Clinical interface with CMC and specifications – Patient Centric Specifications

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INTRODUCTION—Specification setting for biologicals is often based on manufacturing experience and does not necessarily reflect the true safety and efficacy expectations for the product. This presentation will show some perspectives on how to address this issue.

CHALLENGES—Early Clinical Quality Attribute (CQA) identification and acceptance criteria are key, but are challenged by limited platform/prior knowledge and reliance on nonclinical models is not always obvious for vaccines. If an attribute is expected to show varying values due to instability or challenges to control (manufacturing/ testing), clinical justification should be considered.

APPROACH BEING TAKEN—Patient centric specifications approach is a multidisciplinary effort. Key drivers are Quality by Design approach (observation of CQAs changing over time, analytical procedure selection and development to monitor CQAs in stability, acceptance criteria clinically justified) and prior product knowledge (formulation, analytical testing, manufacturing process, toxicology profile, clinical design). Continuous interactions between CMC and Clinical function is key to the design and trial execution in order to support justification of specifications. Early engagement with Health Authorities on CMC and Clinical approach is critical. An illustrative example will be provided to show how all these elements have been implemented for a vaccine (Menveo liquid).

CONCLUSIONS—Acceptance criteria for product related critical quality attributes based on patient centric approach ensure: strong specifications; delivery to the patient of future commercial lots equally potent as those tested in clinical trial at the desired shelf life; robust rationale for product comparability; higher flexibility in commercial supply by assuring a reduced lot rejection rate.