



*From diagnostic technologies
to diagnosis in the field*

Annual Report
2009

Our vision is of a world where
everyone will have equitable access to high quality diagnosis

Our mission is to drive the development
and implementation of accurate and affordable
diagnostic tests that are appropriate
to patient care in low-resource settings

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Moving diagnosis closer to the community



Photo FIND/C. Boelme

Message from the Chairman of the Board and the Chief Executive Officer

The year 2009 has been both an eventful and fruitful one for FIND. We have been able to make some great strides towards achieving our vision of a world where everyone will have access to high quality diagnosis. FIND's strategy continues to evolve, but now focuses on three overarching elements:

Extending the value chain

Although FIND was initially created to focus specifically on the development of new technologies, we and our partners have come to realise that we can't stop here. The greatest impact at the country-level will only be achieved if our work extends beyond the point where a product receives approval from the World Health Organization (WHO)'s Strategic and Technical Advisory Group (STAG). There is a real need for further support at various points of the value chain, all the way up to patient access and impact at country level. FIND aims to fill this gap.

Targeting all levels of the health system

FIND focuses on developing easy-to-use tools for all levels of the health system, particularly the community level, to address the lack of effective and appropriate technologies for the detection of poverty diseases.

Developing technological platforms

FIND is building on current investments by expanding the number of diseases that can be diagnosed using existing technological platforms. We recognize that individual disease programmes operate within the context of a broader health system. FIND supports integrated care while reducing the burdens on health care workers and laboratory technicians.

While FIND's various projects and achievements are described in detail in the following chapters, we wanted to showcase some specific highlights from 2009.

Tuberculosis Programme

FIND's primary focus in tuberculosis (TB) research continues to be a push towards the development of rapid diagnostic tests (RDTs) that could be used at point-of-treatment where the majority of patients first seek care in remote, rural areas. These would require little training and provide results within minutes. In addition, we continue to develop and improve technologies that can enhance diagnosis at all levels of the health system in disease-endemic countries.



*Dr. Gerald Möller
Chairman of the Board*



*Dr. Giorgio Roscigno
Chief Executive Officer*

The year 2009 saw the completion of demonstration studies by FIND and WHO in 27 microscopy centres and 12 supervisory sites across 9 countries of the Primo Star iLED - a fluorescence microscope that can identify TB bacteria 10% more efficiently and detect TB bacilli up to four times faster than conventional microscopy. This microscope was designed to be efficient and robust, features targeted to the needs of high burden TB countries. The studies were aimed at assessing the impact of this new technology on improving the efficiency of microscopy in resource-constrained settings, and FIND hopes to support scale-up as soon as WHO issues policy guidance in 2010.

FIND also continued negotiations with Carl Zeiss MicroImaging GmbH (Germany), the manufacturer of these microscopes, to reduce their price. The company demonstrated its ongoing commitment to the global fight against TB by extending a favourable price for the LED fluorescence microscope from an initial 24 to 74 high burden countries.

We have seen great advances during 2009 in our demonstration studies on the automated rapid test for TB and multidrug-resistant (MDR) TB strains using the GeneXpert® platform, a self-contained and automated system that can deliver test results in less than 90 minutes. FIND plans to bring the performance dossier of this technology to WHO's STAG for consideration in September 2010.

Malaria Programme

FIND's malaria programme reached an exciting milestone in 2009, as FIND teamed up with the WHO Regional Office for the Western Pacific and the WHO-based Special Programme for Research and Training in Tropical Diseases to carry out the largest-ever independent, laboratory-based evaluation of RDTs for malaria. Together with a second round of testing published in 2010, initial evaluations demonstrated marked variability in commercially-available tests: some performed exceptionally well in tropical temperatures and were capable of detecting even low parasite densities in blood samples, while other tests were only able to detect high parasite densities.

FIND and WHO, in collaboration with national reference laboratories, have been developing tools and protocols to routinely lot-test RDTs, to verify their quality when procured. The programme involves establishing facilities, procedures, and an entire suite of training materials and job-aids, developed with extensive field testing. As a result, National Malaria Control Programmes can now purchase and use malaria RDTs on a wide scale with confidence that the results can be relied upon for treatment decisions. The programme also allows for quality assurance for point-of-care tests at a community level on an unprecedented scale, an essential step in the implementation of new WHO global guidelines on management of malaria-like fevers.

Meanwhile, the loop-mediated isothermal amplification test for malarial DNA, developed by FIND and partners, is on track for release into the market in 2011. For the first time, molecular diagnosis and detection of very low parasite density infections will be possible outside of high-capacity laboratory facilities. A high-throughput version of this technology, currently in early development, is expected to make the same test widely available for surveillance and screening purposes, sought by countries entering the phase of malaria elimination.

HAT Programme

The sleeping sickness or human African trypanosomiasis (HAT) programme also took off this past year with an extended agreement between FIND and the University of Geneva (Switzerland) to renew efforts to create diagnostic test for this neglected tropical disease. The University of Geneva researchers, working with partners

at Makerere University (Uganda), and the Institute of Tropical Medicine (Belgium), have made progress in identifying biomarkers in cerebrospinal fluid that indicate the stage of the disease. This continued partnership will enable further studies that we expect will lead to the development of a simple, rapid test to diagnose HAT throughout Africa, even in areas with only basic resources.

At the 60th Anniversary Conference of the International Scientific Council for Trypanosomiasis Research and Control in Kampala (Uganda) this year, Dr. Joseph Ndung'u, Head of FIND's HAT programme, was awarded a gold medal by the African Union (AU) in recognition of his contribution to the research, control and eradication of tsetse flies and trypanosomiasis in Africa. Dr. Ndung'u played a leading role in establishing the HAT programme at FIND when he first joined in 2006, and continues to drive its steady progress in the development of new diagnostic tools.

Scaling-up

In 2009, the Expanding Access to New Diagnostics for TB (EXPANDx-TB) project extended its activities to cover an additional 11 high burden countries. EXPANDx-TB is a UNITAID-funded joint collaboration between the WHO, the Global Laboratory Initiative and the Stop TB Partnership's Global Drug Facility. This initiative aims to diagnose 15% of the global MDR-TB burden, by ensuring that (i) countries have access to new and effective diagnostic technologies; (ii) these technologies are properly integrated into TB control programmes; (iii) the laboratories which need to support these efforts have the requisite capacity for implementation; and (iv) technology transfer efforts promote local know-how and sustainability. With additional funding of almost US\$ 61.5 million, the number of high burden TB countries to be covered by this project will increase from 16 to 27.



In addition to our TB laboratory scale-up activities in Lesotho and Uganda, we have been working with the Ethiopian Ministry of Health (MoH) to establish a state-of-the-art National TB Reference Laboratory and five regional reference laboratories with quality standards equivalent to those in many high income countries. FIND created a project management system to carry out all related activities in 2008, which was agreed upon by the Ethiopian Health and Nutrition Research Institute and the Ethiopian MoH, together with other partners, including WHO, the US Center for Disease Control and Prevention, the US President's Emergency Plan for AIDS Relief and Johns Hopkins University (USA). In March 2009, the Ethiopian MoH announced the opening of two Biosafety-Level 3 laboratories in the capital Addis Ababa that have the capacity to use liquid culture and drug susceptibility testing, as well as the line probe assay - all WHO-approved technologies for the diagnosis of TB and MDR-TB. Ethiopia thus became the fourth nation on the African continent with the capacity to use these cutting edge diagnostic methods.

Since signing a Memorandum of Understanding with the Ugandan MoH in 2007, FIND has been supporting the development of a national health policy and strategic plan on laboratory services for the country. This process came to fruition in September 2009 with the launch of the first ever national policy on laboratory services. The policy will provide a framework for improving the organization, coordination and management of laboratory services, human resources for the laboratory sector, procurement and supply chain systems for laboratories, infrastructure and safety, quality systems, monitoring and evaluation, financing and partnerships.

Financial results and organizational changes

In 2009, FIND moved to a larger office in Geneva in order to accommodate a growing team of professionals dedicated to diagnostics. We were gratified to see that efforts to bring high quality practices to all our offices were rewarded: FIND India and Uganda have now joined the Geneva office in receiving ISO 13485:2003 and 9001:2008 certifications, which demonstrates the high standard of work in the design, development, manufacture, evaluation and demonstration of *in vitro* diagnostics, as well as project management.

Financially, the year 2009 was a period of consolidation for FIND, as several projects moved into late phase demonstration studies. Analytical and project expenditure was down 10%, from US\$ 25.5 million in 2008 to US\$ 22.9 million, and total expenditure decreased by almost the same percentage, from US\$ 28.8 million to US\$ 26.3 million. Continuing tight management controls on support and infrastructure costs enabled project spending to be maintained at 87% in 2009, compared with 88% in 2008, 85% in 2007 and 84% in 2006.

Accurate and prompt reporting, using the latest software and computer systems is a key feature of FIND's financial management and has played a major role in helping project leaders to manage their project portfolios. These financial systems have been designed to facilitate future expansion, thus safeguarding the efficient project management standards that are a hallmark of FIND's work with project partners.

Accounting standards for revenue recognition allow contributions from donors to be recognised over the full term of each grant agreement. In 2009, revenue thus determined (plus sundry income) amounted to US\$ 24,629,000 (2008 - US\$ 27,786,000), which resulted in an excess of expenditure over income of just over US\$ 1.7 million. This was deducted from previous accumulated surpluses of US\$ 2.2 million to leave a total of almost US\$ 528,000 at the end of 2009. Further information on FIND's financial results in 2009 can be found in the Auditors' Report, Financial Statements and Notes elsewhere in this Report.

We remain grateful for the continued and generous support from our funding partners, which include the Bill & Melinda Gates Foundation, the Government of the Netherlands, the European Union, UNITAID, the UK Department for International Development, National Institutes of Health (USA), and the Government of Ireland.

About FIND

FIND is a not-for-profit organization devoted to the development and implementation of accurate and affordable diagnostic tools for poverty-related diseases.

Since it was established in 2003, FIND's aim has been to address the urgent and unmet need in the developing world for affordable and more suitable diagnostic technologies, as well as to facilitate their rapid uptake in disease endemic countries. Focusing initially on tuberculosis, the scope of our activities has expanded to include malaria, human African trypanosomiasis, and FIND is looking into moving into other related disease areas as well.

Why diagnostics?

Good health is essential to breaking the cycle of poverty that afflicts hundreds of millions of people across the planet. But before using medicines to treat disease in the world's least developed countries, one must first correctly diagnose and manage infections, particularly ones such as HIV, tuberculosis and others requiring long-term treatment. This is how FIND is making a difference: by opening new doors for the prompt and adequate treatment of poverty-related diseases.

From diagnostic technologies to diagnosis in the field

The key to improving diagnostic capacity in poorer countries is to make them easy to use and affordable, while simultaneously upgrading local healthcare systems and laboratory standards, so that the new tools can be implemented, their impact measured and their effectiveness improved through a continuous flow of information and feedback from the field. This is the focus of FIND's work.



Photo FIND/C. Boehme

Partnerships that make a real difference

Research by the World Health Organization (WHO) has shown that although poverty-related diseases have not always received the attention they deserve from the established diagnostics companies, there is considerable work going on in this field in smaller biotechnology companies and academic research groups. However, even when diagnostic tests are developed for infectious diseases, they are seldom tailored to the needs of resource-poor settings.

FIND's business model, which is based on public-private partnership agreements, stands at the intersection of all who are working to improve public health services in developing countries. In the field of diagnostics, we promote collaboration and cultivate relationships that accelerate the transformation of proven biological principles into effective products, with a demonstrated impact on disease control.

We have active collaborations with over 160 partners, including Ministries of Health (MoHs), bilateral and multilateral organizations, research and academic institutes, commercial partners, NGOs and over 80 clinical trial sites.

Only through a concerted effort involving the research community, private companies, the public sector and governments of affected nations will it be possible to generate the momentum necessary for rapid progress in delivering better diagnostics to the developing world.

The opening ceremony of the new Malaria Lot Testing Center at EHNRI in Addis Ababa, which took place on 25 February 2009 in the presence of the Honorable Minister of Health, Dr. Tedros Adhanom.





Major Programme Activities

*Introducing faster, affordable and more accurate
tests where patients first seek care*



Tuberculosis Programme

Tuberculosis remains one of the deadliest global health threats today. In 2008 alone there were 9.4 million new cases and 1.3 million deaths from TB worldwide. We continue to focus on the development of simple, innovative and rapid diagnostic tools that can be used in low income countries, with a high burden of TB. Together with our partners, we are improving the standard of diagnostic tools, targeting them to the most under-resourced areas. Three such technologies - liquid culture (LC) and drug susceptibility (DST), rapid speciation, and the line probe assay (LPA) - are already being scaled up in laboratories across the developing world and being integrated into national diagnostic algorithms.

FIND has had many successes throughout 2009. Key milestones include (i) bringing the self-contained, automated, 90-minute Xpert® MTB/RIF test for detection of TB and MDR-TB to demonstration studies; (ii) advancing feasibility studies on the manual loop-mediated isothermal amplification (LAMP) assay that amplifies TB DNA with high specificity, efficiency and rapidity, and allows for a visual readout of results in under two hours; and (iii) conducting additional demonstration studies on LPA to test for accuracy of MDR-TB detection in a variety of geographical settings and to investigate further positive benefits for patients. A brief description of the progress made on each project is provided below.

Reference materials project

An important obstacle to the development of diagnostics across diseases has been the unavailability of sample banks. The FIND TB Reference Material project was set up to address this problem, and to provide high quality clinical sample specimens from well-characterized patients.

We have active collection sites in South-East Asia, Africa and South America that periodically send aliquots from patients to our central repository located in Bangkok. The current collection includes serum, urine and sputum samples, and includes a total of over 34,000 aliquots from 2,100 patients across six countries (Vietnam, Peru, Bangladesh, Brazil, Uganda and South Africa). Alongside the routine collection activities, a number of study-specific collection efforts have been undertaken to meet the needs of individual projects requiring non-frozen samples.

Several of our projects have benefited from the sample banks this year, above all the biomarker discovery projects, for which the availability of well-characterized testing materials is a key element.

The FIND TB Reference Material project, which was established in 2006, has proved to be an extremely valuable asset in supporting our research into new TB diagnostics. The demand for high-quality sample material has been steadily increasing, particularly for TB/HIV co-infected specimens, as TB is usually more difficult to diagnose in samples from patients who are HIV-positive. In order to address this demand, a number of new collection sites in HIV endemic areas are now being considered.

Antigen discovery

Our objective with this project is to discover novel antigens and validate existing antigens proposed as TB biomarkers to accelerate development of a rapid diagnostic test for active TB. FIND's partnership with the Forsyth Institute (USA) and the Tablin Proteomics Laboratory at Harvard University (USA) has delivered several novel *Mycobacterium tuberculosis*-specific peptide sequences from well documented urine samples from patients with active TB in Africa, Asia and Latin America. Studies are currently being expanded to HIV co-infected TB patients - one of the major clinical target populations.

One of the most promising antigens has been produced in recombinant form and antibodies were generated to establish a sandwich immunoassay. Preliminary results, suggesting high detection rates in clinical samples, are being supported by additional efforts to develop high affinity monoclonal antibodies to improve assay sensitivity.

A newly established collaboration with the National University of Singapore, employing proprietary ultra-high resolution mass spectrometry of sputum samples, resulted in the identification of a panel of *M. tuberculosis*-specific lipid molecules that could be used in TB case finding, both in HIV-negative and -positive TB patients. This project adds another encouraging layer to FIND's "-omics" driven approach for novel diagnostic target identification.

Antibody detection

Through our antibody detection work, we hope to determine the best possible combination of serological targets and to use these biomarkers for a rapid diagnostic test (RDT) for TB. In 2008, we reported the generation of the first ever whole proteome array for *M. tuberculosis* serology. This whole proteome screen had identified a panel of 61 TB-specific target antigens for improved TB serology.

The major focus of work in 2009 was on protein expression, production and purification of the identified biomarkers. The success rate was greater than 80%. Technical and clinical validation plans were developed, and purified proteins are being used to develop individual immunoassays that are to be consolidated into a multiplex testing platform for target validation. FIND is expecting a small to medium number of combined targets to be finally translated into a rapid serological test for active TB.

Dipstick for Tuberculosis

Since one of our high priority goals is to develop a rapid POC test which can be used at the community level of the health system, Lipoarabinomannan (LAM) was identified as a promising target for antigen detection because of its temperature stability and the existence of published data demonstrating the possibility of detecting it in urine. This project is aimed, firstly, at developing an assay for LAM antigen detection that meets target specifications, and secondly at identifying more potential antigens in urine.

FIND has been working with the Swedish Institute for Infectious Diseases (now at the Karolinska Institute), Genovac (Germany), and Future Diagnostics BV (The Netherlands) to develop a new LAM-based assay using monoclonal antibodies. By June 2009, an ELISA prototype assay was developed which showed very high analytic sensitivity (low nmol/l range) for the detection of the LAM antigen.

Two pilot lots were manufactured and evaluated in 200 TB suspects in South Africa and Zimbabwe. However, the assay showed unexpected low sensitivity in both settings and the study was discontinued. Local testing with LAM calibration antigen confirmed that the microtiter ELISA plates, manufactured by Future Diagnostics, were working satisfactorily. As a result, FIND will run additional studies in 2010 to explore these contradictory results.

Urinary TB nucleotides

The initial goal of this project was to develop a simple DNA extraction procedure for urine, coupled with a LAMP assay for *M. tuberculosis* DNA, to produce a diagnostic test that could be used at the level of microscopy centres to detect adult and paediatric patients with pulmonary or extra-pulmonary TB.

The majority of the work has been conducted by the Tuberculosis Trans-renal DNA Consortium, whose active efforts have been establishing DNA stability in urine, comparing methods of DNA extraction from urine, and detecting trans-renal DNA (trDNA) using a small amplicon target. A contract has also been established with the Alland laboratory at the University of Medicine and Dentistry of New Jersey (USA), which will undertake a parallel effort to prove or refute the presence of trDNA, and provide independent validation for the outcomes of the consortium.

Unfortunately, proof of principle has not been convincingly demonstrated. Several publications have reported the findings of urinary DNA stability and extraction studies, but inadequate sensitivity and specificity have been observed throughout the feasibility trials of the consortium. To date, well-conducted experiments using the sensitive GeneXpert (Cepheid, USA) technology platform have been unsuccessful in detecting spiked DNA in urine.

However, TB trDNA may be present at the limit of Polymerase Chain Reaction (PCR) detection. Current feasibility investigations include: (i) urine testing of TB patients thought to be highest yield (e.g., smear positive, just beginning TB treatment); and (ii) use of a DNA stabilizer from the moment of urine collection. The results of these feasibility studies will determine the future of this project.

Volatile organic compounds

Identification of TB volatile organic compounds (VOCs) in breath or in the headspace of sputum specimens is a highly attractive target for TB diagnosis. This year, FIND proposed a work plan to establish a collaboration with field leaders, and to validate initial feasibility data in well-defined samples and patients.

The research experience of testing the electronic nose (E-nose) – together with the Royal Tropical Institute in the Netherlands (KIT) and two other Dutch academic institutions – has steered research activities towards VOC discovery rather than dependence on VOC pattern recognition.

An intriguing proof of principle for the utility of VOCs for TB detection is currently coming out of APOPO vzw (Belgium), which uses sniffer rats for the detection of TB in sputum. FIND does not necessarily expect that the rat system will be appropriate for programme implementation, but rather that investigations into specific VOCs detected by the rats may be useful in developing a more appropriate technology. Establishment of an important new collaboration for VOC detection from sputum (and possibly eventually breath) is under consideration with the Charles Stark Draper Laboratory (USA), which receives support from Becton, Dickinson and Company (USA).

We continue to explore the practical feasibility of using VOC detection as a paradigm, given the high concentrations of compounds needed for detection, poor reproducibility, and current lack of micro-machines for field use. FIND remains connected to leading international VOC investigators: several publications and presentations at international conferences this year include the work of Mona Syhre (University of Otago), Claire Turner (The Open University), the APOPO group, and the KIT-Amsterdam collaboration.

Manual TB DNA detection

With this project, FIND aims to establish and validate a LAMP assay that could replace microscopy at peripheral clinics in the developing world. There were no key milestones in 2009, as this project was in the development phase.

During the year, we partnered with Eiken Chemical Company Ltd. (Japan) to carry out a rapid prototyping process in the field to simplify the assay components with a focus on key technical features including (i) precision transfer of sputum; (ii) design and development of a direct sputum sampling device; and (iii) minimization of DNA contamination. To verify each of the key technical features, we carried out a feasibility study in Vietnam with the modified components. By the end of the year, some technical challenges remained, but once resolved, evaluation and registration studies should take place throughout 2010.

Automated TB DNA detection

The objective of this project is to develop and validate a fully-automated system that has the potential to revolutionise TB case detection by dramatically reducing the time for detection, maximizing ease of use, replacing culture methods, and delivering additional data on drug sensitivity.

Over the course of 2009, and in partnership with Cepheid, FIND (i) finished the beta trial and trial report for GeneXpert® technology; (ii) concluded the CE-Mark technical file and registration; (iii) established the joint logistics team for the demonstration phase of the project; (iv) started the demonstration phase activities; and (v) completed the customer support plan.

In 2010, FIND and Cepheid will complete the demonstration phase activities and submit the required documentation, hopefully leading to WHO-STAG approval. FIND and partners will continue extended demonstration projects and begin collecting evidence for scale up.



Line probe assays for MDR-TB diagnosis

In 2008, the WHO's Stop TB Department issued a recommendation for the use of molecular line probe assays (LPAs) for the rapid diagnosis of MDR-TB in high TB burden, low-income settings. These recommendations were based on numerous published laboratory-based studies, as well as preliminary data from a large, FIND-sponsored demonstration study in South Africa. The published data indicated that LPAs are highly accurate in the detection of MDR-TB, while the FIND study suggested that the LPA would have significant patient benefits and would be highly cost-effective when compared with TB culture and DST.

Throughout 2009, we carried out further demonstration studies in Uganda, Thailand, the Philippines and India. These studies, together with a laboratory-based study of over 700 MDR-TB isolates from seven countries conducted by the U.S. Centers for Disease Control and Prevention (CDC) in partnership with FIND, indicated that LPA test accuracy for MDR-TB was high in a variety of geographical settings. Additional data from these projects continues to suggest positive patient benefits. Some national programmes have revised their diagnostic algorithms for MDR-TB to eliminate routine culture and DST for patients with valid LPAs that do not show MDR-TB. LPAs are also being rolled out by FIND and partners in 27 high MDR-TB burden countries under the EXPANDx-TB programme, supported by UNITAID.

Diagnosis for latent TB infection

We provided support to several studies on the QuantiFERON®-Gold In-Tube (QGIT) test, a whole blood interferon-gamma release assay (IGRA) for the diagnosis of latent TB infection (LTBI). IGRAs are increasingly being used in place of the tuberculin skin test (TST) for LTBI diagnosis in industrialized countries because of superior performance. However, IGRAs are more costly and technically more complex to perform than TST.

In order to address the role IGRAs can play in high TB burden, low resource countries, FIND undertook a number of evaluation studies, the largest of these conducted in Zambia and South Africa where a cohort of approximately 8,000 TB cases and adult contacts were enrolled. They will be followed over a three year period. Smaller studies in childhood TB contacts, paediatric TB suspects, HIV-infected adults, and potential adult immigrants to the USA are being conducted in South Africa, India, and Vietnam. Data from these studies will be compiled and submitted to WHO-STAG for a review in the third quarter of 2010.

Expansion of existing technological platforms for HIV

We are currently working to extend the application of current FIND molecular test platforms to include HIV. To date, we have (i) initiated exploratory discussions with Cepheid on the feasibility of a programme to develop real time quantitative PCR for HIV viral load using the GeneXpert platform, and (ii) initiated an evaluation of potential additional uses of the LAMP technology, in partnership with Eiken.

A programme of work was set up with Eiken to develop a real time LAMP assay. This involves refining the Customer Requirement Document, selection and initial optimization of the HIV-1 primers, and selection of external consultants. Finally, Eiken and FIND will work in concert to select gene targets, identify appropriate clinical materials, viral isolates and other developmental controls, and select collaborative partners for feasibility studies.

Demonstration studies on the LED fluorescence microscope

In 2009, FIND completed demonstration studies to assess the feasibility of establishing light-emitting diode (LED)-based fluorescent microscopy (FM) at microscopy centres in low- and middle-income countries with no prior experience using FM. This was achieved by examining over 100,000 smears in 27 sites across 9 countries. Data management for all the international study sites was based at the FIND India office, and all data was included in the report submitted to WHO-STAG.

In November 2009, WHO-STAG acknowledged the superior performance of LED FM over conventional microscopy for identification of acid-fast bacilli, as well as its cost-effectiveness and use of low power systems that can be easily introduced in microscopy centres. It is expected that WHO-STAG will issue policy recommendations in 2010, and FIND hopes to support scale-up of LED FM in reference laboratories and peripheral settings. Additional studies to assess the effect of fading of the fluorescence stain are in progress.

*Contributing to elimination efforts
through better tests*



Photo FIND/J. Ndung'u

Human African Trypanosomiasis (HAT) Programme

Sleeping sickness, or human African trypanosomiasis (HAT), is a deadly, neglected tropical disease that affects impoverished rural communities in sub-Saharan Africa. It is caused by single-celled protozoa belonging to the genus *Trypanosoma*, transmitted through the bite of a tsetse fly. There are no clinical signs that are characteristic of the disease, which makes it difficult to diagnose, and it is fatal if left untreated. However, if an early and accurate diagnosis is made, treatment is safe and relatively inexpensive.

The disease progresses from an early generally milder stage 1 to a devastating late stage, associated with serious damage to the central nervous system. During stage 2, patients display a range of psychotic signs that lead to stigmatization by their families and communities. The few drugs that are used to treat people in this stage are administered over prolonged periods of hospitalization, and are associated with potentially fatal adverse reactions.

Diagnosis of HAT is a two-step process: case detection, followed by staging in order to choose the appropriate treatment. Currently, HAT patients have to undergo a lumbar puncture to determine staging – a painful procedure that requires a skilled health worker, carries with it the risk of infection, and does not always yield accurate results.

FIND has been working with partners to develop diagnostic tests for HAT that are cheap, easy to use, sensitive and specific enough not only to accurately detect cases of sleeping sickness but also to determine the stage of disease, confirm cure after treatment, and detect relapses after a failed treatment.

Biomarker research

In 2009, FIND signed an extended three year agreement with the University of Geneva (Switzerland) whose research team, headed by Dr Jean-Charles Sanchez and working with partners at Makerere University (Uganda) and the Institute of Tropical Medicine (Belgium), has made considerable progress in identifying biomarkers in patients' cerebrospinal fluid (CSF) that indicate the stage of the disease. The agreement promises to fund further studies to determine how these biomarkers can be used in the development of a simple POC test intended for use in rural communities throughout Africa.

Analysis of CSF from HAT patients continued to reveal biomarkers that clearly distinguish stage 1 from stage 2 cases. One panel comprising CXCL10, CXCL8 and GSTP was published, and new biomarkers have been identified. Validation of these was initiated in the summer of 2009 on a cohort of 600 HAT patient samples.

Antibody detection test

Also this year, 32 recombinant and native antigens were screened against patient and endemic control sera using dot-blot and ELISA. Two cycles of screening have been completed, resulting in a short-list of 10 antigens that are undergoing a final assessment to identify one or two to be used in the development of a lateral-flow assay (LFA). This has made the prospects of developing a single format antibody-detection rapid diagnostic test for HAT a realistic prospect, which will be further pursued in 2010.

Antigen detection test

A limitation of antibody detection tests is their inability to distinguish active infections from past or subclinical exposures. A direct test for parasite proteins will offer better specificity for active infection. We are targeting single-chain antibodies, which are small enough to penetrate the variable surface glycoprotein coat of trypanosomes, and bind to invariable sites on the parasites. The feasibility of using single chain variable fragment (scFv) antibodies, camel heavy-chain antibodies (nanobodies) and aptamers is being explored with the Seattle Biomedical Research Institute (USA), VIB (Belgium), and the Darmstadt Biotechnology Institute (Germany), respectively. Work with VIB has identified a number of promising nanobodies that are undergoing feasibility testing.

In the last quarter of 2009, screening of antigens to be used in a POC test entered its final phase, with selection of specific antigens completed at the end of the year.

Test of cure

After treatment, it is difficult to determine whether or not a sleeping sickness patient is cured. With the current diagnostic tools, patients have to come back every 6 months for up to 2 years to have their CSF examined for the presence of parasites. As a result, many do not return for the follow-ups. FIND, the University of Geneva and the Institute of Primate Research (Kenya) have started research that could lead to the development of a simple method to confirm cure after treatment.

Advocacy

A Strategic Plan for Advocacy on African Trypanosomiasis, undertaken in partnership with the Pan African Tsetse and Trypanosomiasis Eradication Campaign (PATTEC) was initially implemented in 5 endemic countries, including Angola, Southern Sudan, Kenya, Uganda and Tanzania. Another 5 countries adopted the plan in August 2009, after formal agreements with PATTEC were finalized.

In September, the African Union awarded Dr. Joseph Ndung'u, Head of the HAT Diagnostics Programme at FIND, a gold medal in recognition of his contribution to research, control and eradication of tsetse flies and trypanosomiasis in Africa. The gold medal and certificate of appreciation were presented to Joseph during the 60th Anniversary Conference of the International Scientific Council for Trypanosomiasis Research and Control (ISCTRC) held in Kampala, Uganda.

Technology platforms for HAT

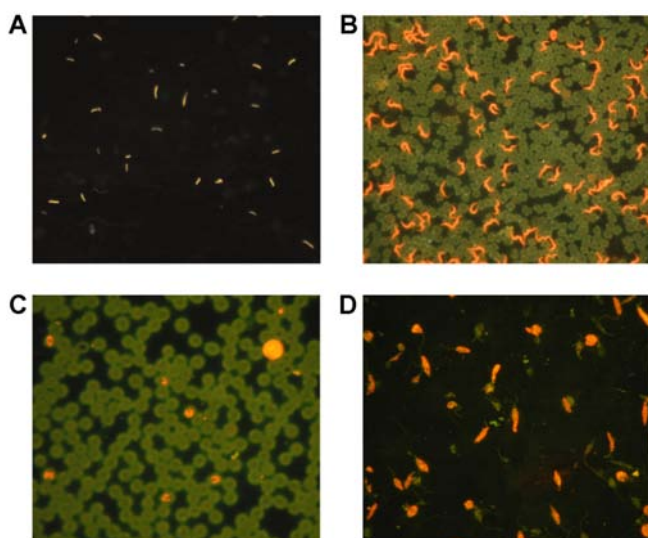
One of the strategies of FIND is to leverage existing investments and diagnostic technologies to serve the needs of different disease programmes. The goal is to reduce the burden on healthcare workers and laboratory technicians by building on technologies with which they are already familiar. In 2009, two FIND-supported technology platforms that are applicable to more than one disease underwent evaluation for HAT.

LED fluorescence microscope

The LED-based fluorescence microscope was first developed for diagnosis of TB by FIND and Carl Zeiss Micro-Imaging GmbH (Germany). It is robust, affordable, uses LED bulbs that have a lifespan of more than 10,000

hours, and does not require a dark room. Since the bulbs use very little energy, the microscope can be operated using solar power, making it easy to use in remote rural settings where sleeping sickness occurs.

The evaluation of LED FM in 4 centres in Africa progressed very well. This was complemented by a simple method of parasite concentration based on lysis of red blood cells. Demonstration studies were started in the second half of 2009, in laboratories in Uganda and the Democratic Republic of Congo (DRC).



The LED fluorescence microscope can be used to visualize various pathogens.

(A) Tubercle bacilli (B) A thin blood smear showing trypanosomes (orange) (C) Malaria parasites (orange) (D) Cultured *Leishmania donovani* promastigotes (orange). (A) stained with auramine O (B), (C) and (D) stained with acridine orange.

LAMP

LAMP technology is a novel method of DNA amplification that is performed under isothermal conditions. The technique uses a set of six primers that recognize eight sections of target DNA, making it highly sensitive as well as increasing the specificity, speed and efficiency of the amplification. Our development partners have developed a LAMP test for *Trypanosoma brucei* using RIME sequences and one for *Trypanosoma brucei rhodesiense* based on the serum resistance-associated gene. LAMP promises to become a good test for field diagnosis and confirmation of cure in sub-Saharan Africa, where facilities are limited. The first prototype kits of a LAMP test based on RIME sequences were finalized at the end of this year.

*Quality assuring rapid diagnostic tests
and developing improved ones*



Photo FIND/H. Hopkins

Malaria Programme

Before treatment with anti-malarial drugs, the WHO now recommends parasite-based diagnosis in all cases of fever. For many malaria-endemic countries, this constitutes a revolution in malaria management and will only be achieved by making point-of-care diagnosis generally accessible: through the widespread use of malaria RDTs. A robust but streamlined quality assurance/quality control system is a critical component of effective RDT implementation, to ensure diagnostics are used safely and produce accurate results.

Over the last few years, FIND and the WHO have been developing quality assurance (QA) systems to ensure that malaria RDTs are working efficiently and delivered to health workers, and that adequate materials to support training and good practice are implemented, even in the remotest areas. We are also working to improve the next generation of malaria diagnostics. Together with the WHO, we are implementing an accelerated three-stage solution to ensure that malaria RDTs that perform well are used in national disease control programmes.

Establishing reference methods and materials for RDT evaluation

As part of a project to establish reference methods and materials necessary for initial and ongoing evaluation of malaria RDTs, FIND, WHO and partners have:

Created a global malaria specimen bank and a network of laboratory and clinical testing sites

Together with the WHO and the CDC, FIND coordinated the development of a global specimen bank of cryo-preserved malaria parasite samples to support the comparative performance evaluation of commercially-available antigen-detecting malaria RDTs. Full characterization of these samples was completed, and forms the basis for malaria RDT product testing, while small panels of cultured parasites are available to manufacturers for internal quality control. Three regional quality-controlled lot testing sites have been established and an expanding number of RDTs, procured by several countries and programmes in Africa and Asia, are now being tested.

A range of recombinant antigens have been identified or synthesized and are now being characterized at the CDC in order to calibrate an antigen-based reference panel that will form the basis of new, lower-cost and sustainable malaria RDT evaluations, and quality control systems.

Developed positive control wells for quality testing of RDTs at point-of-care

One product of the recombinant antigen reference panel project is the development of positive control wells (PCWs), to be packaged with RDTs and easily reconstituted for quality testing of RDTs in the field. These PCWs are being specifically designed (i) for ease of use by healthcare workers; (ii) to be stable in typical field conditions; and (iii) with sufficient antigen to produce a test line on an intact working RDT. The final aim is a product that contains all recombinant proteins of the three main target antigens currently detected in commercial assays (HRP2, pLDH, and aldolase) with an additive to provide viscosity similar to lysed whole blood after reconstitution.

From August to November 2009, a preliminary field study of prototype PCWs was carried out among health workers with experience using RDTs in Uganda. The potential utility and acceptability of PCWs in routine healthcare settings was assessed and pictorial job aids (instruction sheets) and training instructions were developed and evaluated.

Developed an improved blood transfer device

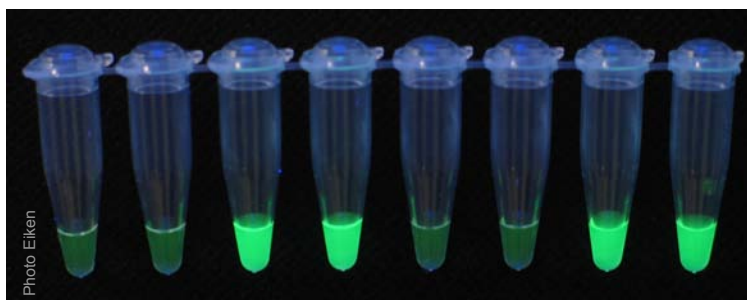
Most commercially available RDT kits include individual-use, disposable blood transfer devices, which are used to collect, transfer and deposit a specified amount of blood (typically 5-10ml) from a fingerprick site to a well on the RDT cassette. To ensure safe and accurate RDT use, these devices must (i) minimize the risk of blood exposure to health care workers, (ii) reliably transfer an appropriate amount of blood to avoid false-negative test results, and (iii) be easy to manipulate.

FIND developed and tested an improved blood transfer device with a “cup” design, based on a promising concept that was never taken forward. Together with our partners, we then evaluated this device among 227 health workers in Nigeria, the Philippines, and Uganda. The new cup mechanism out-performed other devices currently available in RDT kits and was preferred by the majority of health workers. It has now been made available to RDT manufacturers.

Developed new field reference standards for detection of malaria parasites

The LAMP assay for malaria is a simple molecular diagnostic test, adapted by FIND as a highly sensitive field diagnostic. It can be used in malaria screening, surveillance and to support clinical trials, but also as a reference standard against which other diagnostic tests can be evaluated.

This assay uses primers that target the mitochondrial DNA of *Plasmodium* parasites to diagnose infection with any of the *Plasmodium* species, and to differentiate *P. falciparum* from other species. Results are available in



less than 1 hour, from fresh, frozen, or dried blood samples, with sensitivity similar to that of PCR. Eiken Chemical Company Ltd., the manufacturer of LAMP technology, has also developed a Procedure for Ultra Rapid Extraction (PURE) of DNA from blood for malaria diagnosis (initially developed to extract DNA from sputum samples for TB diagnosis).

An initial version of the LAMP malaria kit was recently evaluated in Uganda to assess its completeness, ease of use and to obtain feedback on any modifications needed. Simultaneously, a training manual and SOP were developed. The current LAMP malaria kit is expected to be on the market in 2011, while FIND is embarking on further development towards a low-cost high through-put version of the test, aimed at the screening and surveillance needs of countries with malaria elimination programmes.

Evaluations of the performance and robustness of RDTs

Definition of product specifications for RDTs

The improvement of malaria RDTs requires (i) the identification of new abundant and stable antigens, (ii) the production of specific antibodies with increased sensitivity, (iii) the identification of sample factors affecting the performance of RDTs, and (iv) the use of reagents and materials stable in the environmental conditions of endemic countries (thermostability). FIND and partners are working on these issues in order to resolve the main drawbacks of the current available RDTs. For example:

- a. FIND and the Royal Dutch Tropical Institute (KIT) have identified and produced a number of recombinant proteins as potential *Plasmodium* antigens. During 2009, more than 50 specific monoclonal antibodies

(MAbs) against the proteins GLURP, DHFR, and HDP were obtained. The MAbs were evaluated for their recognition of *Plasmodium falciparum* and *P. vivax* parasites, and some were selected for evaluation in a LFA format. Specific MAbs are now being evaluated for both their thermostability and their recognition of parasites from different geographical origins.

- b. Partners at the Queensland Institute of Medical Research (QIMR) in Australia have been evaluating possible factors that could affect the recognition of the HRP2 protein by antibodies used in current RDTs. The correlation of protein concentrations, sequence variability and antibody binding allowed us to conclude that the level of detection of parasites by HRP2-based RDTs depends mainly on the protein abundance and not on the number of amino acid repeats in its sequence. QIMR is currently evaluating the effect of patient antibody levels and parasite antigens (prozone effect) on the performance of RDTs.
- c. During 2009, FIND established a service and evaluation agreement with AdAlta Pty Ltd (Australia) for the production of thermostable shark antibodies (IgNARs) specific to malarial antigens. IgNARs specific to PfLDH and PvLDH were identified and their thermostability was evaluated. Although these reagents were more stable, their binding capacity was low when compared to MAbs.
- d. We signed a feasibility agreement with ChemBio Diagnostic Systems Inc. (USA) for the evaluation of their highly sensitive Dual Path Technology Platform with malaria antibodies.
- e. This year, we also started collaborating with AbD Serotec/MorphoSys AG (Germany), for the screening of human combinatorial antibody libraries (HuCAL) with malaria antigens to identify highly specific and thermostable antibodies. During the first phase of the project, AbD Serotec established a high-throughput Thermofluor method to measure the thermostability of different antibody fragments and formats.

Developing RDTs for placental malaria

With our partners and the WHO, we are currently embarking on a clinical study to evaluate the accuracy of RDTs in detecting placental malaria, which will provide valuable efficacy data for a new proposed strategy to screen pregnant women with these tests. This would enable the use of more efficacious drugs, eventually replacing Intermittent Prophylactic Treatment in Pregnancy (IPTp), leading to direct public health

Improving roll-out and use of RDTs

FIND is currently developing a business and technical development plan (solutions pathway) in order to improve the accuracy, stability, geographic utility, and availability of malaria RDTs. To this end, we have:

Identified technical and business solutions to improve access

Potential solutions include (i) developing a transport and storage guide for personnel handling RDTs in health clinics, and at central and peripheral facilities; (ii) supporting development of a “cool box” which does not require electricity but which protects RDTs from temperatures exceeding 30°C; and (iii) building a repository of product-specific job aids for RDTs, to be accessed by National Malaria Control Programmes (NMCPs) and other partners.

Carried out temperature monitoring

Portable “tags” were used to monitor the temperature and humidity levels to which RDTs are subjected, as they move through the supply chains. Countries were selected in order to obtain data from a cross section of environmental conditions, to include Burkina Faso, Senegal and the Philippines. The project has brought to light new evidence on the stability requirements of POC tests in tropical and sub-tropical regions.

Developed best practices in RDT implementation

Over the past few years, FIND has been working closely with the Ugandan NMCP, as well as other country programmes and agencies, to develop and demonstrate best practices in planning and rolling out malaria RDT implementation programmes, ranging from structured planning timelines to innovative reporting mechanisms. We participated in the Global Fund grant application processes to guide NMCPs on malaria RDT implementation plans and QA.

On the basis of this experience, we are coordinating the development of a multi-agency, global operational manual to provide clear guidance and support materials for programmes seeking to introduce and scale up the use of malaria RDTs. The suite of documents on malaria diagnostics is currently being drafted by FIND, in partnership with the WHO, MoHs, the CDC, the US President's Malaria Initiative, Roll Back Malaria partnership and other stakeholders. It is on target to be finalized by the end of 2010.

Launched a disease and commodity monitoring system based on text messaging

We partnered with Columbia University's Earth Institute (USA) and the Ugandan MoH to design and launch a monitoring system based on SMS messaging. The project aims to facilitate and support rapid reporting of malaria cases, the use of malaria diagnostics, stocks of anti-malarial commodities and disease surveillance by health units located in remote areas in Africa. The system was introduced in Uganda in early November 2009 and covers 127 health workers from 45 health units in Gulu district; and 247 health workers in 113 health units in Kabale district.



Scale-up Programme

Although FIND was initially set up to focus specifically on the development of new technologies, we and our partners have come to realise that this cannot be the end-point of our involvement. The greatest impact on patient lives will only be achieved if our work extends beyond endorsement from the WHO. There is a real need for further support at country level – particularly in laboratory strengthening and policy implementation, along with supporting the roll out of new diagnostic technologies.

Laboratory Strengthening

In response to the emerging threat of drug-resistant TB, WHO launched the Global MDR-TB & XDR-TB Response Plan in 2007. This called for significant expansion of TB diagnostic laboratory capacity, which plays a vital role in curbing the spread of these deadlier forms of TB. The required increase in laboratory services in high burden countries has been estimated at up to 13,000 centres for smear microscopy, 130 advanced diagnostic centres for culture and drug susceptibility testing, and five national referral laboratories, as well as an increase in the number of supra-national reference laboratories.

In the past six years, FIND has worked on liquid culture (LC) and drug susceptibility testing (DST), Immune-chromatographic rapid species identification and the molecular line probe assay (LPA) technologies, all of which have been endorsed by the WHO as suitable tools to diagnose TB in developing countries. However, the roll-out of these technologies is only feasible if the laboratories in high burden countries are strengthened in terms of their QA systems, SOPs and in-house technical capacity. Recognizing the need for this strengthening, FIND established a laboratory support programme to demonstrate and document the steps needed to translate policy into practice.

One of the first activities in this area was the opening in March 2009 of two state-of-the-art TB laboratories in Addis Ababa in collaboration with the Federal Ministry of Health. One of these Biosafety Level 3 TB labs is based at the Ethiopian Health and Nutrition Research Institute (EHNRI) and the other is at St. Peter's Hospital. Both laboratories have the capacity to use liquid culture and line probe assay technologies, which were approved by WHO for the diagnosis of TB and detection of multidrug-resistant TB in high endemic countries. Ethiopia is now the fourth nation in the African continent to use these rapid diagnostic methods. This undertaking is part of the Ethiopian Diagnostics Access Facilitation (EDAF) project which was set up under the auspices of the Federal Ministry of Health of Ethiopia, EHNRI, CDC PEPFAR, UNITAID, Johns Hopkins University (JHU) and FIND. The Ministry of Health and partners have committed to establish at least four more regional reference laboratories in the regions of Adama, Bahir Dar, Mekelle and Awassa.

In this way, collecting evidence for scale-up and scale-up have become the cornerstones of FIND's laboratory strengthening activities.

Collecting evidence for scale-up

Collecting evidence for scale-up began in Lesotho in 2007 and proceeded some time later in Ethiopia followed by India and Uganda through our field offices. The experience that we gained from these activities enhanced our position with funding partners, as evidenced by the UNITAID-funded EXPANDx-TB project which is comprised of the WHO's Global Laboratory Initiative (GLI), FIND and the Stop TB Partnership's Global Drug Facility (GDF). Both Lesotho and Ethiopia were included as Round 1 countries under this programme for 2009.

FIND activities to collect evidence for scale-up in Lesotho are described below. An overview of collecting evidence for scale-up in Ethiopia can be found in the FIND Annual Report 2008.

Lesotho

In November 2006, FIND conducted an assessment and evaluation of the TB laboratory facilities in Lesotho. In 2007, FIND partnered with WHO and Partners in Health (USA) to refurbish and upgrade the National Reference Laboratory (NRL) in the capital, Maseru, into a quality-assured TB culture facility. Through this public private partnership (i) a biosafety level 3 (BSL-3) laboratory for solid culture was established; (ii) an external quality assessment programme for smear microscopy was developed; and (iii) LC & DST for TB, and the molecular LPA for MDR-TB detection, were introduced.

The laboratory renovations, introduction of new technologies, training of staff, validation and monitoring phases were all completed, demonstrating that WHO policy on diagnostics can be translated into effective action. In addition, the success of LPA in diagnosing MDR-TB has led to plans to introduce this technology into two regional laboratories.

In the second half of 2009, the results of our laboratory strengthening work in Lesotho were published in the *International Journal of Tuberculosis and Lung Disease*.

Scaling up: the EXPANDx-TB project

Without accurate diagnosis and efficient treatment, data indicates that every TB patient can infect 10-15 additional people every year. The WHO estimates that in 2008 there were between 400,000 and 500,000 cases of MDR-TB, which occurs when patients fail to respond to standard first-line drugs. Approximately 3.6% of TB cases across the globe are MDR-TB. To counter the increasing burden of MDR-TB, a number of global health stakeholders came together in 2009 to launch the "Expanding Access to New Diagnostics for TB" or EXPANDx-TB project.

EXPANDx-TB is a UNITAID-funded joint collaboration between the Global Laboratory Initiative (GLI) at WHO, the Stop TB Partnership's Global Drug Facility (GDF), and FIND. Over a span of five years and across 27 countries, EXPANDx-TB aims to narrow the diagnostic gap in MDR-TB control by increasing access to new diagnostic technologies, accompanied by the requisite technology transfer and appropriate laboratory services at country level. The project will also ensure that new technologies are properly integrated into TB control programmes. FIND and partners aim to diagnose at least 129,000 patients with MDR-TB, which would account for over 15% of the global burden.

Building on previous negotiations with suppliers to obtain lower prices, FIND ensures that the cost of WHO-endorsed diagnostics is further reduced by linking volume with price, and by enlarging the pool of current manufacturers. FIND also ensures that customer support is in place, know-how from the product development process is shared, and provides long-term, on-site mentoring for technology transfer.

By the end of 2009, FIND was already working with 16 countries. Six Memoranda of Understanding (MoUs) have been signed, in addition to the four already in place through our laboratory strengthening work in Ethiopia, Uganda, Lesotho and India. Discussions are underway to finalise MoUs with the six remaining countries.

Assessment visits were completed in eight countries in order to (i) investigate laboratory capacity, infrastructure and procedures for TB management; (ii) evaluate what is needed to modernise national TB reference labs; (iii) identify training needs (on global laboratory policy, bio-safety and quality assurance); (iv) assess funding gaps in meeting these challenges; (v) identify potential partners; and (vi) define timelines. Following this step, training workshops were held on the new diagnostic tools for TB (LC & DST and LPA) as well as on specimen processing, medical mycobacteriology, conventional and molecular procedures and laboratory management.

Below are some of the key highlights and activities from 2009 in each of the 16 countries:

Azerbaijan

- Negotiated an MOU with the national health authorities of Azerbaijan, to be finalized early 2010.

Democratic Republic of the Congo

- Completed country visits to oversee renovation of the NRL in Kinshasa to a BSL-3 facility and to assess the ability of the regional laboratories of Lubumbashi and Kisangani to take up new diagnostic tools.

Djibouti

- Coordinated the renovation of the NRL to a certified BSL-3 laboratory.

Ethiopia

- Established two BSL-3 laboratories: at the Ethiopian Health Nutrition Research Institute who will host the NRL for TB; and at St Peter's Hospital, a central hospital responsible for the care of TB/HIV co-infected patients experiencing treatment failure or relapse;
- Identified, assessed and supported the renovation of 6 regional laboratories to BSL-3 standards for the introduction of new tools, and currently expanding the use of the LPA, liquid culture and DST to those labs using PCR for early infant diagnosis of HIV;
- Enabled rapid policy reform on the use of these tests in TB control, documented in the new MDR-TB Management Guidelines, which was accompanied by in-country validation of laboratory capability.

Haiti

- Developed good working relationship with the MoH and the GHESKIO centre, and set up dates for 2010 to conduct validation studies.

Ivory Coast

- Delivered equipment for LC and LPA; translated training packages for these technologies into French; and facilitated the signing of a procurement plan for the tools, which was approved by the National TB Programme.

Kazakhstan

- Prepared and negotiated a MoU to start work with WHO, the Stop TB Partnership and the National Health Authorities of Kazakhstan.

Kyrgyzstan

- Prepared and negotiated a MoU to start work with WHO, the Stop TB Partnership and the National Health Authorities of Kyrgyzstan.

Lesotho

- Early infant diagnosis of HIV using DNA from dried blood samples was introduced at the NRL in Maseru in November 2009, to provide an integrated molecular platform for the detection of TB and HIV;
- Intra-laboratory validation showed 100% proficiency in performance of the introduced assays by laboratory technicians, and thus a scale-up plan was drafted to cover all districts in Lesotho by December 2010. This would allow the country to take over testing completely from the National Institute for Communicable

Diseases (NICD) in Johannesburg, where many samples were still being sent for analysis. FIND, the NICD and the Clinton Health Access Initiative (USA) have partnered to contribute supplies and logistics to this scale-up project;

- Presented new TB diagnostics algorithms for validation in November 2009, including those for MDR-TB rapid identification to expand the reach of LPA facilities to all smear-positive patients;
- Currently planning a workshop to develop an effective patient/specimen referral for the laboratory and discussing safe and timely transportation of sputum specimens to the Central TB Reference Laboratory.

Moldova

- Held a workshop “Ensuring access to TB diagnostics and laboratory services” in Chisinau in December 2009, attended by representatives from NRLs across 10 Eastern and Central European countries.

Myanmar

- Started the introduction of negative pressure and other biosafety measures, including two 80 KVA generators in both the NRL in Yangon and the regional laboratory in Mandalay;
- Following this, training on LC and LPA are planned for early next year; these tests will then be introduced at both sites and, after validation, the results will be used for patient diagnosis and follow-up.

Swaziland

- From November to December 2009, discussions were held with Médecins Sans Frontières who agreed to support laboratory strengthening activities at the National TB Reference Laboratory. Implementation plans and roles are to be determined in early 2010.

Tajikistan

- Set up meetings for April 2010 with the Deputy Minister of Health and Head of Agency for Medical Service Monitoring and Control, to present the EXPANDx-TB project and discuss a draft MoU.

Uzbekistan

- Supplied a LC diagnostic instrument and reagents in September 2009 and provided subsequent training in order to respond to limiting culture capacity in the already functioning BSL-3 laboratory;
- Facilitated the replenishment order for Uzbekistan, which included equipment and reagents for the central laboratory in Tashkent;
- Helped plan the refurbishment of the regional laboratory in Samarkand alongside KfW (German bank for reconstruction) - who provided most of the equipment - with the aim of implementing a negative air pressure laboratory;
- Finalized the protocol, budget and human resources strategy for a drug resistance surveillance pilot project with the WHO Drug Resistance Survey team.

FIND Country Programmes



FIND India

Since 2008, FIND has been working to facilitate access to new tuberculosis diagnostics in India. Due to our in-country position, we have become familiar with national processes and have come to understand the needs for technology uptake in the country's specific context. In collaboration with the Indian National Tuberculosis Programme (NTP), we conducted studies at 10 TB laboratories, collecting evidence for the scale-up of the three FIND-developed technologies endorsed by the World Health Organization.

In 2009, FIND was identified as a key partner in the implementation of the National Laboratory Scale-up Plan for India, developed with the aim of defining the nationwide laboratory strategy for culture and DST services to combat drug-resistant (DR) TB. The plan lays down a road map for implementation. Laboratories are required to provide DR-TB diagnosis to all smear-positive re-treatment patients by 2012, and all smear-positive patients by 2015. Laboratory plans are expanding dramatically in terms of the number of facilities, human resource requirements, and the use of WHO approved high through-put rapid diagnostic technologies. The NTP envisages creating the capacity to perform at least 160,000 diagnostic culture/DSTs and 330,000 follow-up cultures annually, through LC and LPA.

During 2010, FIND will build on its experience of rolling out new diagnostics in India, and work with partners to develop a strategy on how to reach out to the private sector in the country. While the NTP is the backbone of TB control in India, private sector laboratories and hospitals continue to play an important role, and can dramatically expand the reach of new tools to a much greater number of patients.

Highlights from 2009

Projects to increase diagnostic capacity

Our main objective will be to introduce LPA into 43 laboratories and LC/rapid speciation in 33 laboratories over the next four to five years. These projects are to be funded through the Global Fund Round 9 and the EXPANDx-TB programme, expected to be implemented in 2010. Negotiations were held for the expansion of the UNITAID-funded EXPANDx-TB project to 27 countries, which would include India.

FIND was selected as a sub-recipient for the approved Global Fund Round 9 proposal, for which NTP India is the principal recipient. This proposal complements the EXPANDx-TB project, since both ventures focus on the uptake of LPA and LC testing in existing programme laboratories. Through this project, the Government of India will provide the essential requirements for participating laboratories, while FIND will manage technical assistance for assessments, capacity building, monitoring and evaluation, including on-site mentoring by laboratory experts for successful uptake of LPA and LC testing.

Relocation of FIND Office to Central Delhi

In August 2009, FIND India offices were relocated to Connaught Place, one of the largest financial, commercial and business centres in New Delhi. In light of the anticipated EXPANDx-TB and Global Fund activities, it was decided to look for larger premises to accommodate more staff, as well as the increasing need to be closer to the Central TB Division of the Ministry of Health and Welfare, WHO and selected trial sites. Connaught Place houses several offices belonging to Indian and international companies and, from this position, FIND hopes to stay better connected to core stakeholders and activities.

ISO Certification and Standard Operating Procedures

In June 2009, the FIND India office was certified for compliance with the ISO standards 13485:2003 and 9001:2008 by KEMA Quality, a leader in global testing and certification services. The certification confirms that ISO standards are implemented and maintained through the organisation's quality management procedures.

All SOPs were reviewed prior to the external ISO audit and those for regulatory affairs were revised in order to (i) simplify regulatory procedures and archiving in line with FIND's quality management system, and (ii) incorporate procedures for custom duty exemption for various shipments. To facilitate better monitoring of the procedures, specific software with key features, including a periodic alert on logistical issues and auto-generated reports for better analysis of procedures, has been developed with the help of a local IT agency. The revisions to the SOPs and the software development are expected to facilitate the implementation of the EXPANDx-TB and Global Fund projects, particularly with regard to the importation of clinical trial materials.

Demonstration studies

Liquid culture and the line probe assay

FIND India has been conducting demonstration projects for LPA and LC in different NTP laboratories since 2008, and has been nominated to become a member of the National Laboratory Committee (NLC) of the NTP, an advisory body for laboratory issues. Progress and updates on various FIND projects are presented at successive meetings held by the NLC.

During 2009, interim results of the LPA studies were presented to the NLC. The response has been encouraging and we anticipate that the Committee will endorse the routine use of LPA, LC and rapid speciation in programmatic settings under the EXPANDx-TB and Global Fund projects next year.

Xpert® MTB/Rif

India is one of the sites for the Xpert® MTB/RIF demonstration study, described in the chapter on TB projects. The system was installed at CMC Vellore Medical College in the fourth quarter of 2009 and FIND is investigating the operational performance, feasibility and impact of the assay in pulmonary TB suspects and DR-TB suspects. Patient enrolment will continue for a one year period and data from all study sites will be pooled to create a dossier to be submitted to WHO-STAG in 2010.

LED Fluorescence Microscope

India participated in the demonstration study on the LED FM project, which was conducted at nine microscopy centres with three supervising study sites at JALMA Institute, CMC Vellore Medical College, and New Delhi TB Centre. Data management for all the international study sites was based at the FIND India office. The final report was submitted to WHO-STAG in 2009.

Laboratory management information system

With the introduction of rapid diagnostics in NTP laboratories, a dramatic decrease in time to diagnosis and increase in number of tests conducted per day is expected. However, reporting and analysis of proficiency data and tests results are expected to be major challenges.

FIND has developed an electronic data management and information system to streamline data management and reporting of test results to relevant laboratory officials. This software collects all patient-related data from the time of sputum collection through to completion of second line TB treatment, with treatment outcomes, as well as synthesising data on the diagnostic tools available in each laboratory (Lowenstein-Jensen culture & DST, LC & DST and LPA). The software complements the existing register-based data management system used in the laboratories and is expected to facilitate monitoring and evaluation. It is currently in use at three NTP laboratories. Next, FIND India plans to develop a comprehensive online Laboratory Information Management System (LIMS), adding interfaces for human resources, logistics and financial aspects of projects to the existing software.



Challenges

The biggest challenges for FIND India will be to address the gap between the existing laboratory capacity in the country and the envisioned plan under the National Laboratory Scale-up Plan. This will involve needs assessments of all existing laboratories, laboratory design, infrastructure upgrades, an increased supply of equipment and consumables, provision of additional support for human resources, capacity-building of new and existing human resources, and ongoing monitoring and evaluation, including on biosafety standards, for 43 laboratories across the country. Establishing a procurement and supply chain for all the laboratories and a rigorous recording and reporting mechanism at all sites will also be major challenges.

In 2008, the FIND Uganda office was established at the request of the Ministry of Health to focus on technology development from proof of concept through to gathering evidence and scale-up of diagnostics. Today work continues on tuberculosis and malaria programmes, including laboratory capacity strengthening activities.

Throughout this year, FIND Uganda staff participated in a number of local and international conferences, workshops and meetings and also provided logistical and administrative support on a wide range of different activities, including field visits and meetings.

Highlights from 2009

ISO Certification and Standard Operating Procedures

As with the FIND India office, FIND Uganda was awarded ISO certification in mid-2009. An external audit by KEMA Quality was conducted in June 2009 and both the office and laboratory were certified as being compliant with ISO 9001:2008 and 13485:2003. The finance and accounting audit for FIND Uganda took place in December 2009.

The laboratory's 40 standard operating procedures and associated forms (50 in all) were reviewed prior to the external audit and updated and revised where necessary to ensure complete harmonization with FIND's quality management system. In addition, a computerized laboratory information management system (LIMS) is being developed and implemented to improve efficiency and QA of laboratory data.

Tuberculosis programme

TB bead concentration

A feasibility and evaluation study on the use of a magnetic bead technology to concentrate *Mycobacterium tuberculosis* in sputum prior to LED FM was completed. The TB bead concentration technology was compared with three other methods for microscopy and a draft manuscript on results was prepared for review at the end of 2009.

Line probe assay validation study

A local validation study of the line probe assay (LPA) for rapid MDR-TB screening was completed and a manuscript for publication prepared. LPA performance, which correlated highly with conventional methods, was found to be feasible for implementation in the Ugandan setting.

LED fluorescence microscopy demonstration studies

Three commercial LED-based methods for fluorescence microscopy were evaluated in collaboration with the Infectious Disease Institute, Mulago Hospital and the National Tuberculosis Reference Laboratory. Preliminary data from the first phase of the study contributed to the WHO-STAG submission. The second phase is investigating the operational performance of the three systems in a routine setting at Mulago Hospital. Data analysis will be complete by the first quarter of 2010.

Pipette for LAMP

In October, FIND Uganda completed an assessment of a prototype pipette for sputum transfer for the LAMP technology.

Evaluation study of two rapid speciation tests

We are currently performing a laboratory evaluation of the performance of the two rapid speciation tests, developed by Becton, Dickinson and Company (USA) and Standard Diagnostics Inc. (Korea) respectively. The two tests were compared with the predicate assay approved by WHO in 2007, the Capilia TB Neo, developed by Taans Laboratories Inc. (Japan). This included determination of sensitivity, specificity and ease of use for confirmation of *M. tuberculosis* in positive liquid and solid cultures. Results of this study were made available at the end of 2009.

Xpert® MTB/Rif demonstration studies

Uganda is one of the sites for the Xpert® MTB/RIF demonstration study. FIND is investigating the operational performance, feasibility and impact of the assay in pulmonary TB suspects presenting at the hospital emergency department. Patient enrolment started in mid 2009, and will continue for a one-year period.

In October 2009, FIND Uganda completed an assessment of a prototype pipette for sputum transfer for the LAMP technology. We are currently performing a laboratory evaluation of the performance of the two rapid speciation tests (Becton, Dickinson and Company and Standard Diagnostics) compared with the predicate assay approved by WHO in 2007, the Capilia TB Neo. This will include determination of sensitivity and specificity and ease of use for confirmation of Mtb in positive liquid and solid cultures. Results of this study were made available by the end of 2009.

Malaria Programme

Coordination of malaria RDT implementation

FIND works closely with the National Malaria Control Program (NMCP) and WHO Uganda to bring relevant partners together to deliver evidence-based, quality assured and systematic RDT deployment. FIND has continued its active engagement in coordination of QA, procurement and distribution, training and communication, and monitoring and evaluation activities.

We have been active in advocating for RDT funding among in-country partners, and supporting the NMCP in its applications to the Global Fund. In terms of procurement and distribution, we have supported quality assurance by facilitating the storage and distribution chain with temperature and humidity log tags, and relevant WHO/FIND pocket-book guidelines. We continue to advocate for coordinated distribution plans and harmonisation of RDT logistics training and lot testing.

Coordinated sessions were held to formulate and review National Malaria Control Policy Guidelines on malaria case management. Recommendations were made to include parasitological diagnosis, lot testing results of the RDTs for health workers and training institutions, as well as the production of training tools, treatment guidelines and RDT job aids. Furthermore, district-based sensitization of the community about malaria diagnosis was also considered to be of great importance.

We worked with the National Drug Authority to produce the National Malaria RDT Regulatory Guidelines. Based on our input, the Guidelines have been upgraded to a National Medical Devices Regulatory Guideline.

Malaria diagnostics field research studies

FIND carried out a number of activities on field research studies in 2009, as well as planning for upcoming studies:

Evaluation of blood collection and transfer devices for use with malaria RDTs

This study is designed to evaluate a range of devices for ease of use, blood safety, and accuracy and consistency of blood volume transfer. The purpose is to identify the most appropriate blood transfer device/s for use with malaria RDTs in routine health care, and to provide this information to RDT manufacturers and purchasers to encourage marketplace availability of such devices. Field activities for this study were completed in Uganda and Nigeria as of October 2009, and are pending in the Philippines. Results will be published in a peer-reviewed journal and will be disseminated to manufacturers and procurers of RDTs.

Pilot field evaluation of job aid and training messages for positive control wells

Positive Control Wells (PCWs) have been developed for use as a quality control tool, as part of a proposed tiered National QA Programme for malaria RDTs. PCWs are designed to be used by health workers to test stocks of stored RDTs used at their health facilities, to ensure their validity and accuracy. A step-wise approach to field studies to address key questions for PCW development and implementation is being employed.

Between August and October of 2009, PCWs were introduced to health workers in Uganda during pilot training sessions, using newly-developed training materials. Information from these pilot sessions is being used to refine the training materials and inform the final PCW development process. Planning is underway for field work for a preliminary assessment of the utility and acceptability of PCWs in routine healthcare in malaria-endemic areas, to begin in early 2010 with likely clinical sites in Uganda and Senegal.

RDTs in for the detection of placental malaria infection

Malaria prevention measures for pregnant women are necessary and available, but the efficacy and effectiveness of current approaches appears to be dropping with parasite resistance. Preliminary evidence suggests that detection of parasite antigen may provide the best indicator of clinically significant infections and predict pregnancy outcomes. Screening with RDTs, therefore, may offer an accurate and practical way to identify pregnant women who will benefit from targeted therapy for placental malaria infection. We are working with the WHO Special Programme for Research and Training in Tropical Diseases (TDR), advised by key researchers in the area, to develop a protocol to test this hypothesis, with potential for significant policy and public health impact. Participating clinical sites have been identified in Uganda, Nigeria and Burkina Faso, and field work is anticipated to begin by mid 2010.

Laboratory strengthening

Over the course of the year, the national laboratory policy was finalized, published and finally launched with Uganda's MoH and other partners, including WHO and the US CDC during a ceremony on 24 September 2009. Policy dissemination is ongoing. Work has begun on the National Laboratory Strategic Plan which is now in first draft status. This draft is being developed in coordination with the Laboratory Technical Committee (LTC) and is in line with the National Health Policy and Health Sector Strategic Plan.

In the latter half of the year, as a member of the LTC, FIND was engaged in the development of proposals on the national laboratory structure and network, and in establishing a national accreditation system for laboratories in the country. These are still ongoing.

The FIND Uganda Research Laboratory has been preparing for the start of activities for the EXPANDx-TB project, which was extended last year to include Uganda. Three regional centres in Mbale, Mbarara and Gulu are to be assessed by the team in early 2010 so that recommendations for laboratory strengthening can be made. Plans are also underway to establish a TB molecular facility at the National Referral Hospital in Kampala.

In addition, we have been actively engaged in other laboratory strengthening initiatives in the country and have contributed to the NTRL's quality assurance publication for light and fluorescence microscopy, as well as its district and regional laboratory manuals.

A disease and commodity monitoring system based on text messaging

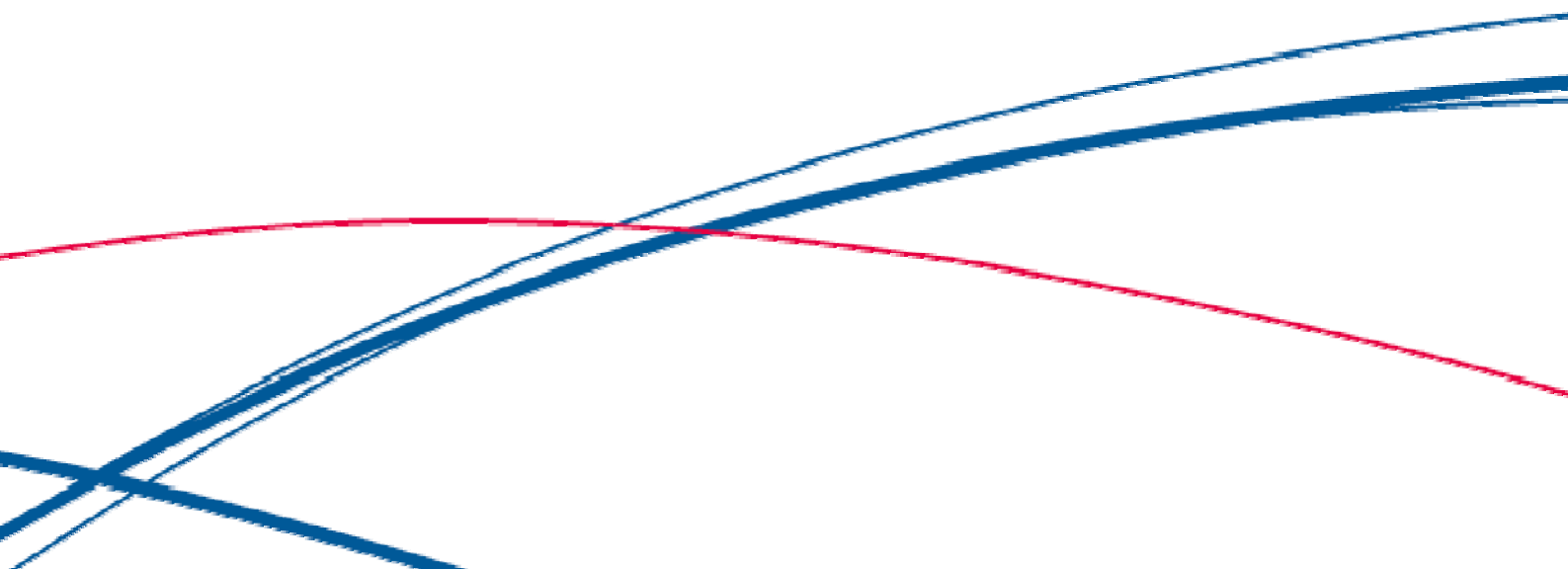
In collaboration with the NMCP and the Earth Institute of Columbia University (USA), FIND recently embarked on a project to develop and pilot the RapidSMS messaging platform for monitoring and evaluation of the malaria RDT rollout in two districts (Gulu and Kabale). RapidSMS is a free and open-source framework for developing short message service (SMS)-based applications that was originally developed by UNICEF. It is being implemented to enable real-time monitoring of facility and district-level data on case management, diagnostics and stock management.

The TB team in Uganda is also developing a project concept note to pilot the RapidSMS technology to monitor TB laboratory performance, both for the TB microscopy external quality assurance programme and the specimen referral system for DST. It is hoped that this technology will also help to monitor the impact of new diagnostic interventions, and that the project will extend to all EXPANDx-TB sites in the future.

On 24 September 2009, the Uganda Ministry of Health and FIND celebrated the launch of the first National Laboratory Health Services Policy in the presence of Mr. James Kakooza, Hon. Minister of State for Health



Financial Statements
for the year ended
31 December 2009 and
Report from the Statutory
Auditor



Report of the statutory auditor

To the Board of the
Foundation for Innovative New Diagnostics (FIND), Geneva

Report on the financial statements

As statutory auditor, we have audited the accompanying financial statements of the Foundation for Innovative New Diagnostics (FIND), which comprise the balance sheet, statement of income and expenditure, cash flow statement and notes for the year ended 31 December 2009.

Foundation Board's Responsibility

The Board of the Foundation is responsible for the preparation of the financial statements in accordance with the requirements of Swiss law and the statutes of the Foundation. This responsibility includes designing, implementing and maintaining an internal control system relevant to the preparation of financial statements that are free from material misstatement, whether due to fraud or error. The Board of the Foundation is further responsible for selecting and applying appropriate accounting policies and making accounting estimates that are reasonable in the circumstances.

Auditor's Responsibility

Our responsibility is to express an opinion on these financial statements based on our audit. We conducted our audit in accordance with Swiss law and Swiss Auditing Standards. Those standards require that we plan and perform the audit to obtain reasonable assurance whether the financial statements are free from material misstatement.

An audit involves performing procedures to obtain audit evidence about the amounts and disclosures in the financial statements. The procedures selected depend on the auditor's judgment, including the assessment of the risks of material misstatement of the financial statements, whether due to fraud or error. In making those risk assessments, the auditor considers the internal control system relevant to the entity's preparation of the financial statements in order to design audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the entity's internal control system. An audit also includes evaluating the appropriateness of the accounting policies used and the reasonableness of accounting estimates made, as well as evaluating the overall presentation of the financial statements. We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our audit opinion.

Opinion

In our opinion, the financial statements for the year ended 31 December 2009 comply with Swiss law and the statutes of the Foundation.


Report on Other Legal Requirements

We confirm that we meet the legal requirements on licensing according to the Auditor Oversight Act (AOA) and independence (article 728 of the Swiss Code of Obligations) and that there are no circumstances incompatible with our independence.

In accordance with article 728a paragraph 1 item 3 of the Swiss Code of Obligations and Swiss Auditing Standard 890, we confirm that an internal control system exists, which has been designed for the preparation of financial statements according to the instructions of the Foundation.

We recommend that the financial statements submitted to you be approved.

Deloitte SA


Peter Quigley
Licensed audit expert
Auditor in charge


Isabelle Babey

Geneva, May 27, 2010
PBQ/IBA/jh

Attached

Financial Statements (balance sheet, statement of income and expenditure, cash flow statement and notes)

FOUNDATION FOR INNOVATIVE NEW DIAGNOSTICS (FIND)

Geneva, Switzerland

BALANCE SHEET AS AT 31 DECEMBER 2009

(all amounts in US dollars)

	<u>2009</u>	<u>2008</u>
<u>ASSETS</u>		
Current assets		
Cash on hand	4 037	2 945
Bank Current accounts	764 352	1 298 072
Short-term Deposits	13 000 000	20 890 000
Rental Guarantee Deposit	164 344	77 965
Accounts receivable	1 505 898	695 476
Prepayments	2 716 923	2 880 087
	<hr/>	<hr/>
	18 155 554	25 844 545
Fixed assets		
Office furniture & fittings	52 595	45 470
Computers & printers	168 407	45 973
Electrical installations	11 153	7 504
Fax machine & telephones	1 626	1 683
	<hr/>	<hr/>
	233 781	100 630
Patents	23 121	30 828
	<hr/>	<hr/>
Total assets	<hr/> <hr/>	<hr/> <hr/>
	18 412 456	25 976 003
 <u>LIABILITIES AND CAPITAL</u>		
Current liabilities		
Accounts payable	2 194 014	2 435 894
Accrued expenses	476 453	297 670
Contributions received in advance	15 173 566	20 924 076
	<hr/>	<hr/>
	17 844 033	23 657 640
Capital and reserves		
Capital	40 430	40 430
General reserve	527 993	2 277 933
	<hr/>	<hr/>
Total liabilities and capital	<hr/> <hr/>	<hr/> <hr/>
	18 412 456	25 976 003

The accompanying notes form an integral part of these financial statements.

FOUNDATION FOR INNOVATIVE NEW DIAGNOSTICS (FIND)

Geneva, Switzerland

STATEMENT OF INCOME AND EXPENDITURE FOR THE YEAR ENDED 31 DECEMBER 2009

(all amounts in US dollars)

	2009	2008
INCOME		
Contributions income	24 484 891	27 370 155
Sundry income	144 238	416 121
Total income	24 629 129	27 786 276
EXPENDITURE		
Analytical & Project Work		
Tuberculosis	15 083 050	18 403 300
Human African Trypanosomiasis	4 252 387	3 591 018
Malaria	3 419 806	3 541 023
HIV	137 548	24 868
	22 892 791	25 560 209
Information & Communication		
Publications production	50 283	147 236
Website	20 897	26 970
Communications consultants	12 748	24 303
	83 928	198 509
Governing & Advisory Bodies		
Foundation Board	11 437	43 081
	11 437	43 081
General Administration		
Staff costs and travel	924 331	804 043
IT expenses	247 294	304 195
Photocopies, stationery, printing & sundries	114 454	117 605
Rent of premises	534 976	391 115
Repairs & maintenance	108 221	77 886
Telecommunications	115 176	118 563
Office moving expenses	204 803	-
	2 249 255	1 813 407
Finance & Service Expenses		
Staff costs and travel	595 357	459 399
Auditing & accounting	65 471	61 720
Bank charges	19 413	19 670
Exchange losses	133 864	308 603
Legal fees	78 851	140 152
Insurance	185 908	164 300
	1 078 864	1 153 844
Depreciation	62 794	89 080
Total expenses	26 379 069	28 858 130
Excess of expenditure over income for year	(1 749 940)	(1 071 854)
Accumulated surplus brought forward	2 277 933	3 349 787
Accumulated surplus carried forward	527 993	2 277 933

The accompanying notes form an integral part of these financial statements.

FOUNDATION FOR INNOVATIVE NEW DIAGNOSTICS (FIND)

Geneva, Switzerland

CASH FLOW STATEMENT FOR THE YEAR ENDED 31 DECEMBER 2009

(all amounts in US dollars)

	2009	2008
Excess of expenditure over income for the year	(1 749 940)	(1 071 654)
Add back non-cash charge - depreciation	62 794	89 080
	<u>(1 687 146)</u>	<u>(982 774)</u>
Cash flows - operating activities		
Increase/(decrease) in contributions in advance	(5 750 510)	4 993 057
Increase/(decrease) in accounts payable	(241 880)	1 413 695
Increase/(decrease) in accrued expenses	178 783	127 808
(Increase)/decrease in accounts receivable	(810 422)	(265 696)
(Increase)/decrease in prepayments	163 164	(2 849 820)
	<u>(6 460 865)</u>	<u>3 419 044</u>
Cash flows - investing activities		
Additional office furniture & fittings	(25 743)	(23 251)
Additional computers & printers	(148 477)	(30 570)
New electrical installations	(12 392)	-
Additional faxes and telephones	(1 628)	-
(Increase)/decrease in rental guarantee account	(86 379)	(5 243)
	<u>(274 617)</u>	<u>(59 064)</u>
Net increase in cash and cash equivalents for year	<u>\$ (8 422 628)</u>	<u>2 377 206</u>
Cash and cash equivalents at start of year		
Cash on hand	2 945	2 730
Current accounts & short-term deposits	22 188 072	19 811 081
	<u>22 191 017</u>	<u>19 813 811</u>
Cash and cash equivalents at end of year		
Cash on hand	4 037	2 945
Current accounts & short-term deposits	13 764 352	22 188 072
	<u>13 768 389</u>	<u>22 191 017</u>
Net (decrease)/increase in cash and cash equivalents for year	<u>\$ (8 422 628)</u>	<u>2 377 206</u>

The accompanying notes form an integral part of these financial statements.

FOUNDATION FOR INNOVATIVE NEW DIAGNOSTICS (FIND)

Geneva, Switzerland

NOTES TO THE FINANCIAL STATEMENTS FOR THE YEAR ENDED 31 DECEMBER 2009

1. General

The Foundation for Innovative New Diagnostics (FIND) is an independent non-profit Foundation created under Article 80 of the Swiss Civil Code, and is registered in the Geneva Register of Commerce under by-laws dated 22 July 2003.

FIND's mission is to support and promote the health of people in developing countries through the development and introduction of new but affordable diagnostics for infectious diseases.

FIND is exempt from federal and cantonal income and capital taxes.

2. Significant accounting policies

2.1 Basis of presentation The financial statements are prepared under the historical cost convention.

2.2 Fixed assets Fixed assets are recorded at cost and are depreciated under the straight-line method at 20% annually for office furniture and fittings, electrical installations and fax machine and telephones, and 33.3% annually for computers and printers.

2.3 Patents The Patents were purchased as part of an agreement completed with a project partner early in 2004, and are subject to amortization under the straight-line method over their remaining useful life (four years).

2.4 Foreign currency Accounting records are maintained in US dollars. Income and expenditures in other currencies are recorded at accounting rates approximating actual rates in effect at the time of the transaction. Year-end balances for assets and liabilities in other currencies are translated into US dollars at rates of exchange prevailing at balance sheet date.

At 31 December 2009 the rate of exchange used for the Swiss franc, the main foreign currency for 2009, was USD/CHF = 1.03 (2008 – 1.06). Exchange gains and losses are included in the determination of net income.

2.5 Recognition of revenue Contributions received are recorded over the grant period agreed with donors, taking into account the timing of the expected disbursements, with amounts received relating to periods extending beyond balance sheet date recorded as contributions received in advance. Donor agreements in effect at 31 December 2009 provide for a total of USD 23.7 million to be paid to FIND between January 2010 and August 2012.

FOUNDATION FOR INNOVATIVE NEW DIAGNOSTICS (FIND)

Geneva, Switzerland

NOTES TO THE FINANCIAL STATEMENTS(continued)

2.6 Accounts payable and accrued expenses With the exception of emoluments payable to staff, which are accounted for when paid, accounts payable and accrued expenses represent expenditures chargeable in the 2009 financial year, for which invoices were not received for payment before year-end. Settlements are charged to the accruals in the following financial period.

2.7 Rental guarantee deposit The guarantee relates to the rental of the FIND office premises and is recoverable in accordance with the rental contract upon vacation of the premises.

2.8 Projects Payments to project partners during 2009 under contracts signed up to 31 December 2009 totalled USD 11,582,189 (2008 – USD 14,370,210). Commitments at 31 December 2009 for future payments under those contracts total USD 6,699,917 (2008 – USD 10,766,905).

3. Fixed assets and intellectual property

3.1 Fixed assets as at 31 December 2009 were as follows:

	<u>2009</u>	<u>2008</u>
Cost price		
Office furniture & fittings	112,507	106,582
Computers & printers	329,177	185,702
Electrical installations	12,392	45,509
Fax machine & telephones	3,155	9,891
	-----	-----
	457,231	347,684
<u>Less:</u> Accumulated depreciation	223,451	247,054
	-----	-----
Net book value	USD 233,780	100,630
	=====	=====

Fire insurance cover as at 31 December 2009 was USD 128,155 (2008 – USD 124,528).

3.2 Intellectual property as at 31 December 2009 was as follows:

	<u>2009</u>	<u>2008</u>
Patents – cost price	53,949	53,949
	-----	-----
	53,949	53,949
<u>Less:</u> Accumulated depreciation	30,828	23,121
	-----	-----
Net book value	USD 23,121	30,828
	=====	=====

FOUNDATION FOR INNOVATIVE NEW DIAGNOSTICS (FIND)

Geneva, Switzerland

NOTES TO THE FINANCIAL STATEMENTS(continued)**4. Contributions received**

During 2009 contributions were received from donors as follows *(non-dollar amounts converted to USD at exchange rates on date of receipt)*:

	<u>2009</u>	<u>2008</u>
Becton Dickinson and Co	50,000	-
Bill & Melinda Gates Foundation	11,553,558	28,378,683
European Union	344,650	249,622
Government of Ireland	-	259,067
Government of Netherlands	-	2,532,383
JSI Research & Training	21,500	-
UBS	149,850	-
UNITAID	6,064,300	-
WHO	556,173	-
	<u>-----</u>	<u>-----</u>
USD	18,740,031	31,419,755
	<u>=====</u>	<u>=====</u>

5. Pension Fund liabilities

No amounts were due to the pension fund at 31 December 2009 *(2008 – nil)*.

6. Rent commitments

At 31 December 2009 FIND had future rent commitments totalling USD 3,052,311 up to 30 June 2014 *(2008 – USD 198,728 up to 30 June 2009)*.

7. Funds

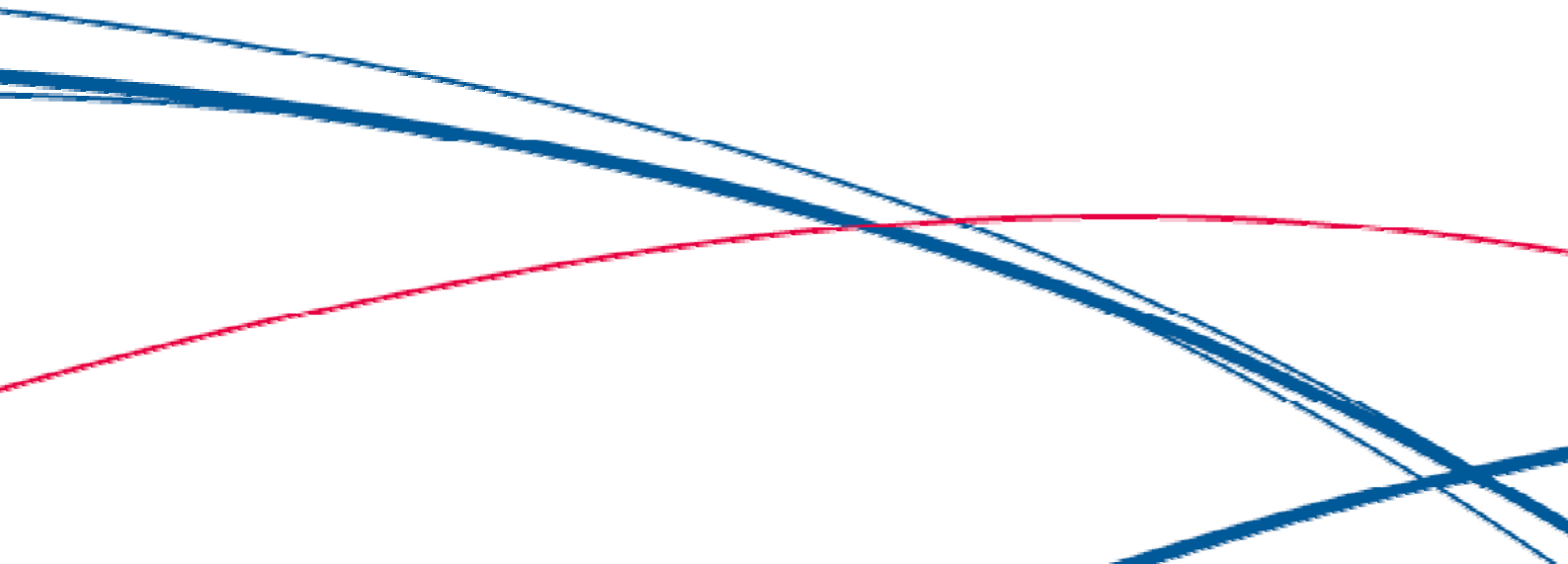
The Endowment Capital of CHF 50,000 is fully subscribed and equates to USD 40,430 at the rate of exchange on the date of payment.

8. Events subsequent to 31 December 2009

There were no events occurring subsequent to 31 December 2009 which could have a material impact on the understanding of these financial statements.

FIND

Board of Directors and Teams



Board of Directors

Dr. Gerard H. Moeller
Chairman of the Board



Dr. Jan Gheuens
Member



Dr. Bernard Mach
Member



Dr. Mphu Ramatlapeng
Member



Dr. Giorgio Roscigno
Member



FIND Geneva Team

Chief Executive Officer

Giorgio Roscigno

Eric Adam, *Project Leader / Project Manager EXPAND-TB*
Audrey Albertini, *Scientific Assistant for Malaria Diagnostics*
Heather Alexander*, *Health Scientist*
Sylvain Biéler, *Project Manager*
Catharina Boehme, *Senior Medical Officer*
Nora Champouillon, *Logistics Officer*
Louisa Chaubert, *Accounting Manager*
Diana Choa, *Personal Assistant to the CEO*
Herbert J. Clemens, *Chief Financial Officer*
Knut Feldmann, *Senior Project Manager - EXPAND-TB*
Francoise Fichet, *Receptionist / Administrative Assistant*
Rossana Gambin, *Human Resources Officer*
Iveth J. González, *Scientific Officer - Malaria*
Beatrice Gordis, *Communications Officer - HAT & Malaria*
Julian Gordon*, *Medical Diagnostic Technologies & IP*
Christen Gray, *Clinical Trials Data Manager*
Cristina Gutierrez, *Senior Project Manager, Laboratory Support*
Linda Hinni, *Accounting Assistant*
Judith Kirorei-Ita, *Scientific Team Administrator - TB*
Peter Koller*, *Quality Manager*
Evan Lee, *Senior Medical Officer*
Solomon Haile Mariam*, *Advocacy Officer - HAT*
Gerd Michel, *Senior Technology Officer*
Pamela Nabeta, *Associate Medical Officer*
Rahul Narang*, *TB Laboratory Support*
Joseph Ndung'u, *Head of HAT Diagnostics Programme*
Richard O'Brien, *Head of Product Evaluation and Demonstration*
Madhukar Pai *, *Consultant for Latent TB Infection*
C.N. Paramasivan, *Head of TB Laboratory Support*
Mark Perkins, *Chief Scientific Officer*
Bärbel Porstmann, *Senior Operating Officer*

Sharon Saacks, *Document Controller & Project Manager TB*
Hojoon Sohn*, *Health Economist*
Ákos L. Somoskövi, *Senior Project Manager, Laboratory Support*
Ranald Sutherland *, *Technology and Business Development*
Jewel Thomas, *Communications Officer – TB*
Tatiana Titova*, *Web consultant*
Mata Toure, *Junior Project Analyst*
Eloise Valli, *Junior Study Coordinator*
Alessandra Varga*, *Events and Image Development*
Julie Vercruysse, *Scientific Team Administrator - Malaria*
Thomas Verges, *Logistics Officer, EXPAND-TB*
Hanna Yirga, *Scientific Team Administrator – HAT*
Diego Zallocco*, *TB Projects*

* *Consultant*

FIND India Team

VV.H. Balasangameshwara, *Senior Programme Manager and Technology Officer*

Jacques Debayle, *Liaison Office Manager*

Uday Gurung, *Data Entry Operator*

Ramesh Mahadevan*, *Logistics Consultant*

R. Narayanaswamy, *Deputy Drugs Controller (I) (RETD.)*

Shailaja Paramathma, *Administrative Assistant*

Neeraj Raizada, *Medical Officer*

Arman Singh, *Data Entry Operator*

* *Consultant*

FIND Uganda Team

Julius Patrick Ademun, *Scientific Officer*

Heidi Albert, Senior Scientist, *Head of Laboratory Research*

Caroline Asiimwe, *Coordinator-Malaria Diagnostics Implementation Project*

Heidi Hopkins, *Medical Officer*

George Lukyamuzi, *Scientific Officer*

Zoe Nakuya*, *Lead Advisor*

Jean Nsekera, *Office Manager*

Barnabas Nyesiga, *Assistant Scientific Officer*

* *Consultant*

Glossary

BSL – Biosafety Level
CDC - US Centers for Disease Control and Prevention
CE - Conformité européenne
CNS – Central nervous system
CRD – Customer Requirement Document
CSF - Cerebrospinal fluid
CTRL – Central Tuberculosis Reference Laboratory
DRC – Democratic Republic of Congo
DR – Drug-resistant
DRC – Democratic Republic of Congo
DRS – WHO Drug Resistance Survey
DST - Drug susceptibility testing
E-nose – Electronic nose
EHNRI – Ethiopian Health and Nutrition Research Institute
ELISA – Enzyme-linked immunosorbent assay
EXPANDx-TB – Expanding Access to New Diagnostics for TB project
FM - Fluorescence microscope
FIND – Foundation for Innovative New Diagnostics
FTO – Freedom to operate
GDF – Global Drug Facility (Stop TB Partnership)
GF – Global Fund to Fight AIDS, Tuberculosis and Malaria
GHESKIO – Haitian Group for the Study of Kaposi's sarcoma and Opportunistic Infections
GLI – Global Laboratory Initiative
HAT - Human African Trypanosomiasis
HIV - Human immunodeficiency virus
HuCAL – Human Combinatorial Antibody Library
IgNAR – New Antigen Receptor antibody from sharks
IGRA - Interferon gamma release assay
IP - Intellectual property
IPR – Institute of Primate Research
IPTp - Intermittent prophylactic treatment in pregnancy
ISO – International Organisation for Standardization
ISCTRC – International Scientific Council for Trypanosomiasis Research and Control
KfW – Kreditanstalt für Wiederaufbau
KIT - Dutch Royal Tropical Institute
LAM - Lipoarabinomannan
LAMP - Loop-mediated isothermal amplification
LC – Liquid culture
LED - Light-emitting diode
LFA - Lateral-flow assay
LIMS – Laboratory information management system
LJ - Lowenstein-Jensen
LPA – Line probe assay
TST – Tuberculin skin test
LTBI - Latent tuberculosis infection
LTC – Laboratory Technical Committee
MAbs - Monoclonal antibodies
MDR – Multi-drug resistant
MoH - Ministry of Health
MoU – Memorandum of Understanding
MRC – Medical Research Council
MSF - Médecins Sans Frontières
NDA – National Drug Authority

NHLS - National Health Laboratory Service
 NICD – National Institute for Communicable Diseases
 NLC – National Laboratory Committee
 NMCP – National Malaria Control Programme
 NRL – National Reference Laboratory
 NTRL – National Tuberculosis Reference Laboratory
 NTI – National Tuberculosis Institute
 NTP - National Tuberculosis Programme
 PATTEC – Pan African Tsetse and Trypanosomiasis Eradication Campaign
 PCR - Polymerase chain reaction
 PCW – Positive control well
 PDP – Product development partnership
 PEPFAR - US President's Emergency Plan for AIDS Relief
 POC – Point-of-care
 PPP – Public private partnership
 PTB - Pulmonary tuberculosis
 PURE – Procedure for ultra rapid extraction
 QA - Quality assurance
 QGIT - QuantiFERON®-Gold In-Tube
 QIMR – Queensland Institute of Medical Research
 RBM – Roll Back Malaria Partnership
 RD-9 – Round 9 (Global Fund)
 RDT – Rapid diagnostic test
 Rif – Rifampin/Rifampicin
 RIME - short and non-autonomous sequences
 RT – Real Time
 SBRI – Seattle Biomedical Research Institute
 scFv – single chain variable Fragment
 SMS – Short Message Service
 SNRL – Supra-National Reference Laboratory
 SOP – Standard operating procedure
 STAG - WHO Scientific Technical Advisory Group
 TB - Tuberculosis
 TDR - WHO Special Programme for Research and Training in Tropical Diseases
 trDNA – trans-renal DNA
 TST - Tuberculin skin test
 VOC - Volatile organic compounds
 VSG – Variable surface glycoprotein
 WHO - World Health Organization
 WPRO – WHO Regional Office for the Western Pacific
 XDR - Extensively drug-resistant
 ZN - Ziehl-Neelsen

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