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The TDR Tuberculosis Specimen Bank: a resource for diagnostic test developers

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SUMMARY

BACKGROUND: The Special Programme for Research and Training in Tropical Diseases established a specimen bank in 1999 to support the development and evaluation of new tuberculosis (TB) diagnostic tools.

OBJECTIVE: To provide a narrative of the bank's development and discuss lessons learned, the bank's limitations and potential future applications.

RESULTS: Collection sites were selected in high- and low-prevalence settings. Patients with TB symptoms, consenting to participate and to undergo human immunodeficiency virus testing were enrolled and diagnosed. Serum, sputum, saliva and urine samples were collected and sent to the bank's repositories. The bank has stocked 41 437 samples from 2524 patients at 11 sites worldwide. Ninety-five requests for specimens have been reviewed and 67 sets have been approved. Approved applicants have received sets of 20 or 200 samples. The bank allowed an evaluation of 19 commercial lateral flow tests and showed that none of them had broad global utility for TB diagnosis.

CONCLUSIONS: The establishment and development of the specimen bank have provided a wealth of experience. It is fulfilling a need to provide quality specimens, but the type and number of samples may not fulfil the demands of future end-users. Plans are underway to review the mechanisms of specimen collection and distribution to maximise their impact on product development.

KEY WORDS: specimen bank; tuberculosis; diagnostics development; diagnostics evaluation; clinical specimens

FOR THE MAJORITY of patients in low- and middle-income countries (LMICs), the diagnosis of tuberculosis (TB) is based on the identification of acid-fast bacilli using sputum smear microscopy. This method has low sensitivity, however, especially in children and in patients with TB-HIV (human immunodeficiency virus) co-infection and extra-pulmonary TB. The Special Programme for Research and Training in Tropical Diseases (TDR), co-sponsored by the World Health Organization (WHO), evaluated the need for better diagnostics and established a TB Diagnostics Initiative (TBDI) in 1997. This initiative soon identified that a key barrier to the development and assessment of new diagnostic technologies was the limited availability of well-characterised clinical specimens from patients with and without TB from a wide variety of geographic origins. In response to this, the TBDI established a specimen bank with the aim to support test development and evaluation through provision of prospectively collected clinical specimens.[1]

The establishment and development of the bank have provided a wealth of experience that could be useful to similar initiatives elsewhere. This study provides a narrative of its development and discusses lessons learned, the bank's limitations and potential future applications.

MATERIALS AND METHODS

Information pertaining to the establishment and management of the bank was reviewed, including internal archives, grey literature, key informant interviews and questionnaires sent to users in 2004 to obtain feedback. Information obtained from these documents was used to describe the process for selection of specimen collection sites, establishment of quality assurance procedures and number of specimens collected and used.

RESULTS

Establishment of the bank

The need for a bank of reference clinical materials to support TB diagnostic test development and evaluation was identified through a series of meetings with various members of the diagnostics industry in 1997–1998.

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The creation of the bank was initiated in 1999 with enrolment through a selection of collaborating centres for specimen collection, the development of collection protocols and the identification of a sample repository. These collection activities were preceded by the acquisition of extant materials that met the standards derived by the WHO Secretariat. To be selected for enrolment of new patients, centres had to meet a number of criteria, including the ability to enrol, classify, treat and follow up at least 300 symptomatic pulmonary TB patients and collect clinical information; the availability of a quality controlled laboratory with technologists competent to perform laboratory diagnostic procedures in accordance with the study protocol, including smear, solid and liquid culture, identification of *Mycobacterium tuberculosis*, HIV testing; the availability of chest X-ray facilities; and the ability to export frozen, aliquoted specimens. Centres were not required to comply with any specific quality standard, such as good laboratory practice (GLP) or good clinical laboratory practice (GCLP), but it was considered an advantage in the selection process. The initial centres were selected from South Africa, Uganda and Gambia* and were visited to verify laboratory standards. Their staff contributed to the development of patient enrolment and specimen processing protocols. Further sites were included to increase the geographic representation of the samples (Brazil, 2000) and the number of patients without TB (Canada and Spain, 2001).

To expand the bank's resource, an open call for applications was issued on the TDR website in 2002. Twenty-nine applications were received and a TDR committee scored all applications according to preset criteria. Seven sites were shortlisted and visited for external quality assessment, and four (Viet Nam, Bangladesh, Kenya and Colombia) were finally selected. Later, one centre conducting field studies with TDR (Peru) and the original South African site were also invited to participate. A further non-competitive third round was initiated in Zambia in 2009 to increase the number of specimens from patients with TB and HIV co-infection.

Participants and collection of specimens

Following local and WHO ethical review committee approvals, each centre serially enrolled 200 subjects aged >18 years presenting with cough of ⩾3 weeks' duration who consented to participate and who fulfilled the selection criteria. Written consent was obtained from all TB suspects included in the study. Patients who had received anti-tuberculosis treatment in the previous 2 months were excluded. Those without culture-positive disease were followed for ⩾2 months with repeat clinical and microbiological examinations to establish a non-tuberculous illness. Asymptomatic patients and those for whom follow-up was deemed difficult were excluded.

Clinical information was collected using standardised case report forms (http://apps.who.int/tdr/diseases/tuberculosis/pdf/case-report-form.pdf), and subjects were requested to provide three sputum specimens, collected as spot, morning, spot. Sputum specimens were concentrated by centrifugation (>2400 × *g* × 15 min). Smears were prepared, stained using the hot Ziehl-Neelsen method and examined using light microscopy. Two concentrated specimens were cultured in solid and liquid media. In accordance with results of the smear examinations and culture, the patients were classified as smear-positive, culture-positive TB; smear-negative, culture-positive TB; smear-negative, culture-negative TB (clinical diagnosis with good response to anti-tuberculosis treatment on follow-up clinical and X-ray evaluations); or TB negative (TB ruled out on the basis of clinical diagnosis and good response to broad spectrum antibiotics). Patients with indeterminate results (e.g., negative or contaminated culture and positive smear microscopy) were excluded.

Sputum specimens were liquefied with glass beads and N-acetyl-L-cysteine (50 mg/ml); half of the sample was processed for culture/microscopy and the other half was stored in quantities of 5 × 0.5 ml. Urine samples were centrifuged for 5 min (500 *g*) and stored in quantities of 5 × 1.5 ml without preservative. Twenty ml blood samples, collected in serum separation tubes, were allowed to coagulate and centrifuged (1200 *g* × 10 min) and serum was harvested and divided into quantities of 20 × 0.5 ml. Saliva was collected by asking patients to soak cotton buds in their gums and centrifuged prior to the preparation of 0.5 ml × 5 aliquots. Centres in Gambia, South Africa and Uganda collected serum, sputum and saliva; the Brazilian centre also included urine; and Canada and Spain collected serum, sputum and urine.

The collection of adequate sputum volumes was problematic, as most sputum specimens were used for diagnostic purposes, and patients unlikely to have TB were often unable to produce suitable volumes. Initially, only patients with complete sets of samples and volumes were enrolled, which resulted in a slow recruitment process. The protocol was therefore modified. The sites in Viet Nam, Bangladesh, Kenya, South Africa, Colombia and Peru did not collect saliva (due to the low demand for this specimen type). Furthermore, the sites were required to enrol only 50 subjects (of a total

* Specimens were collected by Medical Research Council Laboratories, Banjul, Gambia; Case Western Reserve University Research Collaboration, Kampala, Uganda; the National TB Research Programme, Pretoria, South Africa; Hospital Universitário Prof Edgard Santos, Salvador, Brazil; the Respiratory Hospital Health Sciences Centre, Winnipeg, Canada; the Catalan Health Institute, Barcelona, Spain; the Hospital Pablo Tobón Uribe, Medellín, Colombia; the Medical Research Council, Overport, South Africa; the Kenya Medical Research Institute, Nairobi, Kenya; the International Centre for Diarrhoeal Disease Research, Dhaka, Bangladesh; and the Pham Ngoc Thach TB and Lung Disease Center, Ho Chi Minh City, Viet Nam.

Table 1 Number of patients and type of diagnosis by collection sites

Country	TB			TB-negative	Unclassified	Total
	Smear-positive/ culture-positive	Smear-negative/ culture-positive	Smear-negative/ culture-negative			
Gambia	53	23	9	113	1	199
Uganda	198		2			200
South Africa	329	24	16	21	24	414
Brazil	15	2	1	26	1	45
Canada				201	1	202
Spain	4	7	6	157	24	198
Viet Nam	185	19	1	5		210
Bangladesh	109	10	18	9	30	176
Kenya	121	36	7	8	81	253
Colombia	76	10	6	106	6	204
Peru	162		43			205
Zambia	Under collection					

TB = tuberculosis.

of 200) who could produce enough sputum for storage. The remaining 150 patients were only requested to produce enough sputum for the diagnostic procedure.

In total, 2587 patients (Table 1) have been enrolled to date, providing 41 437 aliquots of clinical material (Table 2). The prevalence of TB among subjects varied widely depending on the site of enrolment, with some sites (Uganda, South Africa, Kenya and Peru) enrolling primarily referred patients who were culture-positive for TB, while others (Canada and Spain) enrolled mostly non-TB cases. Gambia, Brazil and Colombia enrolled a mixture of both. The prevalence of HIV infection varied from 0% in Brazil to 59% in South Africa.

Capacity strengthening

TDR created partnerships for the development and implementation of standardised collection protocols, and the shipment of biological specimens; funded essential equipment (freezers, anemometers for biosafety cabinet control, microscopes, manual equipment for Mycobacteria Growth Indicator Tube and training); and facilitated the participation of principal investigators in the bank's steering committee.

Sample transportation

Samples were kept on ice or refrigerated during sample preparation, aliquoting and initial storage. Aliquots destined for the bank were frozen on the day of collection at −70°C. When an appropriate number of aliquots had been assembled they were transferred to shipping containers and sent to the repository without thawing, where they were catalogued and stored. Materials remain frozen throughout storage and distribution. Specimens were classified as infectious substances, Category B, and transported under UN 3373 regulations.[2] Couriers provided International Air Transport Association-approved packaging and labelling and trained staff to prepare shipments. Specimens were initially transported in vapour shippers in liquid nitrogen, which keep temperatures of −150°C for up to 30 days. However, the weight and limited capacity (300–400 1.5 ml tubes) of the shippers resulted in high transport costs. Therefore, during subsequent collection rounds samples were shipped on dry ice, which is less costly but also less secure, as the lifespan of dry ice is shorter. Only courier companies offering to replenish dry ice en route were considered. However, one shipment from Brazil was delayed in

Table 2 Numbers of patients enrolled, aliquots prepared and the average number of samples collected per patient

Country	Patients *n* (% HIV-positive)	Samples			
		Serum *n* (*n*/patient)	Sputum *n* (*n*/patient)	Saliva *n* (*n*/patient)	Urine *n* (*n*/patient)
Brazil	45 (0)	163 (3.6)	181 (4.0)	184 (4.1)	200 (4.4)
Canada	202 (1)	1026 (5.1)	1408 (7.0)	Not collected	1005 (5.0)
Gambia	210 (13)	2475 (11.8)	1186 (5.6)	643 (3.1)	Not collected
Spain	198 (5)	1950 (9.8)	986 (5.0)	Not collected	990 (5.0)
South Africa	195 (45)	954 (4.9)	1059 (5.4)	729 (3.7)	Not collected
Uganda	200 (41)	1980 (9.9)	994 (5.0)	392 (2.0)	Not collected
Bangladesh	195 (0)	3386 (17.4)	394 (6.8)	Not collected	294 (5.1)
Colombia	201 (3)	3423 (17.0)	235 (5.0)	Not collected	235 (5.0)
Kenya	174 (45)	2733 (15.7)	149 (4.0)	Not collected	183 (5.0)
Peru	207 (2)	2357 (11.4)	Not collected	Not collected	Not collected
South Africa	210 (59)	3373 (16.1)	322 (6.9)	Not collected	242 (4.9)
Viet Nam	206 (7)	4119 (20.0)	605 (5.0)	Not collected	601 (5.0)
Zambia	Under collection				

HIV = human immunodeficiency virus.

customs, the dry ice was not replenished and samples had to be discarded.

Repository centres

A professional repository service based in the United States, which offered long-term storage with continuous temperature monitoring and database management, was selected to ensure the integrity of the samples. However, this company was acquired by a larger company, which in turn filed for bankruptcy soon after taking over. The storage facility was acquired in turn by Zeptometrix Corporation, Franklin, MA, USA, without the samples in the bank being compromised. The company has since managed the bank professionally, but the TDR Diagnostics Scientific Advisory Committee (which oversees all activities of the TDR Diagnostics Unit) recommended identifying a new repository in a public institution. After inviting potential collaborators and receiving proposals from four repositories, a French centre linked to the Amiens University Hospital (Biobanque de Picardie, Salouël, France) was selected on the basis of cost, technical facilities and perceived reliability, as the centre is responsible for the bio-repository activities of the hospital. The initial repository continued to store old stocks, while the new centre stored new collections.

Steering committee and approval of specimen requests

A steering committee was established to monitor bank development and to review requests for specimens. It is composed of staff from TDR, the principal investigators from the collection sites and external specialists with expertise on diagnostics development and evaluation, commercial matters and clinical laboratory issues. Requests for specimens are processed through TDR (http://www.who.int/tdr/diseases/tb/specimen.htm). To ensure a transparent and fair allocation, the committee reviews the requests and approves or rejects the application based on set criteria (Table 3). According to these criteria, specimens are usually released for either proof-of-principle projects or prototype evaluations as sets of 20 or 200 aliquots, respectively, but custom requests are considered. The bank does not charge fees for the specimens, but end-users pay a handling fee to the repository and shipping costs. End-users requesting samples of a specific geographic origin and diagnostic patterns may receive samples stored at both Zeptometrix Corporation and Biobanque de Picardie. In such cases, they have to cover the handling and shipping costs from both repositories.

Specimen requests and allocations

Since 2001, TDR has received requests for 23 370 specimens from 53 companies and 42 non-commercial institutions. The most frequently requested specimens are serum (65%) and sputum (22%). Of these, 12 170 (52%) samples have been approved for release and distributed (Table 4). Requests are rejected if the application does not include preliminary data supporting the project; when the technology is deemed not to be suitable for resource-limited settings; and if the application does not contain information on the tests on which the specimens will be used. Sixty-three per cent of requests have been related to antibody detection using lateral flow tests and enzyme-linked immunosorbent assays (Figure). Other requests have been related to use for DNA/RNA hybridisation probes, detection of volatile agents, proteomic fingerprinting in serum,[3] identification of novel target antigens for TB serology,[4] and screening of the whole TB proteome completed by the Foundation for Innovative New Diagnostics (FIND), Geneva, Switzerland, and partners in 2009.[5]

Table 3 Criteria guiding the release of specimens

Level I Preliminary laboratory evaluation
- Open to any end-user, commercial or academic.
- An institutional affiliation is required.
- Tests with a format unlikely ever to be adapted for use in developing countries will be given lower priority.
- The end-user will need to disclose the nature of the test (IgG antibody detection, antigen capture, etc), the matrix needed (sputum, serum or saliva), and at least general comments on the technical methodology (sandwich assay on ELISA plates using polyclonal antibody, etc) of the assay under development.
- A total of 20 specimens will be provided to all bona fide investigators and/or organisations making requests.

Level II Laboratory evaluation
- Open to end-users, commercial or academic, who have an assay to be tested that has demonstrated, in previous laboratory or field evaluations, characteristics (specificity, sensitivity, ease of use, speed or low cost) that make ongoing sponsorship of development reasonable.
- Operating characteristics vary so widely with test conditions and with the nature of the sample population that fixed numerical criteria are not appropriate. In general, however, a test should have a combination of characteristics that makes it attractive for use in settings of endemic disease. Such a combination might include, for example, only moderate sensitivity but excellent specificity and ease of use.
- Tests that are not obviously applicable to developing country settings may be appropriate for study using the material from the bank only if justification or description of low-cost adaptations of the test is included.
- An allotment of 200 specimens will be provided to those end-users with promising (and appropriate) products.

IgG = immunoglobulin G; ELISA = enzyme-linked immunosorbent assay.

Evaluation of lateral flow tests

In 2004, TDR evaluated 19 commercially available rapid tests for the detection of *M. tuberculosis*-specific

Table 4 Number of banked specimens requested and approved

Specimen	Requested *n* (%)	Approved *n* (%)
Serum	15 310 (65)	7 970 (66)
Sputum	5 190 (22)	2 830 (23)
Saliva	2 040 (9)	960 (8)
Urine	1 050 (4)	410 (3)
All	23 590	12 170

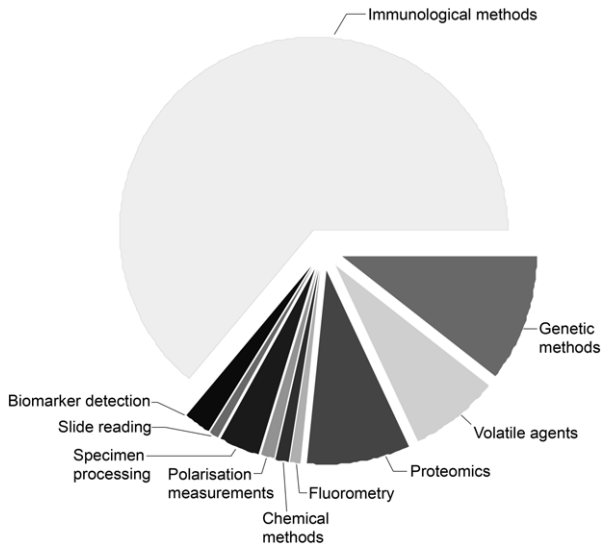

Figure Number of requests by type of research project. Of the 95 requests that the bank has received, the research related to immunological methods ($n = 60$), genetic methods ($n = 10$), volatile agents ($n = 7$), proteomics ($n = 8$), fluorometry ($n = 1$), chemical methods ($n = 1$), polarisation measurements ($n = 1$), specimen processing ($n = 3$), slide reading ($n = 1$), biomarker detection ($n = 2$) and unknown ($n = 1$).

antibodies in the context of the Diagnostics Evaluation Series.[6] Test manufacturers who agreed to participate in the evaluation submitted a set number of tests to the Institute of Tropical Medicine, Antwerp, Belgium, contracted by TDR to perform the evaluation using TB-positive and -negative samples collected at eight sites. Approximately half of the samples were from HIV-positive patients. The evaluation showed test sensitivities ranging from 0.97% to 59.7% and specificities from 53% to 98.7%. Tests with specificities >95% all had sensitivities at or below 20%.

User feedback

Previous users have indicated that the services offered by the bank were useful and that the specimens were adequate for their requirements. Users felt requesting specimens was straightforward and transport costs were reasonable. A few developers indicated that they required multiple types of specimens from the same individual, repeat samples and samples at the end of treatment.

DISCUSSION

The diagnosis of TB in most LMICs relies on the examination of sputum using direct sputum smear microscopy. Although more than 50 million patients are examined yearly using this method, microscopy has low and variable sensitivity, and improved diagnostics for LMICs are needed. The development of new diagnostics has recently been stimulated by an awareness of the critical role of diagnostics in disease control and by increased donor funding to support product development. This work has been facilitated by several factors, including the identification of *Mycobacterium tuberculosis*-specific antigens and genetic markers and by technological developments such as multipurpose and automated platforms.[7–9] The development of new diagnostics requires a network with technological, clinical, scientific and commercial expertise capable of bridging the gap between an incipient idea and a finished product that is endorsed by the WHO. This is a critical challenge, and many promising products fail due to the lack of such expertise. A key issue is the availability of well-characterised, prospectively collected clinical specimens to facilitate the development and independent evaluation of new diagnostic tests.

The bank's inception in 1999, in an area of research that was neglected, was a timely and important step to facilitate the development and evaluation of new diagnostics for TB. The decision to start a specimen bank is not trivial, however, and institutions considering this option should approach it with caution, as bio-banks require long-term commitment. Although documentation is incomplete and some costs were incorporated within separately funded research studies, TDR has invested around US$1 million to develop and support the bank over the past 11 years. Costs include compensation for specimen collection, capacity building, site monitoring, database management, ethical approval, transport and storage, staff time, convening the steering committee and other recurrent costs. Well-characterised specimens are expensive and time-consuming to collect and curate, requiring resources that are not always apparent to potential donors and users. Commercial banks of many types of specimens exist, but generally not for diseases of poverty. TB-related materials, given the clinical and microbiological complexity of the disease, are particularly expensive to collect following correct procedures. The bank is financed through donor funding to TDR, and its functioning depends on the good will of motivated collaborators and the continued commitment of TDR's senior management.

The choice of repository is critical, as the movement of specimens in bulk is risky and expensive. The unfortunate experience with the first storage facility filing for bankruptcy put focus on the importance of the selection. In this case it resulted in the identification of a new publicly owned repository. As a consequence, however, running costs increased (as samples are deposited in two centres), and transport costs for end-users requiring subsets of specimens located in the two repositories doubled.

Although the bank has filled an apparent need, as attested by the 95 requests for materials to support test development and evaluation, it is becoming clear that the type, processing methods and number of specimens collected may not fulfil all requirements of all

end-users. The small numbers of specimens provided are insufficient to drive the development of products from start to finish, a process which may require thousands of specimens. Furthermore, sample provision does not create enough leverage to establish binding agreements with test developers on negotiated prices or future test distribution in LMICs.

Future test developers may also require repeated aliquots to assess test repeatability, stability and robustness; paired, sequential pre- and post-treatment specimens to monitor treatment response and identify markers that could shorten drug trials; and other specimens such as stools and blood constituents incubated with specific antigens. New diagnostic tests should also be evaluated in populations that are currently neglected in TB diagnostics, such as children, pregnant women, the elderly, patients with other coinfections such as HIV or visceral leishmaniasis, and in a wider range of disease presentations, such as latent and extra-pulmonary TB. These issues need to be considered for future specimen collection.

Bank developers should also consider that the parameters used to classify participants into subgroups can change over time. For example, the case definitions for smear-positive TB have changed in the last few years, and diagnostics that are more sensitive than solid culture, such as molecular methods and liquid culture, have become established since the creation of the bank. As in any long-term process, therefore, case definitions may need to be re-visited to keep up with developments.

A further important lesson is that the bank did not have pre-established targets for size or character. Specimen collections have been initiated on approval by the advisory committee when TDR staff have identified the need to replenish stocks or to include specific populations. This reactive approach often reflects funding availability and is not conducive for long-term financial planning or for approaching donors, as they often request specific targets. However, the increased focus on TB test development opens opportunities for partnership building with donors such as the European Union, the Bill and Melinda Gates Foundation or FIND. The bank could contribute to cutting developing costs by continuously allowing for the assessment of novel technologies. Promising tools can be moved forward while other techniques would be eliminated early in the process.

The bank established mechanisms for the enrolment of patients suspected of having TB and ensured the accessibility of specimens for feasibility studies.[6] The process resulted in an access plan for publicly collected and funded materials that was open, fair and productive. However, the landscape for test development has changed during the 10 years of operation of the bank and a new strategy is being developed to adapt to the new environment. This strategy will continue to support the development of promising technologies and will include mechanisms for independent evaluation of new tests and regular reassessment of end-users' needs for different types of specimens and numbers. Currently, specimens are not available for drug and vaccine development, and basic research, but this may change to meet future demands.

The process has generated a wealth of experience related to sample collection and characterisation in resource-limited settings, transportation and storage. The interaction with test developers has provided a better understanding of the specimen needs of test developers and a good overview of present and emerging technologies that may be appropriate for LMICs. The steering committee has ensured a transparent and scientific approach to the management of the bank. This experience and knowledge may be useful to inform the initiation of other specimen collections and repositories supporting research in TB and other diseases associated with poverty.

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RÉSUMÉ

CADRE : Le Programme Spécifique pour la Recherche et la Formation en Maladies Tropicales a créé une banque d'échantillons en 1999 pour soutenir le développement et l'évaluation de nouveaux outils de diagnostic de la tuberculose (TB).

OBJECTIF : Raconter l'histoire de l'élaboration de cette banque et discuter les leçons qu'on en a tiré, les limitations de la banque et les applications potentielles pour l'avenir.

RÉSULTATS : Les sites de collecte ont été sélectionnés dans des contextes à prévalences élevée et faible. Ont été enrôlés et diagnostiqués les patients ayant des symptômes de TB et consentant à participer et à subir un test pour le virus de l'immunodéficience humaine. On a prélevé le sérum, les crachats, la salive et l'urine et on les a envoyés vers des dépôts. La banque a stocké 41 437 échantillons provenant de 2524 patients de 11 sites de par le monde. On a revu 95 demandes d'échantillons et 67 ensembles ont été approuvés. Les demandeurs approuvés ont reçu des ensembles de 20 ou de 200 échantillons. La banque a permis une évaluation de 19 tests latéraux commerciaux et a montré qu'aucun d'entre eux n'avait une large utilité mondiale pour le diagnostic de la TB.

CONCLUSION : La mise en route et le développement de la banque ont fourni une riche expérience de banque. Cela répond à un besoin de fournir des échantillons de qualité, mais le type et le nombre d'échantillons peuvent ne pas répondre aux demandes des utilisateurs finaux futurs. Des plans sont en route pour revoir les mécanismes de la collecte d'échantillons et de leur distribution afin de maximiser leur impact sur le développement des produits.

RESUMEN

MARCA DE REFERENCIA: Con el Programa Especial de Investigación y Capacitación en Enfermedades Tropicales se estableció un banco de muestras en 1999, con el propósito de respaldar el desarrollo y la evaluación de nuevas herramientas diagnósticas de la tuberculosis (TB).

OBJETIVO: Describir la construcción del banco y analizar las lecciones aprendidas, las limitaciones del banco y las posibles aplicaciones futuras.

RESULTADOS: Los centros de recogida de muestras se escogieron en entornos con alta y baja prevalencia de TB. Se incluyeron en el programa los pacientes con síntomas de TB que dieron su consentimiento y aceptaron la prueba de la infección por el virus de la inmunodeficiencia humana y se estableció un diagnóstico. Se recogieron muestras de suero, esputo, saliva y orina, que luego se remitieron a los repositorios. El banco ha almacenado 41 437 muestras provenientes de 2524 pacientes en 11 centros alrededor del mundo. Se han analizado 95 solicitudes de muestras y se han aprobado 67 series. Las solicitudes aprobadas recibieron series de 20 o 200 muestras. El banco autorizó una evaluación de 19 pruebas comerciales de flujo lateral, la cual mostró que ninguna de ellas ofrecía gran utilidad mundial en el diagnóstico de TB.

CONCLUSIÓN: La creación y el desarrollo del banco han aportado abundantes experiencias. El banco satisface la necesidad de proveer muestras de buena calidad, pero el tipo y la cantidad de muestras quizás no sean suficientes para cumplir con las solicitudes de los futuros usuarios finales. En la actualidad, se llevan a cabo planes de revisión de los mecanismos de recogida y distribución de las muestras, con el propósito de potenciar su impacto en el desarrollo de productos.