input as well.

Dr. Perez added that for the dosing question, people were allowed to receive doses from 19 to 42 days in the efficacy analysis. The doses that hovered around the 19 to 21-23 days were allowed in the analyses.

Dr. Show indicated that for any local reaction or SAE, in the vaccine group there are 362 cases (8.8%) and 84 cases (2.05%) in the placebo group.

Dr. Gruber indicated that they could break this down to include the SAEs and not the local reactions and report back.

Dr. Mather indicated that the 2 cases of anaphylaxis that were reported from the UK were both women. One case occurred within min utes and the other one said “within minutes” of vaccine receipt.

Dr. Atmar noted that the briefing document indicated that residents in LTCFs were a potential target for enrollment and he wondered whether there were any participants enrolled from LTCFs.

Dr. Gruber said that to his knowledge, they have not been successful in recruiting/enrolling participants from the LTCF environment. One of the challenges is the nature of trying to contain those environments because of the incredible risk and potential for spread, along with the challenge of getting informed consent. His hope is that the evidence they are presenting based on risk and age condition combined that has shown efficacy will translate into effectiveness in those populations. There are plans to look at special populations, such as LTCFs, post-licensure.

Dr. Atmar said that his reading of the briefing document in terms of efficacy or looking at cases in seropositive individuals was that there were 8 cases, 7 in the placebo recipients in persons who had prior evidence of infection. He also inquired as to how many people were PCR positive at Dose 2 and what the split was.

Dr. Gruber responded that it is a challenge with that 1 to 7 split to say that it must mean that all of those individuals were seropositive or had evidence of prior infection. Suffice it to say that someone either has had prior infection or they have not. To be identified as not having had prior infection requires specific criteria. There can be nothing that suggests that someone is positive by either PCR or serology. However, the second category that includes with and without includes individuals who can be documented as having prior infection, as well as individuals for whom there is insufficient information to know whether they were positive. There were 5 individuals in the placebo group were missing a PCR or serology, so all they could say was that they were infected but not whether they did or did not have infection. The breakdown otherwise in terms of PCR positivity was 1/1 seropositive and 0/1 for individuals identified by PCR. The other 5 did not have information either way. He did not think they had the number of people who were PCR positive at Dose 2 and the split readily available, but will report this back.

Dr. Perez indicated that 1 person in the vaccine group and 1 person in the vaccine group were positive at baseline for COVID-19 after Dose 2.

In terms of Pfizer's plan to loo at further data cuts in con unction with discussions with the FDA, Dr. Atmar asked whether there is an estimate from Pfizer or Dr. Fink in terms of when the next data cut may be to add further information about efficacy a month later and perhaps with more information in the subgroups.

Dr. Gruber said that they have not yet engaged in a discussion about the next step in terms of what the best timing is from Pfizer's perspecti e. O er time, they ha e the potential to gain more information about total cases, enrich the numbers based on demographics groups, and potentially will have more information that can inform durability of protection and severity of disease. These are things they want to do and in relationship to the Biologics License Application (BLA) filing. The question regards whether there is a time between now and then that it makes sense. Dr. Fink (FDA) agreed that they will still have to have these discussions.

Dr. Ault observed that from the data shown in terms of VE in a number of subgroups, there did not appear to be a group or characteristic identified that seemed associated with vaccine failure. Looking at all of the data, he wondered whether such a characteristic or group identified that might have been associated with vaccine failure.

Dr. Gruber pointed out that when a vaccine has this degree of success, it is hard to identify common themes. They had a number of hypotheses, one of which was that it is not an actual issue in terms of people failing to make an immune response. Perhaps the vaccine did not get to where it needs to be. For instance, perhaps the needle does not get into the muscle in people who are morbidly obese and there is not appropriate antigen presentation. However, there has not been any evidence to convince them that this is the prevailing reason why 8 individuals who were previously negative failed. Sadly, more cases are needed over time to be able to dissect this. One of the key ingredients is going to be looking at the immune response in those individuals. They have sera on everyone in the trial. When they ultimately perform serologic testing, that may offer a clue as to the reason someone may not have made a good immune response.

Dr. Szilagyi asked whether there were exclusion criteria for prior anaphylaxis in this study. Regarding the common AEs (fatigue, headache, fever), he asked whether a sub-analysis was performed about how common these events were among a much younger age group like 16 to 30 years of age.

Dr. Gruber indicated that there was one exclusion criterion, which basically excluded an individual who had an anaphylactic or severe allergic reaction that was associated with a prior vaccine of any kind, or they actually were known to have had a reaction to any of the excipients or constituents within the current vaccine. Prior history of allergy by itself was not an exclusion. He did not know whether there was anyone in the trial with a prior history of anaphylaxis, but individuals were not excluded except those who fit this narrow definition, which corresponds to what typically appears in labels. In terms of AEs, they have conducted some analyses in individuals 18 to 25 years of age. There was a general tendency to have some increase in reactogenicity moving down the age range, but that still was felt to be within a tolerable and acceptable range in comparison to other vaccines. That has become the key metric used for looking at the 12 to 15 year olds to give them comfort to continue to dose in that group. They have dosed the first 100 in a staged way to ensure that they were not creating undue reactions and then did a comparison. After that comparison, they elected to expand from the 100 to the full 2000. The DMC looked at this independently and instructed the investigators to proceed as planned.

Dr. Perez added that the 18 to 25 year olds look similar to the 18 to 55 year olds in that reactogenicity was somewhat worse after the second dose, but was still within a reasonable range. They also compared the reactogenicity data of the 100 subjects 12 to 15 years of age in order to continue and did not see the increase in reactogenicity rates seen in the 18 to 25 or 18 to 55 year olds. That encouraged them to continue to involve that age group.

Ms. Bahta asked whether Pfizer had any idea when they might hear about the results from the DART study.

Dr. Gruber indicated that they are moving forward as quickly as possible and anticipate having enough information by the end of the first quarter of 2021 to be a position to have that undergo an appropriate review by the FDA.

Dr. Frey asked whether any new cases of or flares in any autoimmune diseases were observed, if they saw any cryptogenic or idiopathic pneumonia that was worrisome, or there were any cases related to increases in a Th2 response.

Dr. Gruber responded that they saw no evidence of anything unusual and no Th2 bias. The DMC has continued to look at data beyond the November 14, 2020 data cut. Even with the more comprehensive data, to his knowledge there has been no indication of autoimmune disease, idiopathic or odd manifestations or presentation of disease, and nothing to suggest Th2 bias. However, they have not looked at Th2 bias beyond the German trial in terms of the original responses to the vaccine. The fact that the nature of what they are seeing in terms of protection beginning after the first dose against severe disease gives him comfort in a certain sense in that they know there is huge and growing exposure in the US.

Ms. McNally requested that Dr. Gruber speak briefly about the safety of this vaccine for women who may be pregnant or may want to become pregnant.

Dr. Gruber thought this may be a question to come back to the FDA. All he could say at this point was that they purposefully did not include pregnant women in the study. There is no a priori reason to suspect that this vaccine would be associated with increased risk of problems in pregnancy. They will have a fuller understanding once the DART studies are completed.

Dr. Wharton inquired about the appendicitis cases described in the briefing document in terms of the imbalance between the vaccinated and placebo groups, although the overall numbers were not large. She was interested in the distribution of time post-vaccination for the appendicitis cases among the vaccinated group and whether there was any evidence of temporal clustering. Because the vaccine resulted in lymphadenopathy in many recipients, it seems biologically plausible that the vaccine could be associated with appendicitis because the appendix contains lymphoid tissue, which is why she was interested in timing.

Dr. Gruber said that off the top of his head he did not remember any details about temporal clustering. The reason this bubbled to top was because when they first started seeing appendicitis cases, they took that seriously as a potential life threatening event. They looked at these cases with a great deal of scrutiny and matched them up with what would be expected in a population this size for the types of demographics and nature of the population. The frequency with which this was occurring seemed not to be outside the bounds of what would be expected in a population at large. In addition, all of these data were presented in a blinded fashion to the DMC, which has the ability to look at this unblinded. The DMC has not indicated that they see this as an important signal.

Dr. Mathers added that she could talk about the 12 cases grouped together, but not in an unblinded down to individual patient level. The latency in the cases that occurred after Dose 1 ranged from the same day of Dose 1 up to 16 days after Dose 1. The cases that occurred after Dose 2 ranged from 11 days to 28 days post-Dose 2. Only a single case occurred on the same day as Dose 1. One of the challenges they faced and tried to manage carefully is that with an ongoing trial, they could not unblind individuals at a subject level. They can speak with the DMC and perhaps can provide some of that information. The DMC was privileged to know that information and has a fair degree of sophistication around the potential for AEs associated with immune response and saw fit to have Pfizer continue the trial. The FDA spoke to their evaluation of this in their briefing document and felt that this was not something that suggested a relationship to the vaccine, which the FDA could speak to further.

Dr. Sanchez asked whether post-vaccination the vaccine contributes to any positive antigen detection when antigen tests are used for SARS-CoV-2 infection. Given vaccine hesitancy throughout the country for all vaccines, he also wondered whether any fetal tissue or cells obtained from abortions were utilized in the making of this vaccine.

Dr. Gruber said that he was unaware of any ability to detect antigen on the basis of vaccination. Obviously, minute amounts are being produced locally.

Dr. Dormitzer added that they have not specifically tested whether antigen can be detected post-vaccination. He agreed that it is extremely unlikely that the quantity of antigen would be enough or that there is a clear path for it to get from expression in a muscle or local lymph node to be shed so that it could be detected with a nasal swab. The probability is very low. In terms of whether fetal tissue or cells obtained from abortion were used in the making of this vaccine, the making of the vaccine involves a cell-free synthetic process. Cell lines established long ago have been used in assay work that has been done in medical research that would have had that origin, but the actual production of the vaccine does not use cell lines.

Ms. Stinchfield (NAPNAP) inquired as to whether subjects were asked about mask wearing, hand hygiene, and social distancing and if so, whether there were any differences in the two groups.

Dr. Gruber said that to his recollection, they did not ask specifically about those sorts of precautions. It is his sense that the investigative science emphasized that they could not guarantee that this vaccine would prove effective, so it would be important for people to continue social distancing, masking, et cetera. However, he did not recall anything specific for tracking those behaviors.

Dr. Middleman (SAHM) said that as a practitioner, because many people are behind on vaccines giving COVID-19 vaccine offers a wonderful opportunity to help catch people up. She asked whether there are any data that would help guide practitioners about the safety of co-administration of other vaccines and whether the FDA commented on whether it would be best to give COVID-19 vaccine alone and co-administration would be ill-advised or recommended.

Dr. Gruber responded that Pfizer does not have data one way or another. They plan to assess influenza vaccine in particular if it turns out that COVID-19 is a seasonal illness. They recognize that when patients present for influenza vaccine, it would be an ideal time to administer COVID-19. However, they do not have data on co-administration with other vaccines as there was a temporary delay criterion that people had to get their vaccines spaced away from when the COVID-19 vaccine was given.

Dr. Schmader (AGS) asked whether Pfizer could share the frequency of local and systemic reactions only in the 65 to 85 year old group.

Dr. Gruber said that he was comforted by the fact that the older they got, there seemed to be less reactions. In the original Phase I study, there was a breakdown with 65 years of age and above. They start getting diminishing numbers of individuals as they get higher in age, but they do have the age spectrum now above 85 years and can gather that information.

Dr. Fryhofer (AMA) asked what evidence there is that the mRNA is degraded and what happens to the mRNA and the lipid nanoparticle after it is injected and has done its job in terms of how long it hangs around, how it is broken down, and if there are any concerns that this could cross the placenta.

Dr. Dormitzer indicated that the lipid nanoparticle probably does not last very long once it enters the cell. At that point the lipid fuses with the cell membrane, releasing the RNA. The RNA is metabolized by the usual pathways. The lipids have different things such as cholesterol, which we have anyway. There is some information on how the other lipids are metabolized. To some degree they are either broken down and others wind up secreted through the liver. While they have not measured specifically whether this would cross the placenta, the placenta poses quite the barrier. Therefore, it is hard to imagine a pathway by which an intact lipid nanoparticle could cross the placenta.

Dr. Drees (SHAE) observed that preparations were underway to begin vaccinating HCP as early as the next week, yet there are still populations for whom there are no data such as pregnant women and immunocompromised individuals. She asked whether there would be any recommendations about specific contraindications for this vaccine. They are getting a lot of questions from people with a history of autoimmunity issues for example. She also asked how long people should be monitored post-vaccination and if that would differ for people who have a history of allergic reaction versus those who do not. She also wondered whether they should expect to receive the EUA Fact Sheet, which she assumed would include some of this information, at the same time that an EUA is issued or if there would be a delay on that.

Dr. Gruber emphasized that Pfizer does not have data in immunocompromised populations or pregnant women at this time. Negotiations are ongoing in terms of the label. Monitoring is also to some extent a labeling or recommendation issue. From his perspective, he did not see any reason that one would respond any differently to people than is typically done in terms of monitoring individuals in a setting. Within many if not most labels for vaccines, there are precautions about being prepared to deal with an allergic reaction if it occurs and monitoring individuals for a period of time. He deferred to others who have to make the recommendations and from a regulatory perspective to have that in the label.

Dr. Fink added that in terms of authorized use and any contraindications, the VRBPAC vote the previous day was for an indication for use in individuals 16 years of age and older—period. That is what the committee voted on. Therefore, any populations who are not specifically contraindicated for use would be included in that indication. FDA expects that there will be at least a label contraindication for use in individuals who have any known allergies to any of the components of the vaccine. Prescribing information and fact sheets will describe those components. One of the things the FDA was discussing during the day regarded whether any additional warnings or precautions are needed related to the severe allergic reactions that occurred in the UK. Certainly, those data will be described. The fact sheet and prescribing information must be provided with the vaccine when made available under an EUA. He did not anticipate that there would be any delays with respect to that.

Dr. McKinney (APTR) asked whether the lymphadenopathy affirmed in vaccine recipients is regional at the site of injection only or if it was generalized, whether it was transient or persistent in nature, and if it was present in those persons with appendicitis or Bell's Palsy.

Dr. Gruber answered that the nature of lymphadenopathies was that individuals were vaccinated in their non-dominant arm. The one case of lymphadenopathy that was considered to be related by the investigator was found on the opposite side from the deltoid where the individual had been injected. In most instances, it was transient. This is known to exist with other vaccines and is in the label for other vaccines. Sometimes it is picked up in clinical trials and sometimes it is picked up after approval. One of the reasons Pfizer may have picked up the

0.3% incidence sooner than other trials is because this is a huge database of 32,000 individuals for whom there is a median follow-up time of 2 months.

Dr. Perez added that the lymphadenopathy was transient, tended to occur after 5 days or so, and generally was reported as lateral to the injection site in the neck.

Dr. Mather added that there was no lymphadenopathy in the patients with facial paralysis. There was no reported enlargement of lymph nodes in those 4 patients, or in the appendicitis patients. They looked closely to see if there was any mention of lymph nodes in surgical pathology reports or in any of the imaging studies, and there were not in the data they received. Lymphadenopathy is listed in other labels such as meningitis vaccine and bacille Calmette-Guerin (BCG). While Pfizer identified the lymphadenopathy as a AE, the actual frequency was low at 0.3% so it was not common.

Dr. Whitley-Williams (NMA) thanked Pfizer for sharing the data on the under-represented minority population. She recalled that the percent of African Americans was 9.6% and that the actual N is pretty small at only 2000. The Latino and Hispanic population was much higher at 26%. While she applauded the effort, she expressed hope that future trials and follow-up would continue to enroll under-represented minority subjects. She emphasized the importance of continuing to apply lessons learned to increase the percentages enrolled and retained in these trials, at least for the follow-up.

Dr. Gruber stressed that Pfizer recognizes that racial and ethnic minorities have a much greater risk and are very keen on including them in trials, and they continue those efforts. The observation studies post-licensure will emphasize and assess those populations as well.

Regarding the anaphylaxis issue, Dr. Duchin (IDSA) asked whether there are any other medical or other products that might have ingredients contained in the mRNA vaccine that people would not be aware of by looking at the chemical names of the vaccine ingredients.

Dr. Gruber said that was a challenging question. The presumption would be that if someone had an anaphylactic reaction to something like a product that people would work hard to figure out what was in that product and that person would know. If they had a minor reaction, it may not even be investigated. His hope would be that if someone has had true anaphylaxis or a severe reaction, there would be some investigation that would inform the individual. There was a fair amount of discussion the previous evening amongst the CISA group about this. The vaccine contains polyethylene glycol (PEG) as an excipient for which there has been a history of some individuals having a specific allergic reaction to that component, but this seems to be a rare phenomenon.

Dr. Dormitzer added that a similar product is a lipid nanoparticle formulated RNA product. Of the 4 lipids in that formulation, 2 are the same, cholesterol and 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC), and 2 are different but similar.

Dr. Maldonado (AAP) emphasized the importance of the issue regarding 16 to 17 year olds, which came up frequently during the VRBPAC vote the previous day, especially among pediatricians. She stressed that this should not hold up the rest of the work from being vaccinated and should not be an obstacle to the US in terms of vaccinating children. She re uested additional details about Pfizer's plans to pursue acc ine in pediatric trials in terms of next steps, the timeline for moving to younger age groups, potential policy implications due to the equity issues involving young frontline workers who are under 18 years of age who otherwise might qualify for dosing, and confidence in the vaccine for people who are already disenfranchised who may be frontline and who are pediatric patients as well.

Dr. Grubner stressed that Pfizer considers the pediatric population to be very important and obviously have requirements. Beyond the requirements, they recognize that although disease appears to be less frequent in the younger age groups, nonetheless there are hospitalizations across the country and the potential for spread among the younger age groups has yet to be fully defined. Obviously, everyone wants to keep schools open and children engaged. Right now, Pfizer has included the information in the current file for 16 and 17 year olds and continues to enrich that database. Individuals who are not part of the current EUA filing who are 12 to 15 years of age are being actively enrolled. They had a cohort of about 100 and are now at about 500, with a goal to enroll a total of 2000 participants in this age group. It is the intent to have safety and immunogenicity approximate to the time the BLA is filed to potentially be able to get an indication in that age group. Pfizer anticipated seeing more reactogenicity in the lower age groups, but has been comforted and reassured that this does not seem to be noticeably different than what has been seen among 18 to 25 year olds. Therefore, they have continued the 30 µg dose for the planned enrollment of the full 2000 participants 12 to 15 years of age. However, this could differ moving into younger age groups 5 to 11 years of age. The current plan is to conduct a dose ranging study in children 5 to 11 years of age predicated on what has been learned in children 12 to 15 years of age, and then gradually move down from there. Pfizer anticipates starting that trial in the April 2021 timeframe, which would give them enough time to have completed the study in the children 12 to 15 years of age and submit that to the FDA and other regulatory authorities. While they may see an attack rate in children 12 to 15 years of age that offers some information about efficacy, the assumption at this point is that there will not be enough cases and immunobridging will be done.

Dr. Poehling recalled that there were more cases of Bell's Palsy in the a ccine than the placebo group and as e d about the timeframe between the accine dose and the de e lopment of Bell's Palsy.

Dr. Gruber said that Pfizer has paid close attention to this just as the FDA has to ensure that they can be confident that there is not a signal there. The frequency of what was seen in terms of the overall trial was well within the range of what would be expected looking at the population at large. Given that, 4 cases would be expected 1/16th of the time to appear in that distribution if the vaccine was not related.

Dr. Perez indicated that among the 4 cases of facial paralysis reported in the vaccine group, the first occurred 3 days after Dose 1 and resolved 3 days after that. The second subject developed facial paralysis 9 days after vaccine, the third developed facial paralysis 48 days after vaccine, and the fourth person developed facial paralysis 37 days after vaccination.

Dr. ald onado (AAP) noted that the Bell's Palsy population incidence ranges from - 30/100,000.

GRADE: Pfizer BioNTech COVID-19 Vaccine

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Dr. Gargano presented the ACIP COVID-19 Vaccines WG's Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) of the Pfizer BioNTech COVID-19 vaccine. The policy question under consideration is: "Should vaccination with Pfizer BioNTech COVID-19 vaccine (2-doses, IM) be recommended for persons 16 years of age and older under an emergency use authorization?" In terms of the PICO (Population, Intervention, Comparison, Outcomes) question, the population under consideration is persons ages 16 years and older, the intervention is 2 doses of the Pfizer BioNTech COVID-19 vaccine administered 21 days apart, and the comparison is no vaccine. The WG identified 7 outcomes as the as the most important for the policy question, which are shown in this table with their level of importance and description:

Outcome	Importance[a]	Description
Benefits		
Symptomatic lab-confirmed COVID-19	Critical	Primary outcome; current studies use PCR + specific symptoms
Hospitalization due to COVID-19	Critical	Phase 3 trials not designed to detect statistical differences between treatment groups for this outcome
All-cause death	Important	Death from all causes; phase 3 trials not designed to detect statistical differences between treatment groups for this outcome
SARS-CoV-2 seroconversion	Important	Measured using antibodies to non-spike protein to differentiate seroconversion due to natural infection from immunogenicity to vaccine; no data available
Asymptomatic SARS-CoV-2 infection	Important	Measured using serial PCR; no data available
Harms		
Serious adverse events	Critical	Evaluating balance of events between arms; also reporting on number deemed vaccine-related
Reactogenicity	Important	Evaluating grade ≥ s e erity of systemic e ents and local reactions

[a]Three options: Critical; Important but not critical; Not important for decision making

Of note, in the case of the vaccine trials, hospitalization due to COVID-19 and deaths are less common and the phase 3 trials may not be designed or powered to evaluate differences between treatment groups. The WG does not necessarily expect the direct evidence for these outcomes at this point, and to some degree could infer that decreases in symptomatic COVID would also translate into decreases in hospitalizations and deaths. Additionally, for the outcomes of seroconversion and asymptomatic infection, no data are currently available, so these outcomes were not included in the evidence profile that Dr. Gargano presented. Data on seroconversion eventually will be available in an ongoing Phase III trial, but asymptomatic infection is not currently being studied. However, the WG did consider it an important outcome.

The WG conducted a systematic review to identify evidence related to the policy question. They identified published articles using the Medline, Embase, and Cochrane Library databases written in English and restricted to 2020. The following search terms were used to identify data on vaccination with the specific vaccine formulation under consideration: coronavirus, COVID-19, SARS-CoV-2, respiratory (symptom, disease, illness, condition), vaccine, immunization,

trial, double blind, single blind, placebo, comparative study, phase 3, immunogenicity, efficacy, effective, adverse, evidence, and variations on these terms. Articles were included that provided data on vaccination with BNT162b2 and: 1) involved human subjects; 2) reported primary data; 3) included adults (ages 18 and older) at risk for SARS-CoV-2 infection; 4) included data relevant to the efficacy and safety outcomes being measured; and 5) included data for the dosage and timing being recommended (µg, doses at and days). The WG also sought out additional resources, including obtaining unpublished data from vaccine manufacturers. Over 2700 records were identified through database searching and 1 record was obtained directly from the sponsor of the Phase III trial. Ultimately, 2 resources were included in the evidence synthesis.

GRADE evidence type assesses the certainty of estimates from the available data. The highest level of certainty is Type 1, which means the WG is very confident the true effect lies close to that of the estimate. Type 2 means the WG is moderately confident in the effect estimate, but there is a possibility the true effect could be substantially different. Type 3 means low certainty, indicating the 's confidence in the effect estimate is limited. Type 4, indicates very low certainty, meaning the WG has little confidence in the effect estimate. The evidence type is not measuring the quality of individual studies, but how much certainty the WG has in the quantitative estimates of effect for each outcome.

Initial evidence type is determined by the study design. A body of evidence from randomized controlled trials (RCTs) starts with an initial evidence type of 1, indicating high certainty. A body of evidence from observational studies starts with an evidence type of 3, indicating low certainty. The evidence type can be downgraded due to the following GRADE criteria:

- **Initial Evidence Type** (certainty level) determined by study design
  - Initial evidence type 1 (high certainty): A body of evidence from randomized controlled trials
  - Initial evidence type 3 (low certainty): A body of evidence from observational studies

- **Risk of Bias:** Can include failure to conceal allocation, failure to blind, loss to follow-up. Risk of bias may vary across outcomes.

- **Inconsistency:** Criteria for evaluating include similarity of point estimates, extent of overlap of confidence intervals, and statistical criteria including tests of heterogeneity[2].

- **Indirectness:** Considers the generalizability of the evidence to the original PICO components (e.g., patients, intervention, comparison, or outcomes differ from those of interest[1]).

- **Imprecision:** Considers the fragility of the relative and absolute effect measures based on the interpretation of the 95% CIs and the optimal information size.

- **Other Considerations:** Includes publication bias or indications of dose-response gradient, large or very large magnitude of effect, and opposing residual confounding.

[Guyatt GH, Oxman AD, Kunz R et al. GRADE guidelines: 8. Rating the quality of evidence--indirectness. *J Clin Epidemiol.* 2011. DOI:10.1016/j.jclinepi.2011.04.014].

To review the evidence of benefits, for the critical outcome of symptomatic COVID-19, one study provided data. This was the Pfizer-BioNtech Phase II/III RCT and the data were obtained directly from the sponsor. The data cutoff date was November 14, 2020. Primary analyses were performed for an evaluable efficacy population defined as "all eligible randomized participants who receive all vaccination(s) as randomized within the predefined window and have no other important protocol deviations as determined by the clinician, who did not have evidence of prior SARS-CoV-2 infection." For these analyses, there were over 36,000 persons, about 18,000 per arm, who contributed over 4000 person-years of observation, about 2200 per arm. Some secondary analyses included persons with prior infection and there were about 40,000 persons and 4600 person-years. Analyses also were done for an all-available efficacy population, which includes all randomized participants who received at least one dose, with outcome counting any time after that. The number of persons is somewhat larger at over 43,000, but the number of person-years is quite a bit larger at almost 8000 or 4000 person-years per arm. It may be helpful to think of the evaluable efficacy as similar to a per protocol analysis and the all-available efficacy as more similar to an intention-to-treat (ITT) analysis.

Using the available efficacy population for all persons aged at least 16 years, there were 8 cases among 17,411 persons in the vaccine arm and 162 cases among 17,511 persons in the placebo arm. This resulted in a vaccine efficacy estimate of 95% and a 95% confidence interval of 90.3% to 97.6%. This is the outcome used for GRADE. Vaccine efficacy was also over 90% in a number of key subgroups, including those aged 65 and older, 75 and older, those at risk due to presence of a comorbidity or obesity, and those who were aged at least 65 years and at risk. For some subgroups, the number of person-years was small and the confidence intervals were wider. In a comparison of primary and secondary outcomes, varying the timing of outcome assessments and with inclusion of persons who had evidence of prior infection had little influence on efficacy estimates. In terms of the results for the all-evaluable efficacy population, which includes everyone who received at least one dose of vaccine or placebo, there were 50 cases reported among 21,314 persons who received the vaccine and 275 cases among 21,258 persons who received the placebo, for a vaccine efficacy estimate of 82% and a 95% confidence interval of 75.6% to 86.9%.

In terms of the GRADE evidence table for the outcome of symptomatic COVID-19, because the data were from an RCT, the evidence type started at 1. Regarding risk of bias, there was some concern related to blinding. Participants and study staff were blinded to assignments, but they may have inferred receipt of vaccine or placebo assignment based on reactogenicity. This was deemed unlikely to overestimate the efficacy results; therefore, the WG considered the risk of bias Not Serious. Because there was only one study, there were no serious concerns of inconsistency. Some concern for indirectness was noted due to the short duration of observation in the available body of evidence. The vaccine efficacy observed at a median 2-month follow-up may differ from the efficacy observed with ongoing follow-up. However, in consideration of the strength of association and precision observed for this outcome in particular, it is unlikely that the efficacy estimate for symptomatic COVID-19 would change substantially enough to fall below the FDA-defined efficacy threshold for licensure under an EUA; that is, to <50% efficacy. The WG acknowledged some concern for indirectness because of exclusions from the clinical trial. The WG judged this to be not serious, in part because all available subgroup evaluations were so consistent. The relative effect was very strong, as indicated by the VE estimate of 95% with a narrow confidence interval. There were no other serious concerns affecting the certainty assessment. The WG assessed the level of certainty as high, or type 1, for this critical outcome.

The second outcome for consideration was hospitalization for COVID-19. The protocol included a definition of severe COVID-19, but this did not require hospitalization. The data on hospitalization were obtained from the sponsor. The definition used for severe COVID included the following:

- ❑ Severe COVID-19[a]: COVID-19 case with at least 1 of following:
  - Clinical signs at rest indicative of severe systemic illness;[b]
  - Respiratory failure;[b]
  - Evidence of shock;[b]
  - Significant acute renal, hepatic, or neurologic dysfunction;
  - Admission to an intensive care unit; or
  - Death

- ❑ Severe COVID-19 per CDC definition: hospitalization, admission to the ICU, intubation or mechanical ventilation, or death

[a. Severe COVID-19 as defined in protocol using guidance from FDA.
b. **Severe systemic illness**: respiratory rate ≥30, heart rate ≥125, SpO_2 ≤ % o n room air at sea le el or PaO_2/FiO_2<300 mm Hg; **respiratory failure**: needing high-flow oxygen, noninvasive ventilation, mechanical ventilation, ECMO; **evidence of shock**: SBP <90 mm Hg, DBP <60 mm Hg, requiring vasopressors].

The two analyses using the available efficacy population corresponds with the population used in the primary efficacy analyses for symptomatic COVID, and the same outcomes analyzed using the all-available efficacy population. The severe COVID-19 outcome was used as defined in the Phase II/III protocol, as well as the hospitalization outcome per the PICO question. In the analysis used in GRADE, 5 cases of COVID resulted in hospitalization that occurred at least 7 days post-Dose 2 among persons who did not have evidence of prior infection, all in the placebo group. The vaccine efficacy was 100% and the 95% CI included the null value. Note that the analyses in the all-available efficacy population included more than twice as many events, and the confidence intervals showed statistical significance.

In terms of the GRADE evidence for the outcome of hospitalization for COVID-19, the initial evidence type of 1 was downgraded 1 point due to serious concern over indirectness of outcomes because of the short duration of follow-up. COVID-19 leading to hospitalization measured in such a short time frame is an indirect measure and some hospitalizations may not have occurred yet for some cases included in the analysis. Certainty also was downgraded 1 point for imprecision. The final certainty estimate for the outcome of hospitalization for COVID-19 is Type 3.

The next outcome of interest was all-cause death, which the sponsor regarded as descriptive only. This was not an efficacy endpoint in the trial protocol. There were few deaths among trial participants, including 2 among vaccinated persons and 4 among placebo recipients. No person-time analysis of deaths was available. The available data indicate a relative risk of death of 0.50, with a 90% confidence interval of 0.09 to 2.73. For the GRADE evidence for all-cause death, no serious risk of bias was identified and there was no serious concern of inconsistency. There was serious concern for indirectness due to the short duration of follow-up as deaths due to COVID-19 may not have had time to occur during the follow-up period. There was very serious concern of imprecision. The relative risk of 0.5 favored vaccination, but the very wide 95% confidence interval did not rule out harms. The certainty estimate was Type 4.

Two studies provided data on harms. These included the Pfizer/BioNTech Phase II/III RCT unpublished data obtained from sponsor and the Pfizer/BioNTech Phase 1 randomized trial [Walsh EE, Frenck RW, Falsey AR et al. Safety and Immunogenicity of Two RNA-Based Covid-19 Vaccine Candidates. NEJM. 2020. DOI: 10.1056/NEJMoa2027906]. The Phase I study by Walsh included data on adults aged 18-55 and 65-85 years, including 12 who were vaccinated with the relevant dose and 9 who received placebo in each age group. The WG evaluated the safety data from this study, including local and systemic reactions and SAEs.

In terms of the raw data on the critical outcome of SAEs, from the Phase I trial, 1 SAE was identified in the vaccinated group that was unrelated to vaccination and 0 in the placebo group. In the Phase III trial, there were 126 events among the vaccine group and 111 among the placebo group. The FDA classified 2 SAEs as related to vaccination, a shoulder injury and lymphadenopathy. In terms of the GRADE evidence table for SAE, the relative risk indicated a relative balance of SAEs between the vaccinated and placebo groups, with a relative risk of 1.14 and a 95% confidence interval of .89 to 1.47. The certainty assessment was reduced 1 point due to serious concern of indirectness of outcomes because the body of evidence does not provide certainty that rare SAEs were captured due to the short follow-up, so the final certainty was Type 2.

Reactogenicity was evaluated using the same 2 studies. The Phase III trial did not solicit this data on everyone, but on a subset of over 8000 participants. Both Pfizer studies used the same events and grading scales, shown here:

- Local reactions (pain at injection site, redness, swelling)
  - Grade 3: pain at injection site that prevents daily activity; redness > 10 cm; and swelling > 10 cm
  - Grade 4: emergency room visit or hospitalization for severe pain at the injection site, necrosis (redness and swelling categories) or exfoliative dermatitis (redness category only).

- Systemic events (fever, vomiting, diarrhea, headache, fatigue, chills, new or worsened muscle pain, new or worsened joint pain)
  - Grade 3: fever >38.9°C to 40.0°C , vomiting that requires IV hydration; diarrhea of ≥ l oose stools in hours se ere fatigue, se e re headache, severe muscle pain, or severe joint pain that prevents daily activity.
  - Grade 4: fever >40.0°C, fatigue, headache, muscle pain, joint pain, diarrhea, or vomiting that require emergency room visit or hospitalization.

In the Phase I study, Grade 3 local reactions or systemic events were reported in 8.3% of persons in the vaccine arm and 5.6% of persons in the placebo arm. In the Phase III study, Grade 3 events were reported by 8.8% of persons in the vaccine arm and 2.1% of persons in the placebo arm. Pooling the data from the two trials, the WG estimated that the relative risk for any Grade 3 or 4 event was of 4.27 with a 95% confidence interval from 3.39 to 5.38. There was no serious concern for risk of bias, inconsistency, indirectness, or imprecision. The final certainty was type 1.

This table summarizes the ’s current GRADE assessment for the Pfizer-BioNTech COVID-19 vaccine:

Outcome	Importance	Design (# of studies)	Findings	Evidence type
Benefits				
Symptomatic lab-confirmed COVID-19	Critical	RCT (1)	Pfizer-BioNTech COVID-19 vaccine is effective in preventing symptomatic COVID-19	**1**
Hospitalization due to COVID-19	Critical	RCT (1)	Pfizer-BioNTech COVID-19 vaccine may prevent COVID-19-resulting in hospitalization, but the uncertainty is high because this is a rare outcome	**3**
All-cause Death	Important	RCT (1)	Pfizer-BioNTech COVID-19 vaccine may prevent death, but the uncertainty is high because this is a rare outcome	**4**
SARS-CoV-2 seroconversion	Important	No studies	Data not yet available from any studies	**ND**
Asymptomatic SARS-CoV-2 infection	Important	No studies	Data not available from any studies	**ND**
Harms				
Serious adverse events	Critical	RCT (2)	SAEs were balanced between vaccine and placebo arms. Two SAEs were judged to be related to vaccination.	**2**
Reactogenicity	Important	RCT (2)	Severe reactions were more common in vaccinated; any grade ≥ react ion was reported by . % of accinated s. . % of placebo group	**1**

In terms of benefits, the available data indicate that the vaccine is effective for preventing symptomatic COVID-19, with an evidence type of 1. For hospitalization and death, the available evidence favors the intervention, but because so few events were observed during the median 2-month follow-up, the certainty is lower, with evidence types 3 and 4, respectively. No data were available to assess the other two potential benefits. In terms of harms, the available data indicate that SAEs were balanced between the vaccine and placebo arms, and 2 SAEs were judged to be related to vaccination among over 21,000 persons vaccinated. Severe reactions were more common in vaccinated persons. About 8.8% of vaccine recipients vs. 2.1% of placebo recipients reported Grade 3 or 4 reactions. The evidence type for reactogenicity was type 1.

In conclusion, Dr. Gargano reiterated that the policy question focused on what will be an interim recommendation issued during an EUA. Regarding benefits, the Phase III trial is ongoing and effect estimates may change with additional follow-up. This raised concerns for indirectness of outcomes as ideally, the WG would like to look at efficacy over a period of longer than 2 months. The WG judged that it is unlikely that the efficacy estimate for symptomatic COVID-19 would change substantially enough in the months following vaccination to fall below the FDA-defined efficacy threshold for an EUA. Direct evidence of efficacy for hospitalization and deaths is limited at this time due the small number of events that had been observed through the cutoff date of November 14, 2020. From the efficacy against symptomatic disease, the WG inferred that vaccination also would reduce hospitalizations and deaths. No data were available to assess prevention of asymptomatic infections at this time. Regarding harms, Grade 3 reactions were not uncommon in vaccinated persons. SAEs occurred at a similar frequency in vaccine and placebo groups, but only 2 SAEs were associated with vaccination.

Discussion Points

Dr. Lee requested confirmation that the way this was framed was for the period of the EUA and that there would be another GRADE assessment at the time of licensure or this could be re-evaluated. In addition, she inquired as to what the anticipated interval will be between the EUA and the BLA in terms of thinking about the durability of this GRADE.

Dr. Oliver confirmed that the assumption is that there would be an additional review of the evidence when additional data are available, including for a BLA.

Dr. Fink responded that the time period between the EUA and the BLA would depend upon the timeline for additional data to be collected, primarily in terms of additional safety follow-up from clinical studies and additional data on certain aspects of vaccine effectiveness. While he was not able to provide a specific timeframe, the FDA is working with the manufacturer to get to a BLA as quickly as possible.

WG Interpretation and Next Steps

Sara Oliver MD, MSPH
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National Center for Immunization and Respiratory Diseases
Centers for Disease Control and Prevention

Dr. Oliver presented the ’s interpretation of the clinical trial data, Evidence to Recommendations (EtR) Framework of benefits and harms, and safety surveillance and discussed next steps.

In terms of the clinical trial data, the WG reviewed the safety data from the Pfizer/BioNTech vaccine. Local reactions occurring within 7 days were common. Pain at the injection site was the most common reported. Systemic reactions within 7 days were common as well, with fatigue headache, and muscle pain as the most common reported. This symptom onset was usually 1 to 2 days post-vaccine receipt and most symptoms resolved with a median of 1 day.

Regarding highlights of select local reactions by dose in two different populations, persons aged 16 to 55 years and persons over 55 years of age. Among these participants, approximately 70% to 80% had pain at the injection site after each dose of vaccine. While a majority of older adults still had pain at the injection site, the proportion was slightly lower.

Concerning select systemic reactions in the younger and older population, for any fever ≥ 8.0°C, nearly 16% of persons 16 to 55 years of age had a fever after the second dose. This proportion is slightly lower among adults older than 55 years of age. There is a plan to have a document summarizing this reactogenicity data after each dose on the CDC and ACIP websites to help inform providers and patients about possible expected symptoms post-vaccination.

There were a few other events discussed among the WG to highlight. Lymphadenopathy had a higher frequency in the vaccine group compared to the placebo group. As localized lymph nodes are involved in the vaccine response, it is plausible that this could be related to vaccine. Occurrence of Bell’s Palsy also was noted with higher frequency in the vaccine group compared to placebo. The incidence within the vaccine group was consistent with the expected population

rate. There is no known or expected causal relationship between the vaccine and Bell's Palsy known at this time. Overall, SAEs were similar between the vaccine and placebo.

Efficacy data were reviewed by the WG as well. The primary efficacy endpoint, which was subjects without prior infection beginning 7 days after the second dose, yielded an efficacy of 95%. High efficacy was noted for additional post-hoc efficacy analyses, including those with evidence of prior infection across age, sex, race, and ethnicity categories and those with underlying medical conditions. For example, the efficacy among adults 65 and older was 94.7%. Most recipients in the trial received 2 doses of the vaccine. However, an efficacy of 52.4% was noted between Dose 1 and Dose 2.

Efficacy was noted against severe disease as well, although the confidence intervals are quite wide. Efficacy using two different definitions of severe disease was measured, which were: 1) the FDA definition Respiratory Rate ≥ , He art Rate ≥ , SpO ≤ % on room air at sea level or PaO2/FIO2< 300 mm Hg; OR Respiratory failure or Acute Respiratory Distress Syndrome (ARDS), defined as needing high-flow oxygen, non-invasive or mechanical ventilation, or ECMO; OR evidence of shock (systolic blood pressure <90mmHg, diastolic BP<60mmHg or requiring vasopressors); OR Significant acute renal, hepatic or neurologic dysfunction; OR Admission to an intensive care unit or death; and 2) the CDC definition: Hospitalization, admission to ICU, intubation or mechanical ventilation or death. Both analyses showed sufficient efficacy, but with small numbers and wide confidence intervals. The Phase III trial overall was not powered to assess efficacy of the vaccine to prevent hospitalization and death.

Overall, the WG discussed several aspects of the Phase III safety and efficacy data. Communications around expected local and systemic reactions after vaccine receipt will be important. Post-authorization safety and effectiveness studies will be critical as well. Specifically, surveillance for Bell's Palsy could help determine any possible causal relationship. A high efficacy in adults ≥ y ears of age is reassuring. Continued studies are needed to assess the duration of protection. Additional studies also are needed to assess the impact of the Pfizer/BioNTech vaccine on viral shedding and transmission.

The WG previously provided an overall presentation to ACIP of the EtR Framework without characteristics for a specific vaccine, but has not previously presented judgments on the "Benefits and Harms" domain as the Phase III trial data were needed to complete that assessment. During this session, the WG presented its thoughts on the "Benefits and Harms" domain after reviewing the data, and at the time of the next ACIP meeting will present the full EtR Framework for the Pfizer/BioNTech vaccine.

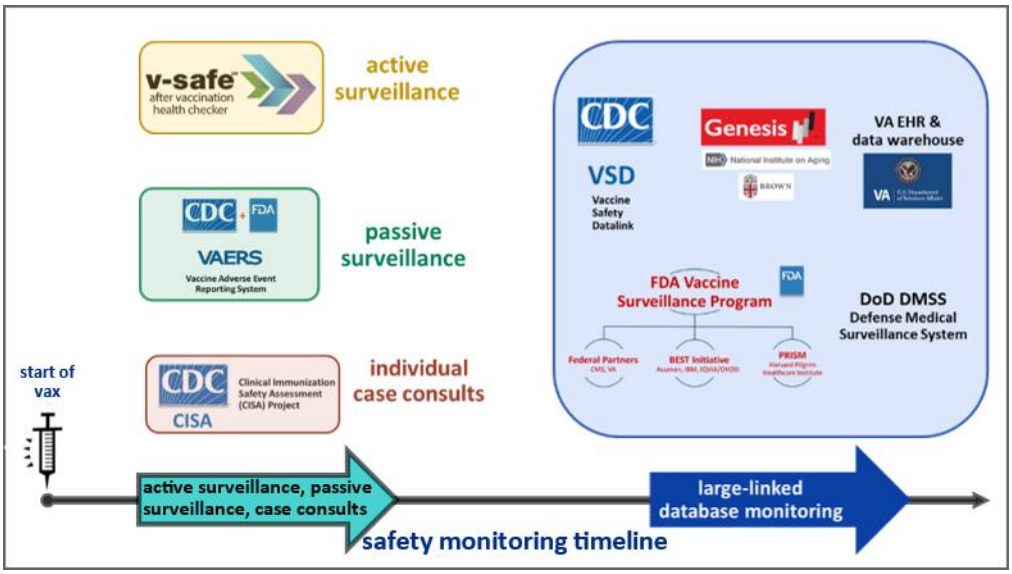
The first criterion for the "Benefits and Harms" domain is the magnitude of desirable anticipated effect, specifically regarding how substantial the anticipated effects are for each main outcome for which there is a desirable effect. The WG felt that the anticipated desired effects were large. The second criterion was the magnitude of undesirable anticipated effects, specifically regarding how substantial the anticipated undesirable effects are for each main outcome. The WG felt that the undesirable anticipated effect were small. The third criterion is the balance of the desirable and undesirable anticipated effects, specifically with regard to what the balance is between the desirable effects relative to the undesirable effects. The WG felt that this balance of effects favored the intervention at this time—the Pfizer/BioNTech COVID-19 vaccine.

In terms of safety surveillance, the WG wanted to bring up a specific safety issue that has been raised recently. Issues of anaphylaxis or an anaphylactoid reaction were noted in UK recipients, 2 healthcare workers with a history of severe allergic reactions. The first has a history of severe allergic reaction to eggs and other food items and the second to a drug. A third healthcare worker with no history of allergies developed tachycardia. CDC is following along with the Public Health England (PHE) authorities to understand these cases. The night before this ACIP meeting, CDC convened an external group with experiences in vaccine safety, immunology, and allergy, CISA, to collate expert knowledge regarding possible cases. The FDA is obtaining more data from the UK regulatory authorities and will consider if additional information would need to be included in an EUA regarding this issue. The WG anticipates further information and clinical considerations to come around this issue prior to vaccine use in the US and will discuss this again with ACIP once the FDA has issued a decision on the Pfizer vaccine. This issue emphasizes the importance of having close safety surveillance.

Dr. Oliver briefly highlighted the COVID-19 Vaccine Safety Technical (VaST) Subgroup. This group was built off of lessons learned from H1N1 vaccine safety monitoring. VaST will ensure transparency and independence regarding safety surveillance. The composition of VaST includes Co-Chairs: Grace Lee (ACIP member) and Bob Hopkins (NVAC Chair), ACIP and NVAC representation, 7 independent expert consultants, ACIP *ex officio* members (NIH, FDA, OIDP, CMS, HRSA, IHS), VA and DoD liaisons, and CDC co-leads.

The objectives for VaST are to: 1) review, evaluate, and interpret post-authorization/approval COVID-19 vaccine safety data; 2) serve as the central hub for technical subject matter experts (SMEs) from federal agencies conducting post-authorization/approval safety monitoring; 3) advise on analyses, interpretation, and data presentation; and 4) liaise with the ACIP COVID-19 Vaccines WG on issues of safety data presentation to the ACIP and application of safety data to policy decisions. Currently, VaST is meeting weekly to refine procedures and hear updates on monitoring systems. Plans include periodic safety data summaries to the COVID Vaccine WG and to ACIP.

This graphic highlights the many specific systems conducting safety surveillance monitoring and the safety monitoring timeline:



In terms of next steps, the WG awaits a final decision from FDA regarding the issuance of an EUA. After an FDA decision, ACIP will have an emergency meeting. The full EtR Framework will be presented at that time. In addition at that meeting, there will be a presentation for various clinical considerations. The WG will present draft considerations for dosing intervals; co-administration with other vaccines; and vaccination of special populations, including those with immunodeficiencies and pregnant women. Finally at that meeting, there will be a vote on the recommendation for Pfizer/BioNTech COVID-19 vaccine.

Dr. Oliver opened the floor for ACIP discussion focused on the safety and efficacy data of the Pfizer-BioNTech COVID-19 Vaccine, posed the final benefits and harms uestion, "What is the balance between the desirable effects relative to the undesirable effects for the Pfizer-BioNTech COVID-19 vaccine?" to determine if ACIP agreed with the in terpretation on the balance between the desirable effects relative to the undesirable effects of the vaccine.

Discussion Points

Dr. Romero said that based on the data present throughout the day, he thought overall that the desirable effects are favorable relative to the undesirable effects of the vaccine. While he remained somewhat leery about the younger age group of 16 to 17 years of age, he felt better about it than he did coming into the meeting. O erall, he tho ught the data supported the 's interpretation.

Dr. Lee said that she believes the efficacy of this vaccine is substantial. While there are some side effects from the vaccine, these should be anticipated. In her mind, the benefits clearly far outweigh the risks at this point. She is comfortable with GRADE Level 1 for the prevention of symptomatic disease and has no doubt that the efficacy is extremely high—much higher than she originally anticipated prior to hearing the data. In terms of durability of immunity, she recognized that during the EUA period there would be an opportunity to re-review the data prior to licensure, she is comfortable with the Level 1 in this context under the assumption it would be 3 to 6 months during the EUA period. If the interval is anticipated to be a year or more, she might feel differently about the level of certainty about the efficacy over that period of time. This is an important and unusual issue in GRADE that they do not typically encounter.

Dr. Poehling agreed with Dr. Lee. She recalled what Dr. Bell reminded them of earlier, that during the 3.5 hours they had been working, roughly 450 people were estimated to have died. Therefore, the desirable effects do outweigh the undesirable effects in her opinion. It is known that because the vaccine is immunogenic, it also is reactogenic. Like Dr. Romero, she initially had questions about the children 16 to 17 years of age. However, 154 children have died so far of COVID-19. That exceeds the number of deaths among children in most influenza epidemics. Following up the data is very important and she expressed appreciation for the VaST Subgroup and all of the post-marketing surveillance that will be important to continued close monitoring.

Dr. Bell reiterated that while the answer to the uestion is a resounding "yes" in this conte t, it is in the context of a pandemic and an EUA and many important questions remain for which there are no data (e.g., durability of protection and subgroups). This lack of data is amplified by the fact that this is a new vaccine platform so there is really no basis for extrapolating. It is very important to continue to accumulate the data that ACIP will need in order to make longer-term recommendations and fill the data gaps that have been identified.

Dr. Bernstein concurred with the concerns about children 16 to 17 years of age. He wants this vaccine to be available as soon as possible and get it into as many arms as possible. However, the data are limited for 16 to 17 year olds and he does not feel the same sense of urgency for this group that he does for the other groups (e.g., HCP, people of color, 65 and older) who are disproportionately impacted by COVID-19. His concern also extends to the fact that he would not want there to be an AE in this younger age group that in turn would only magnify vaccine hesitancy amongst families.

Dr. Ault concurred with what was being said. He asked whether they had an estimate about how many essential workers and HCP might be 16 to 17 years of age.
Dr. Oliver said that while they do not have an exact estimate, they do anticipate there could be some HCP, essential workers, and workers in LTCFs in the 16 to 17 year old age group.

Dr. Kimberlin (AAP Redbook) speaking on his own rather than on behalf of the AAP, he reiterated that for the 16 to 17 year olds, there could be equity issues. Biologically, he thinks of a 17-year-old as not different from an 18-year-old. Since the trial enrolled individuals 16 years of age and older and since the totality of the evidence looks so strikingly positive, he personally would favor inclusion of individuals 16 and 17 years of age in recommendations, recognizing that it would not be a recommendation that all 16 and 17 year olds get vaccinated, but that as their groups come up through the phased allocation of an increasing amount of vaccine that they would not be excluded.

Dr. Hunter expressed his support for the fact that the desirable effects relative to the undesirable effects for this vaccine are very clear, especially in the context of the pandemic. He wanted to express his deep gratitude for and remember their neighbors, coworkers, friends, and family members who have suffered or are suffering from this disease or who have died from it; to honor the healthcare workers who are working very, very hard to care for those people who are ill; and especially to support the public health professionals who are working to prevent further cases.

Dr. O'Leary (PIDS) agreed with Dr. i mberlin's points and noted that while of course they want to make recommendations for vaccination to protect individuals and those at highest risk of severe disease, it also is true that a lot of the considerations regarding the phases of allocation also consider the multiplier effects. Given that older teens are among the highest groups in terms of incidence of disease, if they are working in those settings (healthcare, LTCFs, grocery stores, et cetera) it is going to be important to protect a 16-year old just as much as it is important to protect an 18-year old.

Dr. Szilagyi agreed that there is a remarkable balance of the desirable effects of this vaccine. From an efficacy and safety standpoint, he could not think of a reason why 16 and 17 year olds would be that different from younger adults. He was reassured by the answer to the questions about reactogenicity among 18 to 25 year olds. Even if there is somewhat more reactogenicity among younger adults, those are not severe. The impact of the pandemic on 16 to 17 year olds has been profound, not just from getting COVID-19 but also from the psychological impact of being out of school. Therefore, he favored including 16 to 17 year olds in the recommendation.

Dr. Sanchez said he felt strongly that the desirable effects far outweigh any undesirable effects, and he supported the inclusion of 16 to 17 year olds in the recommendation. They were included in the trials, they were randomized, they were part of the assessment, and should not be penalized for not having huge numbers like the rest. There were still 283 in that age group. While he understood that pregnant women would be assessed, he also feels strongly about assessing whether lactating women should be vaccinated and whether there are any the effects in babies who are being breastfed as another category beyond just pregnancy.

Dr. Ault said he had been thinking about breastfeeding women since Dr. Sanchez first mentioned this, but was having a difficult time coming up with a biological mechanism by which a ccine would get through the mother's body, through the breast, to the child's stomach to cause a problem with breastfeeding. Compared to the risk from COVID from transient decrease in the milk supply due to maternal fever, the vaccine did not seem like a big risk to him.

Dr. Lee asked whether anyone had any thoughts on the timing of post-partum vaccination and any pathophysiologic reasons to make a recommendation about timing.

Dr. Ault said he could not think of any pathophysiologic reasons to give a recommendation about timing, with one possible exception. There are some data about women remaining at higher risk than baseline for respiratory illnesses such as influenza and pneumonia for several months post-partum, which was identified during the 2009 influenza pandemic. It is probably too early to know whether that will be true for this respiratory pathogen, but he wonders whether giving the vaccine during the immediate post-partum period might not be a bad idea. The MMR vaccine is given to women who are not immune to rubella during that time, along with other things in that 48-hour period while women are in the hospital.

Dr. Eckert (ACOG) agreed with Dr. Ault that there are good data to show that other viral illnesses are more impactful in the post-partum period than in women who are beyond that period, likely because of the fatigue and all of the other risk factors that go with being post-partum.

Dr. Fryhofer (AMA) greatly appreciated all of the comments about pregnant women and looks forward to the DART study results. She emphasized that in terms of the HCP in Phase 1a, 75% of healthcare workforce are female. That translates to approximately 330,000 HCP who could become or may be recently post-partum at the time that these vaccinations are going to start. It would be helpful to have the DART information by the end of December instead of the first quarter. This is new vaccine platform and there are women who need this for all of the reasons that have been stated, but it is important to ensure that the vaccine is safe and that they do no harm.

Dr. Cohn stressed that there will be additional public ACIP meetings whenever there are new data to inform the current policy regardless of whether the data suggest that the recommendations need to be changed.

Dr. Poehling noted that the Society for Maternal-Fetal Medicine (SMFM) and ACOG have been meeting to discuss and she wanted to give them a chance to share their thoughts on COVID vaccine.

Dr. Eckert (ACOG) indicated that ACOG has issued a statement to ACIP publicly and reiterated it the previous week during the NVAC meeting that ACOG supports allowing pregnant women to have a conversation with their providers based on their risk-benefit ratio, such as the risk of acquiring the virus based on their job, the prevalence in their community, their own health risks, et cetera and working with their provider to make an informed decision. ACOG is planning to have information available to providers as soon as possible after the EUA and ACIP makes its decisions to try to help providers. ACOG is advocating for pregnant women to be able to have a choice to get this vaccine provided the EUA allows for that, and is hoping to equip providers and pregnant women with as much information as possible in order to make those decisions.

Dr. Ault added that for the past 10 to 15 years, he and Drs. Eckert and Riley have been part of groups like ACOG and ACIP that have tried to ensure that all of their recommendations are congruent and anticipates continuing to do that for COVID vaccine.

Dr. Cohn reminded everyone to be prepared to join the ACIP meeting on either December 12th or 13th, depending on whether FDA issued an EUA before 10 AM on the 12th. If so, the ACIP meeting would convene at 11 AM on Saturday the 12th instead of on Sunday the 13th. A public comment session would be scheduled during that time as well.

December 12, 2020 Opening Session

José Romero, MD, FAAP
ACIP Chair

Amanda Cohn, MD
Executive Secretary, ACIP / CDC

Dr. Romero called to order the December 12, 2020 emergency meeting of the Advisory Committee on Immunization Practices (ACIP), the focus of which was to review the full evidence to support a recommendation and vote for the Pfizer/BioNTech COVID-19 mRNA vaccine BNT162b2. He welcomed and thanked everyone for giving up their weekend to attend this meeting, emphasizing that the work they were about to undertake was of national importance. He expressed appreciation for all of the time and effort everyone has dedicated to this project.

Dr. Cohn greeted everyone and thanked Dr. Romero and all of the ACIP voting members for all of the time and countless hours they all had put in to get to this meeting. She especially thanked the FDA for the huge lift that they had made over the last several days to authorize the Pfizer COVID-19 vaccine on Friday night. That meant that ACIP could consider a vote for recommendation of the Pfizer vaccine product. She then reviewed the agenda for the day, noting that in addition to voting on the Pfizer vaccine recommendation, ACIP would vote on amendments to the 2021 Childhood/Adolescent and Adult Immunization Schedules. While these schedules were voted to be approved in October 2020, consideration would be given to adding the language for the COVID-19 vaccine to these immunization schedules for 2021.

She indicated that all of the meeting materials for the day soon would be available on the ACIP website for the public and that the slides were made available through the same ShareFile link for ACIP Voting, Liaison, and *Ex-Officio* members as the previous day. She requested that Dr. Romero call the roll for just the voting members to identify any COIs and reminded everyone

that members who have participated in any of the COVID-19 vaccine clinical trials would be recusing themselves from the vote for the product-specific recommendations, but would be permitted to vote on the amendments to the immunization schedules.

Dr. Romero conducted a roll call of ACIP members during which the following COIs were identified:

- Dr. Robert Atmar is serving as the Co-Director of the COU of the NIH-funded IDCRC that is working within the CoVPN to evaluate SARS-CoV-2 vaccine candidates in Phase III clinical trials, including those produced by Moderna, AstraZeneca, Janssen, Novavax, and Sanofi.

- Dr. Sharon Frey is employed by SLU, which has a VTU that is part of the IDCRC. She is currently a Site PI for two Phase III COVID-19 vaccine clinical trials.

- Dr. Paul Hunter owns a small amount of stock in Pfizer and has received a small grant from Pfizer to conduct a QI project on pneumococcal vaccines.

Coronavirus Disease 2019 (COVID-19) Vaccines

Introduction

Beth Bell, MD, MPH
ACIP, COVID-19 Vaccine WG Chair
Clinical Professor, Department of Global Health
School of Public Health, University of Washington

Dr. Bell introduced the COVID-19 Vaccines session. She announced that on December 11, 2020, the Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) for emergency use of Pfizer-BioNTech COVID-19 Vaccine for the prevention of COVID-19 for individuals 16 years of age and older. During the December 11, 2020 emergency ACIP meeting, presentations were provided on the Pfizer-BioNTech COVID-19 vaccine clinical development, GRADE for Pfizer-BioNTech COVID-19, and the WG's interpretation of the data on benefits and harms.

For the December 12, 2020 emergency ACIP meeting, the presentation topics included review of the EtR Framework for the Pfizer-BioNTech COVID-19 vaccine, clinical considerations for use of the vaccine, public comment, and votes on the use of Pfizer-BioNTech COVID-19 vaccine and inclusion into the Child/Adolescent and Adult Immunization Schedules. As a reminder, the vote on the use of the vaccine is an interim recommendation and will be coupled with the interim recommendations on allocation, one of which ACIP already has made and others that will be forthcoming in the future.

EtR Framework: Pfizer-BioNTech COVID-19 Vaccine

Sara Oliver MD, MSPH
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Co-Lead ACIP COVID-19 Vaccine WG
National Center for Immunization and Respiratory Diseases
Centers for Disease Control and Prevention

Dr. Oliver presented the EtR Framework for the Pfizer-BioNTech COVID-19 vaccine. As a reminder, this is the policy question being addressed during this session, "Should vaccination with the Pfizer-BioNTech COVID-19 vaccine be recommended for persons 16 years of age and older under an Emergency Use Authorization?" In terms of the PICO ue stion as the focus of the discussion, the population is persons ≥ y ears of age. The intervention is the Pfizer-BioNTech COVID-19 vaccine and the comparison is no vaccine. The outcomes, which were detailed the previous day, include:

- ❑ Symptomatic laboratory-confirmed COVID-19
- ❑ Hospitalization due to COVID-19
- ❑ All-cause death
- ❑ SARS-CoV-2 seroconversion to a non-spike protein
- ❑ Asymptomatic SARS-CoV-2 infection
- ❑ Serious Adverse Events
- ❑ Reactogenicity grade ≥

These are the domains for the EtR to be discussed. Each domain has a question or questions on which the WG will provide judgment:

Evidence to Recommendations (EtR) Framework

EtR Domain	Question
Public Health Problem	• Is the problem of public health importance?
Benefits and Harms	• How substantial are the desirable anticipated effects? • How substantial are the undesirable anticipated effects? • Do the desirable effects outweigh the undesirable effects?
Values	• Does the target population feel the desirable effects are large relative to the undesirable effects? • Is there important variability in how patients value the outcomes?
Acceptability	• Is the intervention acceptable to key stakeholders?
Feasibility	• Is the intervention feasible to implement?
Resource Use	• Is the intervention a reasonable and efficient allocation of resources?
Equity	• What would be the impact of the intervention on health equity?

oing through this, "the vaccine" or "the intervention" in the questions will be changed to "the Pfizer-BioNTech COVID-19 vaccine" and "the problem" will be replaced with "COVID-19 disease."

The main question and additional questions to help inform the discussion associated with the "Public Health Problem" domain are

Is COVID-19 disease of public health importance?

- Are the consequences of COVID-19 serious?
- Is COVID-19 urgent?
- Are a large number of people affected by COVID-19?
- Are there populations disproportionately affected by COVID-19?

The WG reviewed the available evidence to help answer the questions addressed by this domain. As of December 10th, there have been over 15 million cases of COVID-19 in the US, with increases seen over the last month. The cumulative hospitalization rate between March 1-December 5, 2020 was nearly 280 per 100,000 population. Among those hospitalized, nearly one-third required intensive care and 15% died. As of December 10, 2020, there were 291,000 COVID-19-associated deaths reported in the US. Estimates of the SARS-CoV-2 infection fatality ratio range from 0.5% to 1.4%. There are other biologic factors associated with the increased incidence, including age and presence of underlying medical conditions, which have been discussed during earlier ACIP meetings [https://gis.cdc.gov/grasp/COVIDNet/COVID19_3.html . https://gis.cdc.gov/grasp/COVIDNet/COVID19_5.html. Hauser, A. et al. Estimation of SARS-CoV-2 mortality during the early stages of an epidemic: a modeling study in Hubei, China, and six regions in Europe. PLoS medicine, 17(7), p.e1003189 Yang, W. et al. Estimating the infection-fatality risk of SARS-CoV-2 in New York City during the spring 2020 pandemic wave: a model-based analysis. Lancet Infect Dis. 2020 DOI:https://doi.org/10.1016/S1473-3099(20)30769-6].
Based on the review of the epidemiologic data presented here, as well as epidemiologic data that have been presented during prior ACIP meetings, the WG judgment was that yes COVID-19 disease is of public health importance.

For the "Benefits and Harms" domain there are several main and additional questions, including the following:

How substantial are the desirable anticipated effects?

- How substantial is the anticipated effect for each main outcome for which there is a desirable effect?

How substantial are the undesirable anticipated effects?

- How substantial is the anticipated effect for each main outcome for which there is an undesirable effect?

Do the desirable effects outweigh the undesirable effects?

- What is the balance between the desirable effects relative to the undesirable effects?

A detailed review of the benefits and harms through GRADE was presented the previous day. To briefly summarize the benefits, the clinical trial demonstrated high efficacy against the primary endpoint of symptomatic, laboratory-confirmed COVID-19 with an efficacy of 95%. This was determined to have a high certainty under the time period covered by the EUA. For hospitalization, 5 events occurred that were all in the placebo group. Given low numbers and the short time of follow-up, there was relatively low certainty in the estimate. For all-cause mortality, deaths were uncommon overall, with 2 in the vaccine group and 4 in the placebo group. Given the low numbers, there was low certainty of evidence for this outcome.

To summarize the possible harms, SAEs were reported among recipients of vaccine and placebo (0.6% vs 0.5%). There was moderate certainty in this evidence. In terms of the reactogenicity outcomes, severe reactions were more common in vaccinated recipients. Overall, any Grade ≥ re action was reported by 8.8% of vaccinated vs. 2.1% of placebo group. There was a high certainty for this outcome.

o recap the ’s current GRADE assessment for the Pfizer-BioNTech COVID-19 vaccine, in terms of benefits, the available data indicate that the vaccine is effective for preventing symptomatic COVID-19, with an evidence type of 1. For hospitalization and death, the available evidence favors the intervention, but because so few events were observed during the median 2-month follow-up, the certainty is lower, with evidence types 3 and 4, respectively. No data were available to assess the other two potential benefits. In terms of harms, the available data indicate that SAEs were balanced between the vaccine and placebo arms, and two SAEs were judged to be related to vaccination among over 21,000 persons vaccinated. Severe reactions were more common in vaccinated persons, and about 8.8% of vaccine recipients vs. 2.1% of placebo recipients reported grade 3 or 4 reactions. The evidence type for reactogenicity was type 1.

Therefore, the WG felt that the desirable anticipated effects were large and the undesirable anticipated effects were small. Based on this, the WG felt when considering how the desirable effects balance with the undesirable effects, it favors the intervention (Pfizer-BioNTech COVID-19 vaccine).

For the “Values” domain, there are 2 primary questions and several additional questions, including the following:

Does the target population feel that the desirable effects are large relative to undesirable effects?

- How does the target population view the balance of desirable versus undesirable effects?
- Would patients feel that the benefits outweigh the harms and burden?
- Does the population appreciate and value Pfizer-BioNTech COVID-19 vaccine?

Is there important uncertainty about, or variability in, how much people value the main outcomes?

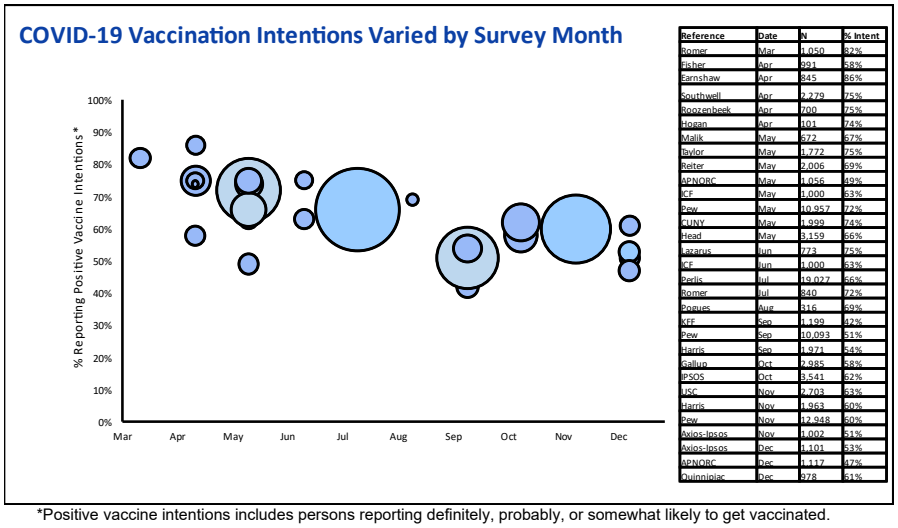
- How much do individuals value each outcome in relation to the other outcomes?
- Is there evidence to support those value judgments?
- Is there evidence that the variability is large enough to lead to different decisions?

For this domain, the WG conducted a review of the scientific literature focusing on vaccine intent, confidence, and attitude with the search terms listed here: SARS-CoV-2/COVID-19 string; vaccine string; intent, confidence, hesitancy, attitude, belief, accept, choice, decision, refusal. The search was updated through December 10, 2020.

The overall acceptability of a COVID-19 vaccine was moderate[1]. The proportion intending to receive the vaccine ranged from 40% to 80%. Nearly all of these surveys were performed prior to news for any specific vaccine. However, recent surveys conducted had preliminary results for the Pfizer vaccine and showed a large proportion who believed the vaccine would be safe and effective and that 70% would receive the vaccine if proven safe and effective by public health officials. Vaccine intentions varied over time, by population, and by vaccine characteristics[1]. Acceptance was lowest among Black respondents and highest among Asian respondents.

Acceptance was greater with higher socioeconomic status, history of a prior influenza vaccine and a higher COVID risk perception, with a higher VE presumed, and a strong healthcare provider recommendation [[1]APNORC; Harris; Fisher *Ann Intern Med*.; ICF; Kreps *JAMA Netw Open*.; Lazarus *Nature Med*.; Malik *EClinicalMedicine*.; Pogue *Vaccines*.; Reiter *Vaccine*.; Thunstrom *SSRN.* Axios-IPSOS. Pew].

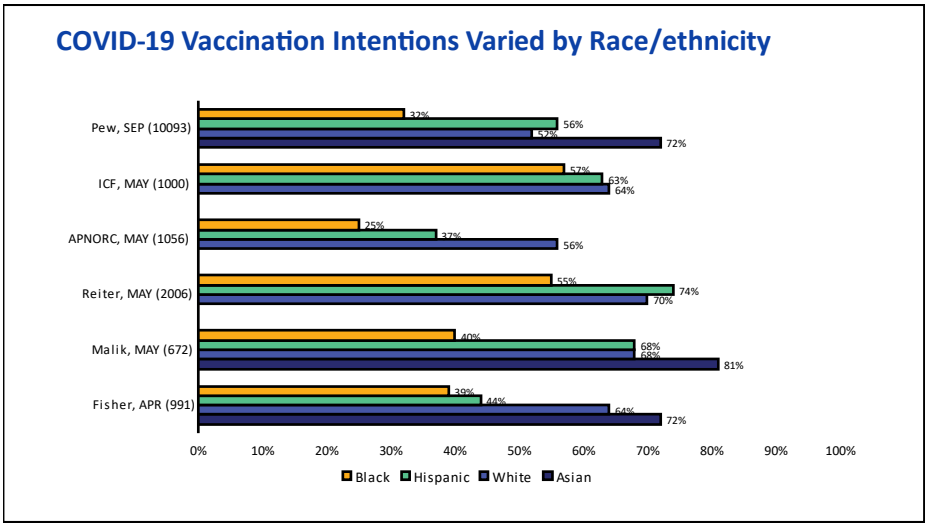
This figure combines data from 31 surveys and shows the proportion reporting positive vaccine intentions by month of data collection, with the bubbles proportional to the survey sample size. Vaccine intent declined since the initial surveys in the spring. However, surveys conducted recently have rebounded slightly. Two of these surveys were done after the press releases showing early efficacy data of the Pfizer and Moderna vaccines:



Reference	Date	N	% Intent
Romer	Mar	1,050	92%
Fisher	Apr	991	58%
Earnshaw	Apr	845	86%
Southwell	Apr	2,279	75%
Roozenbeek	Apr	700	75%
Hogan	Apr	101	74%
Malik	May	672	67%
Taylor	May	1,772	75%
Reiter	May	2,006	69%
APNORC	May	1,056	49%
ICF	May	1,000	63%
Pew	May	10,957	72%
CUNY	May	1,999	74%
Head	May	3,159	66%
Lazarus	Jun	773	75%
ICF	Jun	1,000	63%
Perlis	Jul	19,027	66%
Romer	Jul	840	72%
Pogues	Aug	816	69%
KFF	Sep	1,199	42%
Pew	Sep	10,093	51%
Harris	Sep	1,971	54%
Gallup	Oct	2,985	58%
IPSOS	Oct	3,541	62%
USC	Nov	2,703	63%
Harris	Nov	1,963	60%
Pew	Nov	12,948	60%
Axios-Ipsos	Nov	1,002	51%
Axios-Ipsos	Dec	1,101	53%
APNORC	Dec	1,117	47%
Quinnipiac	Dec	978	61%

*Positive vaccine intentions includes persons reporting definitely, probably, or somewhat likely to get vaccinated.

This chart shows 6 surveys that provided COVID-19 vaccine acceptance by race and ethnicity. Vaccine acceptance was lowest among Black respondents. Some surveys showed a lower acceptance in Hispanic respondents compared to White respondents. Asian respondents reported the highest acceptability:



*Positive vaccine intentions includes persons reporting definitely, probably, or somewhat likely to get vaccinated.

Broadly across national surveys, many adults reported their intention to receive a COVID-19 vaccine with a desire to protect themselves and their community and return to normal. Concerns were raised around side effects, unknown vaccine efficacy, and the speed of the process. Intentions varied substantially by race or ethnicity and by socioeconomic status. Limitations for these surveys include that many were conducted prior to an available vaccine or any specific data about the Pfizer-BioNTech COVID-19 vaccine. Also, convenience samples for surveys or focus groups may not be representative of the US population.

The WG interpretation for the first question regarding whether the target population feels the desirable effects are large relative to the undesirable effects, was that the WG felt that the answer was "probably yes." The WG noted that the extent to which the target population values the vaccine varies by population and over time. Not surprisingly, when asked if there was uncertainty about or variability in how much people value the vaccine, the WG felt that there was "probably important uncertainty or variability."

The main and additional questions for the "Acceptability" domain are as follows:

Is Pfizer-BioNTech COVID-19 vaccine acceptable to key stakeholders?

- Are there key stakeholders that would not accept the distribution of benefits and harms?
- Are there key stakeholders that would not accept the undesirable effects in the short-term for the desirable effects (benefits) in the future?

For this domain, the WG conducted a review of the scientific literature. Preliminary findings were reviewed from CDC evaluations of COVID-19 vaccine attitudes, including a survey with State Health Officers, focus groups with nurses, and online surveys looking at healthcare providers. The WG also looked at broader stakeholders, including professional societies and workers unions, and looked at stakeholder opinions regarding programmatic, financial, and ethical aspects.

There are no published provider knowledge, attitudes, and practices surveys. State Health Officers voiced concerns with vaccine hesitancy, safety, and communications[1]. Focus groups with nurses demonstrated that most supported prioritizing nurses. Some were reluctant to get vaccinated, especially nurses belonging to racial or ethnic minorities[2]. Another vaccine intent survey among HCP showed 63% reported that they would get a vaccine once available. Information from the nurses survey also demonstrate moderate acceptability where 63% were confident the vaccine would be safe and effective[3], but only 57% were comfortable discussing COVID vaccines with patients[4] [[1]CDC COVID-19 Response Team; [2]Jorgenson. *CDC Presentation to ACIP Working Group*; 3Sep 2020; [3]Lindley *et al*, CDC COVID-19 Response Team: Report in progress. 4. ANF, 16 Nov 2020. https://www.nursingworld.org/practice-policy/work-environment/health-safety/disaster-preparedness/coronavirus/what-you-need-to-know/covid-19-vaccine-survey/].

Overall, all jurisdictions have submitted vaccine implementation plans demonstrating at least some level of acceptance with the vaccine. Large and small pharmacy chains are participating in a COVID-19 vaccine program. While State Health Officers have concerns around hesitancy, safety, and communications and nurses report a low percent to receive vaccine, many were willing to be involved in the program.

The WG overall felt that the Pfizer-BioNTech COVID-19 vaccine was "probably" acceptable to key stakeholders.

he primary uestion and additional ue stions pertaining to the “Feasibility” domain include the following:

Is the Pfizer-BioNTech COVID-19 vaccine feasible to implement?

- Is the Pfizer-BioNTech COVID-19 vaccine program sustainable?
- Are there barriers that are likely to limit the feasibility of implementing the Pfizer-BioNTech COVID-19 vaccine or require consideration when implementing it?
- Is access to Pfizer-BioNTech COVID-19 vaccine an important concern?

The WG discussed several barriers to implementation, including financial barriers, complexity of the recommendations, and vaccine storage and handling requirements. For financial barriers, as has been discussed earlier, COVID-19 vaccines will be provided free of charge. However, health systems or health departments could incur the cost for vaccine implementation and clinics. For the complexity of recommendations, please refer to the FDA issued instructions regarding storage, handling, and preparation for the vaccine, but there are several steps in the process overall. Population access to healthcare or vaccine providers could be limited in rural or other hard-to-reach areas. The ultra-cold storage requirements will limit the range of HCPs stocking the vaccine. The minimum size of orders, currently at 975 doses, could limit providers who have access to the vaccine. The requirements for a 2-dose series could impact feasibility in some populations. However, the WG discussed that while there are barriers to implementation that might be insurmountable in traditional circumstances, there have been innovative solutions to overcoming these barriers. These include expanding funding opportunities; pharmacy partnerships; technology, including second dose reminders; unique packing containers to maintain ultra-cold temperatures without a freezer; and detailed state micro-planning.

Taking these barriers and the novel solutions into account, the WG felt that the Pfizer-BioNTech COVID-19 vaccine is “probably” feasible to implement.

he primary uestion and additional ue stions pertaining to the “Resource Use” domain include the following:

Is Pfizer-BioNTech COVID-19 vaccine a reasonable and efficient allocation of resources?

- What is the cost-effectiveness of the Pfizer-BioNTech COVID-19 vaccine?
- How does the cost-effectiveness of the Pfizer-BioNTech COVID-19 vaccine change in response to changes in context, assumptions, etc?

The WG reviewed estimates of economic costs related to COVID-19 vaccinations, disease outcomes, and disease mitigation activities in coordination with the NCIRD and ACIP Lead Economist.

For a summary of the evidence, this involves the balances of the cost of COVID-19 disease and costs of the COVID-19 vaccines. For the cost of the disease, it was estimated that if 20% of the US population is infected with COVID, the direct medical costs could be $163 billion. Health-related costs of COVID disease (e.g., premature deaths, long-term health impairment, and mental health impairment) have been estimated at 8.5 trillion. For costs associated with COVID-19 vaccines, the US government (USG) has committed to at least $10 billion to Operation Warp Speed (OWS) for the provision of vaccines[1]. In addition, vaccine doses purchased with US taxpayer dollars will be given to the American people at no cost[2] [[1]https://www.hhs.gov/about/news/2020/05/15/trump-administration-announces-framework-and-leadership-for-operation-warp-speed.html ; [2]https://www.cdc.gov/coronavirus/2019-ncov/vaccines/faq.html].

For the WG interpretation, there are no published cost-effective analysis currently available. The precise cost-effective analysis and economic impact of vaccination depend on a number of factors that are currently unknown, including the duration of vaccine protection, vaccination coverage levels, and implementation costs associated with a large vaccination program. The WG concluded that cost-effectiveness may not be a primary driver for decision-making during a pandemic and for a vaccine used under an EUA. However, this will need to be reassessed for future recommendations. At this time, the difference by individual vaccine is minimal relative to the overall scale of the pandemic.

Based on these discussions, the WG felt that "yes" the Pfizer-BioNTech COVID-19 vaccine is a reasonable and efficient allocation of resources.

he primary uestion and additional ue stions regarding the new "E ui ty" domain include the following:

What would be the impact of the Pfizer-BioNTech COVID-19 vaccine on health equity?

- Are there groups or settings that might be disadvantaged in relation to COVID-19 disease burden or receipt of the Pfizer-BioNTech COVID-19 vaccine?
- Are there considerations that should be made when implementing the Pfizer-BioNTech COVID-19 vaccine program to ensure that inequities are reduced whenever possible, and that they are not increased?

For a review of available evidence on equity, the WG worked to identify groups that might be disadvantaged in relation to COVID-19 disease burden or receipt of the COVID-19 vaccine. This work was done building upon other work that has been done in this area using the PROGRESS-Plus Framework[1]. PROGRESS-Plus is an acronym to identify factors associated with unfair differences in disease burden such as place of residence, race or ethnicity, occupation, gender or sex, religion, education, socioeconomic status (SES), social capital, disability, or other. A review of the scientific gray literature was conducted in addition to reviewing CDC COVID-19 response data and resources [[1]PROGRESS-Plus is an acronym to identify factors associated with unfair differences in disease burden and the potential for interventions to reduce these differential effects. See O'Neill J, Tabish H, Welch V, et al. Applying an equity lens to interventions: using PROGRESS ensures consideration of socially stratifying factors to illuminate inequities in health. J Clin Epi. 2014;67: 56-64; Welch VA, Akl EA, Guyatt G, et al. GRADE equity guidelines 1: considering health equity in GRADE guideline development: introduction and rationale. J Clin Epidemiol. 2017;90:59-67].

Data on several specific populations were used to inform this discussion and to identify groups which might be unfairly disadvantaged in relation to COVID-19 disease burden or receipt of the Pfizer-BioNTech COVID-19 vaccine for populations from racial and ethnic minorities; populations living in poverty or with high social vulnerability; essential workers[1-3]; residence in congregate settings such as LTCFs, prisons, homeless shelters, and group homes; people with substance use disorders (SUDs); and for gender and sexual minorities [[1]Rho HJ, Brown H, Fremstad S. A basic demographic profile of workers in frontline industries. April 2020. Washington, DC: Center for Economic and Policy Research;2020. https://cepr.net/a-basic-demographic-profile-of-workers-in-frontline-industries; [2]Bui DP, McCaffrey K, Friedrichs M, et al. Racial and ethnic disparities among COVID-19 Cases in workplace outbreaks by industry sector — Utah, March 6–June 5, 2020. *MMWR Morb Mortal Wkly Rep* 2020;69:1133–8. DOI: http://dx.doi.org/10.15585/mmwr.mm6933e3; [3]Waltenburg MA, Rose CE, Victoroff T, et al.

Coronavirus disease among workers in food processing, food manufacturing, and agriculture workplaces *Emerg Infect Dis*. 2021 Jan. https://wwwnc.cdc.gov/eid/article/27/1/20-3821_article].

There are also specific characteristics for the Pfizer-BioNTech COVID-19 vaccine that could impact health equity. Specifically regarding cold-chain storage, handling, and administration requirements, the requirement for storage at -80^0 will likely limit the number and types of facilities that can receive and use the vaccine. This could limit equitable distribution. The vaccine is primarily accessed at large health centers or central distribution sites rather than local community settings. The need for a 2-dose series could lead to challenges in equity as well and will be challenging for some disadvantaged groups (e.g., those who are homeless, live in rural locations, or have limited or no access to healthcare).

It will be important to take advantage of opportunities to increase equitable access to the Pfizer-BioNTech COVID-19 vaccine. The Federal Pharmacy Partnership program for COVID vaccination in LTCFs will facilitate access of the vaccine to LTCF residents and staff and will provide end-to-end management of the COVID-19 process, including cold-chain management and on-site vaccinations. Healthcare facilities that can administer and provide equitable access to the vaccine could offer the potential to increase equitable distribution to the Pfizer-BioNTech COVID-19 vaccine, first in HCP and then broadly.

Several additional considerations regarding equity were discussed by the WG. Although COVID-19 vaccines will be provided at no cost, personal investment in time and travel to obtain the vaccine may be a barrier for some groups. Equity and vaccination programs are closely linked. The WG emphasized that federal, state, and local jurisdictions will require adequate resources to get COVID-19 vaccines to the most affected communities and ensure equitable access. Successful implementation of the COVID-19 vaccination program and confidence in COVID-19 vaccines are pivotal to reducing existing health inequities related to COVID-19.

The WG had additional questions regarding considerations that should be made when implementing the Pfizer-BioNTech COVID-19 vaccine program to ensure that inequities are reduced. These considerations include identifying groups disproportionately affected by COVID-19 or who face health inequities, undertaking focused outreach and education, identifying barriers to vaccination, and conducting active follow-up.

There was a quote that resonated with the WG that Dr. Oliver shared previously that she shared again to emphasize that successful implementation of the COVID-19 vaccine programs and confidence in COVID-19 vaccines are pivotal to reducing health inequities:

> ". . . increasing the availability of an effective intervention within a country or region is not necessarily enough to reduce inequities. The intervention has to be accessible, acceptable, effective in, and used by the most disadvantaged groups within that population to be truly effective at reducing inequities in health."[1]

[[1]O'Neill J, Tabish H, Welch V, et al. Applying an equity lens to interventions: using PROGRESS ensures consideration of socially stratifying factors to illuminate inequities in health. J Clin Epidemiol. 2014; 67: 56-64].

Therefore, the WG interpretation was that the impact of the Pfizer-BioNTech COVID-19 vaccine on health equity would be “probably reduced” given many of the barriers related to the vaccine.

The table summarizes each of the domains for the EtR Framework, the questions, and the WG judgments:

EtR Domain	Question	Work Group Judgments
Public Health Problem	Is COVID-19 disease of public health importance?	Yes
Benefits and Harms	How substantial are the desirable anticipated effects?	Large
	How substantial are the undesirable anticipated effects?	Small
	Do the desirable effects outweigh the undesirable effects?	Favors Pfizer-BioNTech COVID-19 vaccine
	What is the overall certainty of the evidence for the critical outcomes?	1 (high) for prevention of symptomatic COVID-19 3 (low) for hospitalization 2 (moderate) for safety
Values	Does the target population feel the desirable effects are large relative to the undesirable effects?	Probably Yes
	Is there important variability in how patients value the outcomes?	Probably important uncertainty
Acceptability	Is the Pfizer-BioNTech COVID-19 vaccine acceptable to key stakeholders?	Probably Yes
Feasibility	Is the Pfizer-BioNTech COVID-19 vaccine feasible to implement?	Probably Yes
Resource Use	Is Pfizer-BioNTech COVID-19 vaccine a reasonable and efficient allocation of resources?	Yes
Equity	What would be the impact of the intervention on health equity?	Probably reduced

The WG then discussed the balance of consequences overall related to the PICO questions, policy question, and the evidence that has been presented. Overall, the WG felt that the desirable consequences clearly outweigh the undesirable consequences in most settings. Therefore, the WG discussed the type of recommendation to propose to ACIP to consider. The three options include:

- ❑ Do not recommend the intervention
- ❑ Recommend the intervention for individuals based on shared clinical decision-making
- ❑ Recommend the intervention

The ’s conclusion and propositions to ACIP is that they recommend the intervention of the Pfizer-BioNTech COVID-19 vaccine.

Discussion Points

Dr. Szilagyi agreed with the ’s recommendation. In terms of acceptability based on national surveys, he emphasized that the variability in the responses about willingness to get the vaccine means that this is modifiable, that it is mutable, and the hesitancy for the vaccine is not necessarily entrenched. That implies to him that a lot of work is needed in optimal communication and outreach to these populations. Also in those surveys, there was a large proportion who said “unsure.” ha t magnifies his point. In terms of feasibility, though the accine will be available at no charge, there are concerns that a small proportion of adults who are covered by Medicaid with an “Optional Benefits” component who may not be fully co ered f or the vaccine once the public health emergency ends. Regarding second doses, studies of reminder/recall have shown that these are pretty effective for second dose because people who

have received the first dose are not hesitant. This highlights the importance of registries and reminder/recall systems. In terms of costs, the $8.5 trillion mentioned in the total cost was calculated from health-related costs. If indirect costs are included, this is magnified exponentially. With respect to equity, it is very concerning to him that two groups, individuals who are Black and lower education, have both high morbidity from COVID-19 and are the most hesitant to get the vaccine. Therefore, a tremendous amount of outreach and funding of localities for outreach are needed to ensure that equity is truly and properly addressed.

Dr. Goldman (ACP) took a moment to reflect on the gravity of this as ACIP contemplates recommending the vaccine in a global pandemic that has not been experienced in their lifetime. He expressed gratitude and applauded all of the hard work done by the WG, committee members, and physicians, scientists and staff at CDC for their tireless dedication and monumental services. The speed with which this vaccine has been developed is truly a testament to our scientific ability. While the data and evidence do support that the benefits far outweigh the risks, he expressed some caution in recommendations outside the parameters of groups involved in the studies. It is important to ensure that patients are well aware of the potential side effects and that with such a limited supply, they will commit to receiving both doses. This speaks to the importance of acceptance of the vaccine. He supports the approval of this vaccine, but also strongly supports the ongoing studies of both safety and efficacy and using groups other than those specifically studied in the trials. He also reiterated his concerns on the distribution of this vaccine and stressed the importance of sub-prioritization of frontline outpatient physician offices that are not being allocated doses of vaccines by many hospitals and health care systems, even though they remain at some of the highest risk for COVID-19 disease.

Dr. Poehling agreed with the comments on the importance of additional opportunities. She requested further details about support for the recommendation within the WG in terms of whether this was a unanimous recommendation or if there was variation in the opinions.

Dr. Oliver indicated that the WG was unanimous in recommending that ACIP accept the recommendation and that it be recommended in the setting of the EUA.

Dr. Sanchez recalled that the previous day they heard from Pfizer that the ultra-cold storage required for the vaccine is a problem. However, mention was made that it could be stored in the refrigerator for 5 days. That is helpful information that should be shared.

Dr. Cohn indicated that now that the EUA has been approved, multiple communication and education products will be released by the company, such as some great videos on how to prepare and administer the vaccine and some on storage and handling. CDC will ensure that all of its materials align with the EUA and will be sharing communication products focused on storage and handling of this product, which she confirmed can be stored in the refrigerator for 5 to 6 days.

Dr. Romero pointed out that an increasing number of nurses and other HCPs are saying that they would rather wait to accept the vaccine, which is going to place an issue on the implementation of phases moving forward. This issue needs to be considered and will make it somewhat more difficult in terms of trying to progress down the phase ladder.

Dr. Duchin (NACCHO) said it was very gratifying to see this progress. As he mentioned before, the investment in OWS has been unprecedented and has paid off greatly. However, he did not want the significant implications of the implementation challenges to be minimized in any way. In particular, the funding necessary for state and local agencies to carry out this program has been put in the deep freeze with the vaccine. There is a desperate need to carry out an immunization program of unprecedented complexity and importance, with formidable implementation challenges that include what has been noted in terms of the importance of engagement in and education of hesitant communities, vaccination of hard-to-reach populations, the complexity of engaging with community vaccinators and healthcare systems to ensure equitable distribution and allocation of this vaccine throughout the community, and other tasks. He encouraged everyone to do what they can to ensure that this vaccine program is as successful as it can possibly be by making sure that the resources are available on the frontlines to those people who need to implement this program.

Dr. Hayes (ACNM) has heard from her colleagues in the hospitals that some of the nurses and other HCP are unwilling to be vaccinated because they have heard that it is going to affect their fertility among other myths that are floating around. If the main focus on Phase 1a is to vaccinate HCP in the hospitals who are taking care of patients, it is necessary to seriously address these myths that are floating around.

Speaking as a practicing physician, Dr. Fryhofer (AMA) expressed her excitement that this vaccine is now available. However, she was very concerned about implementation after listening to the comments so far. It appears that enough funding has not been allocated to the distribution to get vaccine in the arms of patients. While she is excited that their pharmacy colleagues are helping with implementation and distribution, but patients depend on their physician to give them advice as to whether they should get vaccinated. Physician recommendation is a very important motivator for patients to get vaccinated, and there is going to be a lot to talk to patients about. She also is concerned that hospitals might not offer this vaccine to community physicians and may try to keep it for their own employees and not consider that other physicians who might be on staff who are on the frontlines seeing patients who could have COVID-19 might not have access to the vaccine. She expressed her hope that moving forward, everyone and every organization with access to this vaccine will look at the big picture and not be selfish with what they have, but really do a good job of trying to prioritize and think this process through to help everyone get vaccinated.

Dr. Cohn indicated that as they have discussed during prior ACIP meetings, there will be a limited number of doses for the first several weeks and it will take time to increase the number of provider sites to ensure that access is as wide as possible. CDC is implementing a plan to vaccinate in limited sites, particularly healthcare settings, LTCFs, and public health clinics. As more doses become available, those sites will expand. There will then be reliance on doctors, clinical providers, and pharmacies to help increase coverage. She reiterated what Dr. Fryhofer said that in the interim, all HCP need to recommend vaccination for their patients even if they are not able to give it to them in that moment. The new CDC Communication Toolkit for clinics, clinicians, and HCP has a lot of tools to help everyone recommend and administer vaccine to the people who work around and with them and to the public. The toolkit can be found at: https://www.cdc.gov/coronavirus/2019-ncov/communication/toolkits/clinicians.html

Ms. Stinchfield (NAPNAP) directed her comments to the nursing considerations in terms of moving into the new important vaccination phase of this historic endeavor, with nurses being the largest role in Phase 1a. She was the first nursing member of the ACIP in 2004-2008 and has been a liaison member since then, so she has 16 years with ACIP and could give the public and nurses specifically her full confidence in this process and the scientific incredible breakthrough with mRNA platforms, with the commitment to ongoing safety monitoring and transparent communications. Just as nurses have worked every step of this pandemic from vaccine research, to participating in clinical trials, to expert compassionate direct patient care, to leading hospital pandemic planning—nurses will help implement vaccination at the local level. Like influenza vaccine for which nurses are vaccinated at 90%, she is confident that nurses, after filing their knowledge gap about the novel vaccine, will not step aside but as always will step up and raise that lamp to the path out of this pandemic, which is through vaccination. She was happy to hear about the toolkits, thinks that there needs to be a public communications campaign, and emphasized that they have to help equip nurses and all HCP with education and communication tools. She is confident that nurses will rise to the occasion, be vaccinated, and encourage their patients to do so as well.

Dr. Messonnier emphasized how much CDC values and appreciates all of the advocacy from the liaisons and state and local health departments, and how much the agency is dependent upon it for roll out of this vaccine. The comments raised incredibly important topics, for which the next presentation on clinical considerations might provide more context.

Regarding the EtR framework and implementation, Dr. Lee pointed out that the ACIP charter states that ACIP is responsible for recommendations of use of the vaccine in the US civilian population. She requested confirmation that vaccination implementation efforts also would address vaccination among those who are not citizens or who may be undocumented in terms of coverage, access, and eliminating costs of the vaccine.

Dr. Cohn clarified that the language Dr. Lee described in the charter is the language used for all ACIP recommendations.

Use of Pfizer-BioNTech COVID-19 Vaccine: Clinical Considerations

Sarah Mbaeyi, MD MPH
CDR, US Public Health Service
Medical Officer
National Center for Immunization and Respiratory Diseases
Centers for Disease Control and Prevention

Dr. Mbaeyi reviewed clinical considerations for the use of Pfizer-BioNTech COVID-19 vaccine in the US. These CDC clinical considerations are informed by data submitted to the FDA for EUA of the vaccine, other data sources, best practice guidelines for immunization, and expert opinion. These considerations may be updated as further information becomes available. In addition to these considerations, the EUA conditions of use and storage, handling, and administration procedures described in the package insert should be referenced when using the Pfizer-BioNTech COVID-19 vaccine [https://www.fda.gov/media/144412/download, https://www.fda.gov/media/144413/download, https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/index.html].

Starting with administration, the Pfizer-BioNTech COVID-19 vaccine series consists of 2 doses administered intramuscularly, 3 weeks apart. Administration of the second dose within a 4-day grace period (e.g., between day 17 and 21) is considered valid and is consistent with guidance for other vaccines. If more than 21 days have elapsed since the first dose, the second dose should be given at the earliest opportunity; however, the series does not need to be repeated. Both doses are necessary for protection. Efficacy of a single dose has not been systematically evaluated.

The Pfizer-BioNTech COVID-19 vaccine is not interchangeable with other COVID-19 vaccine products and the safety and efficacy of a mixed-product series has not been evaluated. Persons initiating vaccination with Pfizer-BioNTech COVID-19 vaccine should complete the series with this product. If two doses of different mRNA COVID-19 vaccine products are inadvertently administered, no additional doses of either product are recommended at this time. Recommendations may be updated as further information becomes available or other vaccine types are authorized.

Given the lack of data on the safety and efficacy of Pfizer-BioNTech COVID-19 vaccine administered simultaneously with other vaccines, Pfizer-BioNTech COVID-19 vaccine should be administered alone with a minimum interval of 14 days before or after administration with any other vaccines. If the Pfizer-BioNTech vaccine is inadvertently administered within 14 days of another vaccine, doses do not need to be repeated for either vaccine.

Regarding considerations for vaccination of persons with prior SARS-CoV-2 infection or exposure, data from clinical trials suggest that Pfizer-BioNTech COVID-19 vaccine is safe and likely efficacious in persons with evidence of a prior SARS-CoV-2 infection. Vaccination should be offered to persons regardless of history of prior symptomatic or asymptomatic SARS-CoV-2 infection. Viral or serologic testing to assess for acute or prior infection, respectively, is not recommended for the purpose of vaccine decision-making.

Vaccination of persons with known current SARS-CoV-2 infection should be deferred until the person has recovered from the acute illness (if the person had symptoms) *and* criteria have been met for them to discontinue isolation. While there is otherwise no recommended minimum interval between infection and vaccination, current evidence suggests that reinfection is uncommon in the 90 days after initial infection. Thus, persons with documented acute SARS-CoV-2 infection in the preceding 90 days may delay vaccination until near the end of this period, if desired [https://www.cdc.gov/coronavirus/2019-ncov/hcp/disposition-in-home-patients.html; https://www.cdc.gov/coronavirus/2019-ncov/hcp/duration-isolation.html].

Currently, there are no data on the safety and efficacy of Pfizer-BioNTech COVID-19 vaccination in persons who received monoclonal antibodies or convalescent plasma as part of COVID-19 treatment. Based on the estimated half-life of such therapies as well as evidence suggesting that reinfection is uncommon in the 90 days after initial infection, vaccination should be deferred for at least 90 days as a precautionary measure until additional information becomes available to avoid interference of the treatment with vaccine-induced immune responses.

Persons in a community or outpatient setting who have had a known COVID-19 exposure should not seek vaccination until their quarantine period has ended to avoid potentially exposing HCP and other persons to SARS-CoV-2 during the vaccination visit. For persons residing in congregate healthcare settings such as LTCFs where exposure and transmission of SARS-CoV-2 can occur repeatedly for long periods of time, residents with a known COVID-19

exposure may be vaccinated. In these settings, HCP are already in close contact with residents (for example, by entering patient rooms for evaluation and treatment) and should employ appropriate infection prevention and control procedures. Thus, administering COVID-19 vaccine should not result in additional exposures. Residents of other congregate settings such as correctional facilities and homeless shelters with a known COVID-19 exposure may also be vaccinated, in order to avoid delays and missed opportunities for vaccination given the increased risk for outbreaks in these settings. However, where feasible, precautions should be taken to limit mixing of these individuals with other residents or staff except those essential for the provision of vaccination services who should employ appropriate infection and control procedures [https://www.cdc.gov/coronavirus/2019-ncov/if-you-are-sick/quarantine.html; https://www.cdc.gov/coronavirus/2019-ncov/hcp/infection-control-recommendations.html].

With respect to vaccination of special populations, Pfizer-BioNTech COVID-19 vaccine may be administered to persons with underlying medical conditions who have no contraindications to vaccination. Phase II/III clinical trials demonstrated similar safety and efficacy profiles in persons with underlying medical conditions, including those that place them at increased risk for severe COVID-19, compared to persons without comorbidities. Persons with HIV infection, other immunocompromising conditions, or who take immunosuppressive medications or therapies might be at increased risk for severe COVID-19. Data are not currently available to establish vaccine safety and efficacy in these groups. However, these individuals may still receive COVID-19 vaccination if they have no contraindications to vaccination, but should be counseled about the unknown vaccine safety profile and effectiveness in immunocompromised populations, as well as the potential for reduced immune responses and the need to continue to follow all current guidance to protect themselves against COVID-19 [https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html].

There are no data on the safety of COVID-19 vaccines in pregnant women. DART studies are ongoing and results are expected to be available soon. Studies in humans are ongoing and planned. mRNA vaccines are not considered live vaccines. They are degraded quickly by normal cellular processes and do not enter the nucleus of the cell. Observational data demonstrate that while the absolute risk is low, pregnant women with COVID-19 have an increased risk of severe illness including ICU admission, mechanical ventilation, and death. Additionally, they might be increased risk of adverse pregnancy outcomes, such as preterm birth. If a woman is part of a group (e.g., HCP) who is recommended to receive a COVID-19 vaccine and is pregnant, she may choose to be vaccinated. A discussion with her healthcare provider can help her make an informed decision [https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/pregnancy-breastfeeding.html].

Pregnant women and HCP should consider the level of COVID-19 community transmission, her personal risk of contracting COVID-19, the risks of COVID-19 to her and potential risks to the fetus, the efficacy of the vaccine, the side effects of the vaccine and the lack of data about the vaccine during pregnancy. Pregnant women who experience fever following vaccination should be counseled to take acetaminophen as fever has been associated with adverse pregnancy outcomes. Acetaminophen may be offered as an option for pregnant women experiencing other symptoms as well. Routine testing for pregnancy prior to receipt of a COVID-19 vaccine is not recommended. There are no data on the safety of COVID-19 vaccines in lactating women or the effects of mRNA vaccines on the breastfed infant or milk production/excretion. mRNA vaccines are not considered live virus vaccines and are not thought to be a risk to the breastfeeding infant. If a lactating woman is part of a group (e.g., HCP) who is recommended to receive a COVID-19 vaccine, she may choose to be vaccinated.

Regarding considerations for patient vaccine counseling, before vaccination, providers should counsel vaccine recipients about expected local and systemic post-vaccination symptoms. Unless persons develop a contraindication to vaccination, they should be encouraged to complete the series even if they develop local or systemic symptoms following the first dose in order to optimize protection against COVID-19. Antipyretic or analgesic medications (e.g., acetaminophen, non-steroidal anti-inflammatory drugs) may be taken for the treatment of post-vaccination local or systemic symptoms, if medically appropriate. However, routine prophylactic administration of these medications for the purpose of preventing post-vaccination symptoms is not currently recommended as information on the impact of such use on Pfizer-BioNTech COVID-19 vaccine-induced antibody responses is not available at this time.

Two doses of the Pfizer-BioNTech COVID-19 vaccine are required to achieve high efficacy. Thus, patients should be counseled on the importance of completing the 2-dose series in order to optimize protection. However, protection from the vaccine is not immediate. The currently available vaccine is a 2-dose series and it will take 1 to 2 weeks following the second dose before a person is considered fully vaccinated. Additionally, as no vaccine is 100% effective, some vaccinated people may still get COVID-19 disease. Given the currently limited information on how well the vaccine works in the general population; how much it may reduce disease, severity, or transmission; and how long protection lasts, vaccinated persons should continue to follow all current guidance, including those listed here to protect themselves and others: wearing a mask, staying at least 6 feet away from others, avoiding crowds, washing hands often, following CDC travel guidance, following quarantine guidance after an exposure to someone with COVID-19, and following any applicable workplace or school guidance [https://www.cdc.gov/coronavirus/2019-ncov/index.html].

Regarding contraindications and precautions, severe allergic reaction (e.g., anaphylaxis) to any component of the Pfizer-BioNTech COVID-19 vaccine is a contraindication to vaccination listed in the package insert. Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event that an acute anaphylactic reaction occurs following administration of the vaccine. In addition, because of reports of anaphylactic reactions in persons vaccinated outside of clinical trials, persons who have had a severe allergic reaction to any vaccine or injectable therapy should not receive the Pfizer-BioNTech COVID-19 vaccine at this time. Vaccine providers should observe patients with a history of anaphylaxis (not due to vaccines or injectable medications, as vaccine is contraindicated in these persons) for 30 minutes after vaccination. All other persons should be observed for at least 15 minutes after vaccination to monitor for the occurrence of immediate adverse reactions.

Pertaining to interpretation of SARS-CoV-2 test results in vaccinated persons, prior receipt of the Pfizer-BioNTech COVID-19 vaccine will not affect the results of SARS-CoV-2 nucleic acid amplification or antigen tests. Currently available antibody tests for SARS-CoV-2 assess IgM and/or IgG to one of two viral proteins (spike or nucleocapsid). Because the Pfizer-BioNTech COVID-19 vaccine contains mRNA that encodes the spike protein, a positive test for spike protein IgM/IgG could indicate either prior infection or vaccination. To evaluate for evidence of prior infection in an individual with a history of Pfizer-BioNTech COVID-19 vaccination, a test specifically evaluating IgM/IgG to the nucleocapsid protein should be used [https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/eua-authorized-serology-test-performance].

In closing, Dr. Mbaeyi posted the following questions for ACIP deliberation:

- ❑ Does ACIP agree with the guidance around use in:
  - Immunocompromised persons
  - Pregnant or lactating women
- ❑ Does ACIP agree with the proposed contraindications to vaccination?
- ❑ Are there any other sections of the clinical considerations that ACIP would like to discuss?

Discussion Points

Referring to Slide 23, Dr. Romero pointed out that "in ectable therapy" is a e ry broad category. For example, someone who receives intravenous ampicillin and develops an allergic reaction would be considered ineligible for this vaccine. Putting that in the context of another person who receives oral ampicillin and has an allergic reaction would be eligible for this vaccine. There is going to be some confusion with this.

Dr. Mbaeyi said that more guidance could be provided about situations in which it might be acceptable, such as if the person is under the care of an immunologist. The intent was because the investigation is ongoing with regard to particular excipients that might be involved and some of these could be in other medications. This was kept broad initially as investigation continues, but additional guidance could help to keep people from being excluded unnecessarily.

Dr. Messonnier added that the CDC would appreciate some more conversation on this language, as they are trying to carefully "thread a needle" in a space where they are still not completely clear on all of the available data because it is still being gathered. They do not want to create unnecessary concern or exclude people unnecessarily, but there is a desire to be careful to exclude individuals who may have a higher risk. Someone who had an anaphylaxis reaction 50 years ago is not the same as somebody who had anaphylaxis 18 months ago. The intent is to revisit this quickly as new information becomes available.

Dr. Ault said he thought the language pertaining to pregnancy and lactation was very good. It is difficult to identify an a priori reason to avoid this vaccine in lactating women. In the pregnancy section, he liked that the pregnant HCP was the focus.

Dr. Hunter found this level of detail and thoughtfulness to be very helpful. On an implementation level, he requested clarity regarding whether if a different mRNA is given for the second dose than the first the series would be considered complete.

Dr. Mbaeyi said that at this time, no additional doses are recommended if a mixed series of mRNA vaccines is given. This also will continue to be evaluated over time as more information becomes available and as vaccine supply becomes sufficient to ensure that there are adequate doses.

Dr. Dooling added that the mixed series is not recommended, but the WG felt that given the extreme shortage of vaccine combined with the fact that no more than 2 doses have been studied in subjects, it warranted not repeating any doses if a mixed series was given.

Dr. Hunter said this made sense to him given his level of understanding of immunology and mRNA technology as a practicing family physician and local public health department consultant. If others on the WG agree that this is fine to do, then it is extremely helpful from an implementation point of view.

Dr. Cohn add that it is anticipated, especially early on, that this will happen rarely given the large number of ways to ensure that the recipient and HCP know the first product received based on all of the immunization registries and other data systems put into place. It is not recommended, but when it happens, the individual would not be recommended to receive another dose.

Dr. Goldman (ACP) suggested clarifying the information about how long someone who has had COVID-19 should wait to receive the vaccine after they meet all recovery criteria because they are thought to have some immunity. Perhaps the language could read, "If you ha e documented infection, wait days." If there is an outbrea in a congregate setting, he wondered if the vaccine would still be given to those who are not symptomatic or wait to test whether people are actively infected.

Dr. Mbaeyi clarified that for a congregate setting, the intent of the language can be clarified. Because of how frequently cases or outbreaks are reported in congregate settings, there could be very prolonged periods of recent cases. They do not want these settings to experience unnecessary delays in implementing vaccination or have significant barriers to implementing vaccination. The idea behind the guidance is that in these congregate settings, vaccination could proceed along with implementation of the appropriate infection prevention and control procedures and limit mixing of the population to the extent possible.

Ms. Bahta asked whether anything would be said regarding what to do about a delayed schedule. This would be helpful to have because questions are being raised about that. In terms of contraindications and precautions, she pointed out that it is important for people to understand what "se ere allergic" reaction means by perhaps pro i ding some e amples. h is is a struggle with other vaccines as well. A patient's perception of a se ere allergic reaction may be e ry different from a pro i der's.

In terms of delayed schedules, Dr. Mbaeyi said there is not a maximum period by which the second dose would need to be received as there are not data to inform this at this time. In the clinical trials, people were able to receive the vaccine up to 42 days after their first dose, so that is the extent to which there are data. At this time, the recommendation is to give the second dose as soon as possible after the 21-day period, but no doses would need to be repeated based on a prolonged interval between doses at this time. Regarding severe allergic reaction, CDC is developing materials for HCP including fact sheets and checklists to help them understand the symptoms behind a severe allergic reaction.

In terms of HCP who are in quarantine but are in the middle of their vaccines, Dr. Talbot thought it would be ideal to go ahead and finish their vaccinations so that when their quarantine is over, they also have completed their vaccine series and can go back to work. She wondered if this could be changed for just the HCP at this time. One of the major reasons there is a shortage of HCPs is because of quarantine. If they are already out on quarantine, it is an ideal time to vaccinate.

Dr. Mbaeyi thought this would need to be discussed further. CDC has developed guidance pertaining to HCP and vaccination, which would be posted the next day. At this time, HCP in a quarantine period have not been discussed.

Dr. Romero pointed out that newer recommendations for quarantine have been issued. Shortening the period depends upon not having any symptoms. If the vaccine is administered to an individual and they develop symptoms, quarantine would be prolonged.

Regarding pregnant women, Dr. Fryhofer (AMA) was e ry reassured by Dr. Ault's comment. She also liked the wording that a pregnant woman "may choose" to be vaccinated. She also liked the mention of the nuance about use of prophylactic medicine for fever and the fact that pregnant women who have a fever should take them because the fever itself poses a risk to the pregnant woman. She took issue with the line that "animal de e lopment and reproducti e toxicity studies are ongoing." They heard the previous day from the manufacturer that these studies have been done but the results have not been released. The results need to be published to give physicians and pregnant women access to this information. She is glad that the company plans to closely follow the 23 pregnancies that have occurred in the study trial as those babies are born. She likes the guidelines for reactogenicity that providers should counsel vaccine recipients about expected local and systemic post-vaccination symptoms. However, practitioners need more information and guidance, particularly for HCP in terms of whether they need to plan their vaccinations the day before they have a day off and specifics on how to ascertain whether a symptom is due to vaccination or possibly due to a COVID exposure. There are 330,000 HCP who are likely to become pregnant or be in the post-partum timeframe as this vaccination implementation program begins. This does not include essential workers for whom pregnancy is also a concern. Moving forward as quickly as possible to get this information out would be greatly appreciated, particularly the DART information.

Dr. Mbaeyi indicated that the guidance on reactogenicity and symptoms in HCP would be published the next day along with guidance on vaccination symptoms in LTCF residents, which should address many of the concerns raised.

Returning to Dr. Messonnier's question about additional contraindications proposed, Dr. Bell acknowledged that everyone is doing everything they can to get better information and follow-up on the UK incidents. While she recognized the rationale for including this, she is somewhat nervous about the abundance of caution rationale because oftentimes this is very hard to undo even where there are new data. She wondered whether further language could be added that states something to the effect of, "History of a food, sna e eno m, or en i ronmental allergy" are not contraindications so that there is clear distinction between the concern and the much broader group of allergies that involve many people who they do not want excluded.

Dr. Mbaeyi indicated that this could be added to the language.

Dr. Kimberlin (AAP Redbook) agreed with Dr. Ault's comments regarding breastfeeding and he indicated his support of the wording proposed with regard to contraindications and precautions.

he comment about defining "se ere allergic reaction" got Dr. Drees (SHEA) thinking that they hear hesitancy with regard to allergy not only from people who have a personal history of allergy, but also who have a family history of allergy. Perhaps this could be addressed in the clarification. Regarding history of allergy to any component of the Pfizer vaccine, the fact sheet lists a dozen or so chemical compounds that no one will recognize. She agreed with the pregnancy language and has heard from HCP who are pregnant or lactating and desire a vaccine that if they were told they could not get the vaccine because of that status, they might lie if not showing. In addition, she wondered if a pregnancy registry will be stood up or if they should be following women locally who are pregnant or lactating.

Dr. Sanchez was glad to see that pregnancy and breastfeeding are considered separately. He is in favor of the pregnancy designation stating that it is up to the pregnant woman. A registry would be fantastic for pregnant and lactating women. In terms of the immunocompromised host, the language states "persons with HIV and other immunocompromising conditions." Howe er,

he recalled that the studies enrolled stable HIV-infected individuals and individuals with stable HepB and HepC. Because there are some data on HIV-infected individuals, he thought that should be included.

Dr. Eckert (ACOG) indicated that the CDC convened a call earlier in the morning of several experts in the US in pathology, immunology, kinetics of the vaccine, how it works, et cetera. The overall and complete consensus was that no biological plausibility is seen at this time for placental transfer of the mRNA and the possibility of direct fetal exposure is extremely unlikely. While they clearly look forward to the DART data, at this point ACOG is very supportive of the permissive recommendation and is prepared to support clinicians, obstetricians, and others by providing educational materials as soon as feasible within the next week.

Dr. old man (ACP) suggested changing the language with regard to allergies to "obser ed severe allergic reactions."

Dr. Poehling expressed her gratitude to all who have been working on support of the recommendations on breastfeeding and pregnancy. She agrees with the language and likes the fact that women have the option and that physicians will be able to support them. She wondered whether "se ere allergic reaction" should be "anaphylactic reaction to any a ccine." She is worried that the rest of the language is too broad and that people will be denied vaccine unnecessarily. She recommended saying that it is a "precaution" for people who have had anaphylactic reaction to other medications rather than a "contraindication."

Dr. Atmar agreed with Dr. Poehling's comments about allergy. He also raised a question about the guidance that would potentially be forthcoming the next day. The clinical considerations help deal with individuals and vaccinating them, but does not really address the concerns that healthcare institutions are going to have to deal with in handling the expected side effects that will occur in the 24-48 hours after injection. While he is gratified that there will be some guidance, he wondered whether they could preview it during this meeting so that there could be some public discussion of whatever those recommendations may be. Dr. Cohn confirmed that they could share the language.

Dr. Frey expressed concern about the language regarding how sites should be prepared to manage an anaphylactic reaction. One of the pieces regarded airway protection, relating to intubation she assumed. Most places that give vaccines are not capable of intubating individuals if that is what that was referring to, so clarification is needed about this. Others also expressed concern and indicated that they were getting questions about whether sites need special equipment that they do not normally have for vaccines.

Dr. Bernstein said he was in total agreement that the Pfizer vaccine appears to be remarkably safe and amazingly effective, and there is no question that COVID-19 vaccines are critically important elements in managing the growing public health emergency. He has a lingering concern about the overall inclusion of 16-17 years olds. The study data were very limited for this sub-population in Pfizer's interim analyses. Their protocol amendment to include individuals as young as 16 was only finalized on September 8, 2020. Then this group was followed through November 14, 2020 when data were presented to the FDA. The demographic table in the VRBPAC briefing document lists only 153 total subjects 16 to under 18 years of age, split between vaccine and placebo groups. This timing also did not allow a sufficient number of subjects in this age group to be adequately represented for the median follow-up period of 2 months like the thousands of others in the trial. Systemic reactions were generally more frequent and severe in the younger age group compared with the older age group and after the

second dose compared with the first. Grade 3 reactions of 8.8% in the vaccinated group versus 2.1% in the placebo group were more commonly reported after the second dose. Fortunately, this 16 and 17 year old age group has not had a disproportionate morbidity and mortality as in the other specific groups. He also appreciated that this younger age group can actively transmit SARS-CoV-2 infection to contacts in their families and communities. Unfortunately though, vaccine hesitancy is an overall growing concern. A successful pediatric vaccination program depends on creating and sustaining parental confidence in both the safety and effectiveness of this vaccine. It should be remembered too that serious and unexpected side effects might well occur. In summary for him, if the 16 and 17 year old age group is included as issued by the FDA in its EUA, he would propose that consideration be given to adding this age group as a special population in these interim clinical considerations, explaining that available data are limited at this time. As many as 2000 subjects in this 16 and 17 year old age group are continuing to be studied, so additional data are anticipated in the near future.

Dr. Oliver said that the is happy to discuss the addition of Dr. Bernstein's suggestion in the clinical considerations. Shortly, language for the vote would be shown and additional discussion would be welcomed with regard to this issue during that time as well.

Dr. Maldonado (AAP) expressed support for the ACOG comments and indicated that representatives from AAP also were on that call Dr. Eckert described. AAP was very impressed with the subject matter expertise on the use of mRNA platforms and the lack of evidence for any harm to be caused at this time. AAP is in full support of the 's recommendations and ACO 's input. h ey also recommend that any educational materials also be provided for pediatricians and general providers as well because many pregnant women will be asking for advice and may not be seeking advice directly from their obstetrician providers. For example, they may be at a pediatric visit for other children. AAP is very supportive of allowing pregnant and lactating women to receive the vaccine, because the risk of disease clearly outweighs any potential and theoretical risks form the vaccine platform. Personally, she commented on what she considers to be an issue of equity of not allowing 16 to 17 year olds to receive the vaccine. There is no biologic or physiologic basis for any differences between 16 to 17 year olds and 18 year olds. In her view, absolutely no evidence has been presented in any platform that suggests that there should be any sliding scale of differential safety in those populations. In fact, these are children who are particularly vulnerable because they may be working in frontline situations where they must be in contact with patients and others at risk of infection, yet may not have access to vaccines.

Dr. Mbaeyi referred to the guidance document on the screen about infection prevention and control considerations for HCP with systemic signs and symptoms following COVD-19 vaccination. She indicated that the content of this guidance would be part of the planned Clinician Outreach and Communication Activity (COCA) call on December 14, 2020. The goal of this guidance is to address the concerns raised by a number of committee members about how healthcare systems can manage the expected and common post-vaccination symptoms that people might experience to avoid them being unnecessarily excluded for work when they only have post-vaccination signs and symptoms, and also to prevent them from being inadvertently allowed to be working with potential SARS-CoV-2 or another transmissible infection. A lot of the considerations are based on what has been observed in clinical trials that these systemic post-vaccination symptoms are mild to moderate in severity, occur within the first 3 days of vaccination, and resolve within 1 to 2 days of onset. Some of these considerations might include vaccinating HCP preceding 1 to 2 days off; staggering delivery of the vaccine so that not everybody in a single unit or department gets it at one time; informing HPC about the potential for these short-term systemic signs and symptoms and potential options for mitigating them,

such as acetaminophen or nonsteroidal anti-inflammatory drugs (NSAIDs); and developing a strategy to provide timely assessment of HCP with signs and symptoms of post-vaccination, including viral testing to rule out infectious symptoms; and offering non-punitive sick leave. The rest of the document has some specific approaches. There is a table that addresses HCP with signs and symptoms unlikely to be from COVID-19 vaccination and symptoms that are not consistent with post-vaccination, but are potentially consistent with SARS-CoV-2 that could lead to infection. Specific approaches are recommended. There is a section for HCP who have signs and symptoms that may be consistent either with those symptoms observed following vaccination or SARS-CoV-2 infection since some of these symptoms do overlap. There are specific recommendations about return-to-work criteria, testing, et cetera. Outside consultation was sought on this guidance from SHAE and IDSA.

Dr. Rockwell (AAFP) commented on the slide titled “Immunocompromised Persons” and giving direction for persons with HIV or other immunocompromising conditions. In terms of the language that “these indi idual s may still receive COVID-19 vaccine unless otherwise contraindicated” she wondered if there was any thought that the autoimmune diseases could be addressed as being okay. That is one of the most common questions she is getting from patients and other physicians about patients with autoimmune diseases who are on immunosuppressants, including transplant patients. Part of the fear is a myth that is circulating that autoimmune disease can flare with a hypersensitivity reaction.

Dr. Cohn indicated that CDC is aware that this is a really important group to provide clinical guidance around. At this time, there is no contraindication for vaccination of any of those individuals. For individuals on immunosuppressants, the vaccine may not be as efficacious, but they are believed to be safe in these groups. A section will be added to address those directly in this document.

Looking at the fact sheet for recipients, Ms. McNally requested clarity about what this issue is with those who have a bleeding disorder or are on blood thinner, the relationship to the Pfizer vaccine, and whether that is common to other vaccines as well. In addition, there is language stating “or plan to become pregnant” with no information about what the duration of time would be. Under “What are the risks of the Pfizer-BioNTech COVID-19 vaccine?” anaphylaxis is not listed.

Dr. Mbaeyi indicated that bleeding disorder referred to people whose bleeding disorder is so severe that there might be issues with bleeding after vaccination. This would be something they would discuss with their provider.

Dr. Cohn added that this is similar to what is included in general recommendations for other vaccines. She reminded everyone that the patient fact sheet that they were looking at was the Pfizer fact sheet that was authorized by the FDA, which Pfizer may have additional comments about. The products that CDC will develop will talk about some of the things that are in the Pfizer fact sheet in a way that is more accessible to the individual making this decision or talking to their provider.

In terms of the anaphylaxis issue and the Pfizer patient fact sheet, Dr. Dormitzer from Pfizer indicated that this reaction is currently under investigation for which they are awaiting the results.

Dr. Cohn clarified that the question specifically regarded whether there was any other language in the patient fact sheet that addresses anaphylaxis beyond the contraindication that individuals with a history of anaphylaxis to vaccine or any of the excipients or ingredients in the vaccine should not be vaccinated. She did not think there was and that providers would be relying on additional information from CDC for that clinical guidance.

Dr. Mathers from Pfizer indicated that the language they were reading was the language agreed to with the FDA the previous evening. The language is slightly different for HCP and vaccine recipients.

In terms of the guidance on duration of time before becoming pregnant, Dr. Oliver indicated that CDC will not have recommendations around that. The Pfizer fact sheet is independent of CDC's recommendations with regard to pregnancy. They will make sure that the information CDC has around pregnancy is posted in conjunction with ACOG, AAP, and others mentioned previously.

Dr. Kim (OIDP) observed that for a general community member who is in quarantine for a possible exposure to COVID-19, the proposed recommendation is that he or she would wait until the quarantine period is over to receive the vaccine. While he agreed with the premise behind this proposed recommendation, the quarantine period may overlap with the first dose of the mRNA vaccine. For a person in quarantine, particularly in priority populations, the vaccine is very important if not life-saving. Withholding the vaccine from a general community member who is in quarantine for whom the vaccine would otherwise be indicated, is denying a potentially beneficial medical intervention albeit temporarily.

Dr. Dormitzer, Chief Science Officer for Pfizer, reminded everyone that some questions arose for additional information from Pfizer that he wanted to address. One had to do with the DART studies and the timing of preliminary information. Pfizer plans to have a quality control (QC) report on that study ready for submission to FDA later this month. At this point, the preliminary data show no indication of developmental or reproductive toxicity. The second question regarded the other licensed medication that shares some components with the vaccine, which is ONPATTRO® (patisiran) that is used to treat polyneuropathy caused by hereditary transthyretin-mediated amyloidosis in adults. Like the vaccine, it contains RNA and the lipids cholesterol and 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC), as well as other lipids that are not the same but are of similar classes. It is used in far greater quantities than the vaccine. In terms of contraindications, they brought this up before because they were asked whether there is another medication that shares any components of the vaccine—not because they have any particular concerns.

Dr. Lee noted that in thinking about those who are setting up vaccine programs, she had been thinking about the EUA fact sheet as being the corollary to the Vaccine Information Statement (VIS). In terms of usability and being able to educate more fluidly, some of the CDC communication toolkit information is very helpful also to provide. She was just trying to figure out the most efficient way to educate people. She expressed appreciation for how hard CDC has worked on all of these communications and recognized that it is impossible to build communications when the information gets released less than 24 hours before. She also asked whether as vaccinators, they should be giving out the EUA fact sheet plus more user-friendly fact sheets.

Dr. Cohn confirmed that the patient fact sheet is substantially longer than the VIS. There is a CDC product one-pager that is more consumer-friendly and more similar to the information that would be on the VIS. They are reviewing this with the EUA language to ensure that they align. That will be placed on the toolkit site where all of the other information is. CDC also is working to finalize a screening checklist type of tool for providers to use who need to take patients through a series of a few screening question prior to vaccination to determine whether they would need more information such as information about pregnancy, lactation, or other issues. This will be available in the near future after the clinical considerations are finalized using the input provided during this session. The requirement/intent is to provide the patient with the EUA fact sheet, but CDC will have additional materials they hope providers will use. They will continue to promote the toolkit so that people can download these information sheets to provide to patients.

Dr. Poehling observed that in the screening checklist tool for vaccination, the choice is given to pregnant and lactating women about whether they want to receive vaccination or seek additional information from their physician. She wanted to make sure that in the screening checklist they are not creating a barrier by requiring additional things for pregnant or lactating women.

Dr. Messonnier noted that CDC had the benefit of ongoing counsel with ACOG, AAP, and other partners in this space for weeks as their team anticipated the need to be clearer in this space. They will follow their lead and agree with the concern about not creating barriers and the need for ensuring that pregnant and lactating women are fully informed. The materials are coming, many of which were drafted and mocked up in advance. Since the EUA was approved the pre i ous e enin g and because CDC wanted to get ACIP's feedbac on the clinical consideration, the intent and plan is to have a whole set of materials available before the vaccine is available in jurisdiction on Monday. That said, everyone should anticipate CDC continuing to refine and produce additional material rapidly over the course of the coming week.

Dr. Talbot said that something she would like included in the clinical considerations is the idea of the drive-through vaccination. This is an efficient way of giving this vaccine to reduce contact and spread of COVID-19 among people presenting to get vaccinated. The current guidelines discourage that due to the 15- and 30-minute wait times, but she hopes as they learn more about allergic reactions and can better define them and reduce the risk, it would be nice to comment on the idea of a drive-through vaccination clinic.

Dr. Bernstein inquired as to whether written consent is required for special populations, or if it is just distribution of the EUA fact sheet and possibly other materials from CDC.

Dr. Oliver responded that informed consent is not required under an EUA for any population to receive the vaccine.

Public Comment

David Curry, MS
Foundation President, Center for Vaccine Ethics and Policy, GE2P2 Global Foundation
Affiliate Faculty, Division of Medical Ethics, New York University School of Medicine

Thank you. This is David Curry, President of the GE2P2 Global Foundation and head of its Center for Vaccine Ethics and Policy (CVEP). I am also Affiliate Faculty at the Division of Medical Ethics at ew or Uni e rsity's (U' s) School of Medicine. By way of disclosure, our foundation receives support from a range of individuals and organizations, including Pfizer and the Gates Foundation to support a free weekly digest reviewing peer-reviewed literature and global strategic developments in immunization and public health. Our comment focuses on a key element supporting responsibly and ethically sound deployment of the Pfizer/BioNTech COVID-19 vaccine and others likely to follow very soon. This key element involves the information to be presented to recipients and caregivers as they are offered or seek vaccination. We argue that this information must be clear, must be appropriately written and presented for limited literacy and reading levels, be broadly translated for the diverse populations that will need to be vaccinated and otherwise present alternative vaccine options as they come available, and be otherwise supportive of recipients in making well-informed decisions to accept the vaccine. We recognize that the Food and Drug Administration (FDA) Emergency Use Authorization (EUA) does not require formal informed consent and that the information to be provided at a minimum is via the fact sheet for recipients and caregivers. In examining the EUA fact sheet now posted, we note that it is presented in text only with no graphical information to assist recipient comprehension, even though the fact sheet for providers does include graphical information; is presented at a reading levels does not appear to align with lower reading or literacy levels; and is limited to a document in English with no translations posted or any indication that translations will be posted. We are enthusiastic that Dr. Cohn, at the ACIP meeting December 1st, reported that additional supporting information was in development to enable informed consent for individuals offered vaccines in long-term care facilities (LTCF). The CDC toolkit now posted, apart from that focused to healthcare workers (HCW), appears to be generic and for all recipients. Apart from the limited depth of that content, these resources seem to be available only in English. We are concerned that, especially with the mention of assent today, the posted content will not be robust enough to effectively respond to the information needs of long-term care individuals and caregivers, or to the serious levels of vaccine hesitancy operative across many vulnerable and hard-to-reach populations. We urge, and energetically urge, and are confident that CDC will extend its best efforts to enhance these materials and we urge ACIP to continue to closely assess the supplementary information as it emerges to ensure that it adequately supports the intent of these recommendations. Thank you.

Barbara Loeppke
Loeppke Professional Service

Yes, my name is Barbara Loeppke and I speak on behalf of many concerned Americans like myself. The ACIP committee is the last gatekeeper protecting the American public. We all know that the President has pushed for fast-tracking these vaccines. We all know that the vaccine manufacturers are for-profit companies that stand to make hundreds of billions of dollars. We hope you remember that you have no duty to them. You have a duty to the American public, to each person. A duty to do no harm first. The public, who will rely on your recommendations for this fast-tracked vaccine will have heard the words and phrases I have heard while watching these meetings the last few months where it is like "should" and "probable" and "potentially." Phrases like, " e don't know yet. We'll know as the study progresses. We'll know that in the

future. We hope to have that answer soon. We estimate and we believe." h ere are comments like, " e have no data on reverse transcriptase of the RNA into DNA. While it's possible, we don't think so." Or to what if the accine doesn't prevent transmission, "That's correct. We have no data on that." We know that the Pfizer Chairman, Albert Bourla, has even admitted that the company was not certain if vaccines prevented the coronavirus from being transmitted saying, " his is something that needs to be examined." It is obvious that this vaccine has not been thoroughly tested yet. I have great concern, as do many, as I listened to the committee members find ways to try to explain away the concerns of the vaccine in areas such as pregnancy and anaphylactic reactions rather than turning to the manufacturers to make it safer. If you vote "Yes" will you inform the public that there are many questions that still have not been answered about this vaccine and that there are still questions about the long-term effects, or will you try to dismiss those in order to increase the vaccine uptake? In discussions about vaccine hesitancy by the committee, I never hear the committee admit that the CDC has a spotty history with minorities. The public has not forgotten the CDC's Tuskegee experiment, the MMR (measles, mumps, rubella) experiment on babies, or the years of sterilization procedures done on the incompetent. Don't let this fast-tracked drug become another cautionary tale for the CDC. I hope you take this all seriously. Thank you for your time.

Kermit Kubitz
Individual

Thank you. Based on all the available evidence, including 90% reduction in cases between vaccinated and placebo recipients, antigen titers, and data on adverse events (AEs), the BNT162b2 vaccine appears safe, efficacious, and having a highly positive benefit-risk ratio for patients from 16 to over 75. It is appropriate to allocate the first doses to healthcare workers. According to Dr. Dooling's *Morbidity and Mortality Weekly Report* (MMWR) report of December 3rd, there have been 245,000 cases of COVID-19 and 858 COVID-related deaths among United States (US) health care personnel (HCP). The guidance for identifying injection effects and separating those from COVID-19 infections should also be available for long-term care facilities and staff where a high priority for the age group over 65, in which 70% of death has occurred, is necessary. I have a relative in assisted-living where there have been five coronavirus cases in staff and three among residents. Allocation of the vaccine should also be prioritized for American Indian and Alaska Native (AI/AN) communities, which experience disproportionately high infection and mortality, including among persons aged 20 to 49. Their COVID mortality is around 8 to 10 times higher than among white persons according to Dr. Jessica Arrazola's report of December 11th. The Moderna vaccine, which has a similar structure, mechanism of action, and coding messenger RNA for the coronavirus spike protein, and similar efficacy should also be approved quickly. There also need to be tools for telling the public and doctors about their place in priority allocation phases to avoid tying up doctors' offices and phone lines with people seeking information about vaccine availability and their priority. In addition, the public health infrastructure should have multiple vaccines approved so that urban areas with ultra-cold storage can receive those vaccines and rural areas, which do not have access to the state's regional logistical requirements, can obtain other vaccines. As we know, under an EUA, these are not approved until other vaccines are also available for EUA. Thank you to the ACIP, thank you to the FDA, and as someone said, "Let's get the logistical supply infrastructure out there." Thank you.

Peter Matz
Director, Food & Health Policy
Food Marketing Institute

Good afternoon and what an exciting day it is. I think we can all see the light at the end of the tunnel after FDA's authorization last night. My name is Peter Matz and I am here representing Food Marketing Institute (FMI) the food industry association, where I'm the Director of Food & Health Policy. First and foremost, thank you to the advisory committee for your leadership and tireless efforts to provide guidance, not just to the CDC, but to all of the states and jurisdictions modeling their plans after your recommendations. The importance of the COVID vaccines cannot be overstated and FMI greatly appreciates all of your hard work. By way of background, as the food industry association, FMI works with and on behalf of the entire industry from retailers who sell to consumers and producers who supply the food all the way to supermarket pharmacies to advance safer and more efficient consumer supply chains for both food and pharmaceuticals. In total, FMI member companies operate around 33,000 grocery stores and 12,000 pharmacies, ultimately touching the lives of more than 100 million US households per week and representing an industry with nearly 6 million employees. FMI appreciates this opportunity to share feedback. First, we strongly support ACIP's recommendation to prioritize health care personnel in the initial phase of COVID vaccine allocation and we thank the committee for clarifying that this includes pharmacy workers. Supermarket pharmacies stand ready to be part of this historic vaccination effort and supermarkets are also prepared to offer sites for vaccine administration and support for outreach efforts on the importance of getting vaccinated while they continue providing nutrition, supplements, and pharmacy services in the interim. Having said that, FMI respectfully requests that food industry essential workers be prioritized for COVID vaccinations after that initial phase of vaccine allocations. Designated by the federal government as part of the nation's critical infrastructure, the food industry has continued, bolstered, and at times shifted operations to ensure American families across the country have access to our products. Prioritizing COVID vaccinations for these workers would allow a key intervention to protect the food supply and keep supply chains operating. Therefore, we asked for a safe process to follow the examples set by the National Academy's final framework for COVID vaccine allocation, which recommends prioritizing food industry essential workers behind healthcare workers and certain high-risk populations, and also to CDC's updated COVID a ccination "Program Playbook" which suggests that states and jurisdictions consider including food industry workers in Phase 1b. Finally, we would also ask ACIP to consider prioritizing food industry workers with supporting a supply of personal hygiene, household, and commercial cleaning products. The latter is especially significant as consumers, retailers, and the food sector among others are being directed to use cleaning supplies, sanitizers, disinfectants, and other hygienic supplies to prevent the spread of COVID. So please do keep in mind the importance of those workers supplying critical personal and commercial cleaning supplies, as well as other essential consumer goods. FMI appreciates the opportunity to provide input on this critically important issue. Thank you.

Julie Russell
Coronado Unified School District

Hello. Thank you committee for your hard work in providing the best for our country. As an elected representative of the Coronado Unified School District, I am speaking today to request that the critical decision-makers on your committee prioritize teachers, frontline school staff, and at-risk students in receiving the vaccination. Our teachers have provided distance learning instructions since the imposed school closures. In surveying our stakeholders, students, and parents, we have learned that instruction provided solely through distance learning platforms

cannot fulfill the academic and social/emotional needs of all of our students. Despite our best efforts over the last 9 months, some students are not thriving. We acknowledge that there are still risks from the spread of COVID-19 and that until there is a widespread vaccine available for all, strong mitigating efforts must be maintained. Masks, social distancing, and sanitation efforts will be with us for at least the remainder of the school year. However, access to the vaccine for our staff would ensure that students can be with us in person. We ask that you recognize the importance of the safety of our staff and how many young lives each of them touch. We need our educators to be confident in returning safely to the classroom to resume the valuable and essential work of educating our students. This is especially important in the public sector where a strong union influences hesitation to return teachers back to the classroom. To provide an equitable opportunity for all American children, I will even go out on a limb and say this is a critical thing for our wider economy. It is important to get our kids back into the classrooms and the first step on this would be a prioritization of vaccinating staff. Thank you very much for this critical consideration and those are my comments.

John Allan, MS
Vice President, Regulatory Affairs & International Standards
International Dairy Foods Association

Thank you. Good afternoon. I'm John Allen, Vice President for Regulatory Affairs & International Standards with the International Dairy Foods Association (IDFA), which represents the nation's dairy food manufacturing and marketing industry. However, I am here today representing a broader alliance of food, agriculture, and consumer goods industries associations to ask for your help and to express our thanks to CDC staff and members of the ACIP for your dedication to getting our country through these unprecedented times as quickly and as safely as possible. We fully agree that Phase 1b prioritization of the workforce is a needed defense measure to ensure that our essential workers are protected, remain healthy, and can continue ensuring the production and distribution of safe food and other necessary consumer goods to sustain the US population through the pandemic, but we need your help to make this happen. Please continue to recognize and prioritize access to COVID vaccines for frontline and other essential employees across our critical infrastructure sectors. Without your support for privatization, our supply chains could eventually fall apart creating widespread disruptions to our economy. As the country is on the cusp of initiating the COVID vaccination campaigns, yesterday we submitted written comments into the docket for this meeting laying out suggested guidelines for sub-prioritizing among essential workers within our sectors for vaccination. When necessary, particularly during Phases 1b and 1c when supplies are expected to be limited, we will be sharing these guidelines with state Governors and public health departments at all levels across the country. As vaccine allocation and needs at the local levels will vary inevitably from state to state and locality to locality, these guidelines will likely need to be tailored by local public health officials in coordination with companies within these sectors. To this end, we are encouraging our member companies across the country to reach out to their local health departments to begin discussing plans for vaccination of their employees immediately, including identification of those employees who should receive the first rounds of vaccinations. There is, indeed, very strong support among the public for government partnering with private sector to distribute vaccines to essential workers. I urge you to help us harness that support. To conclude, we offer help and support in working with CDC along with other state and local officials in any way we can before and after vaccines are launched, including help in communicating the benefits of vaccination to our essential employees. So, please don't hesitate to contact us if you see any such opportunities for collaboration. Thank you and thanks again for your time today.

Allison Hagood
Immunize Colorado
Co- " ' : "
Community College Psychology Professor

Good afternoon. My name is Allison Hagood. I am a co-author of the book " our Baby's Best Shot: Why Vaccines are Safe and Save Lives" and a community college Psychology Professor. I am here providing public comment as a private citizen and vaccine advocate. I would like to thank the committee for all of your hard work regarding the development of vaccines for COVID-19, for your transparency throughout the process, and for your willingness to invite public comment. I would like to provide public comment on several issues regarding the COVID-19 vaccines: 1) Communities of color, particularly the African American community, have valid distrust of the medical establishment. Thoughtful work with national and local leaders of communities of color is vital to address these communities concerns in a way that honors their historical experiences. It is important to let these communities take the lead in figuring out what information would be most helpful to address their issues and to develop a system of allocation and distribution that is equitable across demographic groups to avoid exacerbating existing inequities; 2) People who are incarcerated and people experiencing homelessness should be prioritized, given that their situations make it difficult to adequately isolate or quarantine or to obtain masks or facilities for bathing. Incarceration or homelessness should not be a death sentence; 3) An educational infrastructure for the general public is needed to address concerns regarding the rapid nature of the development of these vaccines. The general public is not aware that the research and development process usually involves a great deal of unused time waiting for various approvals and funding sources, and that all of that wait time was eliminated during the process of prioritizing these vaccines. Providing this information to the general public may alleviate many of the concerns expressed regarding how quickly we have been able to get to this point. My co-author and I, in an article published in the journal *Human Vaccines & Immunotherapeutics*, proposed a multi-source model of education to address the concerns of people who are hesitant about vaccines. In such a model, everyone with whom a person comes in contact from public health departments, to Physicians, to nurses in vaccine clinics, to scheduling assistants is a source of accurate information regarding vaccines. In the body of research regarding vaccine education, and in my experience in combating vaccine misinformation, merely providing factual information is unlikely to alleviate concerns regarding vaccine safety and efficacy. Instead, medical and public health professionals would do better by soliciting information on people's specific concerns and target information to those concerns. Since conspiracy theories are already being created regarding these vaccines, the rapid development of an educational program to provide accurate, transparent information is critical. Thank you again for your time.

Ann Lewandowski
Rural Wisconsin Health Cooperative and
Wisconsin Immunization Neighborhood

Good afternoon. My name is Ann Lewandowski and I am representing the Rural Wisconsin Health Cooperative (RWHD) and the Wisconsin Immunization Neighborhood (WIN). We would like to thank the committee and work group members for their hard work during this global pandemic when you have many demands on your time. We are deeply appreciative of the committee's thoughts on rural healthcare personnel. We have been very worried about the feasibility of Pfizer's vaccine with the ultra-cold chain and the large minimum order for rural members in Wisconsin. We would like to thank the committee for their thoughts in considering these logistical challenges during the discussion today. We asked the CDC not to ignore the

challenges of the ultra-cold chain and large minimum order as the thermal shippers only serve one location. Subdivisions at the state level mean that the vaccine is distributed in a refrigerated state, which limits stability to 5 days. Our hospitals are busy with the surge, struggling with staffing challenges driven by exposures in the community and at work. Furthermore, our informational surveys highlight a workforce that is strongly vaccine-hesitant of these vaccines due to the lack of formal information and guidance until very recently. These challenges should not be underestimated. It has been reported that the Pharmacy Partnership for Long-term Care (LTC) partnership will receive thermal shippers of 125 doses. We hope the CDC considers how to ensure equitable access to this reduced minimum order size across locations that need it, including rural areas. We urge the CDC to release the clinical education materials as soon as possible. As previously mentioned, our hospitals and clinics are seeing a surge in COVID-19 cases and need time to allow the staff education required for the storage, handling, and administration of this vaccine. Our providers are anticipating swift delivery of this vaccine with a rapid move to administration. We urge the *MMWR* to include the thoughtful communications and recommendations for healthcare personnel who have allergic reactions, immunocompromising and autoimmune disorders, are pregnant and breastfeeding, and/or other special populations you discussed during your conversation today. We appreciate the committee's thoughtful discussion and personally, I support the comment that autoimmune disorders specifically need to be addressed. I have an autoimmune disorder and I have heard similar comments about worry for a relapse. As somebody working on a prioritization with my state, I urge the committee to be clear and create consistent recommendations that can be easily applied at the state level, particularly as we move into additional phases, such as Phase 1b, that addresses essential workers. Thank you very much for your time and your efforts.

Charles Lee, MD, JD, MBA
President-Elect
American College of Correctional Physicians

Good morning or good afternoon. I am Charles Lee. I am the President-Elect of the American College of Correctional Physicians (ACCP). These are the docs that take care of the inmates and those incarcerated. I'm also talking on behalf of those incarcerated. There are over 2 million persons incarcerated. 250,000 of them have been infected. ha t's times the general population. I'm also representing and talking about those who work in correctional facilities, not only the officers, but also the food workers, handlers, those that take care of the maintenance, as well as the medical people. Definitions. There has been some confusion as to definitions of what is what. For example, congregate facilities. Does that in and of itself include jails, prisons, and juvenile facilities? In some of the state's directives, it is not clear. Correctional facilities, clinics, and hospitals. What if a correction facility doesn't have a clinic? Do they still include their inmates and patients to receive the vaccination? Correctional facility healthcare workers. Are they included in the initial Phase 1a of health care workers? Another factor, generally speaking, is we are concerned about individuals greater than 65 years old. Those incarcerated have an advanced age. Their bodies and generally 10 to 20 years greater than their counterparts on the outside. Therefore, should inmates 55 and greater be considered? Essential workers. There are a lot of essential workers in correctional facilities. Please do not leave them out. Children. Juvenile facilities include them. The state needs some direction. They are all over the place with their guidelines and plans. Some include correctional persons first. Some include them last. Inmates are at risk, a great risk, similar to that of nursing home persons. There is an increased number of minorities, black and brown, in incarcerated facilities. Please take that into consideration. Whereas the black community is 13% of the general population, in jails and prisons it is as great as 40%. Again, I thank you for all the work you've done. We are proud to

represent those that are incarcerated and hope that the ACIP takes my thoughts into consideration. Thank you.

Dorit Reiss, PhD
Professor of Law, Hastings College of the Law, University of California
Member, Vaccine Working Group on Ethics and Policy

Thank you for the opportunity to comment. My name is Dorit Reiss. I am a Professor of Law at the University of California Hastings College of the Law and a member of the Vaccine Working Group on Ethics and Policy. I wanted to ma e points. Let's see if I can get through them. First, I'd li e to than the committee for its intensi e tr ansparent wor since April following the a ccine de elopment, as ing hard uestions, and openly pro i ding e tens i e data on this. ACIP's role in recommending vaccines is unique and critical to ensuring equitable access to safe and effective vaccines. ACIP has been transparently and openly working on this for years and we appreciate your efforts applying your e p ertise to this conte t a s well. I also want to remind you that you're not alone in combating misinformation about the vaccine. Actors like our friends at the National Vaccine Information Center (NVIC) and Vaccinate Your Family work hard to provide information to counter these, as do a large group of online defenses in blogs and comments. We will continue to respond to misinformation. Second, echoing the comments of the previous commenter, it is imperative to consider prisons as a vaccine priority site. In California, every single facility has a COVID outbreak. A third of the entire prison population has been infected with COVID and 96 people have died. That is in one state only. Prison authorities are not always quick in taking measures to allow social distancing and addressing the situation. COVID spikes in prisons correlate to spikes in the surrounding and neighboring counties. Requiring correctional officers to be vaccinated as a condition of employment is essential and the hard work of ensuring compliance must start now. Third, I appreciate that you recognize the need for clear guidance on the issue of severe allergic reactions and the need to update this moving forward as the evidence arises. I want to enforce the comments in the FDA Vaccines and Related Biological Products Advisory Committee (VRBPAC) meeting on this and the points made here and ask the committee to make it a priority to figure out which ingredient in the vaccine may cause a severe allergic reaction, because we need to know what is causing this fast, both for the safely and to respond to concerns of the public. I also hope you will support an urgent study of the safety of the vaccine in those that are known to be allergic to injectables and non-injectables and appreciate your proposed accommodation to such people to be closely observed after vaccination. Finally, although CDC and FDA previously said that you cannot mandate a vaccine under an EUA, I think that is not a good reflection of the law. The law is ambiguous and I hope that the committee will ask the FDA Commissioner to provide clear guidance in the EUA to direct actors on what they can and cannot do. Can they impose consequences for refusing a vaccine? Can they require people to wear more personal protective equipment (PPE) if they refuse? Can they require people to be reassigned? I think business will be looking for ways to encourage vaccines and they need guidance. Thank you for your time.

David Schless
President
American Seniors Housing Association

My name is David Schless, President of the American Seniors Housing Association (ASHA). Our members offer the entire spectrum of senior living, including independent living, assisted living, memory care, and continuing care retirement communities. On December 1st, this committee recommended that the COVID-19 vaccine be offered to both healthcare personnel and residents of long-term care facilities in the initial Phase 1a of the vaccination program. It was widely understood and communicated to the senior living industry by officials of the Department of Health and Human Services (HHS) that residents of long-term care facilities included, in addition to skilled nursing facilities (SNF), the full continuum of senior living care, independent living, assisted living, memory care, and continuing care retirement communities. This was understood when the industry was encouraged to register for the CVS/Walgreens pharmacy program. As a result, operators of all settings registered their communities in anticipation of being treated as a prioritized population for access to the vaccine. However, we are now learning that while assisted living communities will be included among the initial vaccination groups, independent living settings will not be considered in the 1a group and it is unclear whether the independent living section of a building with multiple levels is included. We believe this to be incredibly short-sighted and are deeply troubled by this decision, given the resident population living in these communities and that their risk of contracting the virus is just as great as those living in nursing homes and assisted living communities. Residents of independent living are 82 years old on average and have higher rates of cognitive and functional impairments than those living in private residences. Additionally, many senior living communities offer multiple levels of care. To vaccinate the residents in assisted living but not in the independent living section of the same community would create confusion and emotional harm and is simply not efficient in the delivery of the vaccine to the most vulnerable. Our concerns extend to the staff of independent living communities as well. We believe all senior living workers, such as caregivers, dining staff, and others, including those who work in independent living are an integral part of the essential health care workforce and should not be overlooked in the federal plans for vaccine distribution. We ask that as the committee continues to review vaccine prioritization, consideration be given to recommend that all senior living settings, including independent living, be prioritized in the 1a category. Additionally, it is extremely difficult to serve our vulnerable seniors unless the staff in these communities are also vaccinated and free from COVID-19. Thank you.

Katherine Falk
Parent & Vaccine Advocate

Hi, my name is Katherine Falk and I am a parent and vaccine advocate in Oakland, California. I want to thank the committee for all your hard work. I appreciate and very much share your concern about misinformation. I have been following and countering the spread of anti-vaccine misinformation online for years. There are broad categories of this misinformation, very often spread by people with, to be blunt, a financial interest in selling services or supplements. But, some of this is also passed along by people who are genuinely fearful, who have had a bad experience with the medical system, who don't feel like they can trust mainstream sources. The last 4 years have been terribly corrosive to public trust. Most of all, it has become very clear that racism continues to be a destructive force in our country. I encourage the committee to address the problem of misinformation as much as possible, particularly as it impacts populations that have experienced historical trauma and continue to. Many of these conversations are going to have to take place within communities as opposed to outsiders lecturing. But if the leaders in

these communities can be empowered with resources, that would be very helpful. I also hope that the guidance on how to allocate facts can include a conscious, deliberate effort to avoid reinforcing systemic racism and existing inequities. Thank you very much.

Claire Hannan, MPH
Executive Director
Association of Immunization Managers

I'm Claire Hammond, Executive Director of the Association of Immunization Managers (AIM). Our nonprofit represents the state, territorial, and large urban area public health immunization programs. These amazing government employees have been working with CDC, Operation Warp Speed (OWS), state health officials, Governors, hospitals, and other stakeholders to plan for the distribution of COVID-19 vaccine. Months of vaccine distribution and logistics planning are now coming to fruition. Guidance on subsequent priority groups is needed immediately. Jurisdictions are working now to plan for vaccine allocations coming in the next month. They need to work closely with providers and communicate clearly with consumers about what to expect. Many have advisory committees and ethics groups designed to assure equity and distribution. They cannot effectively plan and communicate expectations without guidance from the ACIP. There is tremendous pressure on Governors. I want to speak specifically to the dilemma facing jurisdictions with essential workers, those over 65, and those with underlying conditions. There is not consensus across states on how to vaccinate these groups. Some Governors have signaled the importance of vaccinating the most at-risk, the highest at-risk first for hospitalization and death (i.e., the older Americans), and those with multiple risk conditions. Yet, essential workers may be in harm's way and can spread the virus in communities. The current definition of "essential workers" is extremely broad. For example, the Cybersecurity and Infrastructure Security Agency (CISA) list for essential workers encompasses almost 60% of the population in North Dakota. These factors could lead to very different approaches across states. I urge the ACIP to provide specific guidance on prioritization as soon as possible. Guidance and educational materials are needed on exactly who should receive the vaccine, especially related to pregnant and lactating women, 16 to 17 year olds, and those with allergies. Screening questions that can be used by providers would be very helpful, so I'm very glad to hear about the CDC " hat You Need to Know: Information for Vaccine Recipients." I'd like to close by reminding the committee and everyone listening of the dire need for additional funding for state, territorial, and local public health agencies. Public health agencies have received just $340 million while more than $10 billion has been invested in vaccine research and production. Public health agencies desperately need funding to continue to enroll tens of thousands of providers, to hire community vaccinators and nurses, to purchase equipment and supplies, and to roll out large-scale communication plans with websites, educational materials, and hotlines. Nothing is more important to the success of this campaign than the trust of healthcare workers, nursing home residents, and eventually all Americans in every community in the safety and effectiveness of this vaccine. Resources are needed. Thank you for the opportunity to provide public comment on this truly historic day.

Gina Harrison
Concerned Parent

My name is Gina Garrett Harrison. My son is permanently handicapped and medically exempt because of your negligent recommendations. I'm ha i ng some issues with the conflicts of interest (COIs) that your panel is saying they do not pose, which I would like to ask you how is it more of a conflict of interest of having an entire panel of pro-vaccine people recommending vaccines to the entire United States? Where are all the opposing voting members who are also scientists and virologists? And since vaccination is for the public, shouldn't your panel be equally diverse with each side being well-represented? We're not only dealing with the pandemic, but we're also dealing with an epidemic of the public's mistrust in your recommendations. In order for something to be considered science, I believe the public needs to have confidence in you. During your 2020 ACIP meeting in February, you had stated that you didn't even know what the term "healthy" meant because it had never been defined. This is a huge problem. In order for something to be rubber-stamped, the public needs to be told exactly how all of these studies are set up. What type of placebo is being used and which form of placebo is being used? We are hoping that you know this information. Do you? Is the placebo another vaccine? Is it the vaccine's adjuvant? Is it the lipids that are questionable at best? The public also needs to know the exclusion criteria from the study and how these test subjects were screened to the fullest. They were physically, mentally, and lab-confirmed to be the healthiest participant receiving this vaccine. It's interesting because one of the things that completely disqualified you as a participant was having a history of vaccine reactions, such as anaphylaxis or any reaction to any of the components in the study intervention. Something tells me that when somebody checked that box, they finally listened and I bet they were shooed off really quick. The public also needs to know that this vaccine has not been proven to prevent transmission. You're recommending all these healthcare employees to take this vaccine that may not even protect them against the infection. he y'll ta e it thinking that they're safe only to have their symptoms reduced just like whooping cough and they become super spreaders without even knowing it. The public also needs to know that the 1976 national swine flu epidemic that spawned a very strong vaccination push also generated numerous lawsuits due to the number of deaths that were caused. This is a repeat. It's history repeating itself. We are so tired of you walking through your job with blinders. We are the ones that are paying for your underhanded lies that you have built this vaccine schedule on. It's past time that you are held accountable because unavoidably, unsafe . . . [allotted time expired].

Tom Rosenberg, MBA
President & Chief Executive Officer
American Camp Association

Thank you, Dr. Romero. I am Tom Rosenberg, President and Chief Executive Officer (CEO) of the American Camp Association (ACA). I appreciate the opportunity to address the CDC/ACIP committee on behalf of the ACA and 47 other national Out of School Time (OST) youth educational organizations. We have submitted written comments to the committee to ensure that all categories of essential childcare workers in all OST settings are prioritized for early allocation of COVID-19 vaccines within the education sector. This position is in accord with the criteria set forth in the guidance provided by the Department of Homeland Security (DHS). Workers supporting the education of our children and adult learners in a myriad of settings qualify as essential critical infrastructure workers as defined by the US Department of Homeland Security. The ongoing availability of healthy staff and continuous operation of these valuable Out of School Time programs is critical to the economic recovery of our country. Workers operating in OST settings, such as organized camps, after school programs, childcare,

community-based centers, and recreation programs provide essential services to early learners and students and to their working parents and caregivers. Hundreds of camps are engaged with their local school districts and municipalities in a variety of ways now as Alternative Learning Centers (ALC). Most of these out-of-school programs provide in-person, early, and K through 12 learning support and enrichment, while others facilitate safe and supervised care for children who are participating in distance learning in partnership with families, local municipalities, and school departments. Our workforce has enabled healthcare and frontline workers to attend to their essential duties with the confidence in knowing that their children, infants to teenagers, are being supervised, well taken care of, and benefiting from in-person education. These workers have carried out these duties despite the loss of substantial revenue due to COVID-19 impacts on the economy. As we move ahead into Spring and Summer, many more community centers, after school programs, recreational areas, and organized camps are planning to open and hire staff to provide continuing service and care to our children, young adults, working parents, and caregivers. We, therefore, urge you to include these workers in the CDC/ACIP vaccine allocation and distribution recommendations for the education sector to be eligible for Phase 1b access to COVID-19 vaccinations when available. I sincerely appreciate this opportunity to present to the committee and look forward to working with the CDC as a valuable partner, as well as others, in the implementation and rollout of vaccines to these workers. Thank you all for your hard work and have a good day.

Votes: Pfizer-BioNTech COVID-19 Vaccine and Adult and Child/Adolescent Immunization Schedules

Sara Oliver MD, MSPH
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Co-Lead ACIP COVID-19 Vaccine WG
National Center for Immunization and Respiratory Diseases
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Dr. Oliver reminded everyone that the policy ue stion is, “Should vaccination with Pfizer-BioNTech COVID-19 vaccine (2-doses, IM) be recommended for persons 16 years of age and older under an emergency use authorization?” he in terpretation of the balance of consequences is that the desirable consequences clearly outweigh the undesirable consequences in most settings, and that the type of recommendation proposed by the WG was to recommend the intervention.

The proposed language for an ACIP vote on the interim recommendation is:

> “The Pfizer-BioNTech COVID-19 vaccine is recommended for persons 16 years of age and older in the U.S. population under the FDA’s Emergency Use Authorization.”

The proposed language for the ACIP vote to amend the 2021 Adult and Child/Adolescent Immunization Schedule is:

> “Recommend the proposed amendment to the 2021 Adult and Child/Adolescent Immunization Schedules.”

For the adult schedule, a text box on the notes page has been that states:

> “ACIP recommends use of COVID-19 vaccines within the scope of the Emergency Use Authorization or Biologics License Application for the particular vaccine. Interim ACIP

recommendations for the use of COVID-19 vaccines can be found at https://www.cdc.gov/vaccines.hcp/acip-recs/vacc-specific/covid-19.html"

The purpose of this statement is to address the timing for coverage under the Affordable Care Act (ACA)-covered health insurance plans. The CARES Act shortens the effective data of ACA coverage from 1 year to 15 business days after the ACIP recommendation and CDC Director adoption. That means that insurance companies will have 15 business days after the Pfizer recommendation vote and adoption until they will be mandated to cover COVID-19 vaccine administration fees by generically listing COVID-19 vaccines rather than just the Pfizer vaccine in the ACIP ACA recommendation. The intent is to cover all COVID-19 vaccines after the initial 15 business days effective date is met so there will be no delay in coverage as additional COVID-19 vaccines are recommended. The Child/Adolescent Immunization Schedule note page includes the same addition.

Discussion Points

Drs. Romero and Cohn reminded the voting members who declared COIs (Atmar, Frey, Hunter) that as they began the deliberation of the proposed recommendation language, these members should abstain from the discussion and the vote.

Dr. Bell thought that there would be an explicit statement about how this recommendation would be tied to the allocation recommendation. Without that, she was concerned that there would be some confusion with this language. There should be clarification that the ACIP was not saying with this recommendation that everyone should go out to get vaccinated, especially given that they were tying it to the schedule though there was nothing in the schedule to indicate that there is an allocation scheme. She would be much more comfortable if there is an explicit statement that this interim recommendation is being made in a time of constrained supply and that the specific populations covered are included in an allocation recommendation.

Dr. Messonnier said that CDC very much concurs as to the importance of not having this language lead to confusion about the current situation of limited supply and, therefore, careful attention to prioritization. While it is not in the actual recommendation language, in the draft *MMWR* there is language that phrases it exactly the way Dr. Bell indicated.

Dr. Oliver read the draft *MMWR* language, " he Pfizer-BioNTech COVID-19 vaccine should be implemented in conjunction with ACIP's interim recommendation for allocating initial supplies of COVID-19 vaccines" with a reference to link directly to the previous publication of the *MMWR* interim allocation recommendations.

Dr. Bell said she would be happier if the *MMWR* language was included in the wording for the vote.

Dr. Messonnier said that while they understood the point, they obtained counsel at CDC and it is not possible to include that language in this way. Part of the issue is that this is a recommendation to use or not use the vaccine. While CDC will ensure that in all of the communications the two are linked, the actual recommendation is for the vaccine or not and they cannot proceed with the language that linked the two recommendations as proposed by Dr. Bell. It is expected that the supply will increase in the next month, so they would move on from the initial prioritization recommendations and would not want to have to come back to ACIP every time the phases change.

Dr. Lee endorses support for ensuring that this recommendation could be used flexibly because they anticipate that it might go into Phase 1b and 1c and would appreciate not having emergency meetings e ery time they mo e into another phase. She agreed with Dr. Bell's intent in making sure that it is communicated clearly that the allocation framework recommended by ACIP should be used accordingly, assuming that there is continued limited supply. She also appreciated that this states "under the FDA's EUA." h is is an important addition with regard to the fact that they discussed the previous day the importance of re-reviewing the GRADE and the EtR with additional information when the BLA comes up.

Dr. Ault made a motion to accept the proposed language for an ACIP vote on the interim recommendation for use of the Pfizer vaccine as presented. Dr. Sanchez seconded the motion.

Dr. Poehling made a motion to approve the language as proposed for the Adult and Child/Adolescent Immunization Schedules. Ms. Bahta seconded the motion.

Dr. Lee requested to make a brief statement before the vote regarding a couple of key points. First, she emphasized to the public listening to this meeting that ACIP has absolutely followed its routine process using the GRADE and EtR Framework in open ACIP meetings as is done for all vaccines. She recognized the concerns that have been raised about the speed of approval at multiple steps, but also emphasized that ACIP has a process that is timely and responsive to the pandemic. She truly hopes that the ACIP deliberations have emphasized that these deliberations have been thorough, transparent, and timely and reassures the public regardless of the outcome of the vote. Second, she highlighted the imbalance that was brought up earlier between investment in vaccine development and supply chain and the investment delivery infrastructure. Part of the EtR Framework does think critical about values, acceptability, resource use, and implementation considerations. Part of that infrastructure is the robust communication and outreach program that is needed in order to actually enhance access, acceptability, and the real-world use of the vaccine. They saw estimates of $8.5 trillion on health impact alone and that does not even consider the economic impact to individuals and families across the US. There was a $10 billion investment in vaccine development and distribution, which has been extremely successful. However, she has heard in the news that only a small fraction of several hundred million has been invested in the delivery infrastructure. Therefore, she made a plea to the lawmakers that they support the public health infrastructure that is really needed to respond to this pandemic. She is confident that they will do their job at ACIP and expressed her hope that others also will follow through in the support that is needed for this work to be successful.

Dr. Messonnier thanked the ACIP members, liaisons, and *ex officio* members for the past two days, as well as for the multiple past months of their careful thought on these issues. As was noted by several members of the public, CDC looks to this committee to be scientifically driven and transparent. ACIP has certainly fulfilled that responsibility. She knows they share the burden and importance of this moment in which they find themselves after so long and so much work by so many parties around the world to have this vaccine in front of them available for this vote. It is a high honor and everyone understands that if ACIP votes for this vaccine, this is only one step. There is much work left to do, but this is a hugely important step.

Motion/Vote: Pfizer-BioNTech COVID-19 Vaccine

Dr. Ault made a motion to accept the proposed language for an ACIP vote on the interim recommendation for use of the Pfizer vaccine as presented, " he Pfizer-BioNTech COVID-19 vaccine is recommended for persons 16 years of age and older in the US population under the FDA's Emergency Use Authorization." Dr. Sanchez seconded the motion. Drs. Atmar, Frey, and Hunter declared COIs. The motion carried with 11 affirmative votes, 0 negative votes, and 3 abstentions. The disposition of the vote was as follows:

11 Favored:	Ault, Bahta, Bell, Bernstein, Lee, McNally, Poehling, Romero, Sanchez, Szilagyi, Talbot
0 Opposed:	N/A
3 Abstained:	Atmar, Frey, Hunter

Motion/Vote: Adult and Child/Adolescent Immunization Schedules

Dr. Poehling made a motion to approve the language as proposed for the Adult and Child/Adolescent Immunization Schedules to "Recommend the proposed amendment to the 2021 Adult and Child Adolescent Immunization Schedules." Ms. Bahta seconded the motion. No COIs were declared. The motion carried with 14 affirmative votes, 0 negative votes, and 0 abstentions. The disposition of the vote was as follows:

14 Favored:	Atmar, Ault, Bahta, Bell, Bernstein, Frey, Hunter, Lee, McNally, Poehling, Romero, Sanchez, Szilagyi, Talbot
0 Opposed:	N/A
0 Abstained:	N/A

Following the votes, Dr. Romero invited ACIP members who wished to do so to reflect on the rationale for their votes.

Dr. Talbot: I just wanted to say thank you to all of the incredible civil servants who have worked tirelessly to make this happen. This is our first kind of big break in this epidemic and many of our civil servants at both the CDC, the FDA, and in the state have been working crazy hours with no extra pay all to make this US a better place. I just want to say thank you from the bottom of my heart.

Dr. Szilagyi: First, I wanted to give a really big thank you to everybody who is on this video from the ACIP voting members, to the liaisons, and affiliated organizations who I so admire. I really wanted to thank the CDC COVID WG, the CDC leaders, and the thousands of people at CDC who are working on this pandemic and on the vaccine. I want to say that I voted for the vaccine because of the clear evidence of its efficacy, safety profile, and benefit/risk profiles based on our evidence to policy framework. I wanted to emphasize that this recommendation is within the context of our prior phased allocation recommendation. As a pediatrician, I wanted to say

strongly that I felt 16 to 17 year olds should be included in the routine vaccine recommendation in the COVID vaccine recommendation because of their risks from the disease and the lack of any evidence to suggest that the efficacy or safety profile should be different for 16 to 17 year olds than for 18 to 25 year olds. I also wanted to re-emphasize what many people and I have said today for the need for substantially increased government funding to actually implement the recommendation. This is government funding for state and local public health organizations and also funding for health systems and health providers. I know we are going to have very tough times ahead because of the surge and a limited vaccine supply, but I am really hopeful that this is the beginning of the end of the coronavirus pandemic. Thank you.

Dr. Bell: I wanted to first of all reflect on all of the suffering that all of us here in the United States and around the world are going through under the pandemic and say that this vaccine and future vaccines do provide a promise of a lot of progress in the future while, of course, for the moment vaccine supplies are going to be limited for quite some time to come I think. I wanted to say that I do believe that the process that we have used here in the ACIP to reach this decision is transparent, is science-based, keeps equity in mind, and is for this moment the absolute best that we can do. I also wanted to recognize people's concerns about this vaccine, and other vaccines, and new vaccines and say that oftentimes one consideration or one factor that people consider is that they say, "Well, would you take this vaccine and would you give this vaccine to your family members?" I can say quite confidently that yes I certainly will take this vaccine when I am able and I would give it to my family members. I think that the risk-benefit is pretty clear. Finally, I wanted to just raise two important points that have been raised by others, but I will just also add my voice. The first is the importance of clear communication and I know that the CDC, as well as many partner organizations, are very skilled in this and are standing ready to provide clear communication over and over again. I would hope that this would be facilitated and this would be recognized as an important component of our vaccination program. The second is the point that has been made several times now, which is about funding. I don't think it is unfair or unreasonable to make a comparison between the amount of money, the billions of dollars that have gone into the development vaccines. Granted, I certainly recognize what a huge accomplishment that has been and continues to be, but I think that the imbalance between that kind of money and the funding that has been provided for the vaccination programs and implementation is really shocking and needs to be corrected, because we are not going to be able to protect the American public if we don't have a way to deliver that seems to them. Thank you.

Ms. McNally: This COVID-19 vaccine offers us hope. It's important to remember that while this vaccine has been developed at an incredible pace and involves new technology, it has gone through all of the appropriate regulatory channels and the approval processes have been transparent. The ACIP has held 9 meetings since February 2020, including this meeting yesterday and today. We heard over 70 presentations on COVID-19 and the COVID-19 vaccines. We have considered the disease epidemiology, benefits and harms, values, acceptability, feasibility, resource use, and equity. Regarding safety, we saw that reactogenicity events were transient and resolved within a couple of days after onset, and the incidence of severe or serious adverse events were similar in the vaccine and placebo groups with 0.6% and 0.5%, respectively. Regarding the effectiveness of this vaccine, we saw that overall efficacy was 95%. There are things we don't know yet, but many issues were addressed during the clinical considerations presentation today. By way of example, there are unknowns regarding the pregnancy and lactating women and there is limited data for 16 and 17 year olds, but additional data will become available and I was reassured by the comments from ACOG and AAP on these issues. The CDC has done an incredible job in spite of the immense time crunch getting information on its website about what to expect after vaccination, the benefits of vaccination,

and latest recommendations for who should be vaccinated. We heard today about the CDC consumer-friendly fact sheet that will be provided to recipients in addition to EUA fact sheet. Over the past several months, as the consumer representative I' e asked questions I think the public has. I believe the ACIP process has worked. I value the expertise of my ACIP colleagues, as well as the CDC's expertise, guidance, and tireless dedication. The theme that has emerged from me is a commitment to continuously collect, review, and report data. The systems are in place and that vaccine safety data will continue to inform clinical guidance and recommendations for COVID-19 vaccines. The need for this vaccine is profound. Because the current data support this vaccine, that it is safe and effective for the majority of people, I voted yes.

Dr. Bernstein: I would like to extend my deep and sincere appreciation to the CDC leaders, COVID-19 WG, the multiple liaisons and partners, and to the public, because together we all will help to make the United States and the world safer. With the pandemic resulting in thousands of deaths each day, keeping equity in mind and knowing 16 and 17 year olds are actively being studied, I voted in favor of both items. I also recognize that this teenage group can actively transmits SARS-CoV-2 infection to contacts in their families and communities. I would still propose that we consider adding this age group as a special population in these interim clinical considerations, explaining that available data is limited at this time. Child health providers will benefit from additional specific detail in recommending and discussing COVID-19 vaccines with parents, families, and communities. Thank you.

Dr. Sanchez: I also want to thank the CDC and the COVID WG for their amazing and ongoing work. It's been really an amazing and well thought out process. I very much agree with the approval of this vaccine as stated based on its strong efficacy and safety, knowing that there will be ongoing evaluation on both ends. Also, I really feel that this is a really important beginning in terms of trying to end this pandemic and deal with it in an effective manner. I also would recommend it for myself and my family. I feel very comfortable with this recommendation, but I also feel very strongly that it needs to be allocated in a fair manner based on risk factors such as weight and others. Thank you for the opportunity to work on this recommendation.

Dr. Poehling: Just 12 months ago COVID-19 pneumonia was first identified. I want to thank the many scientists whose work over decades and the past year has enabled the creation and assessment of vaccines, as well as the many analyses that have been publicly reviewed. I want to thank the many participants of the vaccine trials that have enabled this EUA. I want to thank all those at the CDC, FDA, and many, many more who have worked under an incredible time pressure to transparently share the information needed. The collaborative work and sharing data throughout the process has enabled all the processes needed to submit an EUA and has been fulfilled without any shortcuts. I express tremendous gratitude to all of those in the WG who have diligently informed and prepared us for this moment. The gravity of the COVID-19 pandemic needs to be underscored. Over 15 million Americans have been infected and over 291,000 have died. Many Americans are experiencing negative impacts from COVID-19. The FDA issued this EUA after careful review of safety and effectiveness of the vaccine. While more information will continue to become available, at this time we are asked how to do the greatest good. As the pandemic continues to spread, hospitalizations are at record levels. I vote to make vaccine available by the CDC's prioritization schedule. I will take this vaccine and will recommend it to my family members as well when the time is that it is offered. A highly immunogenic vaccine will also have expected reactions. There are multiple safety monitoring systems and a newly created Vaccine Safety Technical Subgroup to carefully review all data. Revisions and updates of information are expected and reflect that the process is working. As vaccines begin to be offered, it is important that the vaccine is offered to all within each priority

group and will require outreach and communication to achieve the equitable distribution desired. There is much work that needs to be done. Thank you.

Dr. Romero I'll take this moment to add my comments to the to the list of comments that have already been made, and many of these have already been covered. But let me begin by thanking everyone at the CDC, the senior leadership, Dr. Cohn, Dr. Messonnier, Dr. Dooling, Dr. Oliver, Dr. Mbaeyi, our WG Chair Dr. Bell, the voting members, including Dr. Talbot and Dr. Lee, and all of the ACIP members which take too long to read at this point, the liaisons, the *ex-officios,* and also a group that we have not acknowledged as much as we should, which is the subgroup for vaccine safety. Thank you very much for your efforts and deliberations on this. I want to make a comment for the public in general. ACIP has worked to deliver vaccine to the general public that maximizes benefits, minimizes harm, and addresses issues of equity and issues of healthcare disparity. The vote taken today represents the work carried out over 9 months since April of this year. The deliberations have been thorough and have been in-depth. No question that we felt was important was left unturned. All data was presented to us as we ask for it. There has been thorough, robust, in-depth discussion. We now present to you, the general public, the ability to prevent COVID-19 disease. These deliberations are important in coming to the recommendations. I want to stress that we have, throughout this process, looked at safety. I know that safety is an issue that is of concern to the public. At all stages of the development, approval, and further recommendations for this vaccine, safety has been listed as a priority by the FDA and by the ACIP. We hope that the public has confidence in this. Speaking as a person of color, I am grateful that the pharmaceutical company, Pfizer, has included minority populations in the study and we have data from those groups. I want to thank everyone. I want to also mention what has been mentioned before that if and when my turn comes to receive this vaccine, I will receive it without hesitancy.

Certification

Upon reviewing the foregoing version of the December 11-12, 2020 ACIP meeting minutes, Dr. Jose Romero, ACIP Chair, certified that to the best of his knowledge, they are accurate and complete. His original, signed certification is on file with the Management Analysis and Services Office (MASO) of CDC.

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July 1, 2019 – December 31, 2020

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