California Health and Human Services Agency (CHHS)

California Department of Public Health (CDPH)

COVID 19 VACCINE SCIENTIFIC SAFETY REVIEW WORKGROUP

November 12, 2020 - 5:00pm – 6:30pm

MEETING SUMMARY

Workgroup Members Attending

Tomas Aragon, MD, Health Officer, City & County of San Francisco; **Eric Goosby, MD**, Distinguished Professor of Medicine and Director of the Center for Global Health Delivery, University of California, San Francisco; **Rodney Hood, MD**, Trustee, Alliance Healthcare Foundation; **Nicola Klein, MD**, Director, Kaiser Permanente Vaccine Study Center; **Grace Lee, MD**, Professor of Pediatrics and Associate Chief Medical Officer for Practice Innovation, Stanford Children's Health; **Bonnie Maldonado, MD**, Professor and Chief of the Division of Infectious Diseases, Department of Pediatrics, Stanford Medicine; **Arthur Reingold, MD**, School of Public Health Division Head of Epidemiology and Biostatistics, University of California, Berkeley; **Mark Sawyer, MD**, Infectious Disease Specialist, Rady Children's Hospital; **Rob Schechter, MD**, Chief, California Department of Public Health, Immunization Branch; **Peter Szilagyi, MD**, Professor and Vice Chair for Clinical Research, Department of Pediatrics and Mattel Children's Hospital; **Matt Zahn, MD,** Medical Director, Communicable Disease Control Division, Orange County Health Care Agency

California State Representatives Attending

Erica Pan, MD, Interim State Health Officer; **Tricia Blocher**, Deputy Director, Office of Emergency Preparedness, California Department of Public Health **Ron Chapman**, MD, MPH, Former Director, California Department of Public Health.

Western States Representatives Attending

STATE OF WASHINGTON:

John Dunn, MD, Medical Director for Preventive Care and Head of Immunization Program, Kaiser Permanente Washington

Ed Marcuse, MD, MPH, FPIDS, Emeritus Professor, Pediatrics, University of Washington

STATE OF NEVADA:

Ihsan Azzam, MD, Chief Medical Officer, Division of Public and Behavioral Health

Candice McDaniel, Health Bureau Chief, Bureau of Child, Family, and Community Wellness

STATE OF OREGON

Laura Byerly, MD, Chief Medical Officer, Virginia Garcia Health Center

Luke Strnad, MD, Assistant Professor of Medicine, Division of Infectious Diseases, OHSU, Assistant Professor of Epidemiology Programs, OHSU/PSU

Consultants:
Bobbie Wunsch, Founder and Partner, Pacific Health Consulting Group
Laura Hogan, Senior Health Consultant, Pacific Health Consulting Group

Welcome, Review Agenda and Introductions of New Members
Arthur Reingold, MD, Chair
New Workgroup Members' Introductions from Western States

Dr. Reingold welcomed workgroup members and participating representatives from Nevada, Oregon, and Washington. Members and other participants introduced themselves.

Dr. Pan welcomed everyone and offered her thanks for members' time and service to the state of California. We know you are extremely busy and appreciate your willingness to advise us. Ambassador Goosby has agreed to continue on this workgroup along with participating in the National COVID Transition Team.

Dr. Reingold noted the surge of COVID cases across the country and the unfortunate news that California has reached one million COVID cases. He remarked that this underscores the need for the workgroup and the urgency of the safety review. Members will be called together at short notice, soon after approval of any vaccine, to review data and make recommendations.

As discussed at the first meeting, the Scientific Safety Workgroup was intentionally convened with overlapping membership from the Advisory Committee on Immunization Practices and (ACIP) and the Vaccines Related Biological Products Advisory Committee (VRBAC) as a way to coordinate and align efforts. Dr. Reingold also commented that there are ongoing conversations with the Centers for Disease Control and Prevention (CDC) to ensure timely access to vaccine data results for the workgroup.

Follow-Up of Workgroup Organizational Issues
Tricia Blocher, Deputy Director, Office of Emergency Preparedness, CDPH

Ms. Blocher reported that staff are continuing to work on items related to how the workgroup will operate, including public engagement, conflict of interest disclosures, and level of detail for meeting summaries. Meetings will likely include some combination of public comment and workgroup member deliberation. An update with final guidance will be forthcoming soon.

She described the three prong organizational structure of the effort. There is a Scientific Safety Workgroup, a Drafting Guidelines Workgroup, and a Community Advisory Committee. The role of the Scientific Safety Review Workgroup is to review vaccine(s) data and provide independent recommendations to inform vaccine efforts in California and the partner states and to reassure the public about the safety of the vaccine(s). The Drafting Guidelines Workgroup will develop

detailed guidance for local health departments and health systems on the prioritization and equitable allocation of the COVID-19 vaccine(s), especially important for the early phases when supplies will be scarce. The Drafting Guidelines Workgroup will define, categorize, and enumerate the specific priorities within the initial target population of healthcare workers to provide guidance and ensure public transparency about how vaccine(s) are allocated. The Community Advisory Committee is a larger entity, comprised of stakeholders and partners from a broad array of organizations and communities. The main purposes of the Community Advisory Committee are to review information from the Scientific and Drafting Workgroups, engage communities, bring input from constituents to inform planning, and serve as trusted messengers to increase public trust in the vaccine(s).

Member Comments and Discussion

Conflict of Interest

- As you consider operational issues like conflict of interest and public engagement, will there be input to the process from participating states or will California set these expectations?
- CDPH: I will take that issue to the legal team to determine a process.
- We view the overlapping membership with ACIP and VRBPAC as an advantage and not any type of conflict. One of our members also has been asked to join the National Institute of Health, National Institute of Allergy and Infectious, Disease Data and Safety Monitoring Board for COVID-19 vaccines. As with other committees, this membership does not seem to constitute any conflict.
- If anyone is being funded by one of the companies developing COVID-19 vaccines to do studies of the COVID vaccines, it should be disclosed.
- When there is a process for conflict of interest and disclosure in the next few weeks, members will have additional opportunity for discussion.

Clinical Trial Enrollment, Safety and Efficacy for Specific Population Groups

- Links shared by members:
- Pfizer data: https://www.pfizer.com/science/coronavirus/vaccine
- Moderna data: https://www.modernatx.com/cove-study
- SHEA Statement for Healthcare Settings Preparing for COVID-19 Vaccination:
- https://sheaonline.org/images/resources/101420_VaccinePlanningConsiderations.pdf
- The news media reported that Pfizer would have 50% of their population with two doses and two months of follow up by the 3rd week of November.
- Members discussed the availability of data from Pfizer and Moderna related to clinical trial enrollment by race, age, and other population groups. The Pfizer

website mentions that 30% of those enrolled in the clinical trial are under-represented minorities. (see link above).

- There may not be stable estimates of efficacy in subgroups. It is possible the safety data will be more robust since they are larger.
- There was a request made to ACIP to understand whether there are any differences in efficacy or safety profiles by age, race, ethnicity, and co-morbid condition.
- In the past, there have been discussions with experts at the CDC about whether they have evidence of differential vaccine effectiveness by race among the flu vaccine, HPV vaccine or childhood vaccines. Several experts responded they have never seen any evidence of a difference in vaccine effectiveness by race. There is a difference in the likelihood of acquiring COVID for racial and ethnic minorities. It is unclear how much of that is because of being essential workers, or living in more crowded conditions, or other reasons. However, we have not seen evidence for different efficacy by race with other respiratory vaccines.
- Additionally, I have not seen any evidence that there are differential safety data by race.
- I have assumed increased incidence in certain racial and ethnic groups reflect the social determinants of health in our country and nothing genetic. Does anybody have different information?

Public Opinion

- The trust in a vaccine by the public may depend on whether vaccine trial enrollees look like America.
- There are national online surveys every two weeks, of individuals representative of the United States, about their likelihood of getting a COVID vaccine. Black individuals are significantly less likely, right now, to say that they would get a COVID vaccine if it was available. Asian individuals are more likely than Whites to say they are likely to get a COVID vaccine. Latino respondents are about the same as White individuals to say they are likely to get the COVID vaccine. The overall percentage of people who say that they are likely to get a vaccine has dropped by 20% between April and two weeks ago, just before the election. And it appears to be directly correlated to trust in the government evaluation of the vaccine(s).

Preliminary Data and Discussions from ACIP and VRPAC

ACIP Members on Workgroup
Feedback from Members, Scientific Safety Review Workgroup
Art Reingold, MD, Chair

Dr. Grace Lee reviewed slides prepared by staff from the Centers for Disease Control and Prevention. Dr. Lee referenced information on the six vaccines currently in clinical trials in the United States from Pfizer, Moderna, University of Oxford/AstraZeneca, Janssen, Novavax, and Sanofi/GSK manufacturers. She referenced data on the type of vaccine, phase of trial, schedule, age groups enrolled, size and status of the trial. Dr. Lee also reviewed specific information for each vaccine such as the number of doses required, distribution and storage requirements, clinical trial enrollment goals, and status of current enrollment numbers. She commented that the phase three trial enrollment goals are larger than generally available (ranging from 30,000 to 44,000 individuals). From a safety perspective, that will be a positive factor. She referenced immunogenicity and safety information, where available for vaccines. She also reported that all vaccines appear to have local and systemic reactions. There will be a need to educate vaccine recipients to anticipate the local and systemic reactions, so that reactions do not become a contra-indication in the mind of recipients for getting the second vaccine dose. Finally, she presented the COVID-19 Vaccine Clinical Development Timeline with estimated timing for clinical trial phases and submission to the FDA for approval for five of the six vaccines.

Member Comments and Discussion

Case Counts

- Pfizer reports 94 positive cases. Originally, they intended the case cutoff to be about 35 or 36 cases at which time they would go to the Data and Safety Monitoring Board (DSMB). After guidance came out, it seems they waited to reach 50 to 60 cases. During this time, COVID surged and there were more positive cases in the trial. On the plus side, if they had unblinded the trial at 30+ cases, we would have less data and less confidence about the vaccine efficacy estimates in addition to safety.
- For the final analysis, they need to reach something around 134 cases based on adding an interim analysis and adding 14,000 enrollees.

Deployment

- Looking at the Pfizer product, what is it about the mRNA that provides promise, given the logistical issues of storage and the two dose requirements?
- You can make the mRNA faster. The mRNA vaccines are easier to make, and that is why they are the first to the finish line. It does require low temperature storage and I am concerned this raises equity issues on the implementation side, related to the accessibility of this vaccine. For example, it cannot easily deploy in a mobile clinic.
- CDC is working to have pharmacies deliver vaccines to help mitigate concerns on access.
- There are deployment discussions that indicate Pfizer may be deployed primarily to larger facilities. Pfizer may work on a zero degree variant to lower the storage

requirement barrier, but it will take time. Deployment at the community level is a state decision.

- CDPH: California is considering how quickly the vaccine can be available in communities and how the five-day refrigeration window relates to deployment. The state is also tracking how quickly the Moderna vaccine may become available. In addition, local health departments are considering how to partner with hospitals to set up pods to vaccinate skilled nursing facility staff or other organizations that will not get vaccine doses directly.
- One implication of two doses is that there is a need to ramp up capacity quickly to meet the need for first and second doses.

Update on Timing of Phase III Trials
Members, Scientific Safety Review Workgroup
Art Reingold, MD Chair

This issue was covered in the slides previously presented.

Issues for Future Workgroup Meetings
Feedback from Members, Scientific Safety Review Workgroup
Art Reingold, MD, Chair

Dr. Reingold introduced the topic of future meetings. The assumption is that new vaccines will become available over several months on an uncertain timeline. This has implications for whether this group should continue to be available and for what timeframe. In addition, there are issues related to safety that arise from studies conducted after the initial roll out of each vaccine. That raises questions about the duration and role of the group after the initial period of COVID vaccine deployment.

CDPH reported that the term for the workgroup has not been determined.

Member Comments and Discussion

Timeline and role of the workgroup

- If the primary role for the workgroup is to reassure the public that COVID vaccines were properly vetted, the need for this function may evolve and diminish over time.
- Also, the term for this workgroup may depend on the safety profiles and unexpected events that occur down the road. We have confidence in the staff of the FDA and CDC. Our function is “trust but verify”. Given the

current climate, if there are adverse events that require a rapid cycle analysis or other things the public is not familiar with, there may be a need for this group to continue for a time.

- We need a trusted voice of vaccine safety locally. Perhaps that lives with CDPH to become that voice to translate to communities, so the information is not coming from Washington, DC or Atlanta, but from local, trusted leaders.

- A key issue is to balance how to provide additional reassurance without undermining the important national advisory committee structure.

- That balance is key. There is evidence in the vaccine hesitancy literature indicating that, for many people, the level of trust is greater the closer they feel to the group delivering the message. Therefore, it may bring an increased level of confidence for this workgroup to give a stamp of approval in addition to having a recommendation from federal agencies because we are in California and other Western States and closer in terms of public trust.

- On the flip side, we would need compelling evidence to come up with a different conclusion than the FDA. Otherwise, we could exacerbate distrust of the process.

- Some colleagues have expressed concern about the wisdom of creating state level groups, such as this one. However, given the high level of distrust, it sems there is reason for a "trust and verify" function.

- Can we anticipate the groups that may have more concerns about the vaccine and think about how we might "pre-target" natural leaders in the community for briefings that go into detail and demonstrate transparency about what we know and don't know to improve trust in specific communities?

Additional Meeting Topics

- Another topic for discussion relates to sorting out safety data as multiple trials proceed, and vaccines become licensed.

- We should discuss when we would shift to non-inferiority trials instead of placebo trials and the implications of that.

- The majority of safety events will be captured in the post-market safety surveillance systems. The need for continuing trials is going to be related to understanding of the long-term efficacy and effectiveness. It will take time to accumulate that data without blind trials, yet we need to protect people as vaccines become licensed. Perhaps we need a presentation from a clinical trialist expert to discuss these issues.

- CDPH: Providers and consumers will be directed to Vaccine Adverse Event Reporting System (VAERS). All providers will sign requirements on the promotion and use of VAERS. There is high quality surveillance through to the Vaccine Safety Datalink (VSD) in California. We are using the National Health Safety Network (NHSN) data to track outbreaks in congregate care settings.
- The immunization registry will record doses, and participating in the registry is a contractual requirement for receiving vaccines, therefore compliance will be high. The registry does not systematically record adverse events, but it is useful as an ancillary source of data to match doses to other safety data sources.

- A useful tool is the National Healthcare Safety Network (NSHN). It is used by all hospitals and long-term care facilities to report healthcare associated infections and they are building a module to monitor healthcare personnel vaccination status at the aggregate level. It is not at the individual level as immunization registries require. It would be denominator and numerator numbers with numbers of healthcare workers vaccinated and the number of clinically significant adverse events that occur in facilities across the country. California and the Western States would be a huge block of health care facilities if they would agree to use the NHSN. CDC is also promoting the V-Safe system that would do active monitoring of any symptoms post vaccination.

- CDPH: This is not currently mentioned in the CDC provider agreement.

- We should discuss using Chatham House rules (defined as a meeting where participants are free to use the information received, but neither the identity nor the affiliation of the speaker(s), nor that of any other participant, may be revealed).

- Given the vaccine will be limited at first and targeted to healthcare workers, would it be useful to discuss excluding the subgroup of healthcare providers that have had COVID?

- This question has come up. The discussion was that, if you were infected within the last three months, we would not be suggesting you get the vaccine.

- It may be important to discuss what equity looks like for healthcare workers. We are not just talking about healthcare workers as doctors and nurses, but all the people who work in healthcare settings, including respiratory therapists and workers in the laundry.

- Of the 12- 20 million people who are healthcare workers, they are disproportionately minority.

Closing Comments and Adjourn
Arthur Reingold, MD, Chair

Thanks to everyone for attending. Meetings are currently scheduled for November 19, 2020 and December 3, 2020. The meeting on November 19 may be cancelled. The exact timing for meetings remains flexible. There will be a meeting immediately following availability of data.