CMC Considerations in Authorizing Use of Variant-Specific Vaccines

December 6, 2021

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COVID-19 Vaccines: SARS-CoV-2 Variants of Concern

• Multiple SARS-CoV-2 variants have been identified
• Critical to establish impact of variants on vaccine efficacy, as well as other biologics used to diagnose or treat COVID-19
• Critical to establish pathway for the development and testing of vaccines against variants of concern
  • Non-clinical studies needed?
    • Parallel studies with clinical trial?
  • Manufacturing and quality control
    • Product characterization
    • Potency
    • Clinical endpoints - immunogenicity
• Regulatory pathway to authorize or license use of new vaccines
COVID-19 Variant Virus Vaccines

• Vaccine authorization/licensure is based on validated and well-controlled manufacturing process
  • Well-defined manufacturing process to ensure product quality, consistency, and comparability across multiple facilities
  • Product-related data and testing plans adequate to support the manufacturing process in an appropriate facility, to characterize stability, and to ensure consistency of manufacture
  • Facility data to support product quality
    • Compliance with cGMPs
    • Quality systems in place
COVID-19 Variant Virus Vaccines

• Requirements for the authorization of future SARS-CoV-2 variant vaccines will depend on:
  • New vaccine not previously authorized/licensed
  • Prior authorization of “prototype” strain
  • Platform knowledge
  • Development of variant specific assays and reagents
• The regulatory review of each vaccine will be case-by-case and data-driven
CMC considerations for previously authorized products

• If manufacturing process and facilities are identical, no additional process validation will be required
  • Agreement can be reached with sponsors on what data will be necessary to support consistency of manufacturing of new vaccines
    • Will be at least one full scale batch

• If in-process and final release analytical methods are identical, assays do not have to be re-validated for the manufacture and control of variant virus vaccines
  • The exception is critical assays that are variant specific:
    • Potency assay
    • Identity assay

• Stability data from previously authorized/licensed vaccines using the same platform will be considered as supportive information.
CMC considerations for previously authorized products - characterization

• For all vaccine types:
  • Are there any critical quality attributes impacted by the inclusion of a new spike protein antigen?

• For mRNA vaccines:
  • Is the level of protein expression, as measured in an *in vitro* expression assay, similar to previously authorized vaccines?
  • Is the purity profile of DS/DP impacted by variant sequence?

• For vector-based vaccines:
  • Is the level of protein expression similar to previously authorized vaccines?
CMC considerations for previously authorized products – potency assays

• Potency assays for variant virus vaccines:
  • Require demonstration that the potency assay is specific for the variant.
  • Require characterization of variant specific reagents and controls, including antibody reagents and any variant specific antigens used in an assay

• Identity assays for variant virus vaccines:
  • Require demonstration that the identity assay is capable of distinguishing variant vaccine from prototype or other variants.
Additional consideration for variant vaccines

• Monovalent vs. Bivalent vaccines:
  • Potency assay must measure each component of bivalent (or multivalent) vaccine
  • Identity assay must be able to appropriately distinguish each variant virus type in the final drug product.

• Clinical Assays for Immunogenicity:
  • Adapt assay platforms for use with variant vaccines
    • Need to show specificity of the assays for samples from variants
  • Understanding that the availability of variant specific reagents may be limiting
Acknowledgements

• DVP/OVRR/CBER
  • Jerry Weir
  • Swati Verma
  • Anissa Cheung
  • Xiao Wang
  • Gopa Raychaudhuri
  • Cassandra Overking