Review Memorandum Addendum

Date:	**November 18, 2021**
To:	**The File**
From:	**David Cho, PhD (CBER/OD)**
Through:	**Peter Marks, MD, PhD (CBER/OD)**
Applicant name:	**ModernaTX, Inc.**
Application Number:	**EUA 27073**
Product:	**Moderna COVID-19 Vaccine**
Subject:	**Addendum to CBER's review memorandum dated October 20, 2021 entitled, "EUA amendment to support use of a Moderna COVID-19 Vaccine heterologous booster dose following primary vaccination with other authorized COVID-19 vaccines"**

This memorandum documents the Food and Drug Administration's (FDA, the Agency, or we) determination to amend the existing Emergency Use Authorization (EUA) for the Moderna COVID-19 Vaccine to include the use of the Moderna COVID-19 Vaccine as a heterologous booster dose following completion of primary vaccination with another authorized or approved COVID-19 vaccine in individuals 18 years of age and older.

I. Background

On October 20, 2021, FDA authorized for emergency use the administration of a single booster dose of Moderna COVID-19 Vaccine as: 1) a homologous booster dose at least 6 months after completing the primary series of this vaccine in individuals: 65 years of age and older; 18 through 64 years of age at high risk of severe COVID-19; and 18 through 64 years of age with frequent institutional or occupational exposure to SARS-CoV-2; and 2) as a heterologous booster dose following completion of primary vaccination with another authorized or approved COVID-19 vaccine, where the eligible population(s) and dosing interval for the heterologous booster dose were the same as those authorized for a homologous booster dose of the vaccine used for primary vaccination.

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At that time, a single booster dose of the Pfizer-BioNTech COVID-19 Vaccine[1] was authorized for administration 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. And a single booster dose of the Janssen COVID-19 Vaccine was authorized for administration to individuals 18 years of age or older. Consequently, the eligible populations for the Moderna COVID-19 Vaccine heterologous booster included individuals 65 years of age and older and certain individuals 18 through 64 years of age for those individuals who received the Pfizer-BioNTech COVID-19 Vaccine as their primary vaccination, as noted above, or individuals 18 years of age or older for those who received the Janssen COVID-19 Vaccine as their primary vaccination.

Following the authorization of COVID-19 vaccines, 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 of COVID-19 cases appeared to be declining in October 2021 relative to the Delta variant-associated peak globally and in the US, during the month of November 2021 there has been a marked increase in cases in Western Europe and the number of cases in the US has been increasing, rising by about 20% between November 1, 2021, and November 17, 2021. Given the coming winter with more indoor activities due to the cold weather, there is concern that the trend of increasing cases would continue.

As explained in more detail in the review memos entitled "CBER Assessment of booster dose of Pfizer-BioNTech COVID-19 Vaccine (0.3 ml) administered at least 6 months following a primary COVID-19 immunization series in individuals 18 years of age and older" and "CBER Assessment of a booster dose of Moderna COVID-19 Vaccine (0.25 ml) administered at least 6 months following a primary COVID-19 immunization series in individuals 18 years of age and older," the Agency is amending the EUAs for the Moderna and Pfizer-BioNTech COVID-19 vaccines to authorize the use of these vaccines as a single booster dose in individuals aged 18 years of age or older, at least 6 months after completing the primary series of either of these vaccines (i.e., as a homologous booster dose).[2] The eligible populations for the Moderna COVID-19 Vaccine heterologous booster are, therefore, also being expanded to include all individuals 18 years of age and older, regardless of the authorized or approved COVID-19 vaccine used for primary vaccination. The dosing interval for the heterologous booster dose is the same as that authorized for a booster dose of the vaccine used for primary vaccination, and

[1] Reference to the Pfizer-BioNTech COVID-19 Vaccine also includes the use of COMIRNATY (COVID-19 Vaccine, mRNA).

[2] CBER's review and analysis of the use of the booster doses in this population is documented in separate review memoranda: CBER Assessment of booster dose of Pfizer-BioNTech COVID-19 Vaccine (0.3 ml) administered at least 6 months following a primary COVID-19 immunization series in individuals at least 18 years of age, dated November 18, 2021 and CBER Assessment of third dose of Moderna COVID-19 Vaccine (0.25 ml) administered at least 6 months following a primary COVID-19 immunization series in individuals at least 18 years of age, dated November 18, 2021, which are incorporated here by reference.

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the revisions to the Moderna COVID-19 Vaccine EUA and Fact Sheets regarding eligible populations for use of a heterologous booster dose will provide additional clarity to the public, including vaccination providers.

II. Discussion

As noted in our prior review memorandum dated October 20, 2021, in considering the appropriate populations that would be eligible for a heterologous booster dose and the appropriate interval between primary vaccination and a heterologous booster dose, the need for a booster dose is determined by immunity elicited by the primary vaccination. Thus, the eligible population(s) and dosing interval for a Moderna COVID-19 Vaccine heterologous booster dose that would be supported by available data would be the same as those authorized for a homologous booster dose of the vaccine used for primary vaccination.

Therefore, based on the totality of the data, the Moderna COVID-19 Vaccine, when administered as a heterologous booster dose following completion of primary vaccination with another authorized or approved COVID-19 vaccine may be effective in improving protection against serious outcomes of COVID-19 among individuals in whom immunity elicited by primary vaccination has waned. Additionally, the known and potential benefits outweigh the known and potential risks for use of a heterologous booster dose of the Moderna COVID-19 Vaccine when administered to the eligible population, which now includes all individuals 18 years of age and older who have completed primary vaccination with this vaccine or with another authorized or approved COVID-19 vaccine, and where the dosing interval for the heterologous booster dose is the same as that authorized for a homologous booster dose of the vaccine used for primary vaccination.[3]

[3] Another criterion for issuing an EUA under section 564 of the Federal Food, Drug, and Cosmetic Act is that there "is no adequate, approved, and available alternative to the product for diagnosing, preventing, or treating the disease or condition." Although COMIRNATY (COVID-19 Vaccine, mRNA) 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.

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