COVID-19 Conversations

Marion Gruber
Director, Office of Vaccines Research and Review
Center for Biologics Evaluation and Research
U.S. Food and Drug Administration

COVID19Conversations.org
#COVID19Conversations
Authorization & Licensure of Vaccines to Prevent COVID-19

NAM-APHA Webinar on COVID-19 vaccines

November 18, 2020

Marion F. Gruber, PhD, Director
Office of Vaccines Research and Review, CBER, FDA
COVID-19 Vaccine Development and FDA Regulatory Activities

- 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.

- **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.
US Regulatory Framework for making COVID-19 Vaccines available

Licensure

Safety and Effectiveness Data

EUA

IND or Expanded Access
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
COVID-19 Vaccines: Development Strategy & Data Required to Support Licensure

- Manufacturing process to ensure product quality and consistency
- CMC and facility data: compliance with cGMPs requirements
- Nonclinical data
  - Non clinical safety & immunogenicity studies
  - Address the potential for vaccine-induced enhanced respiratory disease
- Clinical data adequate to support the proposed indication and use
  - Efficacy and safety
    - Clinical endpoint that assesses for direct evidence of protection against SARS-CoV-2 infection or disease
      - VE point estimate of ≥50% vs. placebo, with an appropriately alpha-adjusted confidence interval lower bound >30%
    - Characterization of the immune response
- Post-licensure pharmacovigilance plan
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
Data to Support COVID-19 Vaccine EUA

- EUA request for a COVID-19 vaccine may follow a case-driven interim analysis from one or more clinical trials
- To support a favorable benefit/risk determination, taking into account widespread deployment to millions of individuals, vaccine effectiveness should be supported by:
  - Clinical endpoint that assesses for direct evidence of protection against SARS-CoV-2 infection or disease
  - VE point estimate of ≥50% vs. placebo, with an appropriately alpha-adjusted confidence interval lower bound >30%
- In addition to passive safety follow-up an EUA request for a COVID-19 vaccine should include a plan for active safety follow-up of persons vaccinated under the EUA
  - Including but not necessarily limited to deaths, hospitalizations, and other serious or clinically significant AEs
  - To inform ongoing benefit/risk assessments for continuation of the EUA
FDA Guidance for Industry: COVID-19 Vaccines

Development & Licensure of Vaccines to Prevent COVID-19 (June 2020)
Emergency Use Authorization for Vaccines to Prevent COVID-19 (October 2020)

• 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
Possible groups for Phase 1 vaccination

From prior ACIP Discussions:

**Phase 1a:**
- HCP

**Phase 1b:**
- Essential Workers
- High Risk Med Conditions
- Adults ≥ 65 years old

- High Risk Medical Conditions >100M
- Essential workers ~80M
- Healthcare personnel ~20M
- Adults ≥ 65 years old ~53M
Distribution will adjust as volume of vaccine doses increases

**Limited Doses Available**
- Constrained supply
- Highly targeted administration required to achieve coverage in priority populations

**Large Number of Doses Available**
- Likely sufficient supply to meet demand
- Supply increases access
- Broad administration network required, including surge capacity

**Continued Vaccination, Shift to Routine Strategy**
- Likely excess supply
- Broad administration network for increased access

**Example Populations**
- **HCPs**
  - First responders
- **People with high-risk conditions**
  - Older adults, including those living in long-term care facilities
- **Non-healthcare critical workers**
  - People in congregate settings
- **All other older adults**
- **Young adults**
  - Other critical workers
- **All others in the US who did not have access in previous phases**

Illustrative example populations; final prioritization to be decided by ACIP

Illustrative scenario for planning purposes; will be adopted based on clinical/manufacturing information on all OWS candidates & vaccine prioritization.
ACIP Pathway to Recommendation

1. Should COVID-19 vaccine ‘A’ be recommended?
2. Evidence to Recommendation Framework GRade
3. To whom should early allocation of COVID-19 vaccine ‘A’ be recommended?
4. Scientific Evidence Ethical Principles Implementation

ACIP RECOMMENDATION