MEETING OF THE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES (ACIP)

FEBRUARY 28-MARCH 1, 2021

SUMMARY MINUTES

The Centers for Disease Control and Prevention (CDC) convened an emergency meeting of its Advisory Committee on Immunization Practices (ACIP) from February 28 to March 1, 2021. These summary minutes provide an overview of the meeting which was devoted solely to the topic of coronavirus disease 2019 (COVID-19) vaccines. **Dr. José R. Romero** (ACIP Chair) opened the COVID-19 vaccines session.
Dr. Beth Bell (ACIP Work Group (WG) Chair) gave an introduction, reviewed WG activities since the last meeting, and noted the Food and Drug Administration's (FDA) authorization on February 27, 2021 of the Janssen COVID-19 vaccine for emergency use in persons 18 years of age and older.

FEBRUARY 28, 2021

AGENCY UPDATE

FDA: Dr. Doran Fink (Deputy Director, Clinical, Division of Vaccines and Related Products Applications) provided a summary of the February 26, 2021 meeting of the FDA's Vaccines and Related Biological Products Advisory Committee (VRBPAC) which considered the Janssen COVID-19 vaccine. The Committee voted unanimously that the known and potential benefits of the Janssen COVID-19 vaccine outweigh its known and potential risks for the prevention of COVID-19 in individuals 18 years of age and older.

OVERVIEW OF JANSSEN'S SINGLE DOSE COVID-19 VACCINE, AD26.COV2.S

Dr. Macaya Douoguih (Janssen Pharmaceuticals Companies of Johnson & Johnson) presented an overview of Janssen's single dose COVID-19 vaccine, Ad26.COV2.S. Dr. Douoguih provided a detailed review of the preclinical studies, Phase I and II trials, and the ongoing randomized, double-blind, placebo-controlled Phase III safety and efficacy trial. The Phase III study enrolled >44,000 participants and was conducted during the height of the pandemic. Interim findings from the trial, using data from participants with a median of ≥2 months of follow-up, indicated that a single dose of Ad.26.COV2.S offers substantial protection, especially against severe disease including hospitalization and death. Vaccine efficacy was 66% against moderate to severe disease across all countries. Consistent vaccine efficacy against severe disease was observed across all regions, including in South Africa where the B.1.351 variant is highly prevalent. Overall vaccine efficacy was also consistent across subgroups by age, sex, race, comorbidities status, and ethnicity. Vaccine efficacy against COVID-19 related hospitalization was 93% ≥14 days after vaccination and 100% ≥28 days after vaccination. No COVID-19 related deaths occurred in the vaccine group, and all COVID-19 associated deaths occurred in South Africa. Preliminary data suggest that the Janssen COVID-19 vaccine might also provide protection against asymptomatic SARS-CoV-2 infection (vaccine efficacy= 74 %).
The Janssen COVID-19 vaccine demonstrated an acceptable safety and reactogenicity profile. Overall reactogenicity was mild, and Grade 3 reactogenicity was rare. Most adverse events were mild to moderate and resolved in 1-2 days post vaccination. Reactogenicity was overall milder in the older age group. Similar rates of unsolicited adverse events were observed between vaccine and placebo groups. No cases in this Phase III trial met Brighton Collaboration criteria for anaphylaxis. Hypersensitivity was reported in 0.4% of vaccine recipients and 0.3% of placebo recipients; rash and urticaria were the most commonly reported.

There was a numerical imbalance for venous thromboembolic events, but there is insufficient evidence to determine causal relationship. There are plans in place for continued safety monitoring.
The Janssen COVID-19 vaccine offers logistical advantages. It is a single dose and can be stored for 3 months at normal refrigerator temperatures. It has a 2 year shelf life when frozen and can be easily shipped using the existing supply chain. Studies are planned evaluating efficacy of a two dose regimen (results available later this year), evaluating immunogenicity and safety in children 0-17 years of age, evaluating pregnant women (planned to begin late March/early April), and evaluating immunocompromised individuals (planned to begin Q3 2021).

SUMMARY OF DISCUSSION

Janssen Team Members responded to questions from Committee members.

- Question about efficacy in the American Indian/Alaska Native (AI/AN) population
    - Overall low numbers in this subgroup, at 14 days post vaccination vaccine efficacy is 49%, but the confidence intervals are wide. They did not calculate vaccine efficacy for severe disease in this population due to small numbers.
    - Could this lower efficacy be attributed to circulating variants?
        - Do not have sufficient data to answer this at this time, but will continue to evaluate
- Question about efficacy and reactogenicity in participants who had a prior infection
    - About 9% of participants were seropositive at baseline, so there is limited data to evaluate
    - Local and systemic reactogenicity are comparable across people who were seropositive and seronegative at baseline
- Question regarding pregnancy
    - 8 total women who became pregnant after receiving this vaccine, but about 1600 women have been vaccinated with vaccines from the Ad26 platform who were pregnant or became pregnant after vaccination. Have not seen any safety signals to date
- Question regarding why a one dose platform was selected instead of two
    - Influenced by experience with Ad26 platform in Ebola setting, the tremendous advantage of 1 dose in an outbreak setting, and by preclinical data showing protection after a single dose.
    - Always planned to evaluate 2-dose series, but believe the single dose is optimal for a pandemic setting
- Question regarding efficacy including mild cases
    - Very few cases categorized as mild, so effectively no difference in efficacy
- Question regarding coadministration with other vaccines
    - Plans to study, but no data yet available
- Vaccine does not contain any fetal tissue
- Question regarding adults with comorbidities and the small numbers of cases
    - After day 14 the vaccine efficacy is in line with all other subgroups. The lower numbers are only after day 28 with much wider confidence bound and is likely an artifact of small numbers
- Question regarding biodistribution studies
    - Vaccine fragments persist in the body on average for 3 months, no issues have been seen related to this

- Question regarding efficacy against variants. Looks like high efficacy against severe disease, even in setting of variants. Will 2-dose scheduled be evaluated in countries with variants?
    - Yes, this study is enrolling in South Africa and the UK

GRADE: JANSSEN COVID-19 VACCINE

Dr. Julia Gargano (CDC/NCIRD) presented "GRADE: Janssen COVID-19 vaccine." The Work Group used the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach to assess the benefits and harms for the Janssen COVID-19 vaccine; results are summarized in Table 1.

Table 1. Summary of GRADE findings and evidence type for the Janssen COVID-19 vaccine

Outcome	Importance	Design (# of studies)	Findings	Evidence type
Benefits				
Symptomatic lab-confirmed COVID-19	Critical	RCT (1)	Janssen COVID-19 vaccine is effective in preventing symptomatic COVID-19	**2**
Hospitalization due to COVID-19	Critical	RCT (1)	Janssen COVID-19 vaccine prevents COVID-19-resulting in hospitalization	**2**
All-cause Death	Important	RCT (1)	Janssen COVID-19 vaccine is associated with a lower risk of both all-cause death and death due to COVID-19	**2**
SARS-CoV-2 seroconversion	Important	RCT (1)	Data from day 71 serology indicates that Janssen COVID-19 vaccine prevents seroconversion during the available follow-up period; data support an effect on prevention of asymptomatic infection	**3**
Asymptomatic SARS-CoV-2 infection	Important	No studies	No systematically collected PCR data are available to develop an estimate for this outcome	**ND**
Harms				
Serious adverse events	Critical	RCT (3)	SAEs were balanced between vaccine and placebo arms. 3 participants had SAEs judged by FDA to be related to study vaccine	**2**
Reactogenicity	Important	RCT (3)	Severe reactions were more common in vaccinated; any grade ≥3 reaction was reported by 2.5% of vaccinated vs. 0.7% of placebo	**1**

Evidence type: 1=high; 2=moderate; 3=low; 4=very low; ND, no data

EVIDENCE TO RECOMMENDATION FRAMEWORK: JANSSEN COVID-19 VACCINE

Dr. Sara Oliver (CDC/NCIRD) presented the "Evidence to Recommendation Framework: Janssen COVID-19 vaccine." The body of evidence for the Janssen COVID-19 vaccine was primarily informed by one large, international phase III clinical trial that enrolled >40,000 participants aged 18–100 years (median age = 52 years).

Benefits and harms

Dr. Oliver presented the Work Group's assessment of the benefits and harms of the Janssen COVID-19 vaccine within the Evidence to Recommendation Framework (EtR) using data from participants with a median of 2 months of follow-up. Outcomes graded were ≥14 days after vaccination with PCR confirmation from any source.

<u>Benefits</u>

- Overall efficacy was 66.3%. Higher efficacy was observed against the severe outcomes of hospitalization (93%), all-cause death (75%), and deaths due to COVID-19 (100%).

- Between four and ten weeks after vaccination, 10/1346 participants (0.7%) seroconverted, compared to 37/1304 (2.8%) of those receiving placebo. Vaccine efficacy against seroconversion was 74%.
- Similar efficacy was noted across age, sex, race, and ethnicity categories, and those with underlying medical conditions at ≥ 14 days post vaccination.
- Efficacy against severe disease remained high across world regions (73-82%), suggesting protection against severe illness with variant strains.

Harms

- Serious adverse events were reported in a similar proportion among recipients of vaccine and placebo (0.4% vs 0.4%).
- Severe reactions were more common in vaccine recipients; any grade ≥3 reaction was reported by 2.5% of vaccinated versus 0.7% of placebo group. Local reactions within 7 days occurred in ~50% vaccine recipients, with pain at the injection site being the most common. Systemic reactions within 7 days occurred in ~55% vaccine recipients with headache, fatigue, and myalgia being the most common. Most symptoms resolved after 1-2 days.
- Several adverse event imbalances of note: urticaria, tinnitus, and thromboembolic events.

The Work Group's assessment of the benefits and harms of the Janssen COVID-19 vaccine within the EtR Framework was as follows.

- From the GRADE evidence assessment, the level of certainty for the benefits of the Janssen COVID-19 vaccine was type 2 (moderate) for the prevention of symptomatic COVID-19. Evidence was also type 2 (moderate) for the estimated prevention of COVID-19–associated hospitalization and death. Evidence was type 3 (low) for the estimates of prevention of SARS-CoV-2 seroconversion. Regarding certainty of evidence for possible harms after vaccination, evidence was type 1 (high) for reactogenicity and type 2 (moderate) for serious adverse events.

Dr. Oliver reviewed the detailed evidence for each of the remaining domains in the EtR Framework.

Values

- Overall acceptability of a COVID-19 vaccine was moderate, with the proportion intending to receive vaccine ranging from 42-86% across 46 surveys. Vaccination intentions varied substantially by race/ethnicity and socioeconomic status.

Acceptability

- No published provider knowledge, attitudes, and practices surveys were available, but COVID-19 vaccination has been implemented in a variety of settings, with more than 72 million doses being administered as of February 27, 2021.

Feasibility

- The Janssen COVID-19 vaccine is a single dose with more convenient storage (3 months at refrigerator temperatures), but there is the potential for emerging challenges related to managing choice/preferences of providers and consumers for different vaccine products.

Resource Use

- During a pandemic, the best utilization of resources is to employ all vaccines with an acceptable vaccine efficacy.

Equity

- Feasibility of the Janssen COVID-19 vaccine to be implemented in a variety of settings is an opportunity to improve health equity.

The Work Group's judgements for each domain are summarized in Table 2.

Table 2. Evidence to Recommendation Framework domains and Work Group judgements for the Janssen COVID-19 vaccine

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 Janssen COVID-19 vaccine
	What is the overall certainty of the evidence for the critical outcomes?	2 (moderate) for prevention of symptomatic COVID-19 2 (moderate) for hospitalization 2 (moderate) for safety
Values	Does the target population feel the desirable effects are large relative to the undesirable effects?	Yes
	Is there important variability in how patients value the outcomes?	Probably important variability
Acceptability	Is the Janssen COVID-19 vaccine acceptable to key stakeholders?	Yes
Feasibility	Is the Janssen COVID-19 vaccine feasible to implement?	Yes
Resource Use	Is the Janssen COVID-19 vaccine a reasonable and efficient allocation of resources?	Yes
Equity	What would be the impact of the intervention on health equity?	Increased

The Work Group considered the balance of consequences overall for the Janssen COVID-19 vaccine and concluded that the desirable consequences clearly outweigh the undesirable consequences in most settings. Lastly, the Work Group considered the type of recommendation to bring to ACIP for deliberation. The Work Group's decision was "To recommend the intervention".

SUMMARY OF DISCUSSION

Dr. Oliver responded to Committee members' questions.

- Comment that ACIP needs to be very clear on messaging regarding this vaccine being safe and effective and the inability to directly compare across the three authorized vaccines
- Dr. Oliver also cautioned against comparing reactogenicity directly across the three authorized vaccines because it is dependent on how it was asked and other factors
- Question regarding thromboembolic events
    - Janssen responded that there is a slight imbalance but a large proportion of participants that had these events had predisposing factors, and they do not think there is a causal association with vaccine. They are committed to monitoring these events going forward.
- Question about when safety data results from Ebola trial in pregnant women will be published
    - These studies are ongoing, and will be some time before all data is available to be published, but Janssen will make every effort to publish relevant information as soon as possible
- Comment from Dr. Romero that we need stakeholders from Indian Health Services to weigh in on acceptability in the AI/AN population
    - Comment that lower efficacy numbers may be related to small numbers

THE VOTE

Dr. Oliver presented the proposed interim recommendation to the ACIP.

ACIP Vote – Interim Recommendation

> The Janssen COVID-19 vaccine is recommended for persons 18 years of age and older in the U.S. population under the FDA's Emergency Use Authorization.

THE VOTE

- ACIP voted 12-0 (1 recusal) in favor of the interim recommendation for use of the Janssen COVID-19 vaccine. One ACIP member recused themselves because of participation in clinical trials and/or other studies involving companies producing COVID-19 vaccines.

SUMMARY OF DISCUSSION AFTER THE VOTE

Committee members noted the following:

- Emphasized that we continue to face equity and access issues with vaccines, and we need to continue to ensure that equity is at the forefront of how we implement vaccine.

March 1, 2021

IMPLEMENTATION CONSIDERATIONS FOR COVID-19 VACCINES

Dr. Kathleen Dooling (CDC/NCIRD) presented "Implementation considerations for COVID-19 vaccines", reviewing implementation considerations for the Janssen COVID-19 vaccine, COVID-19 vaccine prioritization for all three authorized vaccines, and dosing intervals for mRNA vaccines.

- **Janssen COVID-19 vaccine implementation**
  - ACIP stated no preference in its interim recommendations for any of the three authorized vaccines. The three authorized vaccines are not directly comparable. They were studied at different times, with different circulating variants, and higher background incidence during the Janssen Phase III trial. The Janssen vaccine is one dose, can be transported and stored at 2-8°C, and requires no dilution. Jurisdictions may consider use in locations such as mobile or pop up clinics, newly established vaccine sites, and sites that don't have freezer capacity. The Janssen COVID-19 vaccine would be good for people who can't/don't want to return for a second dose or mobile or homebound populations.
  - The WG recommends offering Janssen COVID-19 vaccine to persons 18 years and older, according to established allocation and eligibility recommendations in a given jurisdiction.
    - This allows for jurisdictional flexibility, supports rapid vaccination, does not single out any group, and allows individuals to be vaccinated with the earliest available vaccine
- **COVID-19 Vaccine prioritization**
  - As of February 27th, more than 72 million doses have been administered, but jurisdictions continue to face constrained supply and reliance on large vaccination centers. Most states have made modifications to the ACIP prioritization framework.
  - Implementation Challenges and Considerations
    - Adjudicating eligibility in large vaccination centers can be challenging, and medical care homes/primary care providers may better be able to assess eligibility based on

underlying medical conditions. Clinical judgment may determine if rare conditions not on the list confer increased risk of severe COVID-19.
        - The size of eligible groups in Phase 1c may exceed vaccine supply and could consider addition of eligibility age band <65
        - To address transmission in congregate settings (prisons, homeless shelter, LTCFs) could consider offering vaccine to all unvaccinated staff and residents at the same time
        - To promote heath equity while ensuring efficient vaccine distribution and administration could use social vulnerability index to place clinics, partner with Federally Qualified Health Centers to help register eligible community members for vaccination, and offer Janssen as an option for populations for whom returning may be difficult.
- **Dosing intervals for mRNA vaccines**
    - Considerations around delaying the second dose
        - Extended inter-dose intervals have been adopted by other national vaccine advisory groups and proposed by individuals in the US as a strategy to increase 1 dose coverage during a time when demand may exceed supply
        - In Phase I and II clinical trials, neutralizing antibodies did not show large increases until after receipt of a 2nd dose, and in Phase III trials, almost everyone received doses on schedule. Early studies of real word efficacy of 1-dose of mRNA vaccines in Israel and Scotland showed efficacy of 78-85%.
        - Pros to delaying: Could provide protection to a larger number of people in the next several months, and boosting is likely to be effective even at a longer interval
        - Cons to delaying: 1-dose could leave individuals susceptible to variants and increase transmission of variants, and it would contradict FDA's EUA
        - The WG thought there was insufficient data to increase recommended intervals and there is important uncertainty regarding protection from variants following one dose of mRNA COVID-19 vaccines
    - Considerations for giving a single dose to people with confirmed prior SARS-CoV-2 infection
        - There have been reports of increased reactogenicity following vaccine for people with prior COVID-19, and reports suggest high antibody after 1 dose for people with prior infection. Two studies evaluated a single dose for people with confirmed prior infection and both showed higher titers following 1 dose for seropositive persons compared to seronegative persons. Systemic side effects occurred at a higher frequency among individuals with preexisting immunity.
        - Pros: Could free up second doses from seropositive persons to provide to seronegative persons, and seropositive persons would not receive 2 doses of a reactogenic vaccine
        - Cons: Performing large scale antibody screening prior to vaccination is not feasible, there is limited data currently available, and a single dose would contradict FDAs EUA
        - The WG felt there was insufficient data to suggest changes to guidance or recommendations, and we should consider promotion of existing guidance that those with prior infection may choose to temporarily delay vaccination for several months
- Any updates to recommendations will be discussed publicly, will be evidence based, and will be made in collaboration with FDA

SUMMARY OF DISCUSSION

- Question regarding death and severe disease by race/ethnicity
  - For minority groups, a higher proportion of deaths occurred among younger age groups
- Question regarding list of high risk conditions on CDC webpage
  - List is not exhaustive and was intended for individuals to understand their risk, not be used to certify eligibility for vaccination. List is currently being updated
- Discussion around specific questions for ACIP
  - **Do you agree that offering Janssen COVID-19 vaccine to persons 18 years and older, according to established allocation and eligibility recommendations, is an effective implementation strategy?**
    - Committee agrees
    - Comment from a committee member that we should discuss how we can target use of this vaccine to help get more people vaccinated and who we should give guidance to further the goal of vaccinating more people and increasing equity
    - Comment from a committee member that it would be less efficient and less evidence based to treat the Janssen vaccine separately
    - Concern that if we recommend the Janssen COVID-19 vaccine be used in mobile clinics or hard to reach populations, it may introduce mistrust
    - The American College of Obstetricians and Gynecologists (ACOG) does not have a preference of vaccine for use in pregnant women
    - Comment from a committee member that the ethical framework and allocation strategy previously recommended are very well thought out and we should maintain these for the Janssen vaccine
    - Comment from a committee member that ACIP needs to message correctly that this vaccine is effective in prevention of hospitalization and deaths and needs to be offered to everyone
  - **What are the key challenges and opportunities of implementation guidance options for**
    - **additional age eligibility brackets <65 years?**
      - Committee members are not in favor of this because while it is easier to distribute vaccine, it leads to inequity
    - **eligibility based on 2 or more high risk condition?**
      - Concern for this to create administrative barriers
      - One committee member expressed that we should continue with our current guidance and not require certification of conditions for vaccine eligibility
      - Concerns that the list of high risk conditions is a problem and there is a need to address that it is not exhaustive
      - Concerns that requiring 2 or more conditions would create inequity
      - Committee member expressed concern that particularly in younger populations, they may only have 1 condition and don't want to exclude them
        - Additionally, pregnancy is a high risk condition, so requiring two conditions would exclude most of these pregnant women
  - **What additional data is needed to inform**
    - **delaying the second dose?**

        - Committee members agree that there is not enough data to support this recommendation
    - **giving a single dose of mRNA vaccine for individuals with confirmed prior SARS-CoV-2 infection?**
        - Some committee members expressed that they feel we have enough data for this and could recommend now
        - One member would like to see more data on harms in this group
        - Several committee members expressed a need more data on longevity of protection from prior SARS-CoV-2, more data on correlates of protection, and more data related to variants
        - Committee member expressed that this needs to be a priority for study so ACIP can make evidence based recommendations

CLINICAL CONSIDERATIONS FOR USE OF COVID-19 VACCINES

Ms. Jessica MacNeil (CDC/NCIRD) summarized clinical considerations for use of COVID-19 vaccines, including proposed updates to currently published clinical considerations to include the Janssen COVID-19 vaccine. Any COVID-19 vaccine can be used when indicated; ACIP has no product preference. Safety and efficacy of a mixed series has not been evaluated. In exceptional situations where 1 dose of an mRNA vaccine has been received, but the patient is unable to complete the series, a single dose of the Janssen COVID-19 vaccine may be administered at a minimum interval of 28 days. COVID-19 vaccines should be administered alone or at a minimum interval of 14 days before or after other vaccines; however, a shorter interval may be used when the benefits of vaccination are deemed to outweigh the risks. Vaccination should be offered to persons regardless of history of prior symptomatic SARS-CoV-2 infection. Vaccination should be deferred until recovery from acute illness and criteria have been met to discontinue isolation. While vaccine supply remains limited people with recent infections may choose to delay vaccination. Any currently authorized COVID-19 vaccine can be administered to persons with underlying medical conditions who have no contraindications to vaccination. Immunocompromised individuals may receive vaccine unless otherwise contraindicated but should be counseled about unknown safety of COVID-19 vaccines in immunocompromised persons. There is limited safety data of COVID-19 vaccines in pregnant women, but clinical trials are planned or underway to evaluate this. Pregnant women may choose to receive COVID-19 vaccine when eligible. Persons with a contraindication to mRNA COVID-19 vaccines have a precaution to Janssen COVID-19 vaccine, and vice versa.

SUMMARY OF DISCUSSION

- Discussion around specific questions for ACIP
    - Does ACIP agree with the proposed clinical considerations related to vaccination?
        - ACIP agrees
    - Are there any sections of the clinical considerations the ACIP would like to discuss?
        - Question from a committee member regarding the precautions – Waiting because of a precaution puts people at risk, so is there a place to clarify that for most people, vaccination is still indicated that day after discussion with staff at the vaccine site
            - Will update to clarify
        - CDC is looking very closely at co-administration and evaluating safety data to determine if the recommended minimum interval can be relaxed

- Comment regarding pregnant women- would the Janssen COVID-19 vaccine be preferrable because of the lower reported fever with that vaccine?
    - Do not want to limit opportunity for vaccination in this group, and guidance does say acetaminophen can be given if temperature rises
- Suggestion to consider a different word than "inactivated" vaccines for clarity

COVID-19 VACCINE SAFETY UPDATE

Dr. Grace Lee (ACIP, VaST Co-chair) gave an introduction and reviewed the purpose of VaST and past and current activities.

Dr. Tom Shimabukuro (CDC/NCEZID) presented a COVID-19 vaccine safety update.

- V-safe update: smart phone based text to web survey with daily check ins for the first week
    - As of February 16, 2021 approximately 55 million doses have been administered and V-safe has 3,897,982 registrants. Reported systemic reactions following the second dose of Pfizer-BioNTech are substantially higher. This is consistent with what was seen in clinical trials. Data for Moderna was not available at the time of analysis.
- VAERS update: national passive surveillance system, not designed to assess causality
    - There are 104,763 reports in VAERS. The initial safety profiles of these vaccines are consistent with what was observed in the clinical trials and is reassuring.
- Update on anaphylaxis following COVID-19 vaccine
    - The updated reporting rate of anaphylaxis is 4.7 per million doses administered for Pfizer-BioNTech and 2.5 per million per doses administered for Moderna.
- VSD update
    - Data are available on 629,523 vaccinees for dose 1, and 200,134 vaccinees for dose 2. No signals have been reported as of February 13, 2021.
    - Will conduct dose and product specific analyses
- CISA responded to 331 clinical inquiries/consultation requests about COVID-19 vaccine safety
- Maternal vaccination safety summary
    - Not seeing substantial differences in local or systemic reactions in pregnant women
    - V-safe pregnancy registry
        - As of February 19th there are 1,815 participants enrolled and there have been 275 completed pregnancies including 232 live births, with no significant difference in pregnancy outcomes or complications compared to background rates
    - Most reports to VAERS among pregnant women involved non-pregnancy specific adverse events

Dr. Grace Lee (ACIP, VaST Co-chair) summarized VaST's assessment of the safety data. Consistent with clinical trial data, local and systemic reactions continue to be the most commonly reporting following vaccination in v-safe, VAERS, and VA-ADERS. Pregnancy and birth outcomes following COVID-19 vaccination appear similar to rates reported in the literature. Maternal vaccine safety data from multiple sources will be regularly reviewed. Future vaccine safety surveillance activities will include the newly approved Janssen COVID-19 vaccine. VaST will continue to update ACIP on a regular basis.

SUMMARY OF DISCUSSION

Dr. Lee and Dr. Shimabukuro responded to Committee members' questions.

- Is there any data from v-safe on limiting daily activity/missing work as a result of reported reactions?
  - VaST will look into this for future meetings
- Are we seeing reports of anaphylaxis or severe allergic reaction to the second dose of mRNA vaccines?
  - Most cases occur after the first dose, there are a few after the second dose, but the data is from early on in the vaccination program
- Committee member noted that venous thromboembolism looks higher than expected
  - Dr. Shimabukuro explained that for some of these rare events enough follow up time has not been accumulated, but when looking at the unvaccinated concurrent comparator analysis that does not rely on follow up time, there is not a difference. Additionally while it may look higher, no statistical signals have been observed.
- Suggestion to consider adding question on lab confirmed SARS-CoV-2 infection before vaccination
- Question regarding background rate of pregnancy outcomes not being controlled for age, race, etc and not matching the group enrolled in the v-safe pregnancy registry
  - Dr. Shimabukuro responded that we capture demographic information in the v-safe pregnancy registry and may be able to do these sub analyses as we have more data
- Question regarding monitoring post-authorization safety data of Janssen being limited by potential lower enrollment in v-safe if used at mass vaccination clinics
  - VaST will conduct enhanced surveillance for the Janssen vaccine in VAERS to ensure it is being monitored closely

EMERGING SARS-COV-2 VARIANTS

Dr. Heather Scobie (CDC/CGH) presented "Emerging SARS-CoV-2 Variants: Considerations for Vaccine." Multiple SARS-CoV-2 variants are circulating globally. Viruses constantly change through mutation, so new variants are expected, but SARS-CoV-2 has a low mutation rate compared with influenza and HIV. The D614G variant likely has increased transmissibility, but is not more clinically severe, and current vaccines are still highly effective. Three variants are of concern have been identified: B.1.1.7, B.1.351, and P.1.

- B.1.1.7 first detected in the UK
  - Detected in 2,400 cases in 46 states
  - Current prevalence in US is 1-2%
  - One modeling study suggest that high vaccine coverage will blunt the public health impact of the variant's higher transmissibility
- B.1.351 first detected in South Africa
  - Detected in 53 cases in 16 states
- P.1 first detected in Brazil/Japan
  - Detected in 10 cases in 5 states
- Impact of variants on vaccine effectiveness
  - Reviewed 26 available studies and the largest impacts were seen for B.1.351, P.1, and B.1.1.7
  - Postponing 2nd mRNA dose may leave some less protected against variants as minimal or no neutralization of B.1.351 is seen after one dose and improved neutralization of B.1.1.7 and

B.1.351 is seen after 2nd dose. However, it is difficult to estimate how these laboratory results might translate to clinical protection.
    - All of the reviewed studies have limitations due to small sample sizes and a lack of generalizability
    - B.1.1.7 has exponentially increased in prevalence in the US, but has a minimal impact on vaccine effectiveness
    - B.1.351 currently has low prevalence in the US, but moderate impact on vaccine effectiveness
    - Current prevention measures and authorized vaccines offer protection against SARS-CoV-2 variants, and periodic update of SARS-CoV-2 vaccines is likely needed
- Response to variants
    - CDC is monitoring variants through genomic surveillance and reviewing epidemiology
    - Moderna and Pfizer are launching booster studies of current vaccines in the US and developing second-generation vaccines against B.1.351
    - We will continue to monitor evidence on the emerging SARS-CoV-2 variants, vaccine effectiveness, breakthrough infections in vaccinated or previously infected persons, and ability of postvaccination serum to neutralize emerging variants

SUMMARY OF DISCUSSION

Dr. Scobie responded to Committee members' questions.

- Question regarding what is known about RNA recombination
    - Limited reports but it is not clear that this is a major source of variation in SARS-CoV-2
- On a local public health level would be great to have more information on how a variant ends up becoming a variant of concern
    - Working on developing more definitions around this
- Someone noted that Florida appears to have more variants and inquired why
    - Potentially related to high transmission in Florida, may also be due to earlier introduction of a variant
- Question regarding increased rate of refractory disease in immunocompromised persons. Will this group be an area of focus?
    - Not aware of current studies but agree this is an important focus
- Comment from committee member that this presentation emphasizes that we should continue with two dose regimen for mRNA vaccines
- Question about if any differences are seen in children with regards to variants
    - Outside of B.1.1.7, overall these variants do not have impact on clinical outcome
    - B.1.1.7 may be associated with increased severity, but there is not currently evidence specific to children
- Question regarding speed to market for a second generation vaccine and recommendations around those vaccines
    - Will need to wait for data to be submitted to FDA for review