Annual Report

2007

Partnering for better diagnosis for all

Message from the CEO and Chairman of the Board

Subsequent to the number of new development activities described in last year's Annual Report, 2007 has been another promising year for FIND.

With respect to our three target disease programmes, significant progress was made on several fronts in our quest for better diagnostic tools for use at all levels of the health system - primary health care level; microscopy (district hospital or health center laboratory) level; and referral laboratories level (national or regional).

We advanced tests aimed at improved detection of tuberculosis; tests to better and more rapidly detect multi- and extensively drug-resistant (XDR) TB; and transformational technologies that could provide platforms that have the potential for broader application to other diseases including malaria, human African trypanosomiasis and HIV/AIDS.

A major accomplishment in our TB programme this year was the endorsement by the WHO of the Strategic and Technical Advisory Groups' recommendations for three products developed by FIND and its partners for use in the public sector of high-endemic developing countries, namely, liquid culture systems for diagnosis of TB and for drug susceptibility testing, and a lateral flow test for *Mycobacteria tuberculosis* complex strains. The decisions were based on a large volume of data from FIND demonstration studies conducted in several countries to show the feasibility, utility and cost effectiveness of these assays when compared with current methods used in culture laboratories of disease-endemic countries. Following STAG approval in June 2007, the WHO issued formal recommendations in November of this year.

The government of Lesotho invited FIND and the WHO to introduce these technologies to improve testing for TB. FIND supervised the upgrading of Lesotho's National Reference Laboratory (NRL) into a quality-assured TB culture facility with the aim to streamline culture and DST facilities in the country.

FIND and Becton Dickinson negotiated a price for the public health sector which is significantly lower than prices commonly paid elsewhere and is an additional commitment to the ongoing FIND and BD contributions and investments in demonstration studies and laboratory support.

FIND also responded to the rise of MDR and XDR TB by consolidating an agreement with Hain Lifescience to fast-track the GenoType® MTBDR*plus* molecular test for the detection of patients infected with drug resistant forms of TB. Large-scale demonstration studies were carried out in four South African provinces in collaboration with the South African Medical Research Council, the Department of Health, and the National Health Laboratory Services. This test gives results within a day as opposed to solid culture which can take up to six weeks.

Furthermore, the feasibility of developing a molecular test to be used at the level of microscopy also deserves special mention. This test, based on Eiken's Loop-mediated isothermal AMPlification (LAMP) technology, has the potential to replace microscopy altogether. The LAMP assay is designed to detect DNA directly from clinical samples with minimal instrumentation. Molecular amplification methods, such as polymerase chain reaction, are proven technologies for the detection of TB but have not been routinely and widely used in developing countries due to their complexity and the need for highly trained staff. What is even

more exciting about LAMP is the potential for use of this technology as a molecular platform for diagnosis of other diseases, including HAT and malaria.

In our thrust to improve options for diagnosis of TB at the microscopy level, FIND and Zeiss collaborated in the development of an affordable and robust LED fluorescence microscope. This microscope has a cross-disease benefit, as the technology can be applied to other diseases. An affordable price for 39 endemic countries has been made possible through an agreement with our partner.

Significant progress was also made in the human African trypanosomiasis programme, with a number of projects at advanced stages in the feasibility phase. The production of the mAECT kit at the Institut National de Recherche Biomédicale, in Kinshasa, DRC, received continued endorsement and assistance from FIND and partners. Since DRC has the highest burden of HAT, this has been a major step towards sustainable production of the kit, and is therefore a key step towards guaranteeing access.

Efforts to develop a better serological test for diagnosis of HAT also made clear progress. The first round of screening of 32 antigens for their reactivity revealed that more than half of them could detect 50% or more of the HAT sera. This has increased our confidence in the likelihood of selecting one or more with a higher sensitivity and specificity than the present card agglutination test (CATT). A second screen on 18 selected antigens by ELISA and dot-blot assays, using a new set of positive and negative sera, will be completed before the end of the year.

Furthermore, the discovery of unique host proteins in the cerebrospinal fluid (CSF) of HAT patients that can distinguish early from late stage disease has been a major breakthrough.

The launch of the Malaria programme was another of FIND's major milestones in 2007. The main accomplishments have been:

- The establishment of a malaria team, including the hiring and secondment to the programme of a highly qualified malaria specialist from WHO/WIPRO
- Development of relationships with the WHO, Roll Back Malaria Partnership, the US Presidential Malaria Initiative, World Bank, The Global Fund, and other agencies involved directly or indirectly in procurement to maximize the impact of the product testing activity
- Securing additional funding from the Government of the Netherlands to allow for R&D work that was not covered under the initial BMGF grant
- The creation of prototype positive control wells and contracting of manufacturing
- Agreement by Eiken to be directly involved in LAMP R&D

Another important development this year was the establishment of country offices to facilitate the introduction of FIND diagnostic tests in national disease control programmes. Together with the Central TB Division (CTD) of the Ministry of Health, Government of India, FIND seeks to strengthen the scope of laboratory diagnosis in India by setting up demonstration studies on liquid culture and DST, and molecular diagnosis of TB and MDR TB, and fluorescent microscopy. In August 2007, we signed a Memorandum of Understanding (MOU) with the Uganda Ministry of Health to establish a model center for TB diagnostic technology implementation in Kampala, complete with an organizational network with several partners.

In June 2007, FIND standard operating procedures and quality management systems were audited by the SWISS TS / TÜV-Süd authority. They confirmed that all processes at FIND were

structured, organized and documented at the highest quality levels and that ISO standards were being implemented throughout all organizational procedures. FIND's Project and Quality Management Systems are now ISO 13485:2003 and ISO 9001:2000 certified.

Financial results for 2007 reflected the steady expansion of FIND's activities throughout the year, with analytical and project expenditure up by 68% to $15.2 million from $9.0 million in the previous year. Total expenditure increased by almost the same percentage from $10.7 million to $17.7 million, but tight management controls on support and infrastructure costs resulted in a higher percentage of spending on projects - over 85% of the total in 2007 compared with 84% in 2006.

Accurate and prompt financial reporting based on sophisticated software and computer systems is a key feature of FIND's financial management and has helped project leaders to manage effectively the heavier volume of projects now making up FIND's project portfolio. Financial systems have been designed to adapt easily to 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 provide for contributions from donors to be recognized over the full term of each grant agreement. In 2007, revenue thus determined plus sundry income amounted to $19,267,000 (2006 - $11,423,000), which after deduction of total expenditure left a surplus of just over $1.48 million. This was added to the General Reserve of $1.87 million at the end of the previous year to give a total of just on $3.35 million at the end of 2007. Further information on FIND's financial results in 2007 can be found in the Auditors' Report, Financial Statements and Notes elsewhere in this Report.

We look to another successful year in 2008 as we increase our efforts in the introduction of POC assays as a top priority. We will continue to maintain and constantly improve our quality of management to ensure adherence to the standards expected of us to maintain ISO certification. We rededicate ourselves, together with our partners and donors, to ensuring that affordable and appropriate diagnostic technologies can reach even the poorest patients in high endemic settings.

Product development activities - overview

Tuberculosis Programme

The activities carried out in this disease portfolio progressed along the following lines, namely, 1) advancing the product pipeline; 2) filling the technology and development gaps; and 3) evaluating global access strategies.

1. Advancing development of products in current pipeline

The products were moved through FIND's pipeline in clearly defined phases, beginning with Feasibility and ending in Access. Between these are the Development, Evaluation and Demonstration phases. The maturity of the product determines the entry phase into the pipeline. Nine TB products and applications that entered the Feasibility phase went into Development or Evaluation this year.

The products cover tests aimed at improved detection of TB disease that represent incremental improvements to existing tools (fluorescent microscopes); tests to improve the detection of MDR TB and XDR TB (MGIT, FAST*Plaque*, MTBDR*plus*); and transformational technologies that could provide platforms that also have the potential for broader application to other diseases including malaria, human African trypanosomiasis and HIV/AIDS (NAAT, LAMP, GeneXpert). The products target the diagnostic needs of all three levels of health care

Primary Health Care Level
For this level, FIND is developing an improved assay for diagnosing active disease through TB antigen and antibody detection. Rights to manufacture a point of care (POC) test based on the developed reagents have so far been restricted to the public sector of high-burden, low-income countries, but these need to be extended in order to strengthen FIND's position in negotiations with possible development and manufacturing partners.

Microscopy level
For this level, FIND joined partners in the development of a LED fluorescent microscope which promises faster detection and a 10% increase in sensitivity; a manual TB DNA detection assay to replace microscopy; and an automated TB DNA test to replace culture.

Referral laboratory level
Several candidate tests in the TB product pipeline have been evaluated for this level of the health system: TK colorimetric solid culture medium; Mycobacteria Growth Indicator Tube (MGIT) for culture and DST; Capilia TB for rapid MTB identification; FAST*Plaque*-Response test for MDR screening; line probe assay for rapid MDR TB screening; and diagnosing latent TB in settings with high TB/HIV co-infections.

Addressing Clinical Infrastructure

Advancing the diagnostics in the FIND portfolio through the development pathway requires a strong clinical research infrastructure. The availability of reference clinical materials and study populations in TB-endemic countries is critical for the efficient completion of the development and clinical trial cycle of new diagnostics.

The number of trial sites has increased primarily in India, followed by South Africa. Continuous infrastructure support is currently provided to two trial sites in Peru and Russia to guarantee a rapid execution of studies. While several feasibility and demonstration studies have been or will soon be successfully completed, a large number of clinical studies are under way.

A central repository to store, manage and distribute the collected specimens and related data has been established in Bangkok, Thailand. Development of a data management and specimen tracking system for sample collection sites and the central repository has been completed and is also used for management of clinical trial data. TB reference materials (urine, serum, sputum) from more than 2000 patients and 5 countries have been collected and transferred to the specimen bank in Bangkok. A number of FIND projects have already benefitted from collected specimens, including the ImmPORT/PHRI antibody discovery, LAM reagent development, LAMP and Xpert molecular tests.

The clinical trial team needs to grow rapidly to cope with the increasing number of studies and workload. The demand for reference materials is expected to further increase when FIND begins more intensive development research on biomarker discovery with partners.

2. Filling gaps in technology and development

Progress towards easy-to-use POC tests for TB has been slowed by the complexity of current specimen processing steps prior to testing, the dearth of validated detection targets, and by the lack of simple-to-use technology platforms with the desired sensitivity. The technology limitations relate to the need to develop sensitive detection of TB at peripheral health clinics, including enhanced sensitivity lateral flow tests for TB antigen detection and POC molecular testing for peripheral health clinics. FIND faces three primary challenges in this respect:

Delays associated with geographic separation of R&D and clinical sites

The establishment of a specimen processing research center and a world-class diagnostics research facility in a high-burden setting would facilitate delays associated with distances between clinical trial sites and areas of R&D. Milestones include infrastructure development and agreements with appropriate partners for research activities, because these are critical in meeting the objectives of the work program due to the need for continued access to clinical specimens.

Following an MOU with the Ministry of Health in Uganda in August 2007, plans for renovation of a section of the National Tuberculosis Reference Laboratory in Kampala were finalized, and contractors identified.

Collaborations with Ugandan partners have been established and negotiations regarding ongoing access to clinical specimens for research activities are underway. These partners include the National Tuberculosis Control Programme, WHO Uganda office, Makerere University, MU-University of California San Francisco, Joint Clinical Research Centre, Infectious Disease Institute and Mulago-Mbarara Joint AIDS Programme.

Initial projects have been identified for implementation in the Uganda Research Programme, including evaluation of the Cepheid device in an HIV prevalent setting; implementation of LED microscopy; demonstration of the Genotype MTBDRplus assay; and improved specimen processing for smear microscopy.

Inadequate definition of biomarkers

Protein biomarkers

The FIND biomarker approach has focused both on a collaboration to discover TB markers in sputum as well as on analyzing the gaps and requirements for a focused approach for TB biomarker discovery.

Project plans have been made to evaluate the potential of developing antibody arrays for detection of a subset of secreted and membrane *M.tb* antigen. Potential industry partners have been identified. Discussions are ongoing with all the partners to determine the best suited technology and search strategy.

Biomarker identification remains a high risk approach but, with the arrival of rapidly improving MS and array technologies, the probability of success is increasing steadily. We need to rapidly allocate appropriate resources to adequately manage collaborations and technology scouting in this area.

Nucleotides

Trans-renal DNA (Tr-DNA) detection as means of TB diagnosis is quite appealing due to ease of specimen collection, and the potential for rapid results at point of care. FIND aims to catalyze feasibility studies through establishment of the Transrenal DNA Consortium. The major goal had been to develop a simple DNA extraction procedure for urine coupled with a LAMP assay detecting *M. tuberculosis* DNA for a diagnostic test to be used at the level of microscopy to detect adult and pediatric patients with pulmonary or extrapulmonary TB.

Since transrenal TB DNA may be present at the limit of detection, completion of the feasibility studies in the next 3 months will determine the future of this project.

Volatile Organic Compounds (VOCs)

Identification of TB VOCs in breath or in the headspace of sputum specimens is a highly attractive target for TB diagnosis. FIND proposed an initial work plan for establishing collaboration with leaders in this field and for validating initial feasibility data in well-defined samples and patients. FIND received additional funding from the Netherlands for catalyzing evolution of the VOC concept into a product and established collaborations with leaders in this field, most importantly KIT and two Dutch academic institutions. However, feasibility of VOC detection is challenged by high limits of detection, poor reproducibility, and lack of micro machines for field use.

Technology gaps for the simple detection of low-abundance molecules

Enhanced sensitivity lateral flow tests for TB antigen detection

Three model molecules were selected to demonstrate feasibility of highly sensitive lateral flow assays formats by fluorescent signal detection using ESAT6, LAM and Phos1. This project is primarily based on collaboration with SBRI and their partner CibiTest.

Point of care molecular testing

Two basic approaches were outlined: (i) a manual approach such as the Eiken TB-LAMP Generation1 product currently supported by FIND, whereby a manual, multi-step assay, "macro" fluidic format is simplified using clever consumable plastics and chemistry for sample

preparation and a single piece of equipment such as a heating block, and (ii) an approach analogous to the LFIs.

3. Evaluating global access strategies

The lack of clear pathways for the successful introduction of new technologies into the public health care sector of developing countries remains a major obstacle to their uptake. If no effort is made to shepherd completed diagnostics into use, there is the risk that implementation will be slow or inappropriately matched to sites of use, or that the important feedback loop between user and developer will be broken. Unlike drugs or vaccines, *in vitro* diagnostics are likely to have a rapid life cycle and require ongoing adaptation fueled by continuous interactions between the market and the developers of the technology after market authorization.

FIND/India: A model for technology implementation in emerging economies

Together with the Central TB Division (CTD) of the Ministry of Health, Government of India, FIND seeks to strengthen the scope of laboratory diagnosis in India by introducing liquid culture and drug susceptibility testing (DST), and molecular diagnosis of TB and MDR TB. FIND will augment case finding through LED-based fluorescent microscopy and help in the diagnosis of childhood TB through IGRA use.

FIND established a training site at SMS Medical College, Rajasthan, for liquid culture, DST, species identification and molecular detection of drug resistance. Utilizing this facility, we carried out training for all other FIND study sites in the public health system.

FIND/Uganda: A model for technology implementation in low-income countries

We established a model center for TB diagnostic technology implementation in Kampala Uganda, complete with sustainable relationships with appropriate partners.

In August 2007, we signed an MOU with the Ministry of Health of Uganda and set up a country office in Kampala. Collaboration has been established with Management Sciences for Health and Royal Dutch Tropical Institute as well, which has been made possible through complementary funding from the Dutch government. These two partners bring expertise in laboratory management and in laboratory quality systems to this project.

Country ownership of health sector initiatives is critical to this project, which involves collaboration between the public and private sectors. The development of an accreditation model for laboratories requires the buy-in of the Ministry of Health of Uganda, which is quite enthusiastic about this concept but whose top priority is the finalization of a national laboratory policy prior to the development of an accreditation model. Given that there were at least two previous efforts to develop this policy which did not reach fruition, FIND has invested in strengthening the relationship with the Ministry of Health and other stakeholders through the establishment of the office and the recruitment of a talented Ugandan national to represent FIND on the ground.

Existing funding mechanisms: PEPFAR, the Global Fund and other initiatives

We have established strong collaboration with key partners, including the CDC, UNITAID, and the Global Fund in several countries, including Ethiopia, Côte d'Ivoire, Uganda, and Tanzania.

These relationships have been strengthened and enhanced through the close relationship FIND has with the Stop TB Partnership and the newly established Global Laboratory Initiative.

At country level, FIND and CDC have planned laboratory strengthening activities to implement new diagnostics in Ethiopia and Côte d'Ivoire. The American Society of Microbiology has also been brought on board as a partner for FIND activities in Côte d'Ivoire, and brings the strength and expertise of its 40,000 members to laboratory strengthening. We have been asked by the Central Division of TB Control of India to submit a proposal for laboratory strengthening as a sub-recipient for the Round 8 proposal process.

At the international level, FIND has engaged the WHO at all stages of the process to ensure that the organization also perceives ownership of the process of examining the evidence, of incorporating new diagnostics into global policy recommendations, and in playing an important role in the implementation and rollout of the new diagnostic technologies.

Human African Trypanosomiasis (HAT) Programme

The focus of this disease portfolio is to develop simple and accurate diagnostic tests for human African trypanosomiasis (HAT). Two types of tests are being developed: 1) a test for infection with *T.b. gambiense* and/or *T.b. rhodesiense,* and 2) a staging test to determine whether the central nervous system (CNS) is affected in order to guide the treatment.

For ease of clarity, the presentation is structured around groups of projects that cover the same target technology. However, only one or two projects in each category will be advanced to the development phase based on performance, expected cost of manufacture, field utility, and ease of use.

Parasite detection methods

The most sensitive method for detection of trypanosomes in blood is the mini Anion Exchange Centrifugation Technique (mAECT). During the current reporting period, the mAECT production unit at INRB in Kinshasa was upgraded and staff trained to produce and market the kit in disease-endemic countries. The upgrading included training, implementation of a rigorous quality control system and in-depth analysis of costs to guarantee sustainability of production. Manufacture of the kit in the newly refurbished facility started in July 2007 and 14,000 kits have already been produced. Meanwhile, minor improvements to the product design that should further increase test performance are currently under evaluation at CIRDES in Burkina Faso and ITM, Belgium. If results are convincing, production of mAECT by INRB will be modified accordingly, and sustainable manufacturing of the new product will be implemented and monitored.

Several projects in the feasibility phase are aimed at replacing light microscopy with inexpensive fluorescence microscopy. According to previous studies, fluorescence microscopy is up to 10% more sensitive than conventional light microscopy (WHO/FIND). In this evaluation, a common fluorochrome stain, Acridine Orange, is being used to detect trypanosomes using the new Primostar iLED fluorescence microscope that has recently been developed by Zeiss and FIND. The evaluation is being conducted by 4 laboratories, in Uganda (NALIRRI) and in Kinshasa, DRC (INRB). They are comparing the effectiveness of trypanosome detection using the fluorescence microscope with conventional light microscopy.

Moreover, FIND is working with partners to develop trypanosome-specific fluorescent probes such as nanobodies, developed by VIB, Belgium, and aptamers, developed by the University of Darmstadt. Different blood preparations will be used to determine the sensitivity of the two, and the best probe selected for further evaluation using the iLED fluorescence microscope.

Additionally, different methods of initial sample preparation and concentration will be evaluated using membrane filters and magnetic separation to capture trypanosomes. The membrane-based filtration project is being performed in collaboration with Makere University and magnetic separation is being conducted by the researchers from VIB, Belgium.

Serological methods

Diagnosis of HAT depends on microscopic demonstration of trypanosomes in blood, CSF or lymph node aspirates. For passive case finding, parasitological examination is only carried out on individuals in at-risk populations who demonstrate anti-trypanosome antibodies with a

screening test. The card agglutination test for trypanosomiasis (CATT) is the primary screening tool used by control programs in areas where *T.b. gambiense* is endemic. No similar test exists for *T.b. rhodesiense*.

The specificity of the CATT test is good, but in populations undergoing screening, where the prevalence of disease is usually below 5%, a large number of positive results are false-positive, meaning that seropositive suspects must be confirmed using other tests prior to treatment. The activities detailed below focus on determination of the feasibility of replacing the CATT test with a simpler, more sensitive and specific serological method.

FIND is working with partners to develop new sensitive and specific antibody detection tests. In order to identify the most promising diagnostic candidates, a panel of 32 different antigens was screened using a collection of well-defined sera from patients infected with *T.b. gambiense* and *T.b. rhodesiense*. The collection of HAT sera consisted of 10 *T.b. rhodesiense* and 40 *T.b. gambiense*. Negative controls included 10 and 50 serum samples from European and African origin respectively. The study was initiated in May 2007 and carried out by Microcoat, Germany.

The screening led to the selection of 14 antigens, 3 of the top 5 of which belonged to invariant surface glycoproteins (ISGs). In parallel, an antigen detection test is being developed.

Molecular methods of diagnosis

Detection of trypanosome DNA in patient blood or other biological materials could substitute for parasitologic examination, with theoretically similar specificity and higher sensitivity. Loop-mediated isothermal amplification (LAMP) of DNA is an amplification method that works in real-time and gives a readout that is visible with the naked eye. It is a promising technique due to its high sensitivity and specificity, and requires only isothermal conditions, meaning that it can be done with minimal equipment and, more importantly, does not require an expensive instrument.

The Universities of Murdoch (Australia) and Obihiro (Japan) have completed feasibility studies on LAMP. Each of them developed primers for detecting *T.b. gambiense* and *T.b. rhodesiense*. Recently, both Universities conducted a LAMP evaluation study. Obihiro University completed the LAMP evaluation, but Murdoch University experienced delays due to staff movement and closure of the lab for renovations, and have only submitted data on RIME LAMP. However, the data already submitted has enabled us to make comparisons, and has increased our confidence in selection of the RIME sequences as a target for test development, since it has demonstrated the highest sensitivity and specificity, when compared with other targets.

Malaria Programme

Projects in this disease portfolio aim to establish standard protocols and methods to evaluate commercially available rapid diagnostic tests (RDTs), along with a network of laboratories and reference materials for testing RDTs. Devices for monitoring the quality and performance of RDTs in the field (positive control wells) are also being developed. Work on development of new point of care diagnostics for malaria is underway, along with research on RDT use to develop a business plan for improvements in quality and accessibility of RDTs.

Reference materials and RDTs evaluation

Well-characterized specimens are needed to serve the evaluation of lateral flow assays and also to support the development of new diagnostic tools. In this project, a malaria specimen bank is being established. The bank will support the development and evaluation of malaria diagnostics, limit the need for field trials, and facilitate quality control. FIND, WHO/WPRO, WHO/TDR, and other partners are working with experienced malaria diagnostic collaborating centers in Latin America, Africa, and Asia to develop materials for the specimen bank. The global specimen bank and product testing sites initially include CDC, but may be expanded in the future.

The collection and preparation of samples according to the standard protocols has been completed in the Philippines, Cambodia, and Nigeria, and more than 50% of the target number of samples prepared in Tanzania and Central African Republic. Contracts for sample preparation have been made with institutions in Madagascar, Kenya, Peru and Myanmar, and all three institutions start collections by mid-November 2007. Characterization of collected samples is underway at US CDC, the Hospital for Tropical disease, UK, and the Army Malaria Institute, Australia. Collection of the negative challenge panel is approximately 50% completed, through contracts with US CDC and Research Institute for Tropical Disease, the Philippines, and by direct commercial procurement. Notification to manufacturers of the first round of product testing was undertaken by the WHO in September 2007 with a deadline for expression of interest at the end of October. It is anticipated that the first round of product testing will commence late in the first quarter of 2008.

Positive control wells

The aim of this activity is to increase the quality of products in use, and to increase the users' confidence in test results. At present, field users have no method of ensuring that RDTs that they are using are functioning properly, or whether they might have been degraded by exposure to heat or humidity. RDTs contain a "positive control" band, but this is composed only of antibodies that bind the conjugated detection antibody, and are present in high concentration. As such, they do not address the capacity of a test to detect malaria antigens, and are not engineered to turn negative with moderate amounts of test degradation.

Positive control wells (PCWs) containing recombinant malaria parasite antigens have been proposed as a way to allow field-testing of RDTs for performance. The aim of this project is to produce PCWs that could be packaged with RDTs, maintained in the same conditions, and reconstituted with water for initial or retesting of RDTs.

For health care workers, the PCWs must be easy to use and stable across the variables of time, temperature, and humidity. The amount of antigen planned for each PCW is intended to mimic

that available in a human blood sample with a low-level of parasitemia such as would result in a weakly positive band in a functioning RDT. Failure of the RDT test line to appear would indicate that the RDT has lost the required sensitivity to detect malaria parasites and that it is no longer reliable.

FIND is working with three partners in the development of the PCWs:

1. National Bioproducts Institute (NBI) in South Africa for the feasibility phase of the project
2. ReaMetrix in India, the PCW manufacturer, and
3. Hospital of Tropical Diseases in London through the laboratory of Peter Chiodini for quantitative testing of PCWs during and after development

Field evaluation of existing RDTs

Currently, more than 50 malaria RDTs are available on the market, and with highly variable performance. WHO and FIND are evaluating currently available assays in controlled laboratory studies using reference materials. The objective of this activity is to evaluate field performance and utility of those malaria RDTs that show good sensitivity and temperature stability in the laboratory environment. The testing program will produce high-quality comparative data on RDT performance in the field as well as address specific questions related to RDT implementation, allowing those responsible for procuring RDTs for national malaria control programs to determine whether the tests meet customer requirements for field use, indicating whether technical improvements are required.

The project is currently undertaking a twelve-month field assessment of RDT job-aids and training in Zambia, to establish evidence of safety and effectiveness using these tools in an African village health worker context. The study is supported predominantly by FIND, and additionally by WHO, with the Malaria Consortium contracted to coordinate field work. The implementation phase is planned to commence before the end of November 2007, in collaboration with the Zambia MoH. The study concentrates on blood safety and test accuracy, and will provide a much-needed evidence base for wide-scale RDT implementation at village level in sub-Saharan Africa.

Loop-mediated isothermal amplification (LAMP) assay for malaria

LAMP has been developed for a relatively wide number of pathogens of all classes, and there is one publication of a *falciparum* malaria application. Development of an optimized product, however, will require a more considered understanding of optimal target sequences, minimization of sample handling steps, and optimization of reagents to take into consideration manufacturing issues. In April 2007, a research agreement was reached with HTD under which Colin Sutherland and colleagues will identify targets for *Plasmodium* genus and *P. falciparum*, design primers, optimize sample processing, and validate the text with patient samples. With regard to manufacture, Eiken Chemical Co. has negotiated first right of refusal on the manufacture of all LAMP assays developed by FIND, and royalty-free access for FIND to the necessary intellectual property for the public sector in developing countries has been recited.

Technical Improvement of RDTs

Many currently available RDTs have reasonable sensitivity in patients with parasite burdens of over 100-200 parasites/µl, but with lower levels of parasitemia their sensitivity decreases. Other drawbacks to current tests, particularly those detecting HRP2, include persistence of the target

antigen, and restricted reactivity of capture or detection reagents due to geographic variability in target antigen epitopes. Lastly, and perhaps most importantly, many of the currently available tests are not stable at temperatures higher than 25-30 degrees C. Thermo-instability is a critical issue leading to variable performance in field settings. To meet the need for the development of more robust RDTs, FIND is working with the Royal Dutch Tropical Institute (KIT) to identify novel antigens that can be used for test development, and to research the potential for improving the stability of the various separate test components and RDT devices as a whole. Additionally, FIND is working with the Queensland Institute of Medical Research to further determine the range of sequence variability in particular Histidine Rich Protein II (HRP2) and to propose alternative similar or duplicate targets to decrease the diagnostic impact of this variability.

Business solutions to improve quality and access to RDTs

The past two years have seen a massive increase in procurement of RDTs, particularly for the public healthcare sector, through funding that has become available through mechanisms including The Global Fund and the President's Malaria Initiative. While some of the technical challenges facing the development of an optimal RDT have been identified, such as the need to improve thermostability and sensitivity, additional information on the logistic and financial obstacles to uptake and use of RDTs is also needed to improve access to RDTs. For example, data on the actual delays and storage and shipping conditions faced by RDTs in the supply chain as they move from the factory to the end-user could help refine technical specifications regarding thermostability and packaging. This project will be carried out in collaboration with partners to examine: i) present use and uptake of RDTs; (ii) identify bottlenecks related to the scaling up of the production of high-quality RDTs; (iii) link an understanding of the market for RDTs to concurrent work being carried out to develop technical solutions to improving RDT performance; and iv) develop a comprehensive strategic/business plan for which addresses both the supply side issues of RDTs as well (development and production) as the demand side (uptake and use). The data required for this study requires research at both global and country levels. During the current reporting period, a scope of work has been developed, and potential partners, including the Malaria Consortium, identified to carry out the field work.

Progress in achieving a Global Access strategy

The activities of this project will help improve access to high-quality RDTs in several ways. First, product testing of available RDTs will help guide procurement of tests of assured quality by national malaria control programs and other partners. The need for this type of guidance has been expressed by procurement agents, technical agencies, and donors such as PMI and the World Bank. Secondly, the establishment of an independent project by FIND to create positive control wells will support access to and the proper use of RDTs by providing a field-based reference for external quality control. Throughout all of the projects, FIND is actively engaged with the WHO, including TDR, GMP, WPRO, AFRO; technical partners active in the field, such as Malaria Consortium; and Ministries of Health. Lastly, FIND has established ongoing outreach and communication efforts through its website and newsletter which keeps the larger international public health community informed of progress in FIND's malaria program and the other areas that FIND is working in.

Fund Raising Activities

2007 was an active year for fund raising activities, supported most ably by Ms Susan Dykes as consultant. The UK, Ireland and Canadian Governments were the main focus. In Ireland, Vinand Nantulya made a presentation to the Foreign Affairs Committee in March, following a previous visit when he briefed Irish MPs and Senators. In Canada, he held a series of meetings with MPs and policy makers at CIDA. In the UK, he met officials at DfID. Following a preliminary visit to the Wellcome Trust, Richard Seabrook and Glen Wells made a visit to FIND, in Geneva, to establish areas of collaboration.

FIND at the biennial conference on African Trypanosomiasis, Luanda, Angola

In a five-day conference focused on recent advances in tsetse control strategies, epidemiology of the disease in both humans and animals, development of drugs, and socio-economic impact FIND was a major participant sponsoring a full symposium on renewed efforts in the development of diagnostics for human African trypanosomiasis. During the conference, FIND and the WHO jointly hosted a symposium entitled *Partnering to develop diagnostic tests for human African trypanosomiasis*, which covered recent trends in the development of diagnostics for sleeping sickness.

FIND attends a donors' conference on African trypanosomiasis, Addis Ababa, Ethiopia

The Head of FIND's human African trypanosomiasis (HAT) Diagnostics Programme, Dr. Joseph Ndung'u, attended a special donors' conference dedicated to the Pan African Tsetse and Trypanosomiasis Eradication Campaign (PATTEC) on 2 February 2007, at the United Nations Conference Centre in Addis Ababa, Ethiopia. Special guests included the Ethiopian Prime Minister, Meles Zenawi, and Minister of Agriculture and Rural Development, Addisu Legesse; African Development Bank (ADB) President Donald Kaberuka and Vice-President O Kane (Ousmane); and the Chairperson of the African Union (AU) Commission, Professor Alpha Oumar Konare.

FIND joins European Diagnostics Manufacturers Association

Reinforcing its objective to promote the development of new and affordable tools that are urgently needed to fight poverty-related diseases, FIND became in January 2007 a member of the European Diagnostic Manufacturers Association (EDMA), the trade association representing the In Vitro Diagnostic (IVD) companies active in Europe.

FIND responds to the request from the Kingdom of Lesotho

Owing to the sudden rise of extensively drug-resistant tuberculosis (XDR-TB) and the call of the World Health Organization (WHO) for a rapid response to this far-reaching crisis, FIND, together with several of its partners signed a Memorandum of Understanding with the Ministry of Health of the Kingdom of Lesotho, in which they agreed to collaborate in strengthening the laboratory services in Lesotho in preparation of the introduction of rapid culture, drug susceptibility testing and species identification systems.

FIND and Columbia University agree to collaborate on the Millennium Villages Project of the Earth Institute

FIND signed a Memorandum of Understanding with The Earth Institute at Columbia University in New York, to introduce, as part of a research project, new tools for diagnosis of tuberculosis (TB) in low-resource settings identified by the Millennium Villages project. The MOU was signed jointly by Giorgio Roscigno and Earth Institute Director Jeffrey Sachs during a ceremony held at Columbia University.

Human Resources

2007 saw FIND bolster its human resources capacity to a total of 23 full time employees in addition to 7 consultants in Geneva. FIND's India office was opened with 2 full time staff and 1 consultant.

FIND Board of Directors, Management and Staff

As at 31 December 2007

Board of Directors

Dr. Gerald Moeller (Chairman of the Board)
Dr. Peter Small (Secretary), Senior Program Officer, Bill and Melinda Gates Foundation
Dr. Bernard Mach (Member)
Dr. Callisto Modavo (Member)

FIND Team

Giorgio Roscigno: Chief Executive Officer

Eric Adam: Project Manager and Regulatory Affairs
Heidi Albert: Senior Scientist, Head of Laboratory Research
Audrey Albertini: Scientific Assistant for Malaria Diagnostics
Sylvain Biéler: Project Manager
Catharina Boehme: Medical Officer
Nora Champouillon: Logistics Officer
Louisa Chaubert: Accounting Manager
Diana Choa: Personal Assistant to the CEO
Herbert Clemens: Chief Financial Officer
Jacques Debayle: Liaison Office Manager, FIND (India)
Beatrice Gordis: Communications Officer
Julian Gordon*: Medical Diagnostic Technologies & IP
Heather Alexander Konopka*: Health Scientist
Evan Lee: Senior Medical Officer
Ralf Linke*: Quality Manager, FIND (India)
Gerd Michel: Senior Technology Officer
Pamela Nabeta: Associate Medical Officer
Vinand Nantulya: Senior Policy and Implementation Officer
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
Shailaja Paramathma: Administrative Assistant, FIND (India)
Mark Perkins: Chief Scientific Officer
Laurence Perret: Human Resources Officer
Bärbel Porstmann: Head of Project Management & Regulatory Affairs
Magdalena Radwanska: Scientific Officer, HAT Diagnostics Programme
Ranald Sutherland*: Technology and Business Development
Jewel Thomas: Communications and Advocacy Coordinator
Alessandra Varga*: Events and Image Development
Julie Vercruysse: TB Scientific Team Administrator
Balasangameshwara Vollepore*: Expert, TB Laboratory Support
Hanna Yirga: HAT Scientific Team Administrator

* Consultants

Foundation for Innovative New Diagnostics (FIND), *Geneva*

Financial Statements for the Year ended December 31, 2007 and Auditors' Report

Deloitte.

Deloitte SA
20, Route de Pré-Bois
Case Postale 1808
CH-1215 Genève 15
Tél: +41 (0) 22 747 70 00
Fax: +41 (0) 22 747 70 70
www.deloitte.ch

REPORT OF THE STATUTORY AUDITORS

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

As statutory auditors, we have audited the accounting records and the financial statements (balance sheet, income statement and notes) of the Foundation for Innovative New Diagnostics (FIND) for the year ended December 31, 2007.

These financial statements are the responsibility of the Board of the Foundation. Our responsibility is to express an opinion on these financial statements based on our audit. We confirm that we meet the legal requirements concerning professional qualification and independence.

Our audit was conducted in accordance with Swiss Auditing Standards and with the International Standards on Auditing (ISA), which require that an audit be planned and performed to obtain reasonable assurance about whether the financial statements are free from material misstatement. We have examined on a test basis evidence supporting the amounts and disclosures in the financial statements. We have also assessed the accounting principles used, significant estimates made and the overall financial statement presentation. We believe that our audit provides a reasonable basis for our opinion.

In our opinion, the accounting records and financial statements comply with Swiss law and the By-Laws of the Foundation.

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

Deloitte SA

Peter Quigley
Auditor in charge

Michael Salama

July 14, 2008

Attached : Financial Statements (Balance sheet, statement of income, cash flow statements and notes)

FOUNDATION FOR INNOVATIVE NEW DIAGNOSTICS (FIND)

Geneva, Switzerland

BALANCE SHEET AS AT 31 DECEMBER 2007

(all amounts in US dollars)

	2007	2006
ASSETS		
Current assets		
Cash on hand	2 730	3 797
UBS Current accounts	399 281	444 445
UBS Short-term Deposits	19 411 800	13 497 488
UBS Rental Guarantee Deposit	72 722	67 121
Accounts receivable	429 780	156 176
Prepayments	30 267	82 889
	20 346 580	14 251 916
Fixed assets		
Office furniture & fittings	40 706	49 808
Computers & printers	67 210	40 268
Electrical installations	16 605	25 706
Fax machine & telephones	3 661	5 639
	128 182	121 421
Patents	38 535	46 242
Total assets	20 513 297	14 419 579
LIABILITIES AND CAPITAL		
Current liabilities		
Accounts payable	1 022 199	1 204 357
Accrued expenses	169 862	144 814
Contributions received in advance	15 931 019	11 162 460
	17 123 080	12 511 631
Capital and reserves		
Capital	40 430	40 430
General reserve	3 349 787	1 867 518
Total liabilities and capital	20 513 297	14 419 579

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 2007

(all amounts in US dollars)

	2007	2006
INCOME		
Contributions income	18 392 263	11 152 692
Sundry income	572 608	270 883
Exchange gains	302 379	-
Total income	19 267 250	11 423 575
EXPENDITURE		
Analytical & Project Work		
Project activities	13 622 902	7 715 135
Partnership building	490 660	525 307
Promotion & external relationships	594 835	361 069
Strategic planning & operations	413 155	359 203
Regulatory activities	113 293	98 664
	15 234 845	9 059 378
Information & Communication		
Donor relations & communications	350 654	192 517
Publications production	84 197	69 811
Website	15 185	8 500
Communications consultants	46 431	-
	496 467	270 828
Governing & Advisory Bodies		
Advisory Committees	-	2 856
Foundation Board	37 744	27 098
	37 744	29 954
General Administration		
Staff costs and travel	791 564	544 758
IT expenses	205 903	93 482
Photocopies, stationery, printing & sundries	153 938	106 307
Rent of premises	334 198	248 129
Repairs & maintenance	116 226	29 803
Telecommunications	107 964	81 133
	1 709 793	1 103 612
Finance & Service Expenses		
Auditing & accounting	45 024	21 983
Bank charges	12 534	5 730
Exchange losses	-	34 191
Legal fees	71 186	98 887
Insurance	110 645	100 931
	239 389	261 722
Depreciation	66 743	51 126
Total expenses	17 784 981	10 776 620
Excess of income over expenditure for year	1 482 269	646 955
Surplus at 31 December 2006 brought forward	1 867 518	1 220 563
Surplus carried forward in General Reserve	3 349 787	1 867 518

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 2007

(all amounts in US dollars)

	2007	2006
Excess of income over expenditure for the year	1 482 269	646 955
Add back non-cash charge - depreciation	66 743	51 126
	1 549 012	698 081
Cash flows - operating activities		
Increase/(decrease) in contributions in advance	4 768 559	10 618 239
Increase/(decrease) in accounts payable	(182 158)	439 864
Increase/(decrease) in accrued expenses	25 048	97 518
(Increase)/decrease in accounts receivable	(273 604)	(117 125)
(Increase)/decrease in prepayments	52 622	(82 889)
	4 390 467	10 955 607
Cash flows - investing activities		
Additional office furniture & fittings	(6 808)	(35 248)
Additional computers & printers	(58 989)	(42 471)
New electrical installations	-	(10 640)
(Increase)/decrease in rental guarantee account	(5 601)	(22 682)
	(71 398)	(111 041)
Net increase in cash and cash equivalents for year	$ 5 868 081	11 542 647
Cash and cash equivalents at start of year		
Cash on hand	3 797	426
Current accounts & short-term deposits	13 941 933	2 402 657
	13 945 730	2 403 083
Cash and cash equivalents at end of year		
Cash on hand	2 730	3 797
Current accounts & short-term deposits	19 811 081	13 941 933
	19 813 811	13 945 730
Net increase in cash and cash equivalents for year	$ 5 868 081	11 542 647

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 2007

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 (six 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 2007 the rate of exchange used for the Swiss franc, the main foreign currency for 2007, was USD/CHF = 1.13 *(2006 – 1.22)*. Exchange gains and losses are included in the determination of net income.

2.5 Recognition of revenue Contributions received are recorded according to the grant period indicated in donor agreements, with amounts received relating to periods extending beyond balance sheet date recorded as contributions received in advance. Donor agreements in effect at 31 December 2007 provide for a total of USD 81.4 million to be paid to FIND between January 2008 and August 2012.

2.6 Accounts payable and accrued expenses With the exception of emoluments payable to staff, which, with effect from 2007, are accounted for when paid, accounts payable and accrued expenses represent expenditures chargeable in the 2007 financial year, for which invoices were not received for payment before year-end. Emoluments payable to staff were previously paid on an accruals basis. 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 Project expenditure Project expenditure during 2007 under contracts signed up to 31 December 2007 totalled USD 8,580,367 *(2006 – USD 5,492,942)*. Commitments at 31 December 2007 for future payments under those contracts total USD 8,377,847 *(2006 – USD 5,600,986)*.

3. Fixed assets and intellectual property

3.1 Fixed assets as at 31 December 2007 were as follows:

		2007	2006
Cost price			
Office furniture & fittings		83,331	76,523
Computers & printers		155,132	96,143
Electrical installations		45,509	45,509
Fax machine & telephones		9,891	9,891
		293,863	228,066
Less: Accumulated depreciation		165,681	106,645
Net book value	USD	128,182	121,421

Fire insurance cover as at 31 December 2007 was USD 116,814 *(2006 – USD 108,200)*.

3.2 Intellectual property as at 31 December 2007 was as follows:

		2007	2006
Cost price			
Patents		53,949	53,949
		53,949	53,949
Less: Accumulated depreciation		15,414	7,707
Net book value	USD	38,535	46,242

4. Pension Fund liabilities

No amounts were due to the pension fund at 31 December 2007 *(2006 – nil)*.

5. Rent commitments

At 31 December 2007 FIND had future rent commitments totalling USD 518,510 up to 31 May 2009 *(2006 – USD 712,670)*.

6. 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.

7. Events subsequent to 31 December 2007

There were no events occurring subsequent to 31 December 2007 which could have a material impact on the understanding of these financial statements.

71, avenue Louis Casaï • PO Box 93 • CH 1216 Cointrin – Geneva
Tel. + 41 (22) 710 05 90 • Fax + 41 (22) 710 05 99 • info@finddiagnostics.org
www.finddiagnostics.org