

Development, Authorization & Licensure of Vaccines to Prevent COVID-19

Vaccines and Related Biological Products
Advisory Committee

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Marion F. Gruber, PhD, Director
Office of Vaccines Research and Review, CBER, FDA

COVID-19 Vaccine Development



- Development, authorization and licensure of vaccines against COVID-19 are critical to mitigate the current SARS-CoV-2 pandemic and to prevent future disease outbreaks
- Numerous COVID-19 candidate vaccines based on different platforms and technologies,
 - E.g., RNA, DNA, protein subunit, inactivated virus, non-replicating and replicating viral vector, live attenuated, VLP
 - Express the spike protein or parts of the spike protein, i.e., the receptor binding domain (RBD), as the immunogenic determinant
- Many vaccine candidates have entered Phase 1 and 2 clinical trials around the globe and some have advanced to Phase 3 clinical trials to evaluate their efficacy and safety

COVID-19 Vaccine Development and FDA Regulatory Activities



- COVID-19 vaccine development may be accelerated based on knowledge gained from similar products and platform technologies
- Adaptive and/or seamless clinical trial designs allow for more rapid progression through the usual phases of clinical development
- **FDA must ensure that vaccines that are approved or authorized under EUA are supported by adequate scientific and clinical data**
- FDA is facilitating COVID-19 vaccine development by
 - Providing expedited reviews of CMC information, preclinical and clinical protocols and clinical trials data
 - Providing timely advice and guidance to sponsors to expedite proceeding to Phase 3 clinical trials
 - Directing efforts at generating adequate data to support access to investigational COVID-19 vaccines

Considerations for COVID-19 Vaccines



- COVID-19 vaccines will be widely deployed and administered to millions of individuals, including healthy people
- Public expectation that COVID-19 vaccines will be safe and effective
 - low tolerance for vaccine-associated risks
- **COVID-19 vaccines that are licensed in the US or authorized under EUA must meet applicable legal requirements**
 - **FDA will apply the same standards to grant a biologics license for a COVID-19 vaccine as for other preventive vaccines**
- Vaccine development can be expedited; however, there needs to be sufficient time to accrue adequate manufacturing, safety and effectiveness data to support potential widespread use of these vaccines

Biologic Licensure

- Section 351 of the Public Health Service Act, 42 USC 262:
The Secretary shall approve a biologics license application (BLA) - on the basis of a demonstration that –
 - the biological product ... is **safe, pure, and potent**; and
 - the facility ... meets standards designed to assure that the biological product continues to be safe, pure, and potent;
....
- Only those vaccines that are demonstrated to be safe and effective, & that can be manufactured in a consistent manner will be licensed by the FDA

Demonstration of Effectiveness of COVID-19 Vaccines



- 21 CFR 201.57: “...all indications [e.g., prevention of disease]...must be supported by **substantial evidence** of effectiveness.”
- Expectation that demonstration of effectiveness is based on **adequate and well-controlled clinical studies** using a product that is standardized as to identity, strength, quality, purity and dosage form
- For COVID-19 vaccines, the goal of development programs at this time should be to generate data necessary to support FDA licensure by conducting clinical trials that directly evaluate the ability of the vaccine to protect humans from SARS-CoV-2 infection and/or disease

COVID-19 Vaccines: Development Strategy & Data Required to Support Licensure

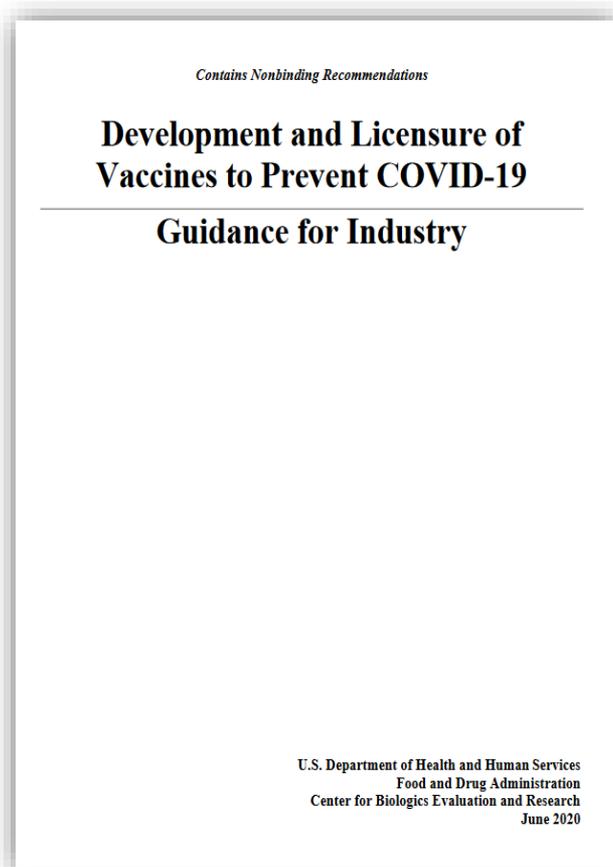


- Manufacturing process to ensure product quality and consistency
- Product-related data and testing plans adequate to support the manufacturing process in an appropriate facility, characterize stability and ensure consistency of manufacture
- Nonclinical data
 - Non clinical safety studies
 - Characterization of the immune response
 - Address the potential for vaccine-induced enhanced respiratory disease
- Clinical data adequate to support the proposed indication and use
 - Efficacy and safety
 - Characterization of the immune response
- CMC and facility data: compliance with cGMPs requirements
- Post-licensure pharmacovigilance plan



FDA Guidance for Industry: Development & Licensure of Vaccines to Prevent COVID-19 (June 2020)

- Helps facilitate the timely development of safe and effective vaccines to prevent COVID-19
- Reflects advice the FDA has been providing over the past several months to companies, researchers and others
- Describes the agency's current recommendations regarding the data needed to facilitate clinical development and licensure of vaccines to prevent COVID-19



Emergency Use Authorization



- An Emergency Use Authorization (EUA) may be issued only after several statutory requirements are met (section 564 of the FD&C Act (21 U.S.C. 360bbb-2))
- Issuance of an EUA requires a determination that the known and potential benefits of the **investigational** product outweigh its known and potential risks
- Use of an **investigational** COVID-19 vaccine under an EUA is not subject to informed consent requirements but vaccine recipients need to be provided a fact sheet that describes
 - the investigational nature of the product
 - the known and potential benefits and risks
 - available alternatives
 - option to refuse vaccination



Emergency Use Authorization (cont.)

- An EUA for a COVID-19 vaccine may allow for rapid and widespread deployment for administration of the investigational vaccine to millions of individuals, including healthy people
- Issuance of an EUA for an investigational COVID-19 vaccine would require
 - Adequate manufacturing information to ensure the product’s quality and consistency
 - A determination that the benefits outweigh its risks based on data from at least one well-designed Phase 3 clinical trial demonstrating safety and efficacy
- Any assessment regarding an EUA would be made on a case-by-case basis considering the proposed target population, the product characteristics, preclinical and human clinical data, and the totality of the available scientific evidence relevant to the product

FDA Guidance for Industry: Emergency Use Authorization for Vaccines to Prevent COVID-19 (October 2020)

Contains Nonbinding Recommendations

Emergency Use Authorization for Vaccines to Prevent COVID-19

Guidance for Industry

October 2020

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research

- Reflects advice the FDA has been providing to vaccine developers
- Describes the agency's current recommendations regarding the data needed to support issuance of an EUA for vaccines to prevent COVID-19

Overview of Today's Agenda



- **FDA introduction and Presentation of Discussion Points**
 - Marion F. Gruber, Ph.D. (FDA)
- **Epidemiology, Virology and Clinical features of COVID-19**
 - Cliff McDonald, M.D. (CDC)
- **NIH activities in the development of vaccines against COVID-19**
 - Hilary Marston, M.D., M.P.H. (NIH)
- **BARDA activities in the development of vaccines against COVID-19**
 - Robert Johnson, Ph.D. (FDA)
- **CDC plans for safety/effectiveness monitoring and evaluation during EUA use and post-licensure**
 - Tom Shimabukuro, M.D., M.P.H., M.B.A (CDC)
 - Stephanie Schrag, D.Phil. (CDC)

Overview of Today's Agenda (cont.)



- **CDER surveillance Systems/Postmarketing**
 - Steven Anderson, Ph.D. (FDA)
- **Operational aspects of COVID-19 vaccine distribution and tracking**
 - CAPT. Janell Routh, M.D., M.H.S. (CDC)
- **COVID-19 Vaccine Confidence**
 - Susan Winckler, R.Ph., Esq. (Regan Udall Foundation)
- **Licensure and emergency use authorization of vaccines to prevent COVID-19**
 - **CMC considerations/Clinical considerations**
 - Jerry Weir, Ph.D. (FDA) /Doran Fink M.D., Ph.D. (FDA)
- **Open Public Hearing**
- **Committee Discussion and Recommendations**



Discussion Items

1. Please discuss FDA's approach to safety and effectiveness data as outlined in the respective guidance documents.
2. Please discuss considerations for continuation of blinded Phase 3 clinical trials if an EUA has been issued for an investigational COVID-19 vaccine.
3. Please discuss studies following licensure and/or issuance of an EUA for COVID-19 vaccines to:
 - a. Further evaluate safety, effectiveness and immune markers of protection
 - b. Evaluate the safety and effectiveness in specific populations