Chicago Scientific Vaccine Work Group Report
December 13, 2020

Based on concerns about potential political pressure on the Food and Drug Administration (FDA) to approve a COVID-19 vaccine, the Chicago Department of Public Health assembled an independent group, the Chicago Vaccine Scientific Work Group, to assess the integrity of FDA processes that resulted in granting an Emergency Use Authorization (EUA) for the Pfizer-BioNTech COVID-19 vaccine. Members of the Work Group have expertise in vaccinology, clinical trials, health disparities, bioethics, data analysis, infectious diseases, pediatrics, reproductive health, regulatory affairs, and public health. The goal of this Work Group was not to perform an independent analysis of safety and efficacy data, or to usurp the FDA's role, but to evaluate the quality of FDA's decision-making process.

Background

The FDA's EUA process was developed after 9/11 in recognition that there might be a need for a rapid review, evaluation, and deployment process to address serious public health risks due to chemical, biological, radiological, or nuclear threats. Notably, for COVID-19, on January 31st, 2020 Secretary of HHS Azar declared it a public health emergency and on March 13th, 2020 the President declared a national emergency.

EUAs for a vaccine can be issued by the FDA when:

1. An agent is identified that can cause a serious or life-threatening disease or condition;
2. Based on the totality of scientific evidence available, including trials if available, it is reasonable to believe that the product may be effective to prevent, diagnose, or treat such serious or life-threatening disease or condition;
3. The known and potential benefits of the vaccine outweighs its known and potential risks and;
4. There is no adequate, approved, and available alternative.[1]

The COVID-19 pandemic has had a devastating impact on the United States, where it is currently responsible for nearly 3,000 deaths each day. In Chicago, nearly 4,000 individuals have died due to COVID-19 since March of this year, along with severe disruption to children's education, the economy and many other aspects of daily life. Although the pandemic has affected all communities, low-income and communities of color have been disproportionately impacted, worsening disparities that existed before the pandemic began. For this crisis to end, safe and effective vaccines must become available for billions of people worldwide, and millions here in metropolitan Chicago. Additionally, general vaccine acceptance and confidence in the process that evaluates new vaccines under the FDA's EUA process is also essential. The Chicago Scientific Vaccine Work Group was assembled to review that process, in hopes of providing additional confidence

[1] Emergency Use Authorization of Medical Products and Related Authorities Guidance for Industry and Other Stakeholders, January 2017. https://www.fda.gov/media/97321/download.

to health care providers and the public, and to inform CDPH should any areas of concern be identified.

When evaluating the safety of a new drug or vaccine the FDA does not have an absolute standard. Safety must be considered in the context of the circumstances in which a drug or vaccine is used. For example, some life-saving cancer chemotherapy drugs have a long list of potentially serious side effects, but when balanced against the risk of dying of terminal cancer, their use is sensible. Important considerations about the safety of vaccines include: 1) they are given to millions of healthy people, and this shifts the balance—vaccine risks should be small; and 2) in our current situation, the risk of not having a vaccine must be recognized. Widespread COVID-19 illness, sometimes severe, is occurring even among previously healthy people. And those with only asymptomatic or mild SARS CoV-2 infection can cause others to become ill—which can result in hospitalization, and death.

On October 6, 2020 (before Pfizer submitted its EUA application), the FDA published new criteria for COVID-19 vaccine EUAs, including vaccine efficacy criteria (at least 50%), and an average of two months of participant follow-up after completion of the full vaccination series.[2]

On November 20, 2020, Pfizer submitted an EUA application to the FDA for use of its COVID-19 messenger RNA (mRNA) vaccine in individuals 16 years of age and older. Pfizer's submission included thousands of pages of safety and efficacy data on over 43,000 clinical trial participants for review by FDA experts.

On December 10, 2020, the FDA held a public meeting with its Vaccines and Related Biological Products Advisory Committee (VRBPAC) to seek input on Pfizer's EUA request. VRBPAC is an independent scientific advisory committee of scientists with a wide range of expertise in vaccine development, virology, clinical trials, statistics, and public health, as well as a consumer representative. Screening for conflicts of interest (COIs) occurs prior to each meeting, and members cannot participate if they have a COI.

Chicago COVID-19 Scientific Vaccine Workgroup Review

Work Group members reviewed numerous materials posted on the FDA website, including FDA COVID-19 Vaccine Guidance documents; FDA and Pfizer "briefing books" (produced independently and based on raw clinical trial data); presentation slides by the Centers for Disease Control and Prevention (CDC), the FDA, and Pfizer; as well as viewing the proceedings. Links to meeting materials and a video of the proceedings are provided in Appendix 1.

Key takeaways and observations from Work Group members from the December 10 VRBPAC meeting and materials and the FDA EUA for the Pfizer-BioNTech COVID-19

[2] Emergency Use Authorization for Vaccines to Prevent COVID-19 Guidance for Industry October 2020. https://www.fda.gov/media/142749/download

vaccine are summarized below. (This summary includes only high-level information about vaccine clinical trial data; in-depth information, including FDA's independent analysis of clinical trial data, is available on the FDA website.)

- The FDA's decision-making criteria were transparent, and the process for granting an EUA for the Pfizer-BioNTech vaccine demonstrated adherence to its October 2020 COVID-19 Vaccine Guidance for Industry, which detailed processes and recommended scientific data and information needed to support an emergency use authorization decision**.** This guidance included a recommendation to convene a VRBPAC meeting prior to making a decision about authorizing any COVID-19 vaccine.

- The information in the FDA's briefing book and VRBPAC presentations are indicative of comprehensive, independent, and in-depth analysis. Information reviewed by FDA scientists included individual case reports for trial participants, not just summary data submitted by Pfizer. FDA scientists' analysis of clinical trial data from trial participants confirmed Pfizer's report that the efficacy of two doses of vaccine in preventing confirmed COVID-19 in Pfizer's clinical trial was 95.0% in the overall study population. In addition, FDA scientists concluded that follow up of trial participants for an average of two months after the second dose indicate a favorable safety profile across a variety of demographic groups, with no specific safety concerns identified that would preclude issuance of an EUA. Side effects were common, but usually mild or moderate and resolved within a few days after vaccination. FDA scientists noted that minimal safety and efficacy data were available for 16-17 year-olds, but concluded that results from older adolescents justified including 16-17 year-olds in an EUA.

- FDA scientists clearly stated that more needs to be learned about various aspects of the Pfizer-BioNTech vaccine's efficacy, as well as its safety profile. This is a new vaccine, so long-term follow-up has not taken place, and rare adverse events (e.g. one in a million) are unlikely to have been detected in clinical trials to date. Examples of important gaps in current evidence are summarized in Appendix 2. Importantly, an extensive process of safety and adverse event monitoring has been established and is planned for at least a 2-year follow-up period. It is anticipated that Pfizer will apply for a Biologics License in 2021, which will entail an additional review process and at least a 6-month follow up period.

- Input from VRBPAC committee members during the December 10 meeting indicated they had vetted the clinical trial data carefully, and did not question the accuracy of FDAs (or Pfizer's) representation of the data. At the conclusion of the meeting, VRBPAC members were asked to vote on the following question, with a "yes" vote indicating support for an EUA: "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?" VRBPAC voted overwhelmingly in favor of an EUA: Yes (17), No (4) and Abstain (1). Three of the "No" votes and the abstention were reportedly due to concerns about inclusion of 16- and 17-year-olds in the EUA, because of their small number in the clinical trial and the low incidence of severe disease in this age range. The fourth "No" vote was

reportedly related to a preference for use of Expanded Access protocols rather than an EUA to support vaccination of healthcare workers and long-term care residents.[3]

- In November 2020, Peter Marks, MD, PhD, Director of the FDA's Center for Biologics Evaluation and Research underscored the FDA's commitment to a thorough review and vowed to resign if an EUA was issued before a vaccine was shown to be safe and effective: "You have to decide where your red line is, and that's my red line. I would feel obligated (to resign) because in doing so, I would indicate to the American public that there's something wrong." Throughout the December 10th VRBPAC hearing, the Committee's independence, input from the public, and presentations by multiple members of the CDC and FDA's evaluation and regulatory areas combined with the prior release to the public of extensive documentation supports the conclusion that this was an unbiased, careful review process.

  On December 11, 2020, FDA issued an EUA for use of the Pfizer-BioNTech vaccine in individuals 16 years of age and older. In an FDA press release, Dr. Marks stated: "Efforts to speed vaccine development have not sacrificed scientific standards or the integrity of our vaccine evaluation process."

Conclusions

The FDA's evaluation of Pfizer's clinical trial data was rigorous, and the decision-making process for issuing the EUA for the Pfizer-BioNTech vaccine was transparent and sound. The FDA's decision to issue an EUA for the Pfizer-BioNTech COVID-19 vaccine was grounded in science, with careful consideration of currently known benefits and risks, in the setting of a public health emergency. Accelerated vaccine development and approval did not sacrifice scientific standards or the integrity of the FDA evaluation process.

As underscored by FDA scientists and VRBPAC, ongoing data collection and evaluation, and more studies are needed in order to address evidence gaps, *e.g.*, the need for more information to inform use of the vaccine in pregnant women and children, and more information related to vaccine use in populations under-represented in Pfizer's clinical trial. Moreover, special efforts will be needed to help communities distrustful of government understand the importance of post-vaccination safety monitoring, and to ensure such monitoring does not increase vaccine hesitancy. Collaboration between Federal, State, City, and community partners is essential for meeting these challenges, and to ensure the public can be confident in COVID-19 vaccines, which hold the promise of ending the pandemic.

[3] https://www.businessinsider.com/why-experts-voted-no-to-pfizers-covid-19-vaccine-2020-12

Appendix 1. December 10, 2020 Vaccine and Related Biologics Advisory Committee Meeting Materials (A recording of the meeting is available at: https://www.youtube.com/watch?v=owveMJBTc2I&feature=youtu.be)

Vaccines and Related Biological Products Advisory Committee 12/10/20 Draft Agenda
Vaccines and Related Biological Products Advisory Committee 12/20/20 Draft Roster
Vaccines and Related Biological Products Advisory Committee 12/10/20 Presentation - FDA Review of Efficacy and Safety of Pfizer-BioNTech COVID-19 Vaccine EUA Request
Vaccines and Related Biological Products Advisory Committee 12/10/20 Meeting Briefing Document- FDA
Vaccines and Related Biological Products Advisory Committee 12/10/20 Meeting Briefing Document- Pfizer
Vaccines and Related Biological Products Advisory Committee 12/10/20 Meeting Presentation - Discussion Questions
Vaccines and Related Biological Products Advisory Committee 12/10/20 Meeting Presentation - Voting Question
Vaccines and Related Biological Products Advisory Committee 12/10/20 Presentation - BNT162b2 Vaccine Candidate Against COVID-19
Vaccines and Related Biological Products Advisory Committee 12/10/20 Presentation - Considerations for Placebo-Controlled Trial Design If An Unlicensed Vaccine Becomes Available
Vaccines and Related Biological Products Advisory Committee 12/10/20 Presentation - COVID-19 Vaccine Post-authorization Safety and Effectiveness Monitoring
Vaccines and Related Biological Products Advisory Committee 12/10/20 Presentation - Distribution Overview
Vaccines and Related Biological Products Advisory Committee 12/10/20 Presentation - EUA Overview and Considerations for COVID-19 Vaccines
Vaccines and Related Biological Products Advisory Committee 12/10/20 Presentation - Epidemiology of COVID-19 in the United States
Vaccines and Related Biological Products Advisory Committee 12/10/20 Presentation - FDA Review of Efficacy and Safety of Pfizer-BioNTech COVID-19 Vaccine EUA Request
Vaccines and Related Biological Products Advisory Committee 12/10/20 Meeting Waiver to Allow Participation- James Hildreth
Vaccines and Related Biological Products Advisory Committee 12/10/20 Meeting Acknowledgement of Financial Interest- James Hildreth

Appendix 2. Pfizer-BioNTech COVID-19 Vaccine Risk, Benefit and Data Gaps

Unknown Benefits/Data Gaps

1. Duration of protection
2. Effectiveness in certain populations at high-risk of severe COVID-19 (e.g., immunocompromised individuals)
3. Effectiveness in individuals previously infected with SARS-CoV-2
4. Effectiveness in pediatric populations
5. Future vaccine effectiveness as influenced by characteristics of the pandemic, changes in the virus, and/or potential effects of co-infections.
6. Vaccine effectiveness against asymptomatic infection
7. Vaccine effectiveness against long-term effects of COVID-19 disease
8. Vaccine effectiveness against mortality
9. Vaccine effectiveness against transmission of SARS-CoV-2
10. Efficacy of a single vaccine dose

Unknown Risks/Data Gaps

1. Safety in certain subpopulations (e.g. children less than 16 years of age, pregnant and lactating individuals, and immunocompromised individuals)
2. Adverse reactions that are very uncommon or that require longer follow-up to be detected
3. Determination of what severe allergic reaction history should be considered a contraindication to vaccine use
4. Vaccine-enhanced disease