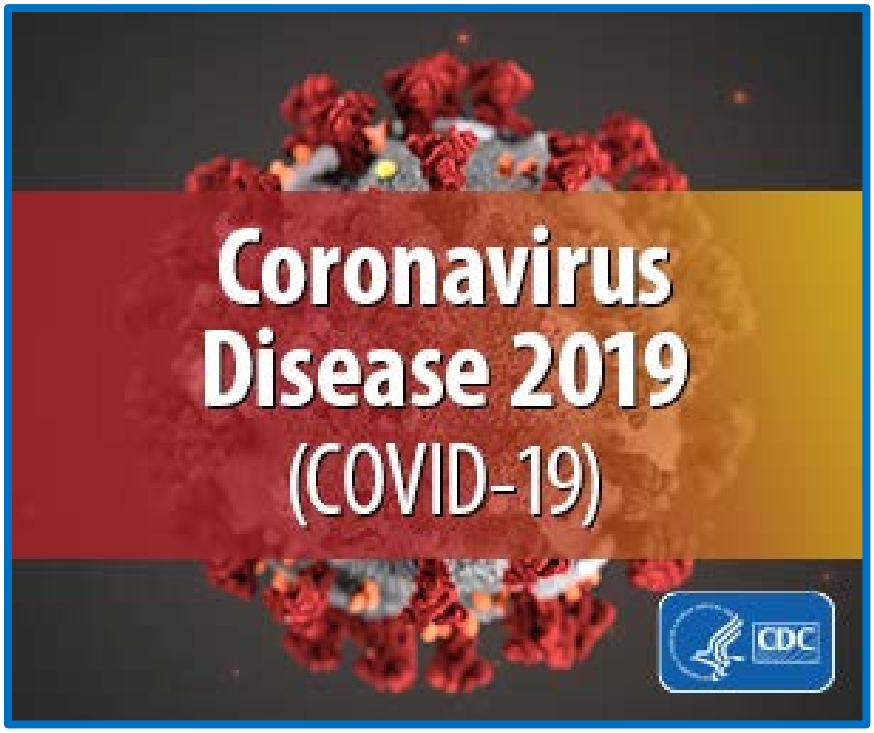
DEPARTMENT OF HEALTH AND HUMAN SERVICES
CENTERS FOR DISEASE CONTROL AND PREVENTION

Advisory Committee on Immunization Practices (ACIP)



Business Summary
Coronavirus Disease 2019 (COVID-19) Vaccines Session
October 30, 2020

The Centers for Disease Control and Prevention (CDC) convened a virtual meeting of its Advisory Committee on Immunization Practices (ACIP) on October 28-30, 2020. This Business Report summarizes the third day of the meeting, which was devoted solely to the topic of coronavirus disease 2019 (COVID-19) vaccines. **Dr. José Romero** (ACIP Chair) delivered the opening remarks. He emphasized that faced with a crisis of historic proportion, basic scientists, clinical scientists, clinical investigators, and volunteers have worked with unprecedented speed to develop, test, evaluate, and manufacture a plethora of potential vaccines against Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2). The mandate given to the ACIP has been to develop equitable, just, and fair policy guidelines for the use of those vaccines that are proven to be safe and effective in preventing and mitigating SARS-CoV-2 disease. The volume of data that have been compiled, analyzed, synthesized, and presented to the ACIP voting members, liaisons, *ex officio* representatives and the public has possibly been more than ever presented for any other vaccine that has come before the ACIP. It can be said without hyperbole or exaggeration that no other national COVID-19 vaccine advisory group has dedicated as much time to addressing questions posed to the ACIP regarding the use of those COVID-19 vaccines. Over the 7 months since its creation, the ACIP's COVID-19 Vaccine Work Group (WG) has met more times than any other non-standing ACIP WG. Dr. Romero publicly acknowledged the extraordinary work in terms of time, effort, and quality that the members of the COVID-19 Vaccine WG have dedicated to this effort. In addition to the official WG members, all ACIP members have given of their time to prepare for, attend, and meaningfully participate in the equivalent of 2 years' worth of open public meetings in a 10-month timeframe. Dr. Romeo also acknowledged the extraordinary leadership of Dr. Nancy Messonnier, Director of the National Center for Immunization and Respiratory Diseases (NCIRD); Dr. Amanda Cohn, ACIP Executive Secretary; and Jessica McNeil, Assistant Executive Secretary for ACIP. In addition, he acknowledged the important support work provided by Ms. Stephanie Thomas and Ms. Natalie Greene who have provided much of the materials to be reviewed prior to the meetings. In closing, he thanked all who have dedicated, are dedicating, and will continue to dedicate their time to ACIP's efforts to provide guidance for the use of safe and effective COVID-19 vaccines, emphasizing that he believed history would not forget their dedication to this task.

Dr. Doran Fink (FDA) provided an update from the Vaccines and Related Biologics Products Advisory Committee (VRBPAC) Meeting on October 22, 2020. During that VRBPAC meeting, the FDA explained the considerations for manufacturing and clinical information needed to support licensure for Emergency Use Authorization (EUA) of COVID-19 vaccines, as described in two recent FDA guidance documents. The purpose of the guidance documents is to provide reassurance that FDA will rely on sound science, established regulatory standards, and a transparent process for evaluating COVID-19 vaccine candidates. Dr. Fink first explained the clinical considerations for an EUA in detail and then summarized the VRBPAC's discussion. VRBPAC expressed concerns about public vaccine confidence. There was broad agreement that data to support issuance of an EUA for a COVID-19 vaccine should not be less than the standards outlined by the October 2020 FDA guidance. Some VRBPAC members expressed concerns that a median follow-up of 2 months after completion of the vaccination regimen would not be sufficient to support an EUA for rapid and widespread deployment. Others considered 2 months to be sufficient and felt that rare adverse events (AEs) and waning immunity could be monitored by surveillance during vaccine use under an EUA. Some VRBPAC members were concerned about COVID-19 of any severity as the primary efficacy endpoint in current Phase 3 trials, given that there may be limited information on severe disease. FDA and some VRBPAC members discussed that primary endpoints were selected based on feasibility and prior experience with preventive vaccines. While analyses to support EUA will include some information on severe disease, insisting on adequately powered analyses of severe disease (which has a lower incidence than less severe disease) could delay the availability of an

impactful vaccine. VRBPAC members expressed concern about clinical trial recruitment of, and accrual of data, in the populations most affected by COVID-19 (e.g., racial and ethnic minorities, elderly individuals, and individuals with medical comorbidities). FDA reported that published guidance and advice to COVID-19 vaccine manufacturers has advocated for inclusion of these populations in trials. While there is no regulatory mechanism for mandating trial recruitment, vaccine manufacturers have been publicizing enrollment demographics for their trials. This is important given that demographic and medical history data from trial participants will be considered in regulatory decisions and will be reflected in vaccine labeling to inform healthcare providers (HCP) and vaccine recipients. There also was discussion regarding considerations for pediatric development and data to support use in pediatric populations, particularly with respect to careful evaluation of immune-mediated reactions or enhanced disease and immunobridging approaches. There was broad agreement among VRBPAC members that blinded, placebo-controlled follow-up in ongoing trials should continue for as long as is feasible, including after EUA. VRBPAC raised questions about expanded access as an alternative to EUA. An expanded access treatment protocol could be considered to allow for deployment of a COVID-19 vaccine. It is important to note that the benefit/risks considerations are similar to EUA, other considerations such as planning and implementation differ from EUA, and an expanded access treatment protocol would be conducted under Investigational New Drug (IND) regulations that require informed consent, Institutional Review Board (IRB) oversight, and investigator responsibilities for vaccine providers. In terms of next steps, FDA will consider the VRBPAC feedback provided and will re-convene the VRBPAC prior to any FDA action to approve or issue an EUA for a COVID-19 vaccine to evaluate and discuss data submitted in support of the licensure application/EUA request and vote on recommendations as to whether the data support vaccine licensure/proposed use of the vaccine under EUA.

Dr. Filip Dubovsky (Novavax) reported on the Novavax NVX-CoV2373 vaccine candidate in terms of vaccine design, the non-human primate protection study, Phase 1 Day 35 safety and immunogenicity data, Phase 2 Dose 1 and Dose 2 reactogenicity data, and plans for Phase 3. The Phase 1 study fully enrolled and safety and immunogenicity follow-up is ongoing. The study sites, investigators, contract research organization (CRO), and participants are blinded to individual vaccine/placebo allocation. Day 35 (14 days after Dose 2) safety and immunogenicity data were reviewed by SMC and FDA in advance of the Phase 2 study. The Day 35 safety summary for NVX-CoV2373 is consistent with previous nanoparticle vaccine with Matrix-M1. No serious adverse events (SAEs) were identified for NVX-CoV2373. There were no adverse events of special interest (AESI), including potentially immune-mediated medical condition AESIs, and no confirmed COVID-19 AESIs. All AEs were mild and moderate and were balanced in active arms. In terms of reactogenicity symptoms, the majority of subjects reported “none” or ”mild” and the mean duration was less than 2 days for both local and systemic reactogenicity symptoms. Novavax Phase 1 study conclusions are that reactogenicity and safety profiles are reassuring for both the 5 µg and 25 µg dose groups when formulated with Matrix-M1 adjuvant. In terms of immunogenicity, the Matrix-M1 adjuvant is required to induce an optimal functional immune response, 2 doses of vaccine administered 21 days apart are superior to a single dose, 5 µg and 25 µg induce comparable immune responses when formulated with Matrix-M1, and Matrix-M1 induces a Th1 biased immune response with high levels of neutralizing antibody. The safety and immunogenicity profile of both 5 µg and 25 µg formulated with Matrix-M1 and administered on Day 0, 21 is acceptable for further clinical evaluation.

The Phase 2 study is fully enrolled, Dose 2 has been administered, and safety and immunogenicity follow-up is ongoing. The study sites, investigators, CRO, and participants are blinded to individual vaccine/placebo allocation. Reactogenicity data were reviewed by SMEs and the FDA in advance of the Phase 3 study. Regarding local reactogenicity events in 2 Dose adjuvanted groups, pain and tenderness were reported most frequently. Increased rates were seen in the adjuvanted groups, especially after Dose 2, and reactogenicity was attenuated in adults ≥60 years of age.

The Phase 3 pivotal safety and efficacy study will be conducted in the United States (US) and Mexico. This is a randomized, observer-blinded, placebo-controlled study in which participants are randomized 2:1 to receive 5 µg + Matrix-M1 vaccine or placebo with 2 doses 0.5ml administered on Day 0 and Day 21. The study will include up to 30,000 adults >18 years of age across the US and Mexico. The plan is to target at least 25% participants ≥ 65 years of age, at least 25% with high-risk co-morbidities, at least 15% black/African Americans, 10% to 20% LatinX, and 1% to 2% Native Americans. This is an endpoint-driven study with efficacy evaluations at 72, 108, and 144 cases. The primary endpoint is prevention of PCR-confirmed mild, moderate, or severe COVID-19 illness occurring 7 days after Dose 2 in baseline seronegative adults. Safety follow-up will be conducted through 2 years.

In summary, the NVX-CoV2373 vaccine candidate is based on the baculovirus/nanoparticle platform technology. The safety database includes over 12,100 nanoparticle vaccinees (RSV, influenza, Ebola) and over 2,500 nanoparticle vaccinees adjuvanted with Matrix-M1. Vaccine presentation will be in 10-dose vials with transportation and storage at 2^0-8^0 C. The vaccine is preservative-free and no admixing or reconstitution is required. A 0.5 ml dose is administered intramuscularly 21 days apart. The preliminary safety profile is reassuring with a favorable reactogenicity profile. A peak immune response is observed 14 days after Dose 2. There is a favorable immunologic phenotype, with a robust neutralizing antibody response and polyfunctional CD4+ Th1-biased cellular immune response. Efficacy evaluation is ongoing.

Dr. Jerald Sadoff (Janssen) presented an update on Janssen's investigational COVID-19 vaccine program. The foundation of Janssen's investigational COVID-19 vaccine is its proprietary AdVac® Technology Platform. Janssen uses a replication incompetent human adenovirus 26 (Ad26), which expresses the target antigen. They have taken a region out of the virus so that it cannot replicate. It invades the cells and makes the transgene and its own antigens, but it cannot assemble them into a replicating virus. The antigen is not on the surface virus. It is only on the surface of the cells that the virus is going into and it is membrane bound. This vaccine has induced very good humoral antibody responses against structural proteins with neutralizing activity and/or other unique functionalities, as well as cellular CD4-T cell responses with a Th1 signature and CD8 T-cell responses. There has been no sign of vaccine-associated enhanced respiratory disease (ERD) in pre-clinical models after breakthrough infection. Janssen has extensive clinical experience with its Ad26-based vaccines, with over 110,000 participants vaccinated. These Ad26-based vaccines have shown to have a favorable safety and tolerability profile in the populations studied to date. On July 1, 2020, Johnson & Johnson received approval from the European Medicines Agency (EMA) for Janssen's Ad26-based preventive Ebola vaccine.

Janssen took the approach of looking at a number of vaccine constructs because of instability problems that were noted before, and to look at theoretical considerations. Janssen has had a lot of experience with its RSV and HIV programs on how to construct stable expression vectors, so they assessed stabilization, signal peptide, expression of antigen, manufacturability of vaccine, and then immunogenicity in pre-clinical animal models. Based on that, they were able to find a vaccine candidate that was clearly superior in terms of its immunogenicity and the other considerations, Ad26.COV2.S. It encodes a full length membrane-bound S-protein with stabilization mutations and a native initial signal sequence. After a single dose of Ad26.COV2.S, they were able to show protection in the lower and upper respiratory tract of SARS-CoV-2 challenged non-human primates (NHP). In other data, they have done down dosing studies and have shown that even when the vaccine is reduced, they have still been able to get substantial protection. This leads to the belief that the immunogenicity achieved will be protective.

Based on that, Janssen began a Phase 1/2 study, COV1001, to assess the safety, reactogenicity, and immunogenicity of this investigational vaccine in healthy adults 18 to 55 (Cohort 1; N=400) years of age and adults 65 years of age and older (Cohort 3; N=375) at 2 different dose levels ($5x10^{10}$ viral particles and $1x10^{11}$ viral particles) administered as a 1 dose or 2 dose regimen. They have the data on the 1 dose regimen and are just accumulating the data on the 2 dose, so Dr. Sadoff focused mainly on the data after 1 dose. Cohort 2 is comprised of 270 participants 18 to 55 years of age in whom duration of the immune response, the ability to boost at various times if necessary, and anamnestic responses will be examined. There were very good seroconversion rates with the enzyme-linked immunosorbent assay (ELISA) at 99% at a slightly lower dose and a similar 99% with very reasonable geometric mean titers (GMTs) for neutralizing antibody levels. There was very little differences in the elderly and younger adults in terms of immune response, and there was a rise between Day 15 and Day 29. With the wild-type virus neutralizing antibodies (wtVNA) showing very good response rates as well of 92% at both doses, with a similar response in the elderly with comparable GMTs. The GMTs rose quicker for the neutralizing antibodies, with a very good response at Day 14. Therefore, in the Phase 3 trials they will start counting cases 2 weeks after single dose immunization. From this data, it is clear that there are not differences in immunogenicity between the younger and elderly groups in terms of ELISA or wtVNA, and they seem to be at the flat part of the dose response curve, which allows them to pick the lower dose as a single dose regimen going forward. There also was a very good T-cell response in both groups. Only 2 individuals responded with Th2 and the rest were completely negative. The ratio in those 2 between the Th1 and Th2 was 28.9 and 20.2. Clearly, a Th1-type response dominated in both younger adults and the elderly with practically no Th2 response at all. With this vector, they also are able to induce fairly high percentages of CD8 T-cell functional responses that express interferon gamma and may play a role in protection as well, although they have yet to prove that.

This vaccine does cause some systemic AEs based on blinded data between the groups. Among the 402 subjects in Cohort 1, approximately 50% to 60% overall had systemic AEs. All were transient and lasted not more than 1 to 2 days. In terms of pyrexia, there was some fever in Cohort 1 that was considered Grade 3. These were very responsive to anti-pyrectics and they did not judge that any-pyrectics needed to be used prophylactically. In Cohort 3, there were far fewer systemic reactions and fever rates were very low with no Grade 3s. Once again, reactogenicity was much lower in the older cohort than the younger cohort but the immunogenicity seemed comparable. Based on this, Janssen designed a Phase 3 efficacy trial, COV3001. This is a multicenter, randomized, double-blind, placebo-controlled, Phase 3 study evaluating the efficacy and safety of Ad26.COV2.S for the prevention of SARS-CoV-2-mediated COVID-19. The primary endpoint is moderate to severe illness. The study is being conducted in

Argentina, Brazil, Chile, Colombia, Mexico, Peru, South Africa, and the US with a target of about 50% of the subjects being in the US. From the beginning, there has been a plan to enroll a diverse population. This study does not have a fixed stop interim analysis. A continuous, sequential monitoring technique is used for safety and efficacy instead. This study is being conducted in healthy adults 18 years of age and above. The estimated enrollment is 60,000 in which participants will receive a single dose pf $5x10^{10}$ of Ad26.COV2.S or placebo. The endpoints are the number of participants with first occurrence of molecularly confirmed moderate to severe COVID-19 with seronegative status. The hope is to have a planned follow-up of up to 2 years. Janssen will attempt to follow participants as long as possible regardless of what happens, but there are plans for how analytically to deal with dropouts and people who want to receive the vaccine or knowing whether they received vaccine or placebo.

In terms of the Phase 3 pause, pauses are not uncommon in these types of studies. Janssen is dedicated to the safety of its participants. This particular pause was in an individual who had a safety event and was subject to automatic stopping or pausing rules. This was judged by the Data Safety and Monitoring Board (DSMB) to be appropriate. Janssen evaluated this case extensively with the DSMB and outside experts. It is a complicated case that had multiple potential causes, which have not completely been determined. However, it is believed that there is no relationship between the vaccination and the event. In consultation with the FDA, the DSMB agreed to restart the trials. The trial has restarted in the US and enrollment is continuing. Janssen plans to disclose the clinical data for its COVID-19 trials once those data are presented or published at prespecified milestones, and will proactively disclose the regulated trial holds as requested by health authorities. Janssen is planning to deploy this vaccine widely once a signal is reached and there is approval from the FDA and other regulatory agencies. The plan is to put it in a 2R glass vial that has 5 doses per vial, 10 doses per carton, and 8 cartons per shipper. The anticipated storage conditions under an EUA would be stored by Janssen at -20^0 C for up to 2 years, in end-user storage at 2^0 to 8^0 C for up to 3 months, and after first use at 20^0 to 8^0 C for up to 6 hours. More data are evolving with the hope that there will be much longer stability of up to 9 months or longer like Janssens other vaccines in this platform.

Dr. Janell Routh (CDC/NCIRD) provided an update on vaccine implementation planning. She reminded everyone that the overarching objectives for the COVID-19 vaccination program are to: 1) ensure the safety and effectiveness of COVID-19 vaccines; 2) reduce mortality, morbidity, and incidence of COVID-19 disease; 3) help minimize disruption to society and the economy, including maintaining healthcare capacity; and 4) ensure equity in vaccine allocation and distribution. She shared an illustrative scenario for planning purposes, explaining that it would be adapted based on clinical and manufacturing information and that distribution would adjust as the volume of vaccine doses increases. Final prioritization will be decided by ACIP. On September 16, 2020, CDC published the "COVID-19 Vaccination Program Interim Playbook for Jurisdiction Operations." All 64 jurisdictions returned a COVID-19 vaccination plan and federal agency plans have been received from the Veteran's Affairs (VA), Indian Health Services (IHS), Department of Defense (DoD), Department of State (DOS), and the Bureau of Prisons (BOP). The plans were reviewed by at least three CDC subject matter experts (SMEs) and feedback was returned. Information about plans will be updated on the CDC website. Jurisdictional plans showed strengths and challenges. Jurisdictions have organized their planning around the allocation phasing assumptions, set out clear plans to train and equip providers on the Vaccine Adverse Event Reporting System (VAERS), laid out deep operational details for second dose reminders (e.g., text, email, automated call) some of which are already live. Challenges include ensuring that public health messaging plans and expedited procedures for emergency communications are in place, that all data systems to administer and track vaccine have been

identified, and that additional planning is in place to ensure equitable access to vaccine distribution in later phases.

In terms of next steps for vaccine implementation, the goal is for jurisdictions to be ready by November 15, 2020. This includes having signed Data Use Agreements (DUAs) to ensure tracking of uptake, identifying pockets of low vaccination, identifying and intervening in coverage disparities, and allocating vaccine product. By this time, vaccination provider sites should be identified and enrolled, especially of those sites that can administer vaccine product to Phase 1 populations and that can position ultra-cold product after possible EUA. Jurisdictions are to confirm that the selected facilities are enrolled in the Vaccine Tracking System (VTrckS) to order and receive product. State capacity will be augmented through federal pharmacy partnerships to support vaccination in long-term care facilities (LTCF). Microplanning will continue to ensure readiness across various scenarios. Pharmacies can help to increase access to vaccines. Once there is an adequate supply of COVID-19 vaccine to support broader vaccination efforts, it will be important to help jurisdictions increase access to COVID-19 vaccine for the general population in Phase 2. The federal government is partnering with pharmacies nationwide to increase access to vaccine. Partners who enroll in this program will receive a direct allocation of COVID-19 vaccine when supply is sufficient and vaccine is recommended for use beyond the initial critical populations. Pharmacy partners under consideration include national chains, large regional chains, and networks of independent pharmacies and regional chains. Of the eligible US pharmacies, 55% have already enrolled. A list of partners will be shared with jurisdictions shortly. Leveraging all resources and public and private partners will allow for the successful administration of the COVID-19 vaccination program. The CDC vaccine website contains information and resources for the general public, providers, and jurisdictions.

Dr. Amanda Cohn (CDC/NCIRD) provided an update on CDC's *Vaccine with Confidence* strategy. There has been a considerable decline in COVID-19 vaccine acceptability in the past 4 months due to concerns about side effects, efficacy, risk perception/need for vaccine, and associated costs. Attributes that make COVID-19 vaccine more acceptable include an HCP saying that the vaccine is safe, that there is no cost for the vaccine to individuals, the potential for the vaccine to help get people back to work and school, and easy access to the vaccine. Individuals across the demand continuum will have concerns, which are understandable and must be addressed with empathy and transparency. Concerns among HCP is a risk for overall vaccine confidence, given that HCP are the most trusted source for health information. Various communities will have unique experiences informing COVID-19 vaccine perceptions, which can be addressed through engagement with community organizations and leaders to communicate clear and accurate information about COVID-19 vaccines. *Vaccinate with Confidence* is a national strategy to reinforce confidence in COVID-19 vaccines with the key priorities to protect communities, empower families, and stop myths. It is not an advertising, marketing or communications campaign. Instead, it is a cohesive framework to support health departments, healthcare providers, immunization partners, and community partners and leaders' promotion of COVID-19 vaccines. This national strategy includes evidence-based content to amplify messages that enable an individual to make the decision to vaccinate, which is critical to ensuring that safe and effective COVID-19 vaccines can help control and reduce the impact of this pandemic. CDC is seeking feedback from a wide range of partners on the *Vaccinate with Confidence for COVID-19 Vaccines Framework*, and will send a short email to share with colleagues to review and provide input.

Dr. Steve Anderson (FDA) reviewed FDA's active post-licensure safety surveillance systems and Center for Biologics Evaluation and Research (CBER) plans for monitoring COVID-19 vaccine safety and effectiveness. FDA and CDC have weekly and bi-weekly coordination meetings on VAERS and pharmacovigilance activities between the CBER Office of Biostatistics and Epidemiology (OBE) and the OBE Division of Epidemiology (DE) and the CDC Immunization Safety Office (ISO). CBER DE physicians will be reviewing the serious adverse event (SAE) reports from VAERS for COVID-19 vaccines. This will include review of individual reports, death reports, aggregate analyses, case-series, et cetera. FDA will utilize statistical data-mining methods to detect disproportional reporting of specific vaccine AE combinations to identify AEs that are more frequently reported. COVID-19 vaccine monitoring data considerations include rapid data access for near real time surveillance, large databases comprised of tens of millions of patients for evaluating vaccine rare SAEs, data representing the integrated care spectrum (e.g., outpatient, physician, inpatient, et cetera), high quality data to assess and confirm potential AEs or safety concerns for COVID-19 vaccines, and data with significant clinical detail or medical chart access. The FDA Biologics Effectiveness and Safety (BEST) system includes several partners, represents a variety of healthcare settings, and has an emphasis on inclusion of electronic health records (EHR), some claims, and linked claims-EHR data. BEST is a modern surveillance system that is able to perform a diversity of queries and studies. There has been an ongoing FDA-CMS partnership on vaccine safety since 2002. CMS data cover a very large population of approximately 55 million elderly US beneficiaries ≥65 years of age. Given that over 92% of US elderly individuals use Medicare, this database represents the elderly population and not a sample. It represents a variety of healthcare settings and consists of claims data with access to medical charts. Not all claims and EHR data systems can be used to address a vaccine safety or effectiveness regulatory question and each data system has its limitations in terms of the populations, healthcare settings, clinical detail, necessary parameters, data lag, exposures, and outcomes that are captured.

In terms of COVID-19 vaccine safety surveillance planning, the FDA will utilize rapid-cycle analyses (RCA) to monitor 10 to 20 safety outcomes of interest to be determined based on: 1) pre-market review of sponsor safety data submitted to the FDA; 2) coordination with federal partners, international regulatory partners and organizations, academic experts, and others; and 3) literature and regulatory experience with similar vaccines, novel vaccine platforms, and using other relevant data. Dr. Anderson shared a draft working list of possible AE outcomes. In terms of experience, the FDA has conducted near real-time surveillance for annual influenza vaccine and Guillain-Barre Syndrome (GBS) since 2007 and Sentinel rapid surveillance for the 2017-2018 seasonal influenza vaccine to evaluate 6 health outcomes of interest. Epidemiological analyses will require the capability to resolve potential safety signals identified from near real-time surveillance, TreeScan® signal detection efforts, and other sources. This may involve rapid queries and small epidemiological studies and/or larger self-controlled, cohort, comprehensive protocol-based studies. There may be limited information available at the time of licensure on the level and duration of effectiveness. Manufacturers may conduct certain COVID-19 vaccine effectiveness (VE) post-licensure studies. FDA may conduct COVID-19 general effectiveness studies, including subpopulations of interest; duration of protection studies; or other types of studies. FDA is coordinating COVID-19 VE efforts with the CDC/NCIRD through monthly and bi-monthly meetings. The FDA, CMS, and CDC have extensive experience with the data and methods needed to conduct VE studies having produced several VE and relative VE for influenza and zoster vaccines and duration of effectiveness analysis of Zostavax® vaccine. Dr. Anderson emphasized that COVID-19 vaccine monitoring is a large US government effort that involves regular meetings, planned sharing of protocols, discussion of safety and effectiveness outcomes of interest, and coordinated planning and conduct of surveillance activities between the FDA, CDC, CMS, VA, and DoD.

Dr. Tom Shimabukuro (CDC/NCEZID) continued the discussion of post-authorization/post-licensure safety monitoring of COVID-19 vaccines. He reported that ACIP has established a COVID-19 Vaccine Safety Technical Sub-Group (VaST) to advise CDC and other federal partners on planning and preparation for post-authorization/post-licensure safety monitoring of COVID-19 vaccines and independently review and evaluate safety data. Post-authorization/post-licensure safety data on COVID-19 vaccines will be presented regularly during public ACIP meetings. During this meeting, he provided updates on Vaccine Safety Datalink (VSD) monitoring and the CISA Project clinical consult service and HCP's role in reporting AEs to VAERS and facilitating patient enrollment into the v-safe smartphone-based active surveillance system. VSD planned monitoring and evaluation for COVID-19 vaccine safety includes: 1) near real-time sequential monitoring using RCA; 2) monitoring for vaccine-mediated enhanced disease (VMED); 3) studies to evaluate COVID-19 vaccine safety during pregnancy, including fetal death and infant outcomes; tree-temporal scan data mining; and 4) a variety of projects to assess changes in healthcare utilization during COVID-19 and impact on AE monitoring; utility of smartphone technology to enhance vaccine safety monitoring; multisystem inflammatory syndrome in children and adults (MIS-C and MIS-A) as vaccine AEs; safety in an expanded underserved VSD population; and knowledge, attitudes, and beliefs around acceptance/refusal of COVID-19 vaccination.

CISA Project clinical consult service supports US HCP and health departments on complex clinical vaccine safety questions and assists with evaluations of patients with AEs after receiving COVID-19 vaccine or in making clinical decisions about administering COVID-19 vaccine to a person who may be at increased risk for an AE. Advice from CDC and the CISA Project is meant to assist in decision-making versus providing direct patient management and is available to US healthcare providers and health departments by contacting CDC-INFO. HCPs have been CDC's longstanding partners for reporting vaccine AEs to VAERS. VAERS depends upon HCPs to identify and report suspected AEs, even if they are not sure if a vaccine caused an AE. The Health Insurance Portability and Accountability Act (HIPAA) permits reporting of vaccine AEs and medical documentation to VAERS for public health purposes. HCP participation in VAERS reporting will enable public health officials to have accurate and timely information on the safety of COVID-19 vaccines. Specific guidance on VAERS reporting for vaccines authorized for use under EUA will be forthcoming.

V-safe is a new smartphone-based active surveillance program for COVID-19 vaccine safety that uses text messaging to initiate web-based survey monitoring and conducts electronic health checks on vaccine recipients. Health checks are conducted daily for the first week post-vaccination and weekly thereafter until 6 weeks post-vaccination. There are additional health checks at 3, 6, and 12 months post-vaccination. V-safe includes active telephone follow-up through the VAERS program with vaccine recipients reporting a clinically important event during any v-safe health check. A VAERS report will be taken during telephone follow-up, if appropriate. V-safe captures information on pregnancy status and enables follow-up on pregnant women as well. V-safe will allow for estimation of rates of local and systemic reactogenicity and rates of clinically important AE following COVID-19 vaccination and symptoms and conditions associated with these AEs. HCPs will play an important role in v-safe enrollment by providing a one-page information sheet to patients at the time of vaccination (to be created by CDC) and counseling patients on the importance of enrolling in v-safe. CDC will provide information on how to briefly counsel patients on v-safe. Of note, v-safe will be translated into at least 5 other languages.

Dr. Melinda Wharton (CDC/NCIRD) described the ACIP COVID-19 VaST in more detail. VaST was organized in June 2020 and is comprised of independent expert consultants, ACIP members, liaison representatives, and federal agency SMEs. The focus of VaST is to prioritize AESI, develop USG plans for safety monitoring, and create a communication framework. VaST was built off of lessons learned from H1N1 vaccine safety monitoring. There was consensus that a Federal Advisory Committee Act (FACA)-chartered subgroup would ensure transparency, independence, and public accountability. VaST is currently comprised of ACIP and National Vaccine Advisory Committee (NVAC) representation, 7 independent expert consultants, ACIP *ex officio* members (NIH, FDA, OIDP, CMS, HRSA, IHS), and a VA and DoD liaison. The VaST's post-implementation objectives are to: 1) review, evaluate, and interpret post-authorization/approval COVID-19 vaccine safety data; 2) serve as the central hub for technical SMEs from federal agencies conducting post-authorization/approval safety monitoring to share vaccine safety surveillance data; 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. The VaST's deliverables include development of frequent COVID-19 vaccine safety technical reports for internal ACIP and CDC and federal partner use, and frequent COVID-19 vaccine safety data summaries for public release.

Dr. Matthew Biggerstaff (CDC Data, Analytics, and Modeling Task Force) presented modeling strategies for the initial allocation of SARS-CoV-2 vaccines. The question posed to the group to model was, "What is the potential impact, in terms of preventing COVID-19 infections and deaths, of initially allocating vaccine to one of the following groups after vaccinating HCP in Phase 1A: Adults aged 65+, adults with high-risk medical conditions, and essential workers?" He described in detail the population stratification, vaccine product assumptions, completeness of protection, vaccine allocation assumptions for Phase 1 and Phase 1b, epidemic dynamics, administration assumptions, and approximate timing of vaccine rollout (before incidence rises, as incidence rises, as incidence falls). In terms of findings, initially vaccinating high-risk adults or essential workers in Phase 1B averts approximately 1% to 5% more infections compared to targeting age 65+. This difference is greatest in the scenario in which the vaccine is introduced before incidence rises. The findings are robust to assumptions of reduced VE in older populations. Initially vaccinating age 65+ in Phase 1b averts approximately 1% to 4% more deaths compared to targeting high-risk adults or essential workers. As before, this difference is greatest in the scenario in which the vaccine is introduced before incidence rises. The percentage of deaths averted changes if VE is reduced in older populations. Initially vaccinating high-risk adults, age 65+, or essential workers in Phase 1b averts a similar percentage of deaths across the scenarios. Initially vaccinating age 65+ in Phase 1b averts approximately 2% to 11% more deaths compared to targeting high-risk adults or essential workers. Again, this difference is greatest in the scenario where the vaccine is introduced before incidence rises. The findings are robust to assumptions of reduced VE in older populations, but the percentage averted drops.

There are limitations to the study. The efficacy and ability of the vaccine candidates to prevent transmission, as well as the time vaccine may become available, is currently unknown. Modeled epidemic trajectories are only for illustration and are not forecasts. Overall averted burden should be interpreted cautiously, given that it will be sensitive to the future trajectory of the epidemic; findings reflect an idealized rollout with minimal delays and 100% uptake; and the aim of this study was to demonstrate the relative impact of different initial vaccine allocation strategies. The following inputs were assumed and will require reassessment as more

information becomes available: 1) all infections confer protective immunity; 2) immunity, either naturally- or vaccine-acquired, does not wane significantly within a year of infection or immunization; 3) given exposure, younger age groups are just as likely to become infected as older age groups (susceptibility independent of age); 4) individuals with comorbidities are just as likely as their peers to practice social distancing and other protective behaviors; and 5) there was no reduction in VE among those with high-risk medical conditions. The findings are consistent in sensitivity analyses where the percentage of the population infected prior to vaccine introduction was varied. In terms of consistency with external literature, a review of peer-reviewed and pre-publication studies that model the impact of vaccination under different initial allocation strategies shows generally agreement across study results with the results presented here.

Dr. Megan Wallace (CDC/NCIRD) provided updates to COVID-19 immunity and epidemiology to inform vaccine policy, including an overview of US COVID-19 epidemiology, COVID-19 post-infection immunity, COVID-19 reinfection, and epidemiology of COVID-19 in pregnant women. As of October 29th, there were 8,834,393 cases of COVID-19 and 227,045 COVID-19 deaths. From March 1, 2020 through October 17, 2020, the number of specimens tested and percent positive for SARS-CoV-2 from combined laboratories reporting to CDC was 6.3% at Week 42. In terms of what happens to anti-SARS-CoV-2 antibodies after infection, Rhesus macaques challenged with SARS-CoV-2 developed binding and neutralizing antibody responses. Re-challenge of rhesus macaques boosted SARS-CoV-2 antibody responses. In humans with SARS-CoV-2 infection, serum antibodies decline between the acute phase and 2 months post-discharge. In HCP with a history of mild SARS-CoV-2 infection, serum antibodies waned 2 months post-infection. Among hospitalized persons with SARS-CoV-2, neutralizing antibody titers demonstrated little to no decrease over 75 days since symptom onset. Pertaining to whether persons infected with SARS-CoV-2 mount cellular immune responses, in symptomatic COVID-19 patients, SARS-CoV-2 memory B-cells did not wane at the same rate as serum antibodies. Recovered COVID-19 patients have SARS-CoV-2-specific CD4+ T-cells and CD8+ T-cells. In conclusion, repeat exposure to SARS-CoV-2 may cause boosting of immune response. Several studies have now observed waning of serum antibodies in COVID-19 patients after a few months. However, the implications for protection are unknown. Neutralizing antibody titers demonstrated little or no decrease at 75 days post-symptom onset. SARS-CoV-2 specific cellular B- and T-cell responses have been detected in COVID-19 patients. Memory B cells did not wane as fast as serum antibody titers.

Dr. Mary Chamberland (CDC/NCIRD) discussed ethical principles for phased allocation of COVID-19 vaccines, which the COVID-19 Vaccine WG developed to assist ACIP in the identification of groups for early allocation of COVID-19 vaccine in the setting of a constrained supply. During the September 2020 ACIP meeting, 5 interim ethical principles were endorsed: Maximizing Benefits and Minimizing Harms, Equity, Justice, Fairness, and Transparency. During the July through August ACIP meetings, possible groups for Phase 1 vaccination were explored, including HCP in Phase 1a and essential workers (non-HCP), persons with high-risk underlying medical conditions, and adults aged ≥65 years in Phase 1b. The WG reviewed COVID-19 vaccine allocation frameworks including those from Johns Hopkins University (JHU), National Academies, and the World Health Organization (WHO). In addition, they reviewed the ethical literature and consulted with experts in health equity, ethics, and Grading of Recommendation Assessment, Development and Evaluation (GRADE). The interim ethical principles were updated to guide phased allocation and a manuscript was drafted on ethical principles to address key questions to guide allocation planning, and a health equity domain was incorporated into the Evidence to Recommendations (EtR) Framework. There are now 4 ethical principles (Maximizing Benefits and Minimizing Harms, Promote Justice, Mitigate Health

Inequities, and Promote Transparency), and updates to the interim version included folding fairness into justice and styling the principles as action phrases. A series of Key Questions was developed to: 1) facilitate "translation" of the ethical principles; 2) assist ACIP in developing its national recommendations for early phase COVID-19 vaccine allocation; and 3) serve as a tool for State, Tribal, Local, and Territorial (STLT) health authorities as they develop vaccination implementation plans. Although ethical principles are fundamental for stewardship of a limited supply of vaccine, they also will be applicable when COVID-19 vaccines are more widely available. Dr. Mary Chamberland described in detail each Key Question for COVID-19 vaccine allocation planning stratified by ethical principles.

Application of the principle of transparency across the entirety of the allocation decision-making process is essential for building public trust and confidence and being clear about the level of certainty in available evidence. Methods and data used for ACIP recommendations are publicly available and include public participation. ACIP meetings are open to the public and are available on-line. Comments can be made to the *Federal Register* and/or during ACIP meetings and when ACIP engages with stakeholders and partners. Allocation of a limited supply of vaccine is complicated by efforts to address multiple goals, most notably reducing morbidity and mortality and minimizing disruption to society, the economy, and healthcare capacity. If the goals of a vaccination program are not clearly prioritized, it will be difficult to draw distinctions between groups for early phase allocation. There is increasing consensus among allocation frameworks for early vaccination of HCP, suggesting that maintenance of healthcare capacity as the highest priority. If vaccine supply remains constrained, ethical principles can help to guide identification of subsets of other groups for subsequent early phase allocation. The next steps for the WG are to seek ACIP's views on the updated ethical principles and key questions, publish ACIP's ethical principles, and engage in further discussion about application of the ethical principles to help inform Phase 1 allocation recommendations. The WG requested feedback on how application of these principles and key questions could be made more useful to STLT health authorities for COVID-19 vaccine allocation planning.

Dr. Sara Oliver (CDC/NCIRD) presented the ACIP COVID-19 Vaccine WG's interpretation of the data. In terms of COVID-19 vaccine and prior infection, data from Phase 3 trials for any possible vaccine-associated enhanced disease or reactogenicity after prior infection are not yet available. In the absence of concerning data from Phase 3 trials, having positive PRC, antigen, or antibody results is not a contraindication to receive COVID-19 vaccine. Any vaccine recommendations that rely on knowledge of prior immunity/antibody testing would be difficult to implement. In terms of COVID-19 vaccine and breastfeeding women in Tier 1a, most WG members agreed that breastfeeding would not be a contraindication to receive a COVID-19 vaccine. However, this needs to be evaluated for each vaccine, especially if any live virus/vector vaccines are authorized/licensed. Regarding pregnant women in Tier 1a, limited data on pregnancy are expected from Phase 3 trials. The WG did not reach a consensus. The majority felt that if a woman is recommended to receive the vaccine in an early allocation phase, pregnancy should be a precaution but not a contraindication to receive a COVID-19 vaccine. The WG emphasized the need to allow women to make an informed decision, providing all current knowledge of COVID-19 vaccines/platforms with pregnancy and risk of disease. Concerning pregnancy diagnosed after receipt of the first dose of COVID-19 vaccine, the majority of the WG felt that the second dose could be given at the recommended interval. A minority of the WG felt that the second dose should be postponed until the second trimester or until after pregnancy, emphasizing the need to allow women to make an informed decision.

Regarding the WG's interpretation of the modeling data, the differences among the 3 strategies are thought to be minimal. Ethical principles and implementation considerations may greatly contribute to selecting the optimal sequence in Phase Ib. The largest impact in averted deaths and infections is the timing of vaccine introduction in relation to increases in COVID-19 cases. It is important to emphasize the need to continue non-pharmaceutical interventions (e.g., wearing a mask, social distancing) while awaiting available vaccine. Many factors will inform interpretation of modeling data and allocation decisions, such as VE in older adults, a vaccine's ability to prevent severe disease or transmission, and whether the goal is to prevent the greatest number of infections or greatest number of deaths. For vaccine candidates, both Novavax and Jenssen are planning and enrolling large Phase 3 efficacy trials of 30,000 to 60,000 people. The primary endpoints include symptomatic, virologically confirmed COVID-19 disease. Both companies are attempting to enroll diverse populations in terms of race and ethnicity, age (<65 years and ≥65 years of age), and underlying medical conditions.

Concerning implementation and distribution, the WG's interpretation is that Phase 2/3 data from the vaccines show induction of binding and neutralizing antibodies as well as T-cell responses, favorable safety/reactogenicity profiles, supporting advance to Phase 3 trials. Both platforms have prior experience from other vaccines. Safety pauses are expected with large clinical trials, indicating the process is working appropriately. For the current Phase 3 clinical trials, the WG stressed the importance of enrolling diverse study participants, the importance of harmonizing safety and efficacy endpoints across all Phase 3 trials to the extent possible, and the need to report maternal and fetal outcomes for women who become pregnant during the clinical trials. The WG supports FDA's guidance for ensuring that Phase 3 trials conduct ongoing assessment of long-term safety and efficacy, and that issuance of an EUA is not grounds to unblind follow-up in an ongoing clinical trial.

Dr. Kathleen Dooling (CDC/NCIRD) reviewed the COVID-19 vaccine policy questions for the EtR framework and critical and important outcomes. As a reminder, the goals of the COVID-19 vaccine program are to: 1) ensure the safety and effectiveness of COVID-19 vaccines; 2) reduce transmission, morbidity, and mortality of COVID-19 disease; 3) help minimize disruption to society and economy, including maintaining healthcare capacity; and 4) ensure equity in vaccine allocation and distribution. The two ACIP policy questions proposed by the WG are: 1) Should COVID-19 Vaccine "A" be recommended to adults in the US?; and 2) Who should be recommended to receive COVID-19 Vaccine "A" during Phase 1? The EtR framework assesses the domains of Public Health Problem, Benefits and Harms, Values, Acceptability, Feasibility, Resource Use, and Equity. Dr. Dooling reviewed the population, intervention, comparison, outcomes (PICO) for vaccine policy for Question #1, including the critical and important benefits and harms identified by the WG. The WG's next steps for Policy Question #1 (Vaccine Recommendations) are to populate the EtR framework, start GRADEing the vaccine evidence and incorporating Phase 3 data when available, and discuss clinical guidance for special populations, concomitant administration, and scheduling. For Policy Question #2 (Allocation Recommendations), the WG's next steps are to publish the ethical principles manuscript and incorporate the latest information regarding science, implementation, and ethics to further refine Phase 1 allocation. For the health equity domain criterion question, the following sub-questions were posed: 1) Are there any groups or settings that might be disadvantaged in relation to the problem or options that are considered?; 2) Are there plausible reasons for anticipating differences in the relative effectiveness of the option for disadvantaged groups or settings?; 3) Are there different baseline conditions across groups or settings that affect the absolute effectiveness of the option or the importance of the problem for disadvantaged groups or settings? Are there important considerations that should be made when implementing the

intervention (option) in order to ensure that inequities are reduced, if possible, and that they are not increased?

Discussion Points/Comments/Questions/Suggestions

- Regarding vaccine candidates:
  - → Blinded, placebo-controlled follow-up in ongoing trials should continue for as long as is feasible, including after EUA.
  - → Safety and vaccine hesitancy must continue to be addressed.
  - → With all of the vaccine candidates, it seems that local and systemic reactions are extremely common and should be anticipated.
  - → As with other vaccines, there is concern that COVID-19 vaccines may not work as well in adults ≥65 years of age.
  - → Inclusion of individuals with human immunodeficiency virus (HIV) in vaccine trials is imperative.
  - → There continue to be concerns about the potential for ERD.
  - → Safe and effective vaccines for children and pregnant women are a high priority.
  - → Transparency is crucial in all aspects of COVID-19 vaccines, including information about the cases that result in trial pauses, as this will impact sentiments pertaining to vaccines in general, vaccine confidence downstream, and the ability to control preventable diseases.
  - → Ultra-cold vaccines remain troubling in terms of logistics (transportation, storage, venues for administration).
  - → Diversity among trial participants and in terms of outreach and communication must be addressed.
  - → Standardization of convalescent sera would be useful for the field.

- From the broader healthcare perspective, there has been under-investment in vaccine implementation planning:
  - → ACIP expressed hope that going forward, CDC and others would be fully supported in this endeavor versus adding one more task to the already complex delivery system. Funding investments in this type of work is critical.
  - → Assuming that COVID-19 vaccine implementation will ramp up from January through March and more to do in April, there is concern that the Coronavirus Aid, Relief, and Economic Security (CARES) Act Provider Relief Fund that has paid for increases in the workforce will run out on December 31, 2020. Consideration must be given to what can be done at the state and local health department levels in terms of implementing COVID-19 vaccine activities if additional funding is not forthcoming.
  - → State and local jurisdiction funds are likely to depend upon local legislatures.
  - → There are major deficits in the healthcare delivery system, especially in primary care. More targeted support is needed for private practice to continue to deliver all types of vaccines.
  - → Implementation is where actual impact will happen or not. The same level of investment that has been made in vaccine development must be made in implementation. There must be national investment. While state support is important, federal support is crucial. This cannot be done in everyone's "free time." In order for implementation to be successful, the federal government must make a significant investment.

- → Typically, ACIP approves a vaccine and then leaves implementation up to the states. This situation offers a good opportunity for ACIP to permanently change the model by which it operates.

- ❑ The planning process for delivering vaccines to children will be very different from the process for adults, given that the majority of children's vaccines are given in pediatric offices and many providers do no participate in Vaccines for Children (VFC). Although children are likely to be the last in line and pediatric trials are just beginning, planning for delivery to children should be done now.

- ❑ Much can be learned from influenza vaccines (e.g., make vaccination simple and easy, use reminders, use already planned visits, fund and support these activities where possible).

- ❑ While each of the 64 jurisdictions presented creative and unique plans based on their own jurisdictional issues that should be beneficial, it is crucial to keep in mind that different communities have different issues regarding vaccine acceptance, such as communities of color and Tribes:

  - → Many communities of color experience issues due to ongoing systemic racism and disparities that lead them to have distrust. Therefore, it is critical to work with communities of color to engender and earn trust, while being completely up front. It is particularly important to engage with community-based organizations (CBOs) and doctors of color who practice in these communities.
  - → Concerns from Tribes focus on the very compressed timeline that does not allow for the IHS to engage in meaningful conversations. Tribes are being asked to make decisions about distribution, prioritization, et cetera without having all of the information they feel they need. Despite efforts to address these concerns, issues remain about how vaccine will be distributed, ordered, and reported on. Many Tribes want to be ready, but they are challenged by whether to choose distribution through states or through HIS. It is preferable to have both doors open.

- ❑ Confidence in receiving COVID-19 vaccine must be increased within the HCP workforce. If the group they trust the most will not take these vaccines, patients are not going to want to take them either:

  - → Lack of confidence among HCPs can be boosted by providing them with language that helps them answer questions about such topics as how vaccine was licensed so quickly when other vaccines take 15 years.
  - → HCPs are constantly being asked about whether they trust COVID-19 vaccines, to which some respond that when CDC and FDA say they trust it is when HCPs will recommend it.
  - → Given that HCPs are the most trusted vaccine deliverers, perhaps language should be included that permits them to be vaccinated in the first phase. Many private practitioners do not have access to personal protective equipment (PPE), yet they are the ones on the frontline to whom patients turn.

- ❑ Workers Compensation must be addressed.

- ❑ CDC is producing content that will be shared with partners in the near future. It is imperative for partners, HCP organizations, and community partners to amplify these messages as this will be much more powerful than messages coming just from CDC or HHS.

- ❑ Private practitioners have expressed interest in being able to order and receive vaccines through VTrckS. CDC encouraged them to speak with their local jurisdictions to enroll as providers in VTrckS, through which they can also order/receive vaccine.

- ❑ The two components of DUAs, identified and de-identified data, need to be separated in order to move quickly as vaccines become available.

- ❑ Many COVID-19 vaccines will require 2 doses, making it critical to be able to ascertain what vaccine was given for Dose 1 and when Dose 2 is needed:

    - → Efforts to determine this information with existing Immunization Information Systems (IIS) can be frustrating.
    - → State IIS for adults have lagged behind.
    - → Ensuring that people received both doses and the correct products is very important to CDC, so immunization cards will accompany ancillary kits in order to have both IIS records and paper and pen solutions.

- ❑ In terms of safety surveillance systems and safety monitoring plans:

    - → Given that safety surveillance is critical, this immense and collaborative effort is impressive.
    - → While the EHR can be a useful tool for data mining, finding AEs, and ensuring vaccines are distributed, it also has pitfalls that need to be stressed. Confidentiality goes without saying, but the biggest concern is that use of the EMR is burdensome in terms of implementation and use when data registration or data mining are involved. For private practice, this is burdensome and costly. If this is required and there is a cost to integrate it into the health record, it could fail in the community setting.
    - → The emphasis on collaboration among government agencies and groups working on vaccine safety in terms of harmonizing outcomes of interest, regular communication, and sharing data is very important and is applauded. This type of collaboration and coordination should continue through the entire process so that signals are investigated. This also should help to ensure that communicating to the public is well-coordinated, transparent, and consistent.
    - → It was observed that safety monitoring may be difficult in settings outside of VAERS and registries, such as monitoring vaccines administered in workplaces where employers have their own health insurance plans. This is an area that FDA is exploring.
    - → Concern was expressed about the ability of the systems described to monitor for MIS-C, wild-type or vaccine-induced, particularly with respect to the case definition requirement of a positive test or exposure to a suspected or confirmed case within 4 weeks prior to symptom onset.
    - → Concern was expressed about access to v-safe in under-served areas. It is important to be mindful that while most people have access to some form of communication, indigent populations may not have ongoing access to care. In addition, v-safe communication must be culturally sensitive.

- → Lessons learned from children being at home and not in school is that there are many barriers. As hard as it may be to believe, not everybody has internet access and many people purchase phone minutes for phones that are not smartphones. It would be beneficial to track or record v-safe use, perhaps by Zip Code, to ensure that it is inclusive of all communities in terms of access and recording long-term effects from the vaccine.
- → Consideration should be given to modernizing VAERS to accept data from EHRs and/or registries.

❑ Regarding modeling strategies for the initial allocation of SARS-CoV-2 vaccines:

- → This is an incredible, elegant, and impressive analysis and enormous amount of work.
- → From a clinical and public health medical consultant point of view, the assumptions in the model make sense. VE may be somewhat high, but it is reasonable.
- → Consider modeling the impact of poor nutrition, falling behind in school, and possible abuse and neglect if older adults are vaccinated first and schools remain closed. The modeling team noted that this is possible but may require more complex framework such as agent-based models that model people and societal parameters.
- → Consider modeling hospitalizations not just deaths. The modeling team noted that they started with infections and deaths because those estimates are easier to obtain, but infections and hospitalizations can be incorporated in future versions.
- → Consider modeling congregate care settings. The modeling team indicated that this was already done and was presented by Dr. Slayton during the August 2020 ACIP meeting. The take-away from that study was that vaccinating staff in these settings may be more beneficial than just vaccinating residents, likely because of infection-blocking such that the infection is not introduced into the congregate setting.
- → It is critical for ACIP to address equity and disproportionate impact on disadvantaged populations. Approaching this from a race/ethnicity standpoint is probably not the best approach.

❑ With respect to COVID-19 immunity and epidemiology to inform vaccine policy:

- → Pregnant and lactating women should not be excluded from high priority populations for COVID strategies and treated separately. More than 75% of the HCP workforce are females. For instance, pregnant HCP and first responders who are pregnant should be prioritized alongside their non-pregnant peers.
- → Though reinfection appears to be uncommon at this point, it will be beneficial to have further guidance on this as soon as possible.
- → The summary about what is known and unknown about reinfection was phenomenal. However, using language such as reinfection is “likely uncommon within 3 months” suggests more is known that actually is. Perhaps “may be uncommon within 3 months” would be less challenging for management.
- → It is imperative for messaging around vaccine to emphasizes that vaccines are not likely to be 100% effective and that other measures must be utilized in combination with vaccines. The vaccine is not a panacea and will not result in immediate full herd immunity.
- → Dr. James Lee invited health care institutions and local/state public health entities interesting in discussing more about reinfections to email eocevent461@cdc.gov.

- Pertaining to ethical principles:

  - → While there was agreement with and endorsement of the principles, some members were struggling with how they fit into the overall pandemic response—especially having seen projections earlier showing that it seems to matter less *who* gets the vaccine first as far as numbers of infections and deaths. That is, the principles seem less important than how soon the vaccine gets deployed.
  - → The WG pointed out that the modeling work measured only one dimension of the impact, aversion of cases and deaths. The ethical principles takes a more holistic view of several dimensions in the context of limited vaccine supply being guided by ethnical, scientific, and implementation considerations.
  - → The Key Questions to help guide and integrate the process seem beneficial and are greatly appreciated.
  - → One thing that will go a long way with the general population, especially in terms of trust and disparities, is a mechanism for reporting how vaccine products are actually being allocated.
  - → One decision with which ACIP will be faced will be assessing the data in terms of benefits and risks for various groups once a vaccine is available. If a vaccine becomes available in the next month or two, this will be a relatively short timeframe for efficacy and safety data. With no long-term safety data, it will be difficult to balance the benefits versus long-term issues that historically have arisen. Balancing the scientific and ethnical aspects is going to be difficult.
  - → The slide on promoting transparency harkens back to the earlier comments about Tribes and the dynamic tension that a compressed timeline is going to create.

- With respect to the WG's interpretation of the data:

  - → The American College of Obstetricians and Gynecologists (ACOG) urged ACIP to incorporate pregnant and lactating women clearly and explicitly in the prioritization framework should an EUA be issued.
  - → The American Academy of Pediatrics (AAP) agreed with the ACOG statement and defers to them on matters of pregnancy and pregnant women. AAP also emphasized the need to move to pediatric trials when the data suggest that it is safe to do so and should monitor fetal outcomes.
  - → It is important for pregnant and lactating women to make an informed decision. CDC is engaging ACOG and AAP and is working with colleagues with expertise in this area to development materials that can be provided at the time of vaccination.
  - → Related to the unblinding of clinical trials should an EUA become available, particularly for participants in vaccine trials in which efficacy and safety are demonstrated, it is troubling that participants potentially will not have the benefit of receiving vaccine once efficacy is demonstrated. These volunteers have assumed the risk of study participation and in most clinical trial circumstance would be among the first to potentially benefit once efficacy is demonstrated. It is recognized that this is an issue that must be dealt with by FDA and VRBPAC.

- Regarding whether ACIP members agree with the proposed COVID-19 vaccine policy questions and outcomes for the EtR framework:

  - → There was support for the two policy questions being evaluated separately and the important and beneficial outcome of serial PCRs for asymptomatic infection.
  - → This is an unprecedented situation in which consideration may need to be given to conditional recommendations, which should incorporate the principles of informed consent and some higher level of clinical decision-making.
  - → Perhaps consideration should be given to getting the vaccine out as quickly as possible to react to the modeling that says the faster vaccines are administered, the more death that will be prevented.
  - → This does not take into consideration any time-phased protection or safety other than the data that will be provided should an EUA come through in a relatively short period of time. This is a virus like nothing they have seen previously, so the unknown and bad possibilities are always a consideration. They can look at objective information and arrive at a conclusion to move forward with allocation, but that presumes that there is not going to be some later problem.
  - → Following participants for a mean of 2 months after the second dose as a timepoint to start making final decisions about safety is troubling. Concerns prevailed on making quick decisions on safety. While it is true that most AEs of interest will be captured in the first 6 weeks, there will be a need for long-term studies, particularly due to the potential for vaccine-enhanced disease. This highlights the need for a dynamic decision-making process.
  - → The WG has considered mortality, morbidity, and preventing spread in a lumped manner. In the context of unknowns, perhaps those should be disaggregated.
  - → The questions fit the PICO perfectly, with the caveat that there may be changes. There must be flexibility over time and flexibility in implementation. Local areas will have to deal with the reality of whether to save doses for Dose 2.
  - → Given the uncertainties, perhaps the WG should review the data on a monthly basis and update the recommendations to account for concerns in balance with benefits and harms.
  - → While the focus on safety is very important, it is also crucial to understand durability of the immune response.
  - → The ethical principles will be very important to local jurisdictions. Concrete guidance will be needed in terms of equity and a sense of fairness in terms of how allocations actually are implemented.
  - → Frequent messaging of information about COVID-19 vaccines will be very important to public confidence.

Acronyms

AAP	American Academy of Pediatrics
ACIP	Advisory Committee on Immunization Practices
ACOG	American College of Obstetricians and Gynecologists
AE	Adverse Event
AECI	Adverse Events of Clinical Interest
AESI	Adverse Events of Special Interest
BEST	Biologics Effectiveness and Safety
BOP	Bureau of Prisons
CBER	Center for Biologics Evaluation and Research
CDC	Centers for Disease Control and Prevention
CMS	Center for Medicare and Medicaid Services
COI	Conflict of Interest
COU	Clinical Operations Unit
COVID-19	Coronavirus Disease 2019
CoVPN	COVID-19 Prevention Network
CRO	Contract Research Organization
DE	Division of Epidemiology
DFO	Designated Federal Official
DNA	Deoxyribonucleic Acid
DoD	Department of Defense
DOS	Department of State
DSMB	Data Safety Monitoring Board
EHR	Electronic Health Record
ELISA	Enzyme-Linked Immunosorbent Assay
EMA	European Medicines Agency
EMR	Electronic Medical Record
ET	Eastern Time
EtR	Evidence to Recommendation
EUA	Emergency Use Authorization
FDA	Food and Drug Administration
GMT	Geometric Mean Titers
GRADE	Grading of Recommendation Assessment, Development and Evaluation
HCoVs	Human Coronaviruses
HCP	Healthcare Personnel / Providers
HCW	Healthcare Workers
HHS	(Department of) Health and Human Services
HIPAA	Health Insurance Portability and Accountability Act
HIV	Human Immunodeficiency Virus
IDCRP	Infectious Disease Clinical Research Program
IHS	Indian Health Service
IIS	Immunization Information Systems
IM	Intramuscular
IND	Investigational New Drug
IRB	Institutional Review Board
ISO	Immunization Safety Office
JHU	Johns Hopkins University
LTCF	Long-Term Care Facilities

NCEZID	National Center for Emerging and Zoonotic Infectious Diseases
NCIRD	National Center for Immunization and Respiratory Diseases
NVAC	National Vaccine Advisory Committee
OBE	Office of Biostatistics and Epidemiology
PCP	Primary Care Practitioner
PCR	Polymerase Chain Reaction
PICO	Population, Intervention, Comparison, Outcomes
PPE	Personal Protective Equipment
RSV	Respiratory Syncytial Virus
RT-PCR	Reverse Transcriptase Polymerase Chain Reaction
SAE	Serious Adverse Event
SARS	Severe Acute Respiratory Syndrome
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus-2
SLU	Saint Louis University
SME	Subject Matter Expert
STLT	State, Tribal, Local, and Territorial
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 Sub-Group
VE	Vaccine Efficacy
VE	Vaccine Effectiveness
VMED	Vaccine-Mediated Enhanced Disease
VRBPAC	Vaccines and Related Biological Products Advisory Committee Meeting
VSD	Vaccine Safety Datalink
VTU	Vaccine Treatment Evaluation Unit
WG	Work Group
WHO	World Health Organization