

Development Stages in Scope Vaccines

The earliest eligible stage for CARB-X funding is Hit-to-Lead, and CARB-X defines a “Hit” as meeting the following MINIMAL entry criteria:

- Vaccine antigen(s) has been identified, and supportive immunogenicity data in appropriate animal models have been generated. Specifically for the case of maternal vaccines against neonatal sepsis, the envisioned mechanism of protection of the neonate by maternal immunization should be explained, along with how the observed immune response will be aligned with this mechanism.
- Presence and sequence heterogeneity of antigen(s) across clinical isolates that are epidemiologically relevant to the proposed patient population have been determined.

Typical activities during Hit-to-Lead (Lead Generation)

- Characterization of the immune response to the antigen(s) *in vivo*, with mechanism for protection defined
- Determination of the optimal antigen expression (or vaccine production) system
- Preliminary characterization for product quality attributes (lab scale) such as purity, protein conformation, stability, yield, etc., as appropriate
- Adjuvant/formulation screening studies
- Standardization of methods to assess immunogenicity in relevant animal models

Typical activities during Lead Optimization

- Determination of final vaccine product composition (e.g., adjuvant, delivery platform, etc.)
- Identification of Key Quality Determinants
- Qualification of assays to assess immunogenicity and functional antibody and/or cellular response
- Determination of Immunogenicity/efficacy in animal models with route of immunization, regimen, and endpoints to reflect clinical plans
- Assay development to quantitate potency
- Cell bank generation (research)
- Reproducibility runs performed at lab scale and appropriate analytical characterization
- Assessment of stability profile
- Tech transfer and scale-up of vaccine production
- Development of analytical assays for vaccine product release
- Elaboration of a clinical development plan
- Pre-IND consultation (or guidance sought from another relevant regulatory body)

Typical activities during Pre-Clinical (IND Enabling)

- Production and release of Master (and Working, if appropriate) Cell banks
- Qualification and validation of the analytical release assays
- Upstream and downstream process development for GMP scale
- Engineering CMC run
- Toxicology studies
- GMP manufacture of vaccine material for clinical study
- Product characterization at production scale to demonstrate purity, stability, and potency, and product released as per regulatory guidelines
- Submission of IND to US FDA (or clinical trial application to another relevant regulatory body)

Typical activities during Phase 1

- First-in-human, dose-escalation study in healthy volunteers to determine safety, to include endpoints for assessing immunogenicity and potential vaccine efficacy
- Activities related to Phase 2 readiness, (e.g., vaccine manufacture, assay validation, plans for onward clinical development, etc.)