Vaccines and Related Biological Products
Advisory Committee meeting
October 14, 2021

Moderna COVID-19 Vaccine
Application for Emergency Use Authorization of a booster dose

Applicant: ModernaTX Inc.,

Sudhakar Agnihothram, B. Pharm., Ph.D.
Division of Vaccines and Related Products Applications
Office of Vaccines Research and Review/CBER/FDA
Background Outline

- Moderna COVID-19 Vaccine and EUA Request for Booster Dose
- Considerations for EUA of a COVID-19 Vaccine Booster Dose
- COVID-19 Vaccines Available for Use in the U.S.
- Overview of Today’s Agenda
- Voting Question for the Committee
Modern COVID-19 Vaccine

- Emergency Use Authorization: December 18, 2021

- Indication and Usage: Active immunization to prevent COVID-19 caused by SARS-CoV-2 in individuals 18 years of age and older

- Dosing Regimen: Two doses administered one month apart
  - Third dose at least one month after the second dose authorized August 12, 2021, for use in certain immunocompromised individuals

- Each 0.5 mL dose contains 100 mcg of a nucleoside-modified messenger RNA (mRNA) encoding the viral spike glycoprotein of SARS-CoV-2 (Wuhan strain) formulated in lipids.
Submission Date: September 3, 2021

Proposed use of booster dose under EUA: a **50 mcg dose (0.25 mL)** to be administered at least 6 months after completing a primary series to 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 whose frequent institutional or occupational exposure to SARS-CoV-2 puts them at high risk of serious complications of COVID-19 including severe COVID-19.

The clinical package includes safety and immunogenicity data from 171 clinical trial participants who received a 50 mcg booster dose of Moderna COVID-19 Vaccine approximately 6 months after completing the Moderna COVID-19 Vaccine two dose (100 mcg) series.
Rationale for COVID-19 Booster Doses

- The emergence of the highly transmissible Delta (B.1.617.2) variant of SARS-CoV-2 has led to considerations of the potential need for booster doses for fully vaccinated individuals.

- Data from post-authorization effectiveness studies conducted suggest that the currently U.S. authorized, or licensed vaccines remain effective in protecting against severe disease; however, some data suggest that effectiveness may be waning against mild disease and against severe disease in elderly individuals.

- Concerns have been raised that declining neutralizing antibody titers or reduced effectiveness against symptomatic disease may herald significant declines in effectiveness against severe disease.
Emergency Use Authorization

FDA may issue an Emergency Use Authorization (EUA) of an unapproved medical product following an EUA declaration, if the following statutory requirements* are met:

− The agent referred to in the EUA declaration can cause a serious or life-threatening disease or condition
− The medical product may be effective to prevent, diagnose, or treat the serious or life-threatening condition caused by the agent
− The known and potential benefits of the product outweigh the known and potential risks of the product
− No adequate, approved, and available alternative to the product for diagnosing, preventing, or treating the disease or condition

*Section 564 of the FD&C Act (21 U.S.C. 360bbb-2)
COVID-19 Vaccines Available for Use in the U.S.

**Pfizer BioNTech**

FDA approved as COMIRNATY:
- 2-dose primary series, individuals ≥ 16 years of age

Available under EUA as Pfizer-BioNTech COVID-19 Vaccine:
- 2-dose primary series, individuals ≥12 years of age
- 3rd primary series dose, certain immunocompromised individuals
- Booster dose at least 6 months after completion of primary series:
  - Individuals ≥65 years of age
  - Individuals 18 through 64 years of age at high risk of severe COVID-19
  - Individuals 18 through 64 years of age whose frequent institutional or occupational exposure to SARS-CoV-2 puts them at high risk of serious complications of COVID-19 including severe COVID-19

**Moderna**

Available under EUA:
- 2-dose series, individuals ≥18 years of age
- 3rd dose, certain immunocompromised individuals

**Janssen**

Available under EUA:
- Single dose, individuals ≥18 years of age
Available data should support the effectiveness of a booster dose, specifically against currently circulating SARS-CoV-2 variants.

- Benefit of the booster dose should be considered relative to the benefit provided by previous vaccination with a primary series.

Available data should at minimum characterize the most common adverse reactions associated with the booster dose.

- Uncertainties regarding risks (e.g., myocarditis) are also considered and would be further evaluated during post authorization surveillance.

FDA’s evaluation of the safety and effectiveness data of a booster dose of the Moderna COVID-19 vaccine, and additional input from the VRBPAC, is essential for weighing the known and potential benefits and risks.
Overview of Today’s Agenda

- FDA Introduction (30 min)
  - Introduction of the Topic (10 min)
    Peter Marks, M.D., Ph.D., Center Director, CBER, FDA
  - Background (15 min)
    Sudhakar Agnihothram, Ph.D., Review Committee Chair, DVRPA, OVRR, CBER, FDA
  - Q/A - 5 min

- Presentation of Data Relevant to the Need for Boosters (60 Min)
  - Presentation of Updated Israeli Vaccination Data (40 Min)
    Speaker 1: Sharon Alroy, M.D., M.P.H, M.B.A., Director of Public Health Services, Ministry of Health Israel
    Speaker 2: Ron Milo, Ph.D., Professor, Weitzman Institute, Israel
  - Q/A - 20 min

Break (15 min)
Overview of Today’s Agenda, cont.

- **Sponsor Presentation (45 min)**
  Safety and Immunogenicity of a 50 µg Booster Dose of mRNA-1273 (Moderna COVID-19 Vaccine)
  Jacqueline Miller, M.D., ID Therapeutic Area Head, Moderna Therapeutics

- **FDA Presentations (45 min)**
  Tina Mongeau, M.D., M.P.H., Medical Officer, OVRR, CBER, FDA
  Hui-Lee Wong, Ph.D., Associate Director for Innovation, OBE, CBER, FDA

  Q/A 10 min

- **Lunch (30 min)**
- **Open Public Hearing (60 min)**
- **Break (15 min)**
- **Additional Q & A Session regarding the Sponsor and FDA presentations**
- **Committee Discussion and Voting (120 min)**
Voting Question for the Committee

Do available data support the safety and effectiveness of Moderna COVID-19 Vaccine for use under EUA as a booster dose (50 mcg mRNA-1273) at least 6 months after completion of a primary series in the following populations:

- 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 whose frequent institutional or occupational exposure to SARS-CoV-2 puts them at high risk of serious complications of COVID-19 including severe COVID-19.
Non-Voting Discussion Question

Considering the information presented today and at the meeting of the VRBPAC on September 17, 2021, including updated information on effectiveness of mRNA COVID-19 vaccines, please discuss whether available data support use of a mRNA COVID-19 vaccine (Pfizer-BioNTech or Moderna) booster dose administered at least 6 months after completion of the same mRNA COVID-19 vaccine primary series in the general population of adults in an age group less than 65 years.

• For the purposes of this question, age groups below 18 years should not be considered
Thank you!