Regulatory Considerations for Moving from Emergency Use Authorization to Biological License Application for U.S. Products

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FDA U.S. FOOD & DRUG ADMINISTRATION

Overview

Vaccine Development

- Pathways to expedite review and licensure
- FDA/CBER's role in facilitating vaccine development

Key considerations for vaccines during COVID-19 pandemic

- Emergency Use Authorized (EUA) & Licensed COVID-19 CBER regulated products under a Biologics License Application (BLA)

Key considerations for going from EUA to full licensure

Summary of development timelines for two COVID vaccines

Guidance

US Regulatory Framework to Make Vaccines Available During Public Health Emergency

Licensure

Traditional Approval

Accelerated Approval

Animal Rule

IND

Unapproved product with no, or limited, human safety and effectiveness data

Expanded access use options

EUA

Unapproved product, or unapproved use of an approved product, in response to a public health emergency

Vaccine Development against Emerging Infectious Diseases

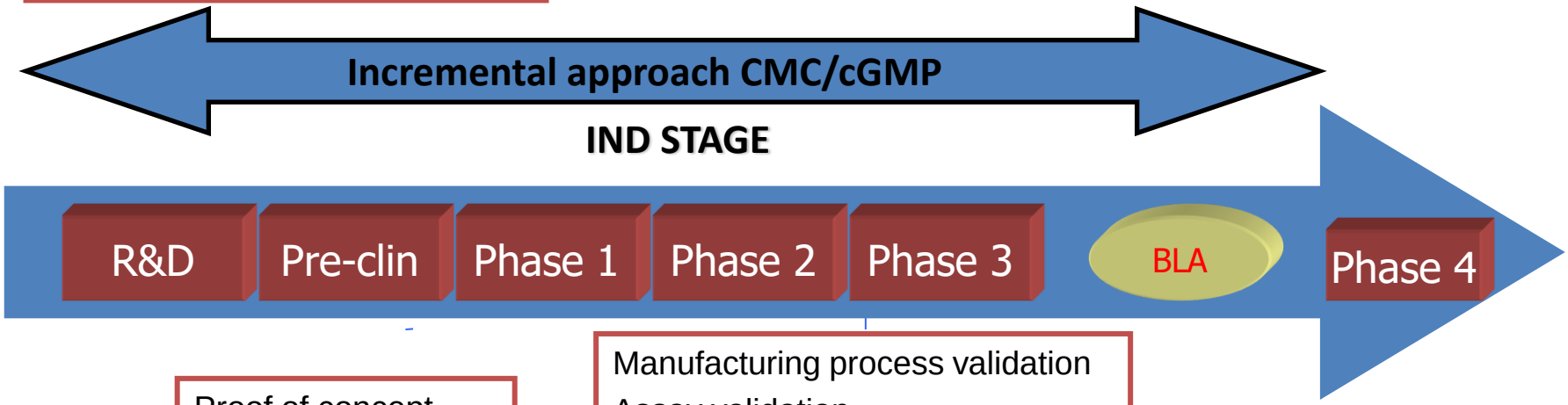
- Follows same paradigm as other preventive vaccines
  - Unique considerations if development occurs in a public health emergency
- Development Strategy
  - Develop and refine manufacturing process to ensure quality product and consistency of manufacture
  - Product-related data and testing plans adequate to support the manufacturing process in an appropriate facility, characterize stability, and ensure consistency of manufacture
  - Pre-clinical data: supportive of initiating clinical studies
  - Human clinical data adequate to support the proposed indication and use
  - Facility data: compliance w/cGMPs, manufacturing controls, QA/QC
  - Post-licensure pharmacovigilance plan

Vaccine Development: Overview

Process Development
- Source characterization
- Raw material qualification
- Cell bank characterization
- DS/DP characterization
- Assay development
- Formulation development
- Process controls

Process Optimization
- In-process controls
- DS/DP characterization
- Formulation optimization
- Assay qualification
- Specification development
- Stability

BLA Supplement:
- Manufacturing changes
- Formulation changes



Proof of concept
Pre-clinical safety

Manufacturing process validation
Assay validation
Final product specification
Final formulation
Stability

Vaccine Development: Expedited Development Pathway

Process Development
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Process Optimization
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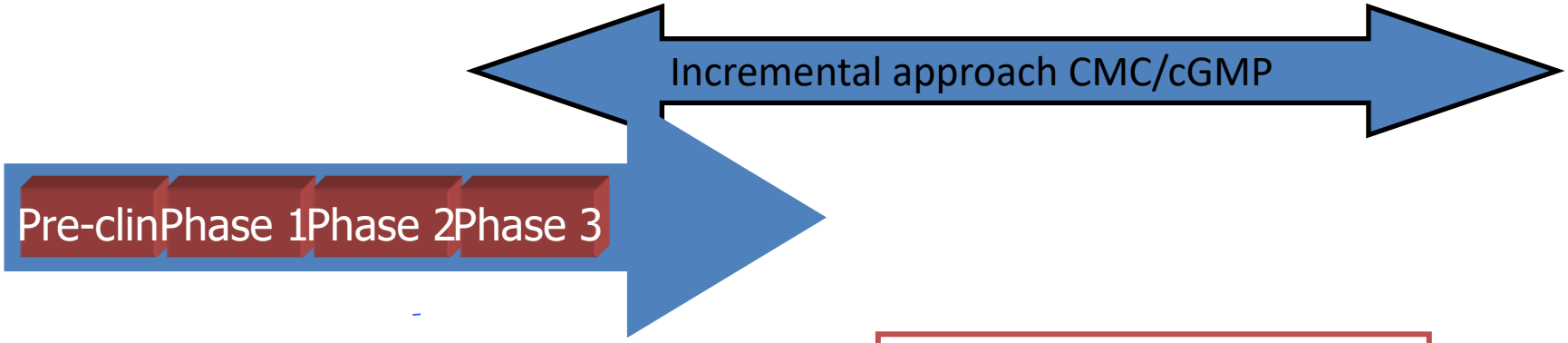

Manufacturing process validation
Assay validation
Final product specification
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Facilitating Expedited Vaccine Development - Role of FDA/CBER

When confronted with an emerging disease with significant public health impact, FDA provides:

- Expedited review of chemistry, manufacturing and controls (CMC) information, preclinical and clinical protocols, and clinical trials data, where available
- Early, expedited review of manufacturing and testing facilities
- Numerous meetings and pathways to licensure for vaccines: Accelerated Approval, Fast Track, Rolling Review Submission, Breakthrough Therapy and Priority Review
- International collaboration among regulatory agencies in review, with goal of regulatory convergence

Facilitating Expedited Vaccine Development - Role of FDA/CBER (cont.)

- Engage in scientific collaboration with industry and academia
  - CBER Participation in the evaluation of the WHO International Standard and Reference Panel for anti-SARS-CoV-2 antibody
- FDA Vaccines Advisory Committee public meetings when necessary
  - Expert advice
  - Transparency for public awareness of critical issues
- **Special emergency programs**
  - Emergency Use Authorization for products used in US population
  - Coronavirus Treatment Acceleration Program (CTAP) *for therapeutics*
    - https://www.fda.gov/drugs/coronavirus-covid-19-drugs/coronavirus-treatment-acceleration-program-ctap

Considerations for COVID-19 Vaccines

- COVID-19 vaccines are being widely deployed and administered to millions/billions of individuals, at risk and healthy people
- Public expectation that COVID-19 vaccines will be safe and effective
  - Low tolerance for vaccine-associated risks
- Vaccine development can be expedited; however, there needs to be sufficient time to accrue adequate manufacturing (including facilities qualification), safety and effectiveness data to support potential widespread use of these vaccines
- Critical to continue global discussion and harmonization to facilitate rapid development, approval/authorization, and global distribution of vaccine
- **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**

Considerations for EUA to BLA

- CMC Data – What is still needed?
- Product quality and testing – Establish Lot Release Protocol?
- Manufacturing Facilities – Is there cGMP compliance?
- Products used under both EUA and BLA – Why is this necessary? How long will the EUA be needed?
- Clinical Data – Are the study reports finalized? Is there sufficient safety and effectiveness data to support licensure?

EUA to BLA – CMC data

- Finalize process validation
  - Process validation completed for both drug substance and drug product
  - Full final study reports for assay and analytical test validation
- Establishment of shelf life
  - Data to support expiry dating of drug product
- Demonstrate manufacturing consistency and comparability between manufacturing sites

EUA to BLA – Lot Release

- No official lot release occurs under EUA
  - Final lot CoAs are reviewed prior to product distribution under EUA.
- Finalize lot release protocol and required testing to be performed by the sponsor and by CBER
  - Establish administrative structure for the submission of lot release protocols and samples. Most important for new sponsors.
  - Critical to determine the suitability of analytical methods used for release of DS and DP. Review final validation reports.
  - Establish and implement release test methods in CBER quality control laboratory.
  - Perform testing and data review of “launch” lots and all subsequent lots to be distributed.

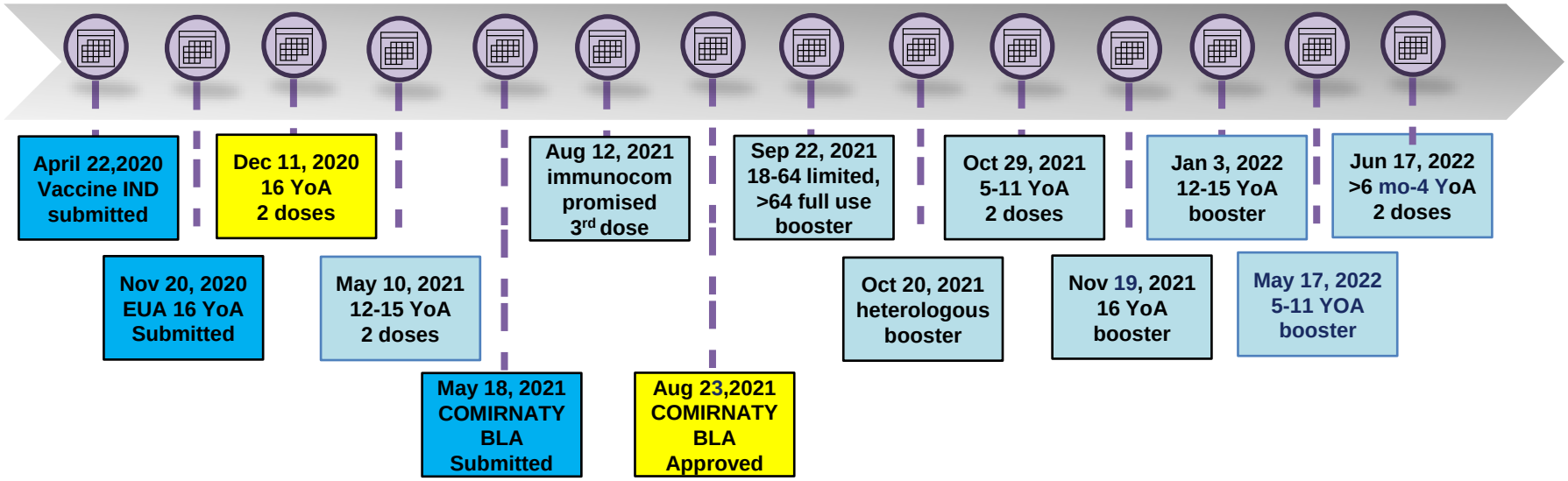
EUA to BLA - Facilities

- Quality of facility to manufacture product for use under EUA
  - Review performed according to requirements for products under development – IND
  - For EUA review, there is an expectation the cGMPs are in place.
    - These expectations are detailed in the EUA Guidance (see below).
  - Depending on the situation, can perform:
    - Site visit – no 483 issued, no classification in the compliance system
    - Investigation
    - Inspection
  - Decision made on a case by case basis and depends on:
    - Inspectional history

- Requirements for licensure of a facility under BLA
  - Expectation that all quality systems are in place

Pfizer-BioNTech COVID-19 Vaccine

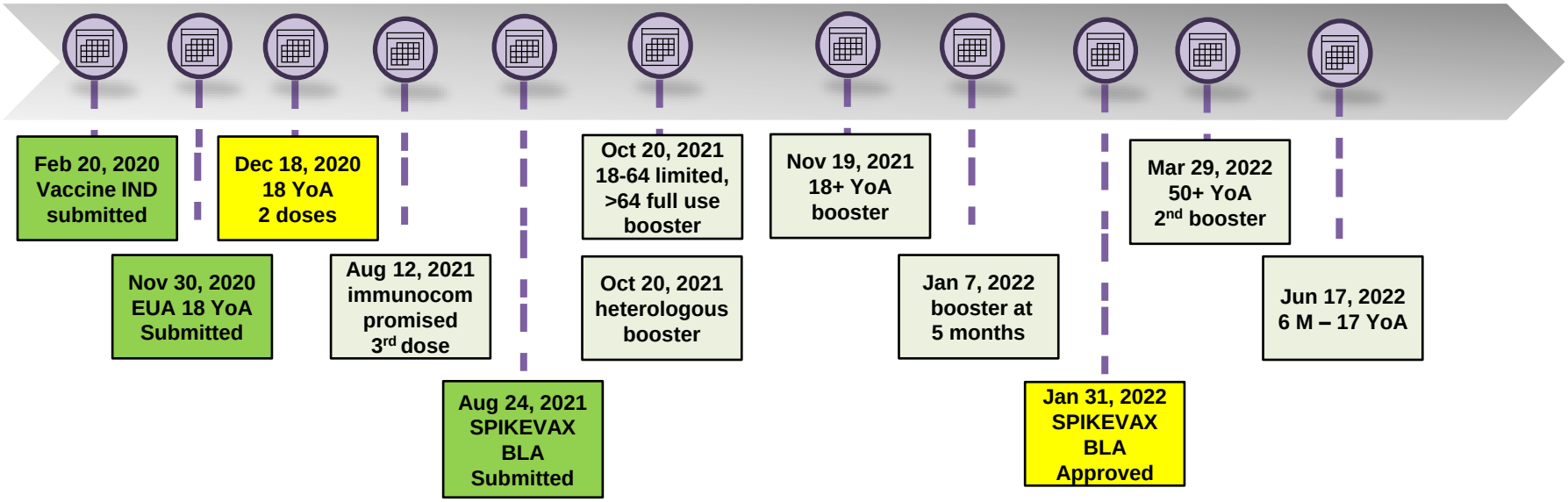
Development Timeline



Comirnaty and Pfizer-BioNTech COVID-19 Vaccine | FDA

Moderna COVID-19 Vaccine

Development Timelines



Spikevax and Moderna COVID-19 Vaccine | FDA

FDA Guidance for Industry: Emergency Use Authorization for Vaccines to Prevent COVID-19 (March 2022)

https://www.fda.gov/regulatory-information/search-fda-guidance-documents/emergency-use-authorization-vaccines-prevent-covid-19

- 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
- Describes the Agency's current recommendations regarding the evaluation of vaccines to prevent COVID-19 caused by variants of concern

COVID-19 Vaccine Guidances: https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/covid-19-related-guidance-documents-industry-fda-staff-and-other-stakeholders

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

https://www.fda.gov/regulatory-information/search-fda-guidance-documents/development-and-licensure-vaccines-prevent-covid-19

- 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 years 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

COVID-19 Vaccine Guidances: https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/covid-19-related-guidance-documents-industry-fda-staff-and-other-stakeholders

Key Considerations for Full Licensure of Expedited Vaccines - Summary

- **The regulatory review of each vaccine will be data-driven**
- Vaccine approval will be based on validated and well-controlled manufacturing process
- Vaccine approval will be based on adequate and well-controlled studies demonstrating safety and effectiveness

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Thank You!