Licensure and Emergency Use Authorization of Vaccines to Prevent COVID-19: Chemistry, Manufacturing, and Controls (CMC) Considerations

Vaccines and Related Biological Products
Advisory Committee (10/22/2020)

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Background

- Chemistry, manufacturing, and controls (CMC) and facility information and data are critical to ensure the quality of vaccines and the consistency of vaccine manufacture
- Licensed vaccines must meet statutory and regulatory requirements for quality, manufacture, and control
  - Vaccines must be safe, pure, and potent
  - Manufacturing and facilities must be in compliance with applicable standards
- Sufficient information must be provided for vaccines to be used under Emergency Use Authorization to ensure vaccine quality and manufacturing consistency

Background (cont.)

- COVID-19 vaccine development may be accelerated based on knowledge gained from similar products manufactured with the same well-characterized platform technology
  - Some aspects of manufacture and control may be based on the vaccine platform
- Any CMC data that will not be available at the time of licensure, or at the time of EUA issuance, must be discussed with FDA in advance, sufficiently justified, and judged to have minimal impact on product quality

Key CMC Expectations for COVID-19 Licensure

- Complete details of the manufacturing process
  - History of process development capturing all changes incorporated into the manufacturing process
  - Information documenting adequate control of all source material
  - Establishment of a quality control system for all stages of manufacturing
- Validation of the manufacturing process
  - Data to support the consistency of the manufacturing process across all manufacturing sites
- Establishment of a quality control unit
  - Demonstration that quality release tests, including key tests for vaccine purity, identity, and potency are suitable for their intended purpose and validated

Key CMC Expectations for COVID-19 Licensure (cont.)

- Establishment of a comprehensive stability program
  - Demonstration of final container stability and expiry date
  - Demonstration that vaccine potency is maintained through expiry
- Compliance with all applicable standards for manufacturing sites, including:
  - Validation of major utilities and qualification of all equipment
  - Validation of aseptic, cleaning and sterilization processes
  - Establishment of a quality control unit that has responsibility for oversight of manufacturing
- Establishment of a lot release protocol for product distribution

CMC Considerations for use of COVID-19 Vaccines under Emergency Use Authorization

- To enable FDA to conduct a meaningful review, an Emergency Use Authorization request for a COVID-19 vaccine must include CMC data, identification of the manufacturing site(s), and information with respect to current GMP
  - It is critical that adequate manufacturing information be provided to ensure the quality and consistency of EUA vaccines
  - Manufacturing and process control data should be submitted in advance of an EUA request
- CMC information and data needed to support the use of a COVID-19 vaccine under EUA are generally similar to that needed for licensure

Key CMC Expectations for COVID-19 Vaccines Used Under EUA

- Complete details of the manufacturing process
- Validation of the manufacturing process
- Establishment of a quality control unit
- *Stability plan that includes tests for product safety, quality, and potency, and stability data from all available developmental and clinical lots to support use under EUA*
- *Stability data to support investigational use under EUA*

Key CMC Expectations for COVID-19 Vaccines Used Under EUA (cont.)

- *Expectations for manufacturing facilities similar to those for licensure; cGMP compliance assessed using site visit or other submitted information*
- *Appropriate quality specifications established for all drug product lots used under EUA and testing results submitted at the time of vaccine distribution*
  - The FDA regulation for lot release does not apply to investigational products, including those distributed in an EUA

Summary - CMC Considerations for Licensure and EUA Use of COVID-19 Vaccines

- A manufacturing process that ensures product quality and consistency is necessary, whether a vaccine is considered for licensure or for use under EUA
- CMC expectations will be the same for all COVID-19 vaccines, but the manufacturing and control data are unique for each product and production process
- Confidence and reproducibility of safety and efficacy results from pivotal clinical trials depends on the establishment and maintenance of high standards of vaccine quality control and manufacturing


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