Food and Drug Administration
Center for Biologics Evaluation and Research

SUMMARY MINUTES
162nd VACCINES AND RELATED BIOLOGICAL PRODUCTS ADVISORY COMMITTEE

December 10, 2020

Committee Members
Hana El Sahly, M.D., Chair +
Archana Chatterjee, M.D., Ph.D.
CAPT. Amanda Cohn, M.D.
Hayley Gans, M.D.
Holly Janes, Ph.D. +
Michael Kurilla, M.D., Ph.D.
Myron Levine, M.D., D.T.P.H., F.A.A.P. +
H. Cody Meissner, M.D.
Paul Offit, M.D.
Steven Pergam, M.D., M.P.H.
Andrea Shane, M.D., M.P.H., M.Sc. +
Paul Spearman, M.D. +
Geeta K. Swamy, M.D. +

Industry Representatives
Paula Annunziato, M.D.
Gregg Sylvester, M.D., M.P.H. <+

Consumer Representative
Sheldon Toubman, J.D. *

Designated Federal Officer's (DFO)
Prabhakara Atreya, Ph.D.
Kathleen Hayes, M.P.H.

Committee Management Specialist(s)
Monique Hill, M.H.A.

* Consumer Representative
+ Not in attendance
< Alternate Industry representative

Temporary Voting Members
Arnold Monto, M.D. (Acting Chair)
A. Oveta Fuller, Ph.D.
David Kim, M.D., M.A.
Eric Rubin, M.D., Ph.D.
James Hildreth, Sr., Ph.D., M.D.
Jeannette Lee, Ph.D.
Juan Gea-Banacloche, M.D.
Mark Sawyer, M.D., F.A.A.P.
Melinda Wharton, M.D., M.P.H.
Ofer Levy, M.D., Ph.D.
Pamela McInnes, D.D.S., M.Sc.
Patrick Moore, M.D., M.P.H.
Ralph Tripp, Ph.D.
Stanley Perlman, M.D., Ph.D.

Speakers and Guest Speakers
Anita Patel, Pharm.D., M.S.
Aron Hall, D.V.M., M.S.P.H., Dipl. A.C.V.P.M.
Doran Fink, M.D., Ph.D. - FDA
Kathrin Jansen, Ph.D. - Sponsor
Nancy Messonnier, M.D.
Steven Goodman, M.D., Ph.D.
Susan Wollersheim, M.D.- FDA
William C. Gruber, M.D. - Sponsor

FDA Participants
Marion Gruber, M.D.
Philip Krause, M.D.
Peter W. Marks, M.D., Ph.D.
CDR. Valerie Marshall, M.P.H., P.M.P.
Celia M. Witten, Ph.D., M.D.
Jerry Weir, Ph.D.

These summary minutes for the December 10, 2020 Meeting of the Vaccines and Related Biological Products Advisory Committee were approved on January 6, 2021.

I certify that I participated in the December 10, 2020 Meeting of the Vaccines and Related Biological Products Advisory Committee and that these minutes accurately reflect what transpired.

_____/s/_____
Prabhakara Atreya, Ph.D.
Designated Federal Officer

_____/s/_____
Arnold Monto, M.D.
Acting Chair

On December 10, 2020 at 9:00 a.m. Eastern Standard Time (EST), the 162nd Meeting of the Vaccines and Related Biological Products Advisory Committee (VRBPAC) met in open session to discuss EUA of the Pfizer-BioNTech COVID-19 Vaccine for the prevention of COVID-19 in individuals 16 years of age and older.

Dr. Arnold Monto, the Acting Chair, called the meeting to order. The DFO made administrative remarks, conducted roll call and invited the committee members to introduce themselves, and read the Conflict of Interest (COI) statement into the public record. It was stated that one conflict of interest waiver was issued under 18 U.S. Code 208 in connection with the meeting and the waiver was posted on the FDA website for public disclosure.

Dr. Doran Fink of FDA provided an introductory presentation titled “Emergency Use Authorization Overview and Considerations for COVID-19 Vaccines.” This was followed by a presentation by Dr. Aron Hall from the Centers for Disease Control and Prevention (CDC) entitled, "Epidemiology of COVID-19 in the United States.” Following Dr. Hall’s presentation, the Committee was released for a 10-minute break. Following the break was a vaccine safety and effectiveness overview presentation by Dr. Nancy Messonnier from the CDC titled “COVID-19 vaccine post-authorization safety and effectiveness monitoring.” Once her presentation concluded, Dr. Anita Patel, also with CDC, presented “Distribution Overview.” Dr. Steven Goodman with Stanford University School of Medicine then presented “Considerations for placebo-controlled trial design if an unlicensed vaccine becomes available.”

After a 45-minute lunch break, the Open Public Hearing (OPH) session was held for 60 minutes during which 21 public pre-registered speakers made presentations and oral comments. The names of OPH speakers and their oral remarks may be obtained from the transcript posted on the website. Following the OPH session, the presentations resumed starting with the Sponsor’s (Pfizer Inc.) presentation by Moderator, Kathrin Jansen, Ph.D., and then by William Gruber, M.D. titled “BNT162b2 Vaccine Candidate Against COVID-19.” Dr. Susan Wollersheim with FDA then presented “FDA Review of Efficacy and Safety of Pfizer-BioNTech COVID-19 Vaccine Emergency Use Authorization Request.”

After the presentations concluded and a 10-minute break, the Committee then proceeded with

discussions and recommendations portion of the meeting. There were two discussion items presented to the Committee, with no vote:

1) Pfizer has proposed a plan for continuation of blinded, placebo-controlled follow-up in ongoing trials if the vaccine were made available under EUA. Please discuss Pfizer's plan, including how loss of blinded, placebo-controlled follow-up in ongoing trials should be addressed.

2) Please discuss any gaps in plans described today and in the briefing documents for further evaluation of vaccine safety and effectiveness in populations who receive the Pfizer-BioNTech Vaccine under an EUA.

The committee discussed potential implications of loss of blinded, placebo-controlled follow-up in ongoing trials including how this may impact availability of safety data to support a biologics license application. Some pointed out the importance of long-term safety data for the Pfizer-BioNTech COVID-19 Vaccine as it is made using a technology not used in previously licensed vaccines. In response to the question whether the ongoing Phase 3 study would still be sufficiently powered if eligible placebo recipients would be vaccinated, Pfizer asserted that even with an anticipated loss of placebo-controlled follow-up of 20%, the study would maintain adequate statistical power and would be positioned to accrue additional data on vaccine efficacy, including efficacy against severe disease, as well as safety, although unblinding of the study would reduce interpretability of results. It was pointed out that non-random loss of placebo recipients from the study, as would be expected when unblinded placebo recipients would receive vaccination based on Advisory Committee on Immunization Practices (ACIP) recommendations, would further reduce interpretability of results. There was also discussion of a blinded trial design proposed by Dean Follmann, Ph.D. of NIH in which duration of efficacy would be compared in clinical trial participants originally vaccinated with the vaccine to those later administered the vaccine as part of a planned blinded cross-over. Pfizer stated that this design was considered but would present logistical challenges including the need for reconsenting subjects and additional study visits.

The lack of data on how the vaccine impacts asymptomatic infection and viral shedding was also pointed out and that this should be addressed prior to study unblinding. Other committee members were concerned about limited data available in certain subpopulations such as HIV-infected individuals, individuals with prior exposure to SARS-CoV-2 and certain demographic groups.

The committee inquired about information regarding anaphylactoid reactions occurring in 2 individuals vaccinated with the Pfizer/BioNTech vaccine in the UK. Pfizer briefly summarized the available information, i.e., the two cases of anaphylactoid reactions were in individuals with a strong past history of allergic reactions both of whom carried an epinephrine auto injector. These individuals developed symptoms of anaphylactoid reaction shortly after receiving the vaccine. Both recovered after appropriate treatment. FDA referred to its analysis of safety data derived from the ongoing pivotal trial that excluded subjects with allergic reactions to previous vaccine administrations but did not exclude subjects with non-vaccine related allergies. A slight numerical imbalance of adverse events potentially representing allergic reactions, with more

participants reporting hypersensitivity-related adverse events in the vaccine group compared with the placebo group (137 vs. 111). None of these were considered to be serious, and none of these events occurred in the immediate post-vaccination period. FDA noted that the fact sheet and prescribing information for Pfizer-BioNTech COVID-19 vaccine will include information under the contraindications section that the vaccine should not be administered to individuals with known history of a severe allergic reaction to any component of the vaccine. Under the warning section, there will be a statement that appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of Pfizer-BioNTech COVID-19 Vaccine.

In reference to the voting question, and prior to the committee members casting their votes committee members asked FDA's perspective on use of the vaccine in pregnancy. FDA explained that data from the preclinical developmental and reproductive toxicity study for this product are expected soon. Even though there are insufficient data to inform vaccine-associated risks in pregnancy, there are also no data warranting a contraindication. Some committee members expressed concerns about including adolescents 16 and 17 years of age in the indication for the vaccine because of the limited amount of safety and efficacy data available in this population. Other committee members encouraged authorization of the vaccine under EUA in adolescents because this would support initiating pediatric clinical trials and because benefits would be expected to outweigh any theoretical risks in this population. Inclusion of vaccines against COVID-19 in the pediatric vaccination schedule will ultimately likely be needed to increase the uptake of the vaccine and to reach herd immunity. Pfizer is planning studies in pediatric subjects using an age-stratified step-down approach. Some committee members raised concerns about the small number of severe COVID-19 cases and limited conclusions about the prevention of severe disease based on the study endpoints. FDA pointed out that vaccine development has a long history and that FDA is not aware of an example of any vaccine that is effective against mild disease that is not also effective against severe disease and that even though limited, data for Pfizer-BioNTech COVID-19 Vaccine suggest efficacy against severe disease.

Following the discussion topics, the Committee then went into the voting portion of the meeting. One voting question was put forward to the Committee:

1) Based on the totality of scientific evidence available, do the benefits of the Pfizer-BioNTech COVID-19 Vaccine outweigh its risks for use in individuals 16 years of age and older?".

The results of the vote were as follows: Yes = 17, No = 4, Abstain = 1. Thus, the committee voted in favor of a determination that based on the totality of scientific evidence available, the benefits of the Pfizer-BioNTech COVID-19 Vaccine outweigh its risks for use in individuals 16 years of age and older.

Following the vote, the meeting was then adjourned on December 10, 2020 at 5:35 PM EST.

Additional information and details may be obtained from the transcript and the recording of the webcast of the meeting that may be viewed at:
https://www.youtube.com/watch?v=owveMJBTc2I&feature=youtu.be