

TB specimen collections – Overview 2009

Well-characterized reference materials are indispensable for the development of novel, effective TB diagnostics in all phases of development. Specimen banks play a major role in 1) Accelerating the development of TB diagnostics; 2) Promoting the discovery of biomarkers; and 3) Facilitating the development of simple and safe specimen processing methods. Reference materials also allow for high-quality comparative studies (using specimen panels) and limit the need for expensive field trials with immature products.

This document provides a short description of currently existing TB specimen collections of significant size, for which trial design, ethical and safety features follow WHO guidelines. It shows that well-characterized specimens are available and relatively easy accessible and encourages academia, public and private research institutes and industry to make use of existing materials. However, there are certainly major gaps in existing collections, notably we lack specimens from pediatric and extrapulmonary TB cases as well as MDR/XDR TB cases. Developers would need specimens from secondary TB cases at early stage of infection from cohorts with long term follow up. Especially for biomarker discovery projects, we would need a greater variety of specimen types and even more intensive diagnostic workup and follow up. These gaps ought to be closed over the coming years.

Central specimen banks

TDR/WHO TB specimen bank

Enrolment from: Adults suspected of pulmonary TB

Patient categories: Smear and culture positive (S+C+); smear-negative, culture positive (S-C+); smear-negative, culture-negative patients, treated for TB based on clinical symptoms with clear response to treatment (CXR); culture-negative patients with TB-like symptoms who were not started on TB treatment and for which TB has been excluded based on clinic and chest radiographs at enrolment and during follow-up (Non-TB).

Origin of patients: The Gambia, Uganda, South Africa, Brazil, Spain, Canada, Bangladesh, Viet Nam, Kenya, Colombia, Peru

Follow-up duration: 2-3 months

Number of serum, urine, sputum aliquots per enrolled patient: Serum - 20 (0.5 ml); sputum - 5 (0.5 ml); saliva - 5 (0.5 ml); urine - 5 (1.5 ml)

Diagnostic gold standard: Concentrated ZN microscopy post-NALC-NaOH treatment, solid and liquid culture, clinical symptoms including chest-radiograph, TB ruled out with non response to TB treatment/response to standard antibiotic treatment as well as a 2-3 months follow up of all patients that were not smear positive.

Patient follow-up: 2 months

Current number of serum, urine, sputum aliquots at central storage facility:

Serum - 21,000

Sputum - 4,100

Saliva - 900

Urine - 3,400

Current distribution in patient categories: 1206 S+C+, 161 S-C+, 73 CXR, 650 Non-TB

Availability of specimens from HIV pos patients: Yes

How to access: Request for specimens with form found at

<http://www.who.int/tdr/svc/diseases/tuberculosis/specimen-bank> sent to Carl-Michael Nathanson (nathansonc@who.int) at TDR

Review process: TDR TB Specimen Bank review committee reviews and approves or rejects all requests.

Average time to release: 1 month

Costs to the specimen user: shipment costs only

[FIND TB reference materials](#)

Enrolment from: Adults suspected of pulmonary TB

Patient categories: Smear and culture positive (S+C+); smear-negative, culture positive (S-C+); smear-negative, culture-negative patients, treated for TB based on clinical symptoms with clear response to treatment (CXR); culture-negative patients with TB-like symptoms who were not started on TB treatment and for which TB has been excluded based on clinic and chest radiographs at enrolment and during follow-up (Non-TB).

Origin of patients: Bangladesh, Vietnam, South Africa, Peru, Brazil

Diagnostic gold standard: Concentrated ZN microscopy post-NALC-NaOH treatment, solid and liquid culture, clinical symptoms including chest-radiograph, clinical symptoms / laboratory findings during patient follow up

Follow-up duration: 2-3 months

Number of serum, urine, sputum aliquots per enrolled patient: Serum - 16 (0.5 ml); Sputum – 4-6 (0.5 ml); Saliva – N/A; Urine - 5 (3.5 ml)

Current number of serum, urine, sputum aliquots at central storage facility:

Serum – 17,821

Sputum – 9,070

Urine – 6,738

Current distribution in patient categories: 1048 S+C+, 250 S-C+, 18 CXR, 148 Non-TB. (In addition, specimens from 1200 endemic controls without pulmonary symptoms will be available shortly).

Availability of specimens from HIV pos patients: Yes, but need to increase numbers

How to access: a Material Request Form (MRF) found at <http://www.finddiagnostics.org/tuberculosis/reference-materials> has to be completed and sent to Eloise Valli (eloise.valli@finddiagnostics.org) by email (as PDF file) or by registered mail.

Review process: FIND Specimen Bank Review Committee reviews technical proposals from current or potential collaborators. Decision is based on relevance to public health.

Average time to release: 1 month

Costs to the specimen user: free

[Grand Challenges in Global Health TB Biomarkers Consortium reference materials](#)

Enrolment from: Newly diagnosed Adult Pulmonary TB patients (HIV-ve/HIV+ve) and TST+ve clinically adult healthy household contacts of these index TB cases (HHC); Adolescent cohorts (South Africa);

Newborn cohorts in South Africa, Malawi, UK

Origin of patients: Ethiopia, Malawi, South Africa, The Gambia, Uganda

Follow-up duration: 24 months (3 time points for HHC – 0, 6, 18m, 2 time points for Index case – 0, 12m). Well characterized and robust follow-up process is in place for all these subjects.

Type of samples per enrolled subject: Serum/Plasma, PBMC, RNA, DNA

All samples are currently stored at each of the field sites, but are planned to be centralized at a later point.

Diagnostic gold standard: Concentrated ZN microscopy post-NALC-NaOH treatment, solid and liquid culture, clinical symptoms including chest-radiograph, clinical symptoms / laboratory findings during long-term patient follow up

Availability of specimens from HIV pos patients: Yes

How to access: The samples will ONLY be made available after fulfilling the committed activities of the current GCGH consortium. Efforts are underway with BMGF to establish a process for a central repository and the pathways of accessibility to the TB scientific community to some of these samples. Also the field sites need to be compensated towards the costs as the current efforts have been sustained with several collateral activities. The samples are envisaged to be made available under code (anonymized) to the scientific community for validating novel test(s)/assay – *not for any explorative pilot studies or such endeavors*. Following completion of the study, the results will be communicated to the investigators from whom the samples originated to break the codes and to make the clinical information available for final analysis with shared ownership. For further questions, please contact Dr. Shreemanta K Parida (parida@mpiib-berlin.mpg.de)

Review process: Yet to be established.

[Aeras TB reference materials](#)

Enrolment from: Pediatric and adult vaccine cohorts

Origin of patients: Focus on Sub-Saharan Africa.

Type of samples per enrolled subject: Plasma, urine

Follow-up duration: up to 24 months

Availability of specimens from HIV pos patients: Yes

How to access: Yet to be established. For further questions, please contact Dr. Lew Barker (LBarker@aeras.org)

Review process: Yet to be established.

[Local specimen collections at trial sites](#)

[Keertan Dheda, UCT](#)

Enrolment from: Adult TB suspects

Origin of patients: South Africa

Availability of specimens from HIV pos patients: Yes

Type of samples per enrolled subject: Urine, saliva, sputum and plasma from well-characterized TB suspects (comprehensive clinical data, LTBI status, and 6 month follow-up are available). Serial samples are available in definite TB cases. Materials include also extrapulmonary specimens (CSF, pleural fluid, and alveolar lavage fluid). Samples are currently being collected from patients with MDR and XDR-TB.

How to access: On a case-by-case-basis with review of the application by the Lung Infection and Immunity Review Committee. UCT has excellent laboratories including molecular biological and proteomics facilities. On-site testing with shared ownership of data is desirable but not essential. Given the resource constraints in South Africa, it is preferred that access be granted through an equitable model, with contributions to capacity development, and infrastructure, that will ensure the sustainability of this specimen collection.

[*Mark Nicol, UCT*](#)

Enrolment from: Pediatric TB suspects

Origin of patients: South Africa

Availability of specimens from HIV pos patients: Yes

Type of samples per enrolled subject: Focus on extrapulmonary specimens (nasal swabs, gastric fluid), induced sputum.

How to access: On a case-by-case-basis; preferably testing on site at UCT research facilities with shared ownership of data. Given the resource constraints in South Africa, it is preferred that access be granted through an equitable model, with contributions to capacity development, and infrastructure, that will ensure the sustainability of this specimen collection.