Review Memorandum

Date:	**December 8, 2021**
To:	**The File**
From:	**Peter Marks, MD, PhD (CBER/OD)**
Applicant name:	**Pfizer, Inc., on behalf of Pfizer and BioNTech**
Application Number:	**EUA 27034**
Product:	**Pfizer-BioNTech COVID-19 Vaccine**
Subject:	**CBER assessment of a single booster dose of the Pfizer-BioNTech COVID-19 Vaccine (0.3 mL) administered to individuals 16 to 17 years of age after completion of a primary vaccination series with the Pfizer-BioNTech COVID-19 Vaccine or COMIRNATY**

This memorandum provides a summary, review, and recommendation on the submission by Pfizer Inc. (Pfizer), on behalf of BioNTech Manufacturing GmbH (BioNTech), to amend the emergency use authorization (EUA) of the Pfizer-BioNTech COVID-19 Vaccine to include administration of a single homologous booster dose to individuals 16 to 17 years of age at least 6 months after completion of a primary series with the Pfizer-BioNTech COVID-19 Vaccine or COMIRNATY (COVID-19 Vaccine, mRNA).

Executive Summary

The Pfizer-BioNTech COVID-19 Vaccine's currently authorized indication is for active immunization to prevent COVID-19 caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals age 5 years and older. The vaccine is authorized for use as a 2-dose primary series in individuals 5 years of age and older, with a third primary series dose authorized for use in individuals 12 years of age and older with certain immunocompromising conditions. A single booster dose of the Pfizer-BioNTech COVID-19 Vaccine is authorized for use in individuals 18 years of age and older following completion of a primary series of the Pfizer-BioNTech COVID-19 Vaccine or COMIRNATY[1] (homologous booster) or following completion of primary vaccination with another FDA-authorized COVID-19 vaccine (heterologous booster). The authorized interval between completion of primary vaccination and booster dose for a homologous booster is at least 6 months, and for a heterologous booster is the same as that authorized for a booster dose of the vaccine used for primary vaccination.

The current submission is a request to expand the eligible population for the use of a homologous booster dose to include individuals 16 to 17 years of age, thereby authorizing the administration of a single booster

[1] COMIRNATY and the Pfizer-BioNTech COVID-19 Vaccine for ages 12 years and older, when prepared according to their respective instructions for use, can be used interchangeably without presenting any safety or effectiveness concerns.

dose to individuals 16 years of age and older at least 6 months after completion of a primary vaccination series with the Pfizer-BioNTech COVID-19 Vaccine or COMIRNATY.

Data reviewed in support of this request included the regulatory submission with a benefit-risk assessment from Pfizer, data submitted previously by Pfizer to support use of a homologous booster dose under EUA in individuals 18 years of age and older, and real-world data from experience with use of a Pfizer-BioNTech COVID-19 Vaccine booster dose in Israel and the United States.

Data previously provided by the sponsor indicated that a booster dose of the Pfizer-BioNTech COVID-19 Vaccine administered to study subjects 18-55 years of age after an average of 6 months following completion of a 2-dose primary series resulted in a neutralizing antibody geometric mean titer ratio of 3.3-fold for the geometric mean titer one month after the booster dose relative to the geometric mean titer one month after completion of the primary series. Additional immunogenicity data supported activity of neutralizing antibodies elicited by the vaccine against the SARS-CoV-2 Delta variant.

Additional data evaluated by FDA included the recent epidemiology of COVID-19 in the United States indicating a widespread increase in the number of cases, as well as real world evidence from Israel and the United States indicating the risk of myocarditis and pericarditis following third doses of the Pfizer-BioNTech COVID-19 Vaccine given to 16-17 year old males (the population at highest risk for vaccine-associated myocarditis and pericarditis) appears to be lower than the risk after the second primary series dose and closer to the risk after the first primary series dose. Based on an assessment of benefits and risks informed by available data, FDA has concluded that the data support the use of a booster dose of the Pfizer-BioNTech COVID-19 Vaccine following completion of a primary series of the Pfizer-BioNTech COVID-19 Vaccine or COMIRNATY in individuals at least 16 years of age.

Review

Disease Background

SARS-CoV-2 is a zoonotic coronavirus that emerged in late 2019 and was identified in patients with pneumonia of unknown cause. The virus was named SARS-CoV-2 because of its similarity to the coronavirus responsible for severe acute respiratory syndrome (SARS-CoV, a lineage B betacoronavirus). SARS-CoV-2 is an enveloped, positive-sense, single-stranded RNA virus sharing more than 70% of its sequence with SARS-CoV, and ~50% with the coronavirus responsible for Middle Eastern respiratory syndrome (MERS-CoV). SARS-CoV-2 is the causative agent of COVID-19, an infectious disease with respiratory and systemic manifestations. Disease symptoms vary, with many persons presenting with asymptomatic or mild disease and some progressing to severe respiratory tract disease including pneumonia and acute respiratory distress syndrome (ARDS), leading to multiorgan failure and death.

The SARS-CoV-2 pandemic continues to present a challenge to global health and, as of December 3, 2021, has caused approximately 264 million cases of COVID-19, including 5.23 million deaths worldwide. In the United States, more than 48.1 million cases and 777,000 deaths have been reported to the Centers for Disease Control and Prevention (CDC). While the pandemic has caused morbidity and mortality on an individual level, the continuing spread of SARS-CoV-2, and emerging variants (such as the highly transmissible Delta variant that is now predominant in the United States) have caused significant challenges

and disruptions in worldwide healthcare systems, economies, and many aspects of human activity (travel, employment, education).

Following EUA of COVID-19 vaccines in December 2020, COVID-19 cases and deaths in the United States declined sharply during the first half of 2021. The emergence of the Delta variant, variable implementation of public health measures designed to control spread, and continued transmission among unvaccinated individuals are major factors in the recent resurgence of COVID-19. Although the number COVID-19 cases appeared to be declining in October 2021 relative to the Delta variant-associated peak globally and in the United States, during the months of November and December 2021 there has been a marked increase in cases in Western Europe and the number of cases in the United States has been increasing. Additionally, in late November 2021, a new SARS-CoV-2 variant, Omicron, was identified initially in the Republic of South Africa and was subsequently found in many other countries. The full significance of this variant in terms of virulence, transmissibility, and level of protection conferred by available COVID-19 vaccines has yet to be determined. However, given the coming winter with more indoor activities due to the cold weather, there is concern that the trend of increasing cases will continue.

COMIRNATY and the Pfizer-BioNTech COVID-19 Vaccine for the Prevention of COVID-19

On August 23, 2021, FDA approved COMIRNATY made by BioNTech in partnership with Pfizer. COMIRNATY is a vaccine indicated for active immunization to prevent COVID-19 caused by SARS-CoV-2 in individuals 16 years of age and older. The vaccine is administered intramuscularly as a series of two doses (0.3 mL each) 3 weeks apart, with each dose containing 30 μg nucleoside-modified messenger RNA (mRNA). COMIRNATY contains mRNA encoding the viral spike glycoprotein of SARS-CoV-2 that is formulated in lipid particles. COMIRNATY is the only vaccine or medical product that is FDA approved for prevention of COVID-19.

The vaccine is also authorized for use under EUA as the Pfizer-BioNTech COVID-19 Vaccine. The EUA for Pfizer-BioNTech COVID-19 Vaccine was originally issued on December 11, 2020, for use as a 2-dose primary series in individuals 16 years of age and older. Issuance of the EUA was supported by safety and efficacy data from a placebo-controlled randomized trial in >37,000 individuals 16 years of age and older. On May 10, 2021, based on additional clinical trial data that was submitted, the EUA was expanded to include adolescents 12 through 15 years of age. On August 12, 2021, the EUA was further amended to allow for an additional primary series dose to be given to certain immunocompromised individuals 12 years of age and older. Based on a clinical trial evaluating immunogenicity, on September 22, 2021, FDA amended the EUA to authorize a single booster dose of the Pfizer-BioNTech COVID-19 Vaccine to be administered at least 6 months after completion of a primary series of Pfizer-BioNTech COVID-19 Vaccine or COMIRNATY to individuals 65 years of age and older, individuals 18 through 64 years of age at high risk of severe coronavirus disease 2019 (COVID-19), and individuals 18 through 64 years of age with frequent institutional or occupational exposure to SARS-CoV-2. Then, on October 20, 2021, FDA authorized the use of the Pfizer-BioNTech COVID-19 Vaccine as a heterologous booster dose following completion of primary vaccination with currently available (i.e., FDA-authorized) COVID-19 vaccines. On October 29, 2021, based on additional clinical trial data, FDA further amended the EUA to authorize use of a Pfizer-BioNTech COVID-19 Vaccine (10 μg mRNA) 2-dose primary series in children 5 through 11 years of age. Additionally, on November 19, 2021, FDA revised the EUA to expand the use of a single booster dose to include all individuals 18 years of age and older after completion of a primary vaccination

series with Pfizer-BioNTech COVID-19 Vaccine or COMIRNATY (homologous booster) or following completion of primary vaccination with another FDA-authorized COVID-19 vaccine (heterologous booster).

During clinical development, the vaccine was called BNT162b2, and it is sometimes referred to below by this working name.

Findings from Post-EUA Surveillance: Myocarditis and Pericarditis

Post-EUA safety surveillance reports received by FDA and CDC identified increased risks of myocarditis and pericarditis, particularly within 7 days following administration of the second dose of a 2-dose primary series of an mRNA vaccine. Reporting rates for medical chart-confirmed myocarditis and pericarditis in VAERS have been higher among males under 40 years of age than among females and older males and have been highest in males 12 through 17 years of age (~71.5 cases per million second primary series doses among males age 16-17 years and 42.6 cases per million second primary series doses among males age 12-15 years as per CDC presentation to the ACIP on August 30, 2021). In an FDA analysis of the Optum healthcare claims database, the estimated excess risk of myocarditis and pericarditis approached 200 cases per million fully vaccinated males 16-17 years of age and 180 cases per million fully vaccinated males 12-15 years of age. Although some cases of vaccine-associated myocarditis and pericarditis have required intensive care support, available data from short-term follow-up suggest that most individuals have had resolution of symptoms with conservative management. Information is not yet available about potential long-term sequelae and outcomes in affected individuals, or whether the vaccine might be associated initially with subclinical myocarditis (and if so, what are the long-term sequelae). A mechanism of action by which the vaccine could cause myocarditis and pericarditis has not been established. Myocarditis and pericarditis were added as important identified risks in the pharmacovigilance plan and included in the Warnings sections of the vaccine Fact Sheets and EUA Prescribing Information. The sponsor is conducting additional post-authorization/post-marketing studies to assess known serious risks of myocarditis and pericarditis as well as to identify an unexpected serious risk of subclinical myocarditis.

Need for Booster Doses

Concerns have been raised that declining neutralizing antibody titers or reduced effectiveness against symptomatic disease may herald significant declines in effectiveness against severe disease. The recent emergence of the highly transmissible Delta variant of SARS-CoV-2 resulted in a new wave of COVID-19 cases in many parts of the world and has led to considerations for administration of booster doses to individuals who received primary vaccination in an effort to enhance immunity, and thus sustain protection from COVID-19. The potential spread of the Omicron variant is also raising concerns. An increasing body of evidence indicates that while the protection of the Pfizer-BioNTech COVID-19 Vaccine remains strong against severe COVID-19 that results in hospitalization (according to a recent MMWR report: 93% with 95% confidence interval = 83%–97%, https://www.cdc.gov/mmwr/volumes/70/wr/mm7042e1.htm), protection does appear to wane over time. The data indicating waning protection come from a variety of sources and have appeared in the published literature. An Israeli study documented waning of protection that was most notably documented five to six months following primary vaccination for severe disease in individuals over 60 years of age, but which also appeared to extend to less severe disease in individuals as young as 16 years of age (https://www.nejm.org/doi/full/10.1056/NEJMoa2114228). Another study

conducted through the Veterans Health Administration showed similar trend for all vaccines authorized or approved in the United States (https://www.science.org/doi/10.1126/science.abm0620).

Requirements for EUA

The EUA process allows the Secretary of the United States Department of Health and Human Services (HHS), in appropriate circumstances, to declare that EUAs are justified for products to respond to certain types of threats. On February 4, 2020, pursuant to section 564 of the Federal Food, Drug, and Cosmetic Act (the FD&C Act), the Secretary of HHS determined that there is a public health emergency that has a significant potential to affect national security or the health and security of United States citizens living abroad, and that involves the virus that causes COVID-19.[2] On the basis of such determination, on March 27, 2020, the Secretary then declared that circumstances exist justifying the authorization of emergency use of drugs and biological products during the COVID-19 pandemic, pursuant to section 564(b)(1) of the FD&C Act.[3]

Under section 564(c) of the FD&C Act, FDA may issue an EUA during the COVID-19 pandemic after FDA concludes that the following statutory requirements are met:

- The agent referred to in the March 27, 2020 EUA declaration by the Secretary of HHS (SARS-CoV-2) can cause a serious or life-threatening disease or condition.
- Based on the totality of scientific evidence available, including data from adequate and well-controlled 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 that can be caused by SARS-CoV-2, or to mitigate a serious or life-threatening disease or condition caused by an FDA-regulated product used to diagnose, treat, or prevent a disease or condition caused by SARS-CoV-2.
- The known and potential benefits of the product, when used to diagnose, prevent, or treat the identified serious or life-threatening disease or condition, outweigh the known and potential risks of the product.
- There is no adequate, approved, and available alternative to the product for diagnosing, preventing, or treating the disease or condition.[4]

If these criteria are met, under an EUA, FDA can authorize unapproved medical products (or unapproved uses of approved medical products) to be used in an emergency to diagnose, treat, or prevent serious or life-threatening diseases or conditions caused by threat agents. FDA has been providing regulatory advice to COVID-19 vaccine manufacturers regarding the data needed to determine that the known and potential benefits of a booster dose outweigh the known and potential risks.

[2] HHS, Determination of Public Health Emergency, 85 FR 7316, February 7, 2020, https://www federalregister.gov/documents/2020/02/07/2020-02496/determination-of-public-health-emergency.
[3] HHS, Emergency Use Authorization Declaration, 85 FR 18250, April 1, 2020, https://www federalregister.gov/documents/2020/04/01/2020-06905/emergency-use-authorization-declaration.
[4] Although COMIRNATY is approved to prevent COVID-19 in individuals 16 years of age and older, there are no COVID-19 vaccines that are approved to provide homologous or heterologous booster doses.

EUA Request

On November 30, 2021, Pfizer, on behalf of BioNTech, submitted an EUA request to expand the authorization of the Pfizer-BioNTech COVID-19 Vaccine to include administration of a booster dose at least 6 months following completion of a primary COVID-19 immunization series of the Pfizer-BioNTech COVID-19 Vaccine or COMIRNATY in individuals at least 16 years of age.

Immunogenicity Data

Reference is made to the Office of Vaccines Research and Review Clinical Review Memo of September 22, 2021, that noted the successful booster dose immunobridging analyses from the Phase 2/3 portion of study C4591001, which supported inference of effectiveness of the booster dose in individuals 18-55 years of age against the reference strain of SARS-CoV-2 (USA_WA1/2020). Booster doses of the Pfizer-BioNTech COVID-19 Vaccine administered after an average of 6 months resulted in a neutralizing antibody geometric mean titer ratio of 3.3-fold for the geometric mean titer one month after the booster dose relative to the geometric mean titer one month after completion of the primary series. This review noted that as outlined in the FDA Guidance document, Emergency Use Authorization for Vaccines to Prevent COVID-19, this inference of effectiveness can be extrapolated to other age groups for which the vaccine primary series has been authorized or approved (e.g., individuals >55 years of age). The review also noted that additional exploratory immunogenicity analyses evaluating neutralization of the reference strain and the Delta variant, although limited by small numbers of samples and use of a non-validated assay, supported the potential for the booster dose to provide additional protection against the currently circulating Delta variant.

Supportive Data from Randomized Placebo-Controlled Clinical Trial of Boosters

Pfizer conducted a randomized placebo-controlled clinical trial in 10,125 individuals receiving booster vaccination with the Pfizer-BioNTech COVID-19 Vaccine or placebo that has not yet been formally reviewed and verified by the Agency. This trial of boosters included randomization of 78 individuals 16 to 17 years of age.

Regarding safety, relevant to the population of individuals 16 to 17 years of age, there was one case of myocarditis and pericarditis reported in this randomized clinical trial. A male individual in this age range developed back, chest, and muscle pain along with joint pain after receiving a booster dose of BNT162b2 and was hospitalized with elevated troponin levels consistent with myocarditis and electrocardiographic changes consistent with pericarditis. The individual received supportive care in hospital and was discharged home following clinical improvement.

Relative vaccine efficacy (RVE) was estimated for booster vaccination with Pfizer-BioNTech COVID-19 Vaccine compared to booster placebo up to the data cutoff date (October 05, 2021) during the blinded placebo-controlled follow-up period. The RVE in the evaluable efficacy population without evidence of SARS-CoV-2 infection prior to 7 days post-booster was observed as 95.3% (2-sided 95% CI: 89.5%, 98.3%), based on 6 cases in the BNT162b2 group and 123 cases in the placebo group. In this analysis, two cases occurred among subjects 16-17 years of age, both of which occurred in placebo recipients. Notably, the cases in this booster RVE analysis accrued during a period of July to the October cutoff

date, during a time that the highly transmissible Delta variant has been the predominant SARS-CoV-2 strain in circulation.

Benefit-Risk Assessment Based on Updated Analyses

Pfizer included a benefit-risk assessment as part of the November 30, 2021 EUA request. Pfizer's methodology to estimate the benefit-risk of using booster doses of BNT162b2 in individuals 16 to 17 years of age is similar to that used to previously evaluate the benefit-risk of booster to all adults 18 to 64 years of age (including subgroups 18 to 39 and 40 to 64 years of age) and to males 18 to 29 years of age.

Summarizing the analysis that the sponsor conducted: predictions per million booster doses administered were calculated using conservative assumptions for hospitalizations:

Table 1. Pfizer's Benefit Risk Analysis

Age Range	**Age 16-17 years**
COVID-19 cases averted	13,843−43,143
Hospitalizations averted	29 to 69
Post-vaccination myocarditis	11-54 (among all 16-17 year olds) 23-69 (among male 16-17 year olds)

In reviewing the data submitted, FDA reviewers note that the key benefit of the booster dose of the Pfizer-BioNTech COVID-19 Vaccine is to prevent breakthrough COVID-19 cases post-primary series of two doses of the vaccine. There is clear evidence that vaccine effectiveness (VE) against COVID-19 is waning for all adult age groups post-2nd dose of the vaccine.[5] The reduced VE is partially due to the waning of immunity and partially to the emergence of the new Delta variant. In its submission, Pfizer referenced real world data from Israel indicating that the waning of vaccine-induced protection against COVID-19 is similar in individuals ages 16 to 17 years as it is in individuals ages 18 years and older.[6] Based on safety surveillance, there were no new or significant safety concerns identified after EUA of the booster dose among high-risk populations. Potential myocarditis risk post-booster dose remains as the key risk in the benefit-risk assessment of the booster dose.

To estimate the number of COVID-19 cases prevented with a booster dose of Pfizer-BioNTech COVID-19

[5] Tartof, Sara Y., et al. "Six-month effectiveness of BNT162B2 mRNA COVID-19 vaccine in a large US Integrated health system: a retrospective cohort study." SSRN, (2021); Barda, Noam, et al. "Effectiveness of a third dose of the BNT162b2 mRNA COVID-19 vaccine for preventing severe outcomes in Israel: an observational study." The Lancet (2021); Klein N. Myocarditis Analyses in the Vaccine Safety Datalink: Rapid Cycle Analyses and "Head-to-Head" Product Comparisons (presented at Oct 21, 2021 ACIP meeting). Centers for Disease Control and Prevention; October 21, 2021. p. Slide 17. Available at: https://stacks.cdc.gov/view/cdc/110921. Accessed 5 November 2021; Andrews, Nick, et al. "Vaccine effectiveness and duration of protection of Comirnaty, Vaxzevria and Spikevax against mild and severe COVID-19 in the UK." medRxiv (2021); Levin, Einav G., et al. "Waning immune humoral response to BNT162b2 covid-19 vaccine over 6 months." New England Journal of Medicine (2021).

[6] Israel MoH. Presentation frim the Epidemic Management Committee and COVID-19 Vaccination Advisory Committee. Waning of protection after a second dose in young ages months after vaccination, Joint analysis by researchers from the Ministry of Health, the Gartner Institute, the Hebrew University, the Technion and the Weizmann Institute. Presented on November 21, 2021. Available at: https://www.gov.il/BlobFolder/reports/vpb-21112021/he/files_publications_corona_vbp-21112021-02.pdf. Last accessed: November 25, 2021.

Vaccine, Pfizer's benefit-risk assessment assumed three scenarios: one with disease burden based on the overall average weekly rate of confirmed COVID-19 cases reported since the beginning of the pandemic (i.e., an average over all peaks and troughs); a second based on the peak incidence during the Delta period in the week ending September 11, 2021; and a third based on the peak infections during the week ending 9 January 2021. Pfizer's benefit-risk assessment assumed VE of two doses prior to a booster was 50% against documented cases of COVID-19 and that this figure increased to 90% after a booster. They assumed the 90% VE was maintained over 6 months. Pfizer also estimated the number of COVID-19-related hospitalizations prevented with a booster of BNT162b2 for two disease burden scenarios described above. They assumed a range of waning VE against hospitalization, from no waning (VE maintained at 90%) to assuming VE after two doses waned to 77% against COVID-19-related hospitalization prior to a booster (based on Self et al.[7]) and returned to 90% after a booster was administered. A range of assumed rates of myocarditis were based on data from Vaccine Adverse Event Reporting System (VAERS) and Vaccine Safety Datalink (VSD) in the 7-day risk window after dose two.

The sponsor's analysis finds one million booster doses will avert between 13,843 and 43,143 COVID-19 cases in individuals 16 to 17 years of age for the scenarios with average and peak incidence rate, respectively. Additionally, the sponsor's analysis finds one million booster doses will avert 29-69 COVID-19-related hospitalizations over 6 months based on a range of weekly average rates of 0.9 hospitalizations per 100,000 from start of the pandemic and 1.5 hospitalizations per 100,000 during the peak Delta week, respectively. Pfizer estimated the risk of myocarditis cases per million booster doses based on the myocarditis case rate reported in VAERS and VSD.[8] As part of their modeling they applied a reduction factor in the rate of myocarditis corresponding to the rate ratio of myocarditis and pericarditis seen in Israeli 16-19 year olds, as data were not available only for 16-17 year-olds. This reduction factor was calculated by Pfizer based on the data to be 0.31 for all 16-19 year olds and 0.33 for males 16-19 years of age.[9] They estimated myocarditis risk per one million booster doses over 6 months as 11-54 cases among all 16-17 year olds and 23-69 cases among male 16-17 year olds.

FDA considers the overall approach of Pfizer's benefit-risk assessment sound with the caveat of limited data on the myocarditis rate post booster dose, and taking into account the single case of myocarditis observed in the randomized clinical trial of boosters conducted by Pfizer. However, FDA agrees that the known and potential benefits of administering a booster dose to individuals 16 to 17 years of age outweighs the known and potential risks given the large number of COVID-19 cases prevented. Although in the worst case modeling scenario, there might be more hospitalizations due to myocarditis than those prevented due to COVID-19, hospitalizations due to COVID-19 are characterized by a generally greater length of hospital stay and acuity of care compared with hospitalizations due to vaccine associated myocarditis. In addition, a reduction in the number of individuals experiencing long COVID-19 is another potential benefit. FDA notes that the benefit-risk assessment of the sponsor uses VSD and VAERS data to estimate the myocarditis risk while data from four health claim databases from the FDA BEST system (Optum,

[7] Self WH, Tenforde MW, Rhoads JP, et al. Comparative Effectiveness of Moderna, Pfizer- BioNTech, and Janssen (Johnson & Johnson) Vaccines in Preventing COVID-19 Hospitalizations Among Adults Without Immunocompromising Conditions - United States, March-August 2021. MMWR Morbidity and mortality weekly report 2021; 70(38): 1337-43.

[8] Male-specific rates were available only from VAERS. VSD rates are for individuals 12 to 17 years of age (rates specifically for individuals 16 to 17-years of age were not available).

[9] https://www.gov.il/BlobFolder/reports/vaccine-efficacy-safety-follow-up-committee/he/files_publications_corona_booster-sr-112021.pdf

Healthcore, CVS Health, and Blue Health Intelligence) generated a relatively higher myocarditis case rate. However, this is unlikely to change the benefit-risk balance of the vaccine. Additionally, Pfizer's estimated waning of VE against COVID-19 cases (50% VE at 6 months post-2nd dose) is greater than FDA's estimates (60-70% at 6 months post-2nd dose) based on CDC vaccine effectiveness study, data from Israel, and other sources of evidence. As a result, the benefits may be somewhat overestimated in Pfizer's assessment, but again it is unlikely to change the benefit-risk balance.

Additional Benefit-Risk Considerations

There are currently limited data on myocarditis and pericarditis following booster doses of the mRNA vaccines. Real world evidence that was used above by Pfizer for its benefit-risk assessment on the incidence of myocarditis and pericarditis from Israel was presented at the Vaccines and Related Biological Products Advisory Committee (VRBPAC) meeting previously, most recently on October 14, 2021, and has since been updated on line (https://www.gov.il/BlobFolder/reports/vaccine-efficacy-safety-follow-up-committee/he/files_publications_corona_booster-sr-112021.pdf). These data suggest that the risk of myocarditis and pericarditis for the Pfizer-BioNTech COVID-19 Vaccine following a third dose several months following the primary vaccination series is not associated with an unacceptable risk of myocarditis and pericarditis. In particular, rather than being as elevated as following the second dose in males 16-40 years of age, the risk of myocarditis and pericarditis after the administration of the third dose appears to be more similar to the risk observed after the first dose. Further pharmacovigilance will be conducted to more completely address this issue.

Recommendation

Based on the data provided by the sponsor, other data available to FDA including real world evidence, and based upon its benefit-risk analysis, the review team concludes that the data support that the known and potential benefits outweigh the known and potential risks, and therefore recommends authorization of the use of a single booster dose of the Pfizer-BioNTech COVID-19 Vaccine to individuals 16 years of age and older at least 6 months after completion of primary vaccination with the Pfizer-BioNTech COVID-19 Vaccine or COMIRNATY.