Review Memorandum

Date:	**December 30, 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 in various situations**

This memorandum provides a summary, review, and recommendation to amend the emergency use authorization (EUA) of the Pfizer-BioNTech COVID-19 Vaccine to:

1. Allow the administration of a single homologous booster dose to individuals 12 through 15 years of age at least 5 months after completion of a primary series;
2. Allow the administration of a single homologous booster dose to individuals 16 through 17 years of age at least 5 months after completion of a primary series;
3. Allow the administration of a single homologous booster dose (or heterologous booster dose as authorized for another COVID-19 vaccine) to individuals 18 years of age and older at least 5 months after completion of a primary series; and
4. Allow a third dose of the primary series in individuals 5 through 11 years of age with certain kinds of immunocompromise.

Executive Summary

The Pfizer-BioNTech COVID-19 Vaccine's currently authorized indication is for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 5 years of age and older. It 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 16 years of age and older following completion of a primary series of the Pfizer-BioNTech COVID-19 Vaccine or COMIRNATY[1] (homologous booster) or for those 18 years of age and older 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 currently at least 6

[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.

months, and for a heterologous booster is the same as that authorized for a booster dose of the vaccine used for primary vaccination.

On December 1, 2021, the first confirmed case of the SARS-CoV-2 variant Omicron (B.1.1.529) was identified in the United States. Since that time, the proportion of cases due to the Omicron variant is estimated to have increased to be over 50% and is rising. This rapid increase in the proportion of cases attributable to the Omicron variant, relative to the previously highly prevalent SARS-CoV-2 variant Delta (B.1.617.2), is contemporaneous with a surge in COVID-19 cases in the United States. Laboratory data indicate that the Omicron variant is more resistant to neutralization by the antibodies generated with the currently available COVID-19 vaccines, and that a third mRNA vaccine dose may provide improved protection against the Omicron variant. In this context, the current action: 1) allows the administration of a single homologous booster dose to individuals 12 through 15 years of age at least 5 months after completion of a primary series; 2) allows the administration of a single homologous booster dose to individuals 16 through 17 years of age at least 5 months after completion of a primary series; 3) allows the administration of a single homologous booster dose (or heterologous booster dose as authorized for another COVID-19 vaccine) to individuals 18 years of age and older at least 5 months after completion of a primary series; and 4) allows a third dose of the primary series in individuals 5 through 11 years of age with certain kinds of immunocompromise.

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.

Data reviewed in support of the current action includes prepublications, accepted publications, published publications, as well as real world evidence on the safety of booster doses provided by the Ministry of Health of Israel. Specifically, based on the Ministry of Health of Israel data from over 6,300 individuals 12 to 15 years of age who received a Pfizer-BioNTech-COVID-19 Vaccine third dose (booster) at least 5 months following completion of the primary vaccination series, there have been no cases of myocarditis or pericarditis reported to date. Additionally, in a study involving approximately 4.7 million individuals 16 years and older in Israel who previously received the primary Pfizer-BioNTech COVID-19 Vaccine series, booster doses administered at least 5 months follow completion of the primary series appeared to be effective with no new safety concerns. Finally, there is a medical need of individuals 5 through 11 years of age with certain kinds of immunocompromise for better primary immunity to protect against COVID-19. Data on safety in this population can be inferred from the experience in healthy children 5 through 11 years of age who were vaccinated with the primary series, and data from vaccine efficacy in individuals 12 years of age and older can be used to extrapolate efficacy to this population.

Based on an assessment of benefits and risks informed by available data, FDA has concluded that the data support: the administration of a single homologous booster dose to individuals 12 through 15 years of age at least 5 months after completion of a primary series; the administration of a single homologous booster dose to individuals 16 through 17 of age at least 5 months after completion of a primary series; the administration of a single homologous booster dose (or heterologous booster dose as authorized for another

COVID-19 vaccine) to individuals 18 years of age and older at least 5 months after completion of a primary series; and a third dose of the primary series in individuals 5 through 11 years of age with certain kinds of immunocompromise.

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 30, 2021, has caused approximately 282 million cases of COVID-19, including 5.4 million deaths worldwide. In the United States, more than 53.2 million cases and 818,000 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 very highly transmissible Omicron variant that is now rapidly spreading and 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 (B.1.617.2) and Omicron (B.1.1.529) variants and their rapid spread across the globe, 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 of 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 was a marked increase in cases in Western Europe and the number of cases in the United States increased starting in early November 2021.

Of particular concern, the Omicron variant was initially identified in the Republic of South Africa in November 2021, with subsequent detection worldwide. On December 1, 2021, the first confirmed case of the Omicron variant was identified in the United States. Since that time, the proportion of cases due to the Omicron variant is estimated at over 50% and appears to be increasing (https://covid.cdc.gov/covid-data-tracker/#variant-proportions). This rapid increase in the proportion of cases attributable to the Omicron variant, relative to the previously highly prevalent Delta variant, is contemporaneous with a surge in COVID-19 cases in the United States.

Although data continue to emerge on a daily basis, the full significance of the Omicron variant has recently

become more clear. This variant appears to be highly transmissible, with a reproductive number that appears to be several times higher than that for the Delta variant (Nishiura H, Ito K, Anzai A, et al., Relative reproductive number of SARS-CoV-2 Omicron (B.1.1.529) compared with Delta variant in South Africa, J Clin Med, 2022; 11:30). Additionally, both laboratory and clinical data indicate that the Omicron variant appears to be significantly more resistant to neutralization by antibodies developed to the prototype Wuhan strain of SARS-CoV-2, and this variant has been associated with breakthrough infections even in fully vaccinated individuals (Cao Y, Wang J, Jian F, et al. Omicron escapes the majority of existing SARS CoV-2 neutralizing antibodies, Nature 2021, in press, https://doi.org/10.1038/d41586-02103796-6; Branal LT, MacDonald E, Veneti L et al., Outbreak caused by the SARS-CoV-2 Omicron variant in Norway, November to December 2021, Euro Surveill, 2021, https://doi.org/10.2807/1560-7917.ES.2021.26.50.2101147). Based on the available evidence, it appears that the primary series of the COVID-19 vaccines currently available in the United States does reduce the risk of serious disease, including hospitalization and death, from the Omicron variant, and the recent administration of a booster dose of a COVID-19 vaccine appears to be associated with an even lower likelihood of breakthrough infection.

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. During clinical development, the vaccine is called BNT162b2, and the memorandum includes references to this working name.

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, at the same dose and volume as for individuals 16 years of age and older. 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, FDA amended the EUA on September 22, 2021 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 the 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 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 the Pfizer-BioNTech COVID-19 Vaccine (10 μg mRNA) 2-dose primary series in children 5 through 11 years of age. Then, 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). Additionally, on December 9, 2021, FDA expanded the use of a single booster dose of Pfizer-BioNTech COVID-19 Vaccine or COMIRNATY (homologous booster) to individuals 16 to 17 years of age after completion of a primary vaccination series with Pfizer-BioNTech COVID-19 Vaccine or COMIRNATY.

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.

The most recent safety data from the Ministry of Health of Israel indicate a rate of myocarditis and pericardits in the overall population of those 16 years of age and older following a booster dose given at least 5 months following the primary vaccination series that is about 1/3 that of the rate seen following the second vaccine dose. Specifically relevant, following the administration of a booster dose at least 5 months after the primary series to over 6,300 individuals in the 12 to 15 year age group, following the third dose as of December 15, 2021, no cases of myocarditis or pericarditis were reported with at least two weeks of active surveillance follow-up.

Need for the Expansion of 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 and Omicron variants of SARS-CoV-2 have resulted in a new wave of COVID-19 cases in many parts of the world and have 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.

In particular, the very large number of recent cases of the Omicron variant is also raising significant concerns, as data indicate that due to the large number of mutations present it escapes neutralization by a variety of monoclonal antibodies and is more resistant to vaccine-induced immunity (Planas D, Saunders N, Maes P, et al., Considerable escape of SARS-CoV-2 Omicron to antibody neutralization, Nature, 2021, in press, https://doi.org/10.1038/d41586-021-03827-2). In this study by Planas and colleagues, a booster dose of the Pfizer-BioNTech COVID-19 Vaccine, as well as primary vaccination of previously infected individuals, strongly increased overall levels of anti-SARS-CoV-2 neutralizing antibodies above a threshold allowing inhibition of the Omicron variant. This finding appears to be relatively robust, as other studies have come to very similar conclusions regarding the potential benefit of a booster dose of the mRNA vaccines (Garcia-Beltran WF, St. Dennis KJ, Hoelzemer A, et al., mRNA-based COVID-19 boosters induce neutralizing immunity against SARS-CoV-2 Omicron variant, Cell, in press, https://doi.org/10.1016/j.cell.2021.12.033; Nemet I, Kliker L, Lustig Y et al., Third BNT162b2 Vaccination Neutralization of SARS-CoV-2 Omicron Infection, N Engl J Med, in press, http://doi.org/10.1056/NEJMc2119358. The totality of available evidence from these and other sources suggests that vaccinated individuals who have completed a primary series and received a subsequent booster with the Pfizer-BioNTech COVID-19 Vaccine are more likely to be better protected against symptomatic infection with the Omicron variant, and especially against severe disease.

Given the potential benefit of a booster dose in providing additional protection against disease due to the rapidly spreading Omicron variant, it is reasonable at this time to expand the use of booster doses to the fullest extent that is scientifically justified. This could include expansion of the eligible age range for boosters as well as reduction in the booster interval. Additionally, ensuring that the benefits of a third dose as part of the primary series for immunocompromised individuals is expanded to the broadest appropriate age range is also reasonable.

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

[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.

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.

Data on a Single Homologous Booster in 12 to 15 Year-Olds at Least 5 Months after the Primary Series

A publication has documented the experience with boosters in approximately 4.7 million individuals in Israel (Bar-On YM, Goldberg Y, Mandel M, et al., Protection against Covid-19 by BNT162b2 booster across age groups, N Engl J Med 2021; 385:2421-30). The real-world effectiveness of booster doses of the Pfizer-BioNTech COVID-19 vaccine administered to individuals least 5 months after completion of the primary series to individuals 16 years of age or older was documented. Those receiving booster doses appeared to be better protected against COVID-19, and this effect was observed throughout the age range.

The most recent safety data available as of December 15, 2021, from the Ministry of Health of Israel based upon over 4.1 million booster doses administered at least 5 months after completion of the primary series indicate a rate of myocarditis and pericardits in the overall population of those 16 years of age and older that is about 1/3 that of the rate seen following the second vaccine dose. Additionally, no cases of myocarditis or pericarditis were reported to an active surveillance system following vaccination of over 6,300 individuals in this 12 to 15 year age group. For purposes of emergency use authorization to address the current situation, it would be reasonable to extrapolate effectiveness of a booster dose in this age group from clinical trial and real world effectiveness data in age groups 16 years and older.

Data on a Single Homologous Booster in 16 to 17 Year-Olds at Least 5 Months after the Primary Series

Effectiveness data on individuals down to 16 years of age is provided in a recent publication using real

[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 for use in individuals younger than 16 or to provide homologous or heterologous booster doses.

world evidence derived from the experience of boosters in Israel (Bar-On YM, Goldberg Y, Mandel M, et al., Protection against Covid-19 by BNT162b2 booster across age groups, N Engl J Med 2021; 385:2421-30). This study included 1,129,585 individuals who were 16 to 29 years of age. The fold-reduction in confirmed cases of COVID-19 in this age range was similar or better than older age groups. Safety data obtained from the Ministry of Health of Israel for this population given the Pfizer-BioNTech COVID-19 Vaccine was previously reviewed following booster administration at 5 months and based on the totality of the available evidence a favorable benefit-risk determination was made. Therefore the revision of the timing of a booster dose from at least 6 months to 5 months in individuals 16 to 17 years of age is supported by real-world evidence that has been available for several months.

Data on a Single Homologous Booster in individuals 18 Years and Older at Least 5 Months after the Primary Series

Two publications have documented the effectiveness in a real-world setting of booster doses administered in Israel after at least 5 months after completion of the primary series (Arbel R, Hammerman A, Sergienko R et al., BNT162b2 vaccine booster and mortality due to Covid-19, N Engl J Med 2021; 385:2413-20; Bar-On YM, Goldberg Y, Mandel M, et al., Protection against Covid-19 by BNT162b2 booster across age groups, N Engl J Med 2021; 385:2421-30). The most recent safety data available as of December 15, 2021, from the Ministry of Health of Israel based upon over 4.1 million booster doses administered at least 5 months after completion of the primary series indicate a rate of myocarditis and pericardits in the overall population of those 16 years of age and older that is about 1/3 that of the rate seen following the second vaccine dose.

Additionally, use of heterologous booster doses with the Pfizer-BioNTech COVID-19 Vaccine was previously evaluated and presented at the October 15, 2021 VRBPAC meeting. As noted at the meeting, the median booster interval for the 51 individuals receiving the Pfizer-BioNTech COVID-19 Vaccine boosted with the Janssen COVID-19 Vaccine was 20.6 weeks (range 12.3 – 41.3); the median booster interval for the 50 individuals receiving the Pfizer-BioNTech COVID-19 Vaccine boosted with the Moderna COVID-19 Vaccine was 16.8 weeks (range 12.0 – 20.9). The data presented support the authorization of heterologous booster doses of the Janssen or Moderna COVID-19 vaccine in individuals older than 18 years of age at least 5 months following a primary series of the Pfizer-BioNTech COVID-19 Vaccine.

Data on a Third Primary Series Dose in 5 to 11 Year-Olds with Certain Kinds of Immunocompromise

A previous review of data led to authorization of a third dose of the Pfizer-BioNTech COVID-19 Vaccine (0.3 ml) administered at least 28 days following the second dose of the two dose regimen of this vaccine for individuals at least 12 years of age who had undergone solid organ transplantation, or who were diagnosed with conditions that are considered to have an equivalent level of immunocompromise. Since that time, the two dose primary series of the Pfizer BioNTech COVID-19 Vaccine received authorization for use in children 5 to 11 years of age.

In considering the use of a third dose as part of the primary series for children 5 to 11 years of age who have undergone solid organ transplantation, or who have been diagnosed with conditions that are considered to have an equivalent level of immunocompromise, the effectiveness of an additional dose in this age group can be extrapolated from data in adults and older children. In terms of safety, prior analyses

conducted as part of the authorization process for healthy children note that myocarditis and pericarditis appear to peak in the 16 to 17 year age range. Given that those with immunocompromising conditions are less likely to have an inflammatory response that could potentially be associated with myocarditis and pericarditis and these 5 to 11 year old immunocompromised individuals at increased risk for severe illness could benefit from the better immune response provided by a third dose as part of the primary series, the overall benefit-risk of the administration of this third dose at least 28 days following the second dose of the two dose regimen of the Pfizer-BioNTech COVID-19 Vaccine appears to be favorable.

Recommendation

Based on the totality of evidence available from the sponsor, the literature, and the Ministry of Health of Israel, and in accordance with established FDA guidance, the review team concludes that the known and potential benefits outweigh the known and potential risks, and therefore recommends the following amendments of the emergency use authorization to:

1. Allow the administration of a single homologous booster dose to individuals 12 through 15 years of age at least 5 months after completion of a primary series;
2. Allow the administration of a single homologous booster dose to individuals 16 through 17 years of age at least 5 months after completion of a primary series;
3. Allow the administration of a single homologous booster dose (or heterologous booster dose as authorized for another COVID-19 vaccine) to individuals 18 years of age and older at least 5 months after completion of a primary series; and
4. Allow a third dose of the primary series in individuals 5 through 11 years of age with certain kinds of immunocompromise.

Continuous, ongoing safety surveillance under the oversight of FDA and CDC will actively and passively monitor for risks of myocarditis and other known and unknown short and long term risks of the booster doses authorized.