

## Q4 2017 – Q4 2018 Activity Report & Updates

### About the specimen bank

FIND has had an established, high-quality biorepository for TB since 2006 with over 300,000 patient samples from endemic countries. Providing access to these specimens serves to support the development and evaluation of new and existing tools to improve TB diagnosis. Sample types include sputum, urine, plasma and serum (special tubes are available as well: e.g. P800 tubes and PAXgene blood RNA tubes and peripheral blood mononuclear cells (PBMCs)). Since 2015, FIND has been adding strains from MDR-TB and pre-XDR-TB patients.

All specimens are collected at qualified clinics under a protocol approved by an Institutional Review Board and with informed consent from patients. FIND follows good clinical and laboratory practice in obtaining and processing samples.

### Distribution of specimens

The FIND TB Specimen Bank dispatched 32 shipments to test developers between Q1 2018 and Q4 2018. A total number of 5,923 aliquots were granted (see table below for details).

#### Summary of requests and aliquots granted/approved

# of requestors	# requests approved	Sputum	Serum	Plasma	Strain & DNA	Urine	PBMC	Total
27	32	1120	2639	350	502	1308	4	Q1-Q4 2018 5923
19	18	1426	680	540	670	459	0	Q4 2016-Q4 2017 3775

### Inventory

The FIND repository currently holds 317,353 TB aliquots from collection sites in Bangladesh, Brazil, Georgia, Moldova, Peru, South Africa, Uganda, Viet Nam and Zimbabwe. FIND also manages the WHO-TDR TB collection, which includes 28,347 aliquots from Spain, Gambia, El Salvador, Peru, South Africa, Tanzania, Uganda, Viet Nam, Canada, Bangladesh, Brazil, Colombia and Kenya.

### Refinement in participant classification system

Participant categories include:

- Clinical TB CXR+: Smear negative, culture negative participants, put on TB treatment based on clinical grounds. Likely subclinical TB: smear negative, culture negative at baseline, culture positive at follow-up
- Latent TB: same as non-TB category but also includes available, positive Quantiferon test results
- Non-latent TB: same as Non-TB category but also includes available, negative Quantiferon test results
- Non-TB: Smear-negative, culture-negative participants that were not put on TB treatment at enrolment, or culture negative/NA and symptoms defined as improved/completely recovered at follow-up
- Microbiologically confirmed TB:
  - S+C+: Smear positive, culture positive and MTB-complex at enrolment
  - S-C+: Smear negative, culture positive and MTB-complex at enrolment

### New collections

FIND is always attentive to the needs of the scientific community and in response to multiple requests from TB test developers, FIND has started a collection of cell-free DNA urine and blood tubes at our collaborating sites in Peru and South Africa.

### Quality control

FIND routinely conducts quality checks to re-test the representative number of specimens from each site at an independent partner laboratory. These quality checks ensure a high standard across different sites and over many years.

### Summary of activities

FIND collection at ZeptoMetrix, USA

Diagnostic category	Patients	Culture Isolate	DNA	Plasma	Serum	Sputum	Urine	Whole Blood
Clinical_TB	156			163	708	721	350	20
Likely_subcl_TB	37			158	202	289	563	16
MDR	1788	39021	8104	8875	7324	11719	102	392
NonTB	1367			5903	4701	5031	4629	216
NonTB_LTBI	503			2745	2620	5501	9738	395
NonTB_NoFU	297			212	1473	403	269	13
NonTB_NonLTBI	518			2474	2244	4489	7813	352
NTM	135			152	813	721	616	34
NTM_MTB	87			138	1082	346	359	7
Possible_TB	158			119	910	795	978	39
S-C+	1104			6626	8902	7320	7192	396
S+C-	26			156	190	175	311	13
S+C+	3608			27212	35506	39022	26398	1811
Xp+S-C-	64			81	285	235	530	25

WHO-TDR collection at Biobanque de Pidardie (FR) & Zeptomatrix (USA)

Diagnostic category	PICARDIE				ZEPTOMETRIX				
	Patients	Serum	Sputum	Urine	Patients	Saliva	Serum	Sputum	Urine
Clinical_TB	57	992	131	149	42	37	63	21	34
NonTB	35	511	11	35	380	88	1012	611	766
NonTB_NoFU	10	143	14	10	107	11	384	374	389
NTM	3	55	1	4	28	5	111	101	110
Possible_TB	61	834	24	83	182	16	479	436	554
S-C+	102	1483	170	170	86	60	395	41	72
S+C-	19	216			4		24	11	14
S+C+	651	9816	905	1006	745	699	3451	772	443

Summary inventory by selected countries/Aliquot types

Country	Patients	# of samples
Bangladesh	89	892
Belarus	132	344
Brazil	176	176
Cambodia	71	1828
Georgia	370	11275
Japan	33	1320
Moldova	578	43833
Peru	2482	90387
South Africa	2638	77854
Uganda	252	1784
Vietnam	4014	87158
Zimbabwe	68	502

### Strains/DNA isolates and matching specimens

Specimens from MDR/XDR-TB patients were collected from globally representative sites in South America, South East Asia, Africa and Eastern Europe. These include sputum, plasma, serum and PAXgene tubes. Strains are characterized by whole genome sequencing and phenotypic testing against first- and second-line drugs and the minimum inhibitory concentration. Over 1,000 strain isolates are currently available.

## The Developers' Toolset

In collaboration with Zeptomatrix, FIND has developed a toolset for developers to support the evaluation of new diagnostic tests for TB, the developer's toolset is expected to be commercially available by mid 2019. As the first component in this toolset, five inactivated, well-characterized strains of *Mycobacterium tuberculosis* complex (MTBC) are now available as reference materials. Individual panel strains are inactivated and stable at 2-8°C, allowing developers to use biosafety level II facilities. Each panel comes with homogenized sputa collected from non-TB patients that can be used as a matrix. FIND is also working to develop an NTM panel that will be available late 2019.

## FINDings

FINDings is a support service that provides an independent report based on the data that is generated through the use of specimens distributed by FIND. The data is submitted to FIND through a standardized reporting spreadsheet. FIND then performs an independent analysis to show the diagnostic accuracy of a new test or biomarker, based on the performance targets set by target product profiles (TPPs). The FINDings report that is produced allows innovators to better understand the performance and development status of their technology.

## Q4 2017 – Q4 2018 requests approved and specimens distributed

Organization	Purpose	Aliquots granted
Beckman Coulter India Pvt. Ltd	Flow cytometry technology to screen TB	8 culture isolates, 4 PBMCs, 28 sputum
Beth Israel Deaconess Medical Center	Glycan microarray technology	210 urine
Chungnam National University School of Medicine	Diagnostic platform to detect the <i>Mtb</i> -specific antigen	60 sera and 60 urine
CSU	Determination and validation of LAM	200 sera and 100 urine
FIND	Head to Head evaluation of targeted NGS solutions	270 culture isolates
FIND	Evaluation of the performance of the Truenat MTB and Truenat RIF assays	150 sputum
Genoscreen	Evaluation of targeted NGS assay	23 strain DNAs
QuantuMDx	Ultra-low cost MDR-TB DST molecular test	238 sputum
ITQB NOVA	TBomics for diagnosing tuberculosis	30 sera
JEI DANIEL BIOTECH CORP	<i>Mycobacteria tuberculosis</i> antigen test	100 sputum
Kinetics	Serological <i>Mtb</i> -specific diagnostic test	300 sera
Meso Scale Discovery	Quantitative multiplex reference test to confirm the diagnostic performance of a non-sputum based biomarker signature	184 sera
Meso Scale Discovery		300 sera
Meso Scale Discovery		80 sera
Microsens Diagnostics Ltd	RapiPREP-TB test is a near patient triage test	150 sputum
NJH	Quality control	154 sputum
PATH	Low cost, nucleic acid (NA) amplification device	200 sputum
Precision Biosensor Inc.	Method for measuring Kallistatin, SYWC and CRP in human serum, plasma and whole blood	20 plasma and 80 sera
Quanterix Corporation	Validation of LAM as a biomarker for TB diagnosis in blood	120 sera
RIT/JATA	Diagnostic accuracy of SILVAMP TB LAM	838 urine
Rutgers	Development of an XDR assay for the detection of TB resistance	50 sputum
Rutgers		11 culture isolates
Rutgers		225 culture isolates and 100 sputum
Salus Discovery, LLC	Development testing of the Salus LAM TB device	100 urine
San Raffaele	Validation of an XDR Assay	214 culture isolates and 100 sputum
Seattle Children Research Institute	Serological assay	40 sera
Serimmune Inc	TB serological assay development.	210 plasma
SomaLogic Inc.	Novel non-sputum based biomarker signature	350 sera
Stanford University	Novel nucleic acid amplification (NAT) blood test	120 plasma
TGen	Evaluation of targeted NGS assay	23 strain DNAs
Brigham and Women's Hospital	Single molecule array (Simoa) technology	130 sera
ZeptoMetrix Buffalo Facility	Performance studies for a specific platform	1 culture isolate
ZeptoMetrix Inc.	CRP project	765 plasma
ZeptoMetrix Inc.	Compare three targeted NGS assays	8 strains DNAs