CARB-X
Combating Antibiotic Resistant Bacteria

Minimal Entry Criteria and Development Stages in Scope
Diagnostics

Minimal Entry Criteria

Consistent with our "Aligned by Design" strategy, we seek diagnostics to support the growing portfolio of potential maternal vaccines to prevent neonatal sepsis. Products focused on rapid triage, bacterial identification and/or antibiotic susceptibility testing are sought. Time-to-result and cost-of-goods are key criteria, and small-sample volumes are critical for this patient population.

For *Neonatal sepsis* products, Minimal Entry Criteria for the diagnostic programs are as follows:

- Programs must be in TRL 3-5, between the beginning of technical feasibility and late-stage product development. For the definition of activities supported in Feasibility and Development see section below.
- Supporting data is required. See below for additional detail:
    a. For **rapid triage tests** -- Proof of concept data on clinical or contrived samples may be used, the tests must target pathogens or markers relevant to neonates (see TPP here). **Preliminary data must demonstrate the following:**
        i. If using host-immune response biomarker detection or transcriptomic markers, clinical sensitivity >90% and specificity >90%, is required.
        ii. If detecting bacterial pathogens directly Clinical or Analytical sensitivity >90% and specificity >90% is required.
        iii. Direct from specimen approach is required.
        iv. Sample volume ≤1 mL is required.
        v. Time-to-result ≤30 mins is required.
        vi. Target COGS of consumable ≤5 USD *is preferred.*

    b. For **pathogen ID tests** -- Proof of concept data on clinical or contrived samples targeting at least one of the pathogens causing neonatal sepsis **is required** (see TPP here). **Preliminary data must demonstrate the following:**
        i. An analytical Limit of Detection (LoD) of <50 cfu/mL **is required.**
        ii. Whole blood as a sample type **is required.**
        iii. Sample volume ≤2 mL *is preferred.*
        iv. Time-to-result ≤8 hours *is preferred.*

    c. For **genotypic resistance or phenotypic susceptibility tests** -- Proof of concept data on clinical or contrived samples targeting neonatal sepsis with demonstration of at least one pathogen/antibiotic combination, pathogen/genetic mutation combination or pathogen/gene detection combination **is required** (see TPP here). **Preliminary data must demonstrate the following:**
        i. Categorical agreement with the reference method of ≥85% **is required.**
        ii. Whole blood as a sample type **is required.**
        iii. Sample volume ≤2 mL *is preferred.*
        iv. Time-to-result ≤8 hours *is preferred.*

Products that are combinations of these tests are acceptable (e.g. pathogen ID plus antibiotic susceptibility test). Please note that these are minimum requirements for entry into the application process only. We recognize that many technologies may be early in the development process, and

therefore they are less stringent than the minimum final product requirements noted in the TPP, as optimization may be necessary.

CARB-X supports diagnostics proposals for bacterial ID and/or AST/AMR in the development stages outlined below (TRL 3-5). Some guidance is provided below as to typical activities that would be considered in or out of scope in line with these stages.

Feasibility: Benchtop feasibility demonstrated with clinical specimens. Sufficient data to support the feasibility of the approach including data that the pathogen of interest can be detected. Plan downstream, critical-path activities, evaluate critical requirements and outline a high-level target product profile. For instrument-based systems, develop and evaluate an initial prototype of the system or of high-risk modules, including software. Demonstrate understanding of relevant clinical care pathway and testing algorithms and how product would be differentiated from competition. Continue prototype testing, as required, to support assay development. Finalize diagnostic target(s) and methods for detecting or quantitating target(s). Develop detailed product development plans and finalize critical design requirements. Finalize initial instrument and software architecture, incorporating input on manufacturability of proposed product. Identify and execute commercial agreements with key external development partners. Begin implementing a Quality Management System; draft regulatory strategy, intended use statement, analytical and clinical study plans. Complete technology transfer from Research to Development.

Development: Develop reagents and buffers. Build and test prototypes of components and subsystems. Code and unit test software. Build first release of instrument software for integration testing. Develop protocols for assay and integration testing. Finalize User Interface specification. Produce initial assay lots with quantities sufficient to initiate real-time stability studies on development lots. Demonstrate key product requirements, including sensitivity and specificity, with fully integrated prototype using clinical samples, preferably in the hands of external users. Continue implementation of a Quality Management System. Prepare for pre-submission with the FDA or relevant Stringent Regulatory Authority (SRA).

Out of scope (too late, beyond CARB-X funding):

- Late-stage product development (Beta System development)
- Verification and Validation testing
- Pilot lot production of reagents and instruments
- Clinical validation of the technology including demonstration in a relevant clinical environment to support regulatory filings
- Longer term studies in support of regulatory filings such as long-term stability studies.
- Marketing support including submission of marketing approvals.
- Manufacturing of the final instrument to be marketed and associated scale-up activities