Summary of Key Changes to Common Protocol (Comparing V2.0 23 April 2024 to Version 2.1 8 July 2024)

1.) Section 4.4 Outcome Measures for Cohort A includes the following changes: a.) **Cured**- "bacteriologically confirmed" was changed to "culture confirmed" and two consecutive cultures "taken at end of treatment at least 4 hours apart" was changed to "taken at any time during treatment" b.) **Clinical failure**- the example of weight loss was changed from "over 10% of loss of usual weight" to "weight loss".

Summary of Key Changes to Common Protocol (Comparing 2016 version to V2.0 23 April 2024)

1.) Cover page has been modified to include changes in RePORT PIs and NIH representatives. The following pages were updated: Table of Contents, List of Abbreviations and Acronyms, Protocol Schema, Protocol Development Team Roster, Protocol Team Cohort Research Unit Investigators, and Protocol Schema.
2.) Section 1.1 Rationale was updated to include the new RePORT networks.
3.) Section 1.2 Study Objectives was modified to include screening, triage, and diagnosis of TB disease.
4.) Section 1.3 Description of the Population was modified (for Cohort A) to "participants seeking care with symptoms of pulmonary TB".
5.) Section 3.0 Study Design was modified. Sample collections of urine and saliva were removed.
6.) Section 4.2 Cohort A: Inclusion and Exclusion Criteria were changed. Participants with MDR TB and XDR TB will no longer be enrolled into Cohort A. Removed sentence stating that there are no age restrictions for Cohort A.
7.) Section 4.2.1 Inclusion Criteria were modified. Clarified TB testing results [Sputum smear or culture positive microscopy **or** Mtb detection by rapid diagnostic test, such as Gene Xpert or Line Probe Assay (LPA)]. Participants now must be 15 years of age or older.
8.) Section 4.2.2 Exclusion criteria were changed. Added language stating that MDR/XDR TB patients may be enrolled in a separate protocol but will not be enrolled in Cohort A.
9.) Section 4.2.3 has been renamed "Late Exclusion Criteria". References to NP and gastric aspirates were removed. Definition of culture-confirmed TB was clarified.
10.) Section 4.3.2 Baseline (Clinical and Laboratory Evaluations for Cohort A) was updated. Added concomitant medication history, completion of MMRC dyspnea scale questionnaire, and Gene Xpert. For Central biorepository storage, removed the requirement for the collection of urine, saliva, sputum, whole blood for PAXgene, IGRA, genetic analyses. Added optional specimen collections.
11.) Section 4.3.3 Month 1 was removed. For Month 2 visit, removed the requirement for the collection of urine, sputum, whole blood for PAXgene, IGRA, and PBMC.
12.) Section 4.3.4 Month 6 visit added (if End of Treatment does not fall in visit window). Includes medical history, CXR (if not done as standard of care), sputum smear and culture (when specimen can be obtained) and the collection of whole blood (plasma) for storage.
13.) Section 4.3.5 End of Treatment Visit was modified. MMRC Dyspnea scale was added. For Central biorepository storage, removed the requirement for the collection of urine, saliva, whole blood for PAXgene, IGRA, PBMC.
14.) Section 4.3.6 6 Month post treatment visit renamed Month 12 Visit/Phone call.

15.) Section 4.3.7 Treatment Failure, Relapse, or Withdrawal Evaluation (TX F/R/W) Visit added MMRC Dyspnea Scale. For Central biorepository storage, removed the requirement for the collection of urine, sputum, whole blood for genetic analyses, PAXgene, IGRA, PBMC.
16.) Section 4.4 Outcome measures for Cohort A was updated. TB Treatment outcomes were modified to align better with the WHO definitions (Cured, Treatment Completed, Treatment Failed, Died, Lost to follow-up, Not evaluated, Treatment Success). Clarified Completion of Therapy Status (3b). Added Additional Classifications section (Bacteriologic relapse, Emerging resistance). Added Study outcomes section (Completed all study activities, Death, Lost to follow-up, Mandatory withdrawal and other).
17.) Section 4.5 Schedule of Events for Cohort A was updated to include all of the changes in visits/activities.
18.) Section 5.1 Design and Procedures (Cohort B Household Contacts (HHCs or Close Contacts of Active TB Patients) was modified, reducing the study length of time from 24 months to 12 months with a 6 week window.
19.) Section 5.2.1 (#1) clarified "exposure" to a pulmonary TB patient.
20.) Section 5.2.2 added "Presumed TB" as an exclusion criterion.
21.) Section 5.3.2 Baseline added language on TST/IGRA testing. Added the completion of the MMRC Dyspnea Scale questionnaire. Added collection of sputum (if producible) for Gene XPert and culture. Added blood draw for HbA1C testing. Deleted collection (for storage) of whole blood for IGRA, and PBMC. Added collection of sputum for storage. Added chest X-ray.
22.) Section 5.3.3 Follow up visits were changed to 6 months and 12 months with -4 week and + 6 week window). Statement about TST/IGRA testing was added. Added statement that list of concomitant medications will be collected.
23.) Section 5.3.4 TB Activation Evaluation Visit was modified. Added the completion of the MMRC Dyspnea Scale questionnaire. Added statement that list of concomitant medications will be collected. Removed collection of urine, PBMCs, and IGRA for storage.
24.) Section 5.3.5 Premature Discontinuation Visit added "Or Phone Call to the title". Added statement that list of concomitant medications will be collected.
25.) Section 5.4 Outcome Measures for Cohort B added "Withdrawal for any reason".
26.) Section 5.5 Schedule of Events for Cohort B was updated to include all of the changes in visits/activities.
27.) Section 6 Off-study Criteria for Cohorts A and B was updated.
28.) Section 7 Sample Size was streamlined, removing language specific to RePORT India.
29.) Section 8 Participating Cohort Research Units was modified to include China, Philippines, South Korea, and Uganda.
30.) Section 9 Individual Country Cohorts was modified. Updated sections for RePORT India, RePORT Brazil, RePORT Indonesia and RePORT South Africa. Added sections for China, Philippines, South Korea, and Uganda.
31.) Section 10 was renamed RePORT International Coordinating Center (RICC). All references to FHI360, Dr. Carol Dukes Hamilton, and Westat were removed. Added description of TB RICC 3.0 and listed new TB RICC institutions (Rutgers, VUMC, Frontier, JHU).
32.) Section 11 Data collection was modified.
33.) Added Sections 11.1 (Clinical data collection), 11.2 (Network Unique Identifiers) and 11.3 (Quality Assurance).

34.) Section 11.4 Statistical and Data Management Center was modified, describing the expanded role of TB RICC and the establishment of routine data transfers.

35.) Section 12 was renamed Specimens for Long-Term Storage at the Network's Central Biorepository and "Network" was added to "Central Biorepository" throughout the section for clarity. Table 12.1 was modified, removing the reference to children.

36.) Section 16 Quality Assurance and Cohort Research Unit Support Visits was updated, removing reference to Westat and periodic site visits.