Review Memorandum Addendum # 2

Date:	**December 30, 2021**
To:	**The File**
From:	**Peter Marks, MD, PhD (CBER/OD)**
Applicant name:	**Janssen Biotech, Inc.**
Application Number:	**EUA 27205**
Product:	**Janssen COVID-19 Vaccine**
Subject:	**Addendum # 2 to CBER's review memorandum dated October 20, 2021 entitled, "EUA amendment to support use of a Janssen COVID-19 Vaccine heterologous booster dose following primary vaccination with other authorized COVID-19 vaccines"**

This addendum documents the Agency's determination to amend the existing EUA for the Janssen COVID-19 Vaccine to include the use of the Janssen COVID-19 Vaccine as a heterologous booster dose at least five (5) months after completion of a primary vaccination series with the Pfizer-BioNTech COVID-19 Vaccine or COMIRNATY (COVID-19 Vaccine, mRNA) 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 Janssen COVID-19 Vaccine 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.[1] The eligible population was subsequently amended on November 19, 2021. FDA authorized the use of the Janssen COVID-19 Vaccine as a heterologous booster dose in individuals 18 years of age or older, where 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. At the time, the dosing

[1] A single booster dose of the Moderna COVID-19 Vaccine and the Pfizer-BioNTech COVID-19 Vaccine 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.

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interval for the Pfizer-BioNTech COVID-19 Vaccine[2] was six (6) months after completion of the primary vaccination series.

Following the authorization, 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 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 single additional vaccine dose may provide improved protection against the Omicron variant.

As explained in more detail in the review memorandum entitled "CBER assessment of a single booster dose of the Pfizer-BioNTech COVID-19 Vaccine (0.3 mL) administered in various situations," the Agency is amending the Pfizer-BioNTech COVID-19 Vaccine EUA to, among other things, authorize the use of a single booster dose of the Pfizer-BioNTech Vaccine at least **five (5)** months after completion of a primary vaccination series with the Pfizer-BioNTech COVID-19 Vaccine.[3] As noted above, 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. Consequently, the dosing interval for the Janssen COVID-19 Vaccine heterologous booster dose following primary vaccination by the Pfizer-BioNTech COVID-19 Vaccine is being amended from six (6) months to five (5) months.

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 Janssen 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. Additionally, the NIH study that originally supported the use of heterologous booster doses, which was evaluated and presented at the October 15, 2021 Vaccines and Related Biologic Products Advisory Committee meeting and discussed in detail in our Oct. 20, 2021 memorandum, also supports the use of heterologous booster doses in individuals 18 years of age and older at least 5 months following primary vaccination under EUA. Specifically, in this study, the median booster interval was 20.6

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

[3] CBER's review and analysis of the use of the homologous booster dose of the Pfizer-BioNTech COVID-19 Vaccine in the various populations is documented in a separate review memorandum: "CBER assessment of a single booster dose of the Pfizer-BioNTech COVID-19 Vaccine (0.3 mL) administered in various situations," dated December 30, 2021, and is incorporated here by reference.

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weeks (range 12.3-41.3) for the 51 individuals who completed primary vaccination with the Pfizer-BioNTech COVID-19 Vaccine and boosted with the Janssen COVID-19 Vaccine.

Therefore, based on the totality of the data, the Janssen 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 have waned. This includes the use of the Janssen COVID-19 Vaccine as a heterologous booster dose at least five (5) months after completion of a primary vaccination series with the Pfizer-BioNTech COVID-19 Vaccine in individuals 18 years of age and older. Additionally, the known and potential benefits outweigh the known and potential risks for use of a heterologous booster dose of the Janssen COVID-19 Vaccine when administered to 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, which now includes at least five (5) months for those individuals who have completed a primary vaccination series with the Pfizer-BioNTech COVID-19 Vaccine.[4]

[4] 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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