FIND
FOUNDATION FOR INNOVATIVE NEW DIAGNOSTICS

Annual Report 2005

© LHI/Sammy 9 and Msizi 4, TB patients in Germiston, RSA/2003/Gary Hampton

© LHI/Slides of sputum being prepared for staining, Uganda/2003/Gary Hampton

FIND Annual Report 2005

FIND's mission is to improve global health by developing safe, affordable and easy-to-use diagnostics to fight diseases of the poor at all levels of the health system

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

2005 was an exciting and transformative year for FIND. We consolidated and systematised our research and development for new TB diagnostics and expanded our portfolio to include human African trypanosomiasis (HAT), also known as sleeping sickness. Following a rigorous scouting and technology selection in 2004, the year 2005 marked some major achievements in the way we operate. FIND has focused on two main technological platforms for the development of diagnostics: nucleic acid amplification and immunodetection.

During 2004-05 it became clear that our strategic approach could be improved by considering more closely diagnostic needs as dictated by the patient rather than by disease epidemiology. This policy would not just take into consideration the levels of the health system where these technologies are used - it would also prioritise testing at point of care.

As part of the developments taking place in point of care active tuberculosis (TB) case detection, FIND formalised its working relations with Eiken, a Japan-based manufacturer of clinical diagnostics, with respectto LAMP, one of the most interesting methods for nucleic acid amplification, and one that may eventually permit public health systems to introduce this powerful technology at point of care. FIND is advancing this technology into feasibility studies in selected evaluation sites in Tanzania, Peru and Bangladesh.

During the year, FIND also continued to work on an important urine lipoarbinomannan (LAM) antigen detection study in Tanzania in collaboration with Chemogen and the University of Munich. With Proteome Systems, we worked to screen for new antigens through proteomics, a unique technology to screen, identify and validate proteins secreted or shed in the blood or sputum of TB patients.

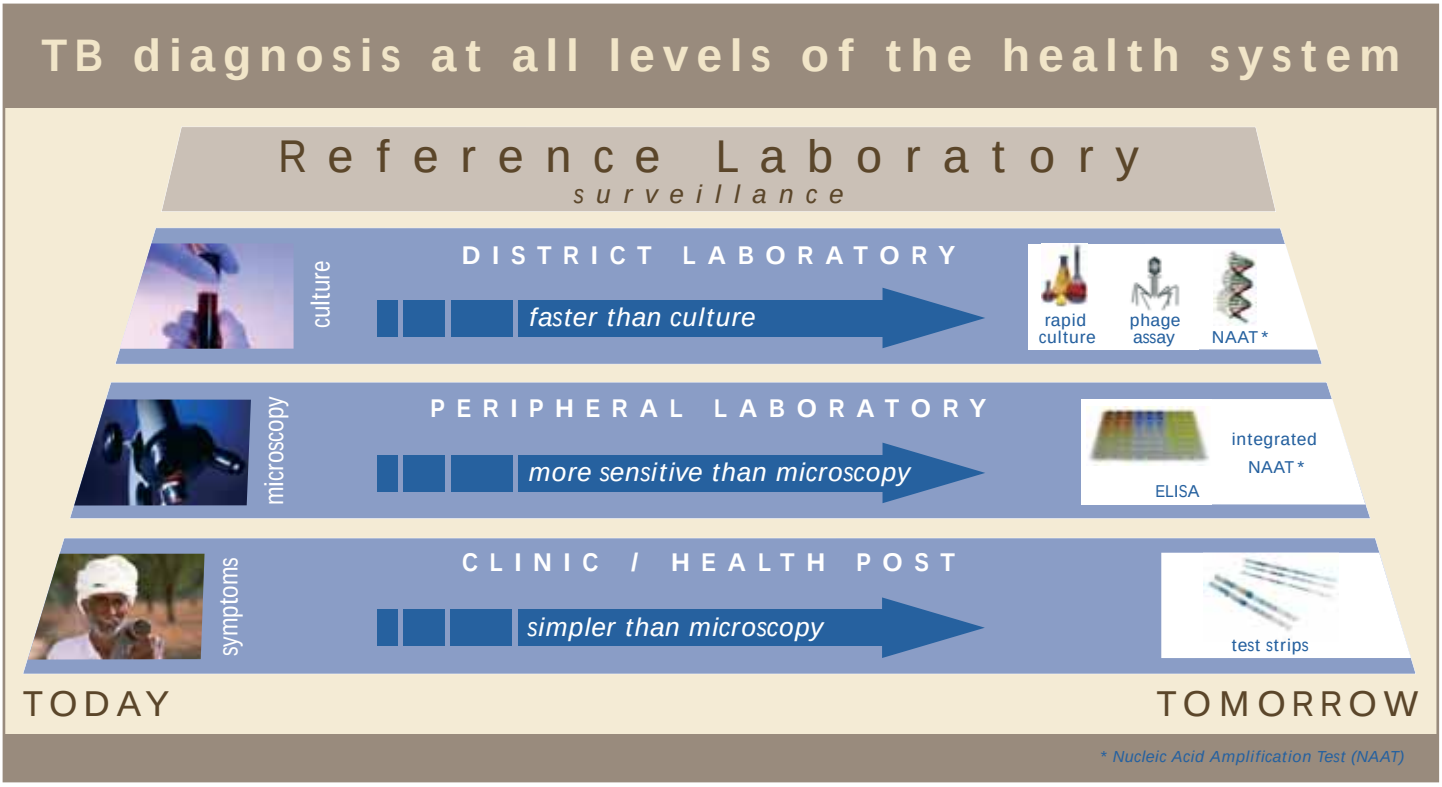
During 2004-05 it became clear that our strategic approach could be improved by considering more closely diagnostic needs as dictated by the patient rather than by disease epidemiology

To address the challenges of multidrug-resistant TB, FIND put together a demonstration study plan to work with Becton, Dickinson and Company's MGIT™ (mycobacteria growth indicator tube) liquid culture and drug susceptibility testing.

Furthermore, through collaboration with Biotec Laboratories, the developers of the FASTPlaque-Response™ *test, FIND also aims to detect resistance to the antibiotic rifampicin, one of the more important and successful of the TB drugs used in therapy, directly from the sputum of patients by using mycobacteriophage techniques to reflect the presence of viable TB bacilli in a sample.*

By the end of this year, FIND signed legal agreements with four diagnostic companies: with Biotec Laboratories for detection, in two days, of mycobacterium tuberculosis (MTB) and rifampicin-resistance from sputum based on phage replication in MTB; with Salubris Inc for the development of new culture systems based on colorimetric solid media; with Becton, Dickinson and Company (BD) for TB culture and drug susceptibility testing using liquid media with fluorescent indicator of growth; and with Eiken Chemical for development of a point of care nucleic acid amplification test based on loop-mediated isothermal amplification (LAMP). What captivated FIND's interest was the great potential LAMP technology promised across a wide range of infectious disease targets, even at the health post level, for example, where conditions are often less than conducive to rapid and unproblematic diagnosis.

In 2005, the Board approved the addition of HAT to FIND's disease portfolio. Current serological and parasitological



tests used in the field for diagnosis of HAT have low specificity and sensitivity and are cumbersome to use. It was agreed that representatives of FIND, WHO, pharmaceutical companies and national control programs would meet in February 2006 to launch this new initiative.

There were several exciting new additions to FIND's staff this year, which you can read about later in this report (see page 20).

Activities carried out during 2005 resulted in an excess of income over expenditure of a little over USD 800,000. All expenditure incurred was in line with budget forecasts and the excess resulted mainly from the application of standards prescribed for the recognition of revenue. The External Auditors' Report is found on page 24, followed by the Audited Financial Statements on pages 25 to 29. The Financial Statements consist of the Balance Sheet as at 31 December 2005, the Income and Expenditure Account for 2005, the Cash Flow Statement for 2005, and Notes to the Financial Statements.

Although FIND has made significant strides so far, we are keenly aware that real success will be measured by our ability, and that of our partners, to bring into use simple, accurate and affordable point of care diagnostics to improve the lives of patients everywhere. These diagnostics should also make a positive difference in the workload of health care workers throughout the developing world.

We look forward to working with you to make this happen and thank you for your interest and support.

Dr Gerald Moeller, Chair
Dr Giorgio Roscigno, CEO

More about FIND

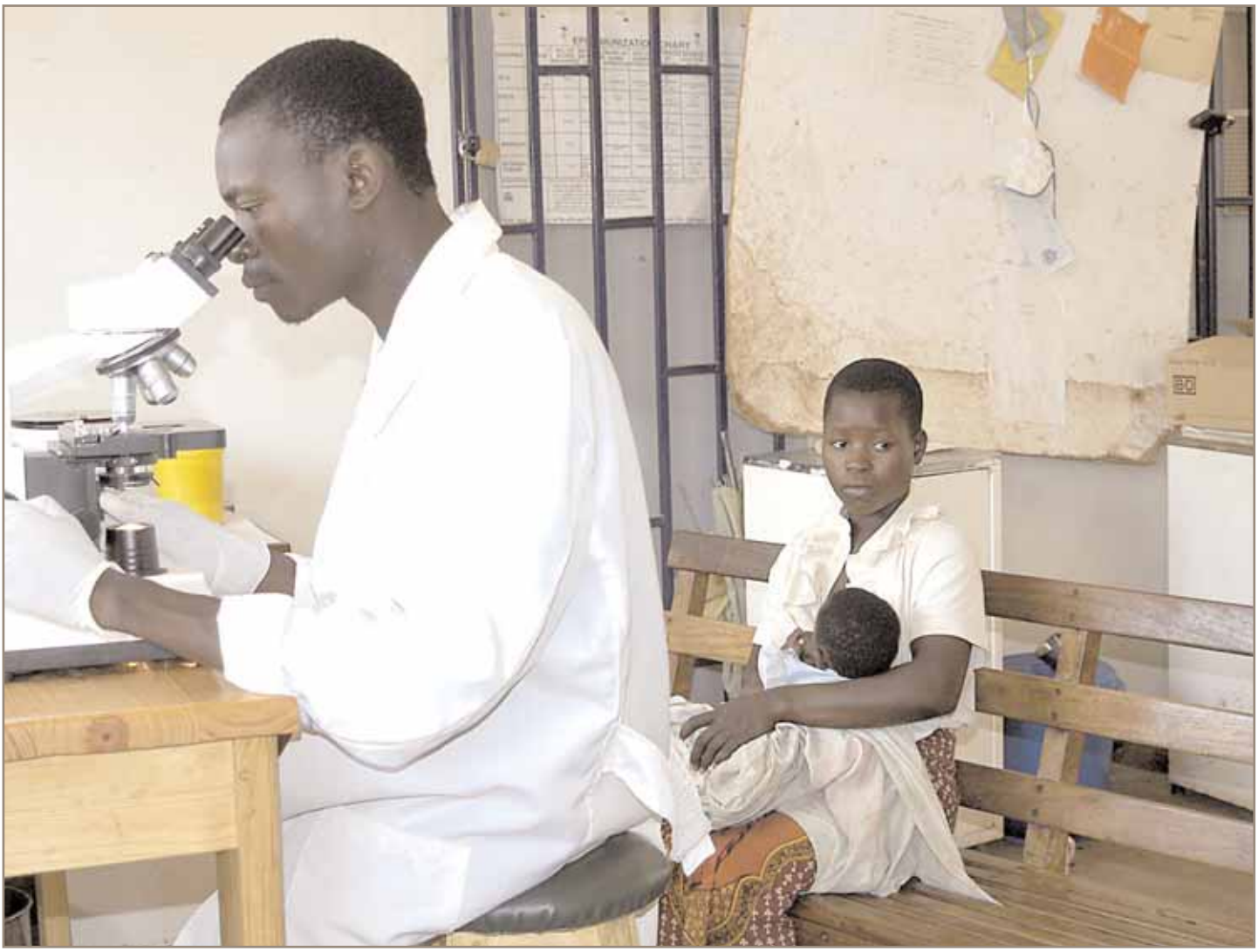
FIND's mission

The Fondation for Innovative New Diagnostics was launched at the World Health Assembly in May 2003 as a public private partnership based in Geneva, Switzerland. FIND aims to identify and develop diagnostic technologies that are robust, efficient, simple and affordable. This mission is based on three beliefs: 1) good health is essential for enabling under-privileged people to end the chronic cycle of poverty; 2) under-privileged people will only be able to achieve good health if the overall health system is strong and accessible; and 3) central to strengthening the health system, and thus impacting the epidemiology of poverty related diseases, is the development and deployment of easy to use, accurate and reliable diagnostic tools that can be accessed at all levels of the health system – including point of care.

FIND's project portfolio

The start-up funding for FIND, made available through a grant from the Bill and Melinda Gates Foundation, targeted the development and evaluation of improved tuberculosis diagnostic tests. Tuberculosis, which claims two million lives a year, is now compounded by coinfection with HIV/AIDS. Around 95% of new tuberculosis cases each year originate in the developing world, where diagnosis still relies on time-consuming and frequently inaccurate microscopy developed over a century ago.

At the end of 2005, FIND added to its disease portfolio a program to develop better point of care tests for diagnosing human African trypanosomiasis (HAT), or sleeping sickness, one of the



A young mother waits with her baby for lab results at the Ntcheu District Hospital, Malawi.

world's most neglected tropical diseases. Today, HAT remains a major public health problem in 36 African countries, with an estimated 50 million people at risk. Initial funding for this project also came from the Bill and Melinda Gates Foundation.

FIND hopes to expand its efforts to other diseases, such as malaria, as more funding becomes available. For continued development of the product portfolio, FIND will rely on new public and private funding.

Why FIND

FIND is a leading non-profit organisation dedicated to the development of new diagnostics for the developing world. There are two unique features to FIND's operations.

First, it is commonly accepted that for diagnostics to be affordable for the developing world, they must be "low tech". FIND believes that it is possible to provide high tech but also affordable solutions for low tech settings. A thorough evaluation of new technologies being developed, both in academic and in industrial laboratories throughout the world, has shown that this is possible. FIND is in the process of making use of "high tech" diagnostic technologies to generate robust, simple and highly affordable diagnostic tests which are compatible with field needs in the developing world.

Second, FIND has adopted a novel commercial model to motivate some of the very best biotechnology companies to innovate high tech diagnostics. Through this approach, partner companies assign all rights to FIND for use of their technologies in the public and the non-profit private sectors of high-endemic countries, while retaining rights on these new technologies for the more lucrative, for-profit private sector. This provides the companies with the incentive to generate profit within the private sector in the industrialised world, while committing to FIND free use of the same technology for the public and non-profit private sector in the developing world.

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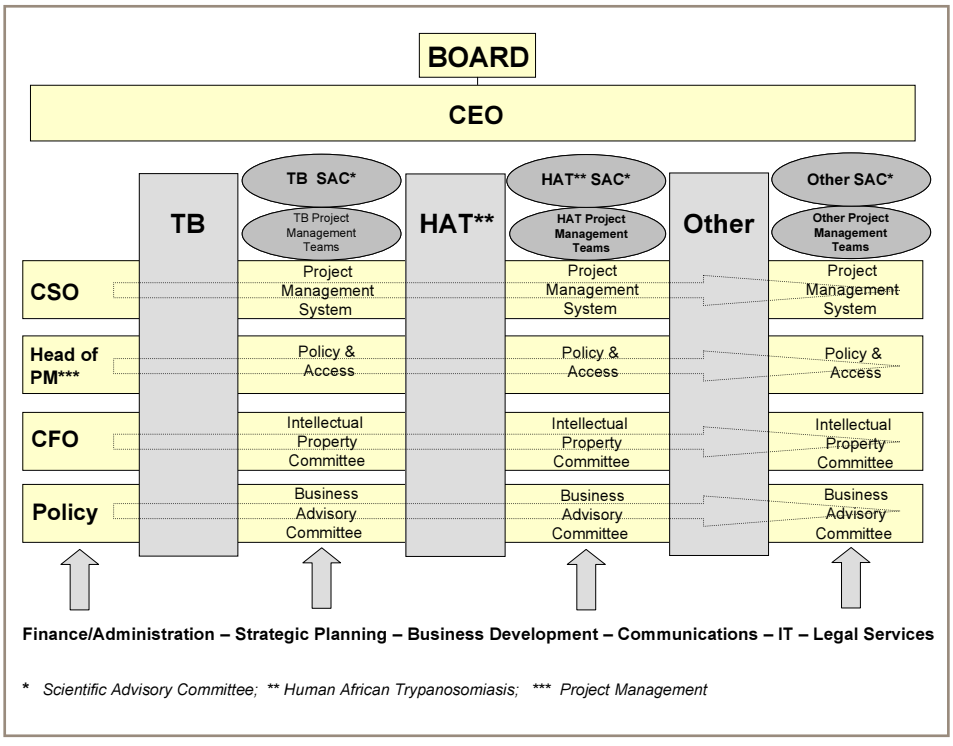
A TB patient in Guraghe, Ethiopia

To accomplish its goals, FIND focuses on the needs of the public sector while basing the operation of its projects on a business model, with practical targets and objectives, as well as accountability for every phase of development. Each disease program is managed as a separate business unit with an independent disease-specific scientific advisory committee (or SAC). All the disease programs are supported by project management systems, policy and access strategy, and a public health advisory committee. To ensure that the products meet the needs of patients and health care providers, FIND works closely with the World Health Organisation (WHO), the STOP TB Partnership, national control programs and civil society.



The FIND business model

© LHI/TB Patients taking medication, Ethiopia/2003/Gary Hampton

© LHI/TB Culture preparation, Peru/1997/Jad Davenport

The Case for Better Diagnostics

There is increasing concern by the global community that life-saving medicines be available to treat diseases in the developing world, in particular AIDS, tuberculosis and malaria. The UN Security Council passed a resolution in 2001 declaring the three diseases to be a global security risk and formed a global financing mechanism known as the Global Fund to Fight AIDS, Tuberculosis and Malaria whose mission is to mobilise resources to enable developing countries to deliver adequate treatment and care.

But focus on the delivery of medicines by itself is not sufficient. A huge challenge remains, namely, taking the right decision on who needs to be treated. The tools or tests available in the developing world for diagnosing these and other poverty related diseases are largely out-dated and ineffective, while newer tools already available in industrialised countries are either not affordable or are not designed for use in the developing world settings. The inability to properly diagnose diseases frustrates care providers, reduces patient's faith in the healthcare system, results in huge mistreatment, and wastes precious resources.

In tuberculosis for instance, the world spends US$ 1 billion on diagnosis globally, but the return on this investment is disappointing. The mainstay for TB diagnosis remains the cumbersome, 100-year old tool, the microscope. Diagnosis via microscopy usually takes up to 5 days as the patient has to provide multiple sputum samples for precise diagnosis. In Malawi, this process costs the patient up to 15 working days worth of wages. What is more, microscopy is insensitive, especially in areas where HIV is prevalent, and many patients are overlooked by false readings. Overall, fewer than 25% of the nearly 9 million new cases of TB each year are reported as having been detected by microscopy.

For malaria, misdiagnosis is also an enormous problem: 50-80% of the fever episodes treated on the basis of signs and symptoms for malaria are not confirmed in parasitologic testing. Simple, accurate, robust and affordable point of care tests are not available for most patients seen in community clinics. A number of rapid tests that can detect malaria antigens in a fingerprick blood sample have been developed over the past decade, but inadequate sensitivity, high cost, and instability at tropical temperatures continue to plague these tests, limiting their impact. One consequence of this lack of accurate local testing is an estimated 500 million treatments for malaria each year in people suffering from some other cause of fever.

For many of the other poverty related diseases, such as human African trypanosomiasis (sleeping sickness), for which there is no commercial market to drive any test development, confirmatory point of care tests are lacking altogether. For sleeping sickness, confirmation depends on microscopic detection of the parasites in blood, lymph glands or cerebrospinal fluid, which is very difficult in field conditions.

While repeat visits and multiple tests can compensate for inadequate diagnostics in industrialised countries, such redundancies are not available in resource-limited health systems. Thus, impoverished populations need diagnostics that are better, not worse, than those in industrialised countries. At the level of the individual, lack of accurate tests leads to delay in treatment, multiple clinic visits, and misdiagnosis, all of which result in direct health and financial costs that developing world patients and health systems can ill afford.





TB Product Portfolio Highligts – 2005

FIND quickly established a project portfolio that was driven by the diagnostic needs of patients and healthcare providers at the different levels of the health system, from district laboratory to peripheral laboratory down to the health post level where primary care.is sought

Evaluation of *FASTPlaque-Response™* test

FIND'S first corporate partnership agreement, signed May 2004 with Biotec Laboratories, Limited, UK, covered development of a 2-day test for rifampicin (RIF) resistance in *M. tuberculosis* using phage technology. Bacteriophage-based tests may be used for the detection of resistance to anti-tuberculosis drugs and for detection of mycobacteria in clinical specimens. When detecting resistance to rifampicin in TB cultures results may be obtained in 48 hours. Bacteriophage tests show high sensitivity for the detection of resistance to rifampicin.

The performance targets for the test included high sensitivity and specificity and the ability to detect resistance directly from sputum in smear-positive TB patients without need to first grow the TB bacilli in culture medium, a process that takes several weeks. Rifampicin resistance indicates a high chance of multidrug-resistant (MDR) TB, which is often fatal if incorrectly diagnosed and treated. Some 450,000 people are thought to develop MDR-TB, worldwide, each year.

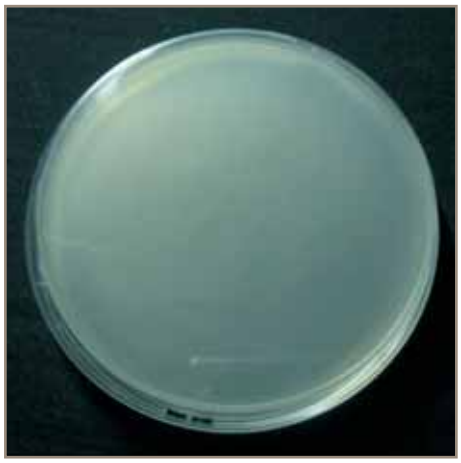
The principle of the test is based on the ability of mycobacteriophages (viruses that infect mycobacteria) to infect and replicate in live (and not in dead) TB bacilli. Phages are added to sputum after processing, and infect live TB bacilli that are present. A potent virucide is then introduced which destroys any remaining phage that is outside the TB bacilli. When the TB bacilli with internalised phage are incubated overnight on solid media along with rapidly growing sensor cells *(M. smegmatis)* that are also susceptible to phage, the replicating phage undergo lysis (or dissolution) with the TB bacilli and nearby sensor cells, creating visible plaques.

When added to the assay, rifampicin will inhibit the uptake and replication of phage in drug-sensitive strains of *M. tuberculosis*. Replication will continue unchecked in drug-resistant strains, thus allowing rapid (2 day) testing, directly from smear-positive sputum, of susceptibility to the most important anti-tuberculosis drug. Conventional susceptibility testing requires several weeks for isolation of bacilli from processed sputum, and several additional weeks for observation of growth in drug-containing and drug-free vials.

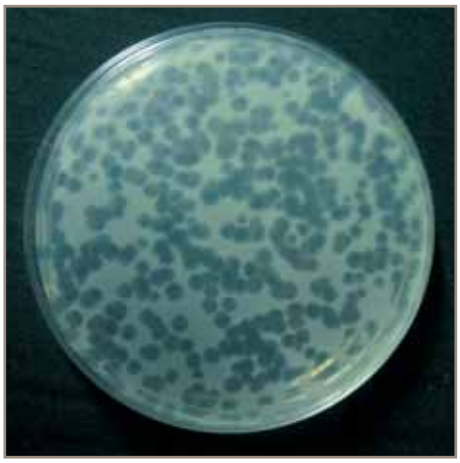
Five major TB projects were launched by FIND in 2005:

1. Evaluation of the *FASTPlaque-Response™* test, an assay for rifampicin resistance, in collaboration with Biotec Laboratories, UK
2. Feasibility study on loop-mediated isothermal amplification (LAMP) for molecular diagnosis of TB, in collaboration with Eiken Chemical Company, Japan
3. Demonstration study of the mycobacteria growth indicator tube (MGIT™), a liquid culture growth test for diagnosis and drug sensitivity testing, in collaboration with BD, USA
4. Feasibility study of urinary mycobacterial lipoarbinomannan (LAM) antigen detection, in collaboration with Chemogen Inc., USA
5. Search for new TB specific antigens for use in development of new assays, in collaboration with Proteome Systems, USA

A large comparative evaluation of the assay developed by FIND and Biotec *(FASTPlaque-Response™)* enrolled 1,500 patients in Lima, Peru, under the direction of investigators from the Tropical Medicine Institute at Cayetano Heredia University, funded by WHO/TDR (The Special Programme for Research and Training in Tropical Diseases) and monitored by FIND. Preliminary results were presented at the annual meeting of the International Union against Tuberculosis and Lung Disease (IUATLD) in 2005. The results showed that the test had high sensitivity and specificity for diagnosis of multidrug-resistant TB (MDR-TB). Interim analysis of results also showed a high contamination rate of the original formulation of the *FASTPlaque-Response™* test. A novel antibiotic cocktail was formulated which could be demonstrated not to interfere with phage infection or otherwise affect the test results. The test was modified by addition of the antibiotic formulation, and, with funding from FIND, several hundred additional patients were enrolled, with good control of contamination demonstrated.
These data will form an important part of the materials required for regulatory filing in order to register the assay in Europe and obtain CE Marking [1].



No phage replication



Phage replication

A multiwell plate format provides a simple and convenient method of screening TB isolates for resistance to rifampicin

Feasibility study on Loop-Mediated Isothermal Amplification (LAMP) for TB

FIND entered into collaboration with Eiken Chemical Co. Ltd., a Japan-based manufacturer of clinical diagnostics, to develop a rapid and simple test for the detection of active tuberculosis. The agreement was announced in July 2005 at the 40th Annual US-Japan Tuberculosis and Leprosy Research Conference, which took place in Seattle, Washington, USA.

As envisaged in the joint development agreement, the TB test will use the Loop-Mediated Isothermal Amplification (LAMP) method developed at Eiken and which is designed to detect DNA directly from clinical samples in less than two hours, and with minimal instrumentation. Molecular amplification methods, such as polymerase chain reaction (PCR), are proven technologies for the detection of TB but have not been widely used in remote settings because of the cost and complexity of existing systems.

The LAMP technology has the advantages of isothermal amplification at relatively high temperatures, high speed, and a visual readout based on turbidity and fluorescence. FIND selected this technology, to be used in numerous molecular amplification platforms, based in some measure on considerations of intellectual property and corporate commitment, but primarily because of the specific advantages of this method that make it particularly

[1] *Before you can sell a medical device or IVD within Europe, you must place a CE Mark (CE Marking) on your product. The CE Mark is not a quality certification nor is it intended for consumers. It is used by the European Competent Authorities (National Ministries of Health) as a way to quickly determine whether your product has met all of the requirements of the Medical Device Directive 93/42/EEC, In Vitro Diagnostic Directive 98/79/EC or the Active Implantable Medical Device Directive 90/385/EEC.*

Visual detection using LAMP technology

suitable for the development of a robust application useful in developing countries.

The joint development agreement which was signed in July 2005 between Eiken and FIND provides the critical support to speed up development and validation of the LAMP test through clinical trials in return for Eiken's commitment to offer this technology at an affordable price to the public and non-profit private health sectors in developing countries. The development plan calls for a first-generation product designed for use at the health system level where microscopy is currently in use, and a second-generation product that might be useable at more peripheral levels of the health system.

Preparatory work began later in the year for a series of experiments designed to test the robustness and analytic sensitivity of the core LAMP technology through a contracted laboratory at the University of Geneva. The speed of the reaction, the straightforward instrumentation and visual readout made LAMP a promising platform for the development of a simple and sensitive tool for molecular detection of TB in developing country settings. Since entering the agreement with FIND, Eiken has modified the technique and transformed it into a more user-friendly, convenient and robust kit format.

By the end of 2005, FIND developed protocols for the clinical trials to test the new simplified assay and secured agreements with local partners to begin clinical feasibility trials in January 2006 in Bangladesh, Peru and Tanzania. In the joint work plan, Eiken agreed to continue to further simplify the test based on the study results and to produce a manufacturable kit by January 2007. FIND will then conduct large-scale clinical evaluation and demonstration trials for the LAMP kit to assess how it can realistically work in developing country contexts.

Mycobacteria Growth Indicator Tube (MGIT™)

One of the tests that FIND is evaluating in collaboration with BD is the MGIT™ (Mycobacterium Growth Indicator Tube) culture system, which allows for the rapid growth and detection of *M. tuberculosis*. BD is providing the technology and FIND is assessing the utility and feasibility of its wide-scale use in developing countries. The agreement between FIND and BD was signed at the end of 2004.

MGIT allows both more sensitive and more rapid detection of *M. tuberculosis* than the standard solid media used for TB culture. The average time to detection is 10-14 days with liquid culture like MGIT as opposed to three to four weeks with traditional solid culture. This is potentially an exciting development for the detection of HIV-infected patients with pulmonary TB who are much more likely to be missed by sputum microscopy as they secrete low numbers of mycobacteria in sputum compared to HIV-negative patients. In high TB/HIV-burden countries, this technology could represent significant progress towards improved management of coinfected patients.

The liquid media is held in a small plastic tube with a silicone plug at the bottom containing chemicals that emit fluorescent light when the bacteria grow and use up oxygen. Inoculation of the media does not require a needle, and the liquid media has no radioactive elements, making it safer and easier to use than its predecessor, the BACTEC™ 460 system.

At present, there is an automated reader available called the BACTEC™ MGIT™ 960 system that holds up to 960 tubes and provides for continuous monitoring of bacterial growth. This technology is widely used in Europe, the US and Japan and is a state-of-the-art culture system. A manual alternative has been developed that may be better adapted to some developing world settings and to laboratories performing smaller numbers of cultures.

The purpose of FIND's initial demonstration projects for assessing the MGIT culture is to demonstrate the feasibility and impact of MGIT technology in two specific areas where new diagnostic TB tests are badly needed, namely, in improved case finding among HIV-infected persons with TB and expanded drug susceptibility testing (DST) for persons at risk of multidrug-resistant (MDR) TB. MGIT is more sensitive than traditional solid culture on LJ media and provides results much more quickly. Thus, access to and sustainable implementation of this technology in high-burden coun-

tries would represent significant progress towards improved TB management.

In areas where TB rates have increased greatly in association with the HIV epidemic, the most widely used TB diagnostic test, sputum smear-microscopy, is inadequate. This is because the large majority of HIV-associated TB cases are sputum smear-negative. In the absence of mycobacterial culture, the complicated and lengthy diagnostic algorithms used to diagnose smear-negative cases are insufficiently precise, and many patients die before the diagnosis of TB is made. Rapid culture methods, such as MGIT, provide the opportunity to quickly and accurately diagnose these cases and implement TB treatment, hence both decreasing HIV-associated TB morbidity and mortality and interrupting TB transmission.

In the initial MGIT demonstration projects for case-finding in TB/HIV, FIND is partnering with CREATE, the Consortium to Respond Effectively to the AIDS TB Epidemic. CREATE is a global research and implementation consortium that targets TB control in areas with severe HIV/AIDS epidemics. The purpose of this consortium is to organise, implement and evaluate novel strategies to reduce morbidity and mortality from TB in populations with high rates of HIV and TB coinfection. MGIT technology is being used for improved TB case detection in CREATE projects in Zambia, South Africa, and Brazil. FIND is also planning similar projects in Tanzania and Kenya, partnering with the US Centers for Disease Control and Prevention (CDC), the Program for Appropriate Technology in Health (PATH), and several academic institutions working in HIV/AIDS.

Above, a laboratory technician in Mbeya, Tanzania, scans MGIT™ tubes in a BACTEC™ 960 system

The ZAMSTAR or Zambia and South Africa tuberculosis and AIDS reduction study completed initial screening, using MGIT culture, of approximately 20,000 persons in 24 geographic communities. The project is now moving to evaluate MGIT culture case-finding among TB suspects in two sites in Zambia.



MGIT can also be used to diagnose multidrug-resistant tuberculosis. FIND, together with BD, is evaluating the tuberculosis drug susceptibility test, MGIT-DST, to determine the feasibility and impact of its wider use in disease-endemic settings. These demonstration projects of MGIT-DST in national TB control programs are presently being carried out in Nukus, Uzbekistan, in collaboration with MSF-Holland; in Samara Oblast, Russian Federation, in collaboration with the UK HPA Mycobacteriology Laboratory; and in Katmandu, Nepal, in collaboration with the German NGO GENET-UP. These projects have benefited from outside technical support from internationally known TB laboratory experts brought in by FIND. A fourth demonstration study is to begin in mid-2006 in Manila, Philippines, with the Tropical Disease Foundation. Dr. Thelma Tupasi, who is the current head of the Stop TB Working Group on MDR-TB, heads this project.

Preliminary data on MGIT performance from these projects will be compiled in late 2006 after detailed discussion by FIND's Public Health Advisory Committee and will be presented to the WHO Strategic and Technical Advisory Committee (STAG) for TB in 2007 with the aim of possible WHO endorsement.

Feasibility study on urinary LAM detection

In April 2005, FIND signed a letter of intent with Chemogen Inc, a startup biotechnology company in Portland, Maine, USA, to develop, evaluate, and launch a point of care test to detect TB antigens in urine in lateral flow or "dipstick" format. Chemogen had already developed a urinary enzyme-linked immunoassay (ELISA) for the detection of the mycobacterial antigen, lipoarbinomannan (LAM), as a basis for the detection of active TB. The "dipstick" is considered to be the ideal format for a point of care test for detecting TB in low-income, high-endemic areas.

The agreement covered an evaluation study of Chemogen's urine LAM-ELISA as a TB screening test in patients with symptoms of pulmonary tuberculosis. Development work on the "dipstick" assay format would start upon successful completion of the feasibility study.

In collaboration with the Department of Infectious Diseases & Tropical Medicine at the University of Munich (LMU), FIND conducted LAM-ELISA feasibility studies. During the past 10 years, LMU, with funding primarily from Walter Reed, has developed an excellent infrastructure for HIV research at the Mbeya Medical Research Program (MMRP) in Mbeya, Tanzania, and recently has developed capacity for high-quality TB studies.

In May 2005 FIND study began enrollment of approximately 700 patients with signs and symptoms consistent with pulmonary tuberculosis. In addition, 200 healthy controls were also enrolled to clarify whether mycobacteria colonizing the urogenital tract would cause false positive results. All patients received an extensive medical check-up, which included voluntary testing and counseling for HIV, sputum culture on both solid and liquid medium, and chest radiograph. Bacteriologically negative study subjects were followed for two months to ensure an accurate clinical diagnosis.

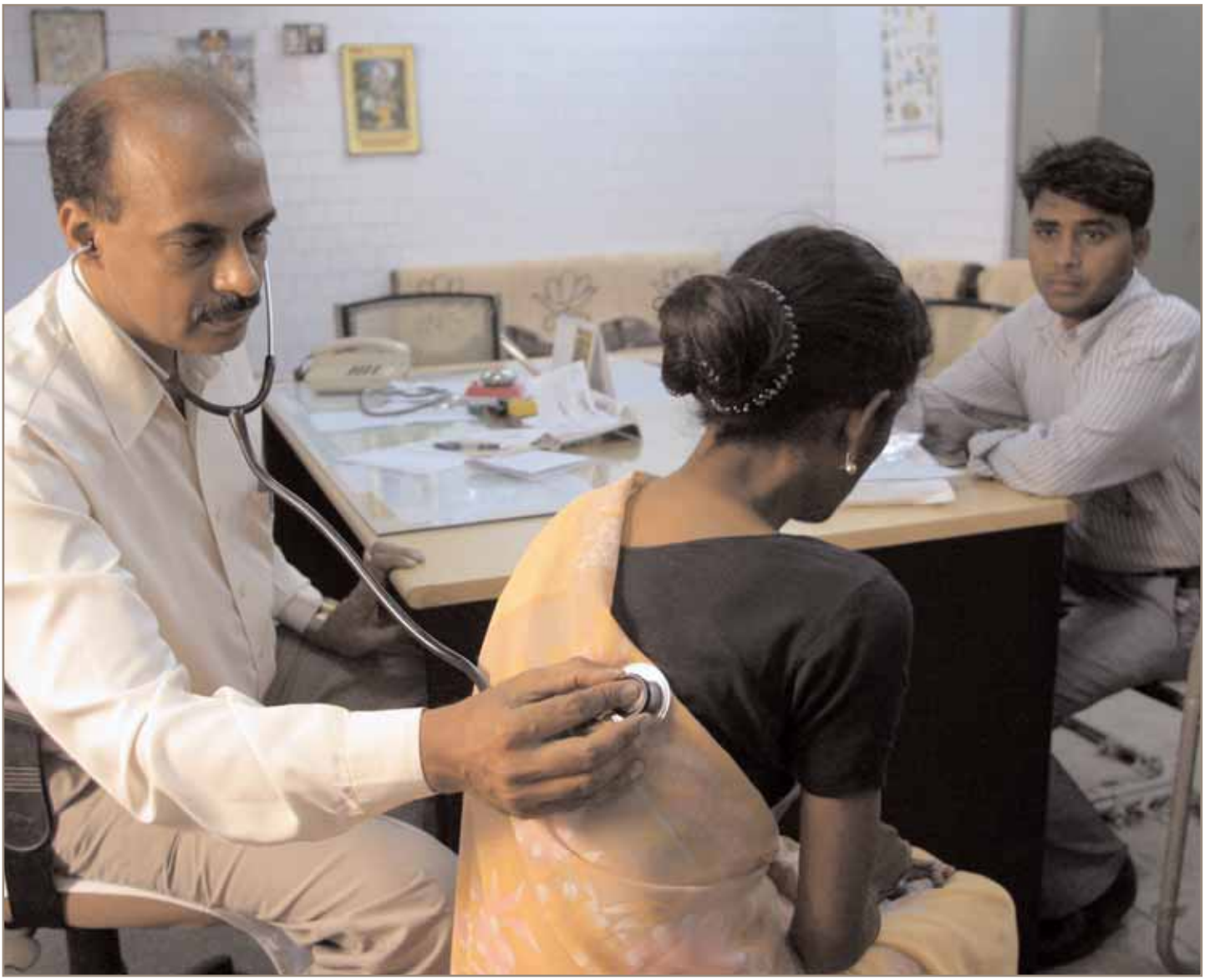
Data from the feasibility study are currently being analyzed, with results expected to be available in the last quarter of 2006.

The search for new TB-specific antigens

At the end of 2005, FIND launched a collaboration with Proteome Systems Limited, an Australian company based in Sydney, towards the development of rapid point of care diagnostic tests for TB.

This project aims to discover specific *Mycobacteria tuberculosis* antigens that are detectable in the sputum or blood of infected individuals and that may be used to develop a point of care assay. Currently, there are no antigen detection tests on the market for the diagnosis of TB. Several point of care TB tests are being marketed which detect antibodies against TB in serum, but none have been found to meet the performance criteria of FIND or WHO.

Ideally, antigen detection assays, if successfully developed, would have the advantages of specificity, correlation with burden of disease, sensitivity unimpaired by immunosuppression, and the ability to measure the severity of an infection. The final goal of the



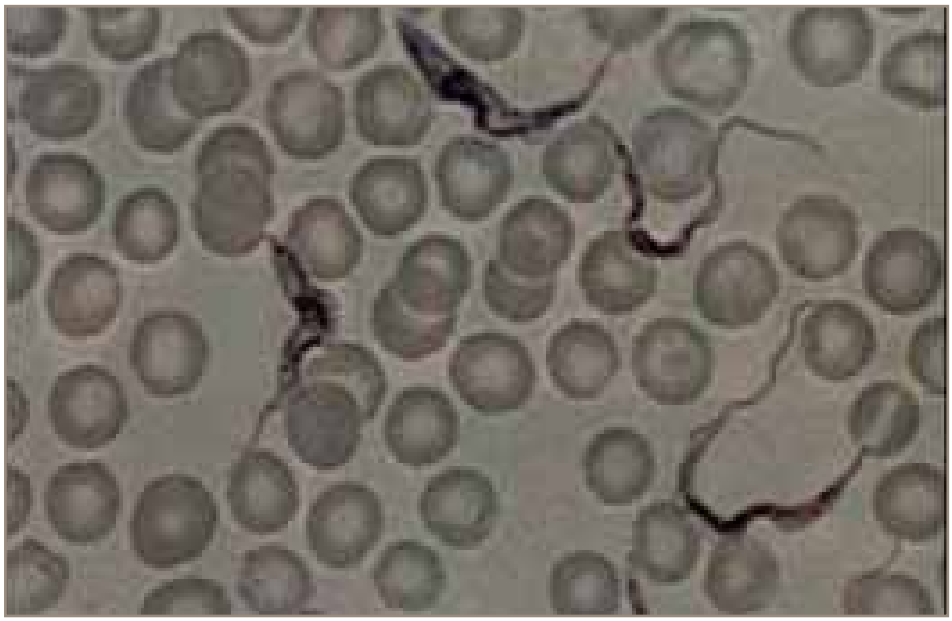
A young husband brings his sister-in-law to see Dr Praveen at the MCD Chest Clinic in Patparganj in East Delhi. The sister-in-law has TB and has now been diagnosed with MDR-TB. She has had TB for 2 years and not got better. In those 2 years, the family has spent 100 000 rupees on her treatment; drugs, injections, home care, nursing home etc. They have finally come to the clinic where they have told her she as MDR-TB.

collaboration with Proteome Systems is the development of a TB test that could be easily administered at point of care, delivering an accurate result within minutes.

Through this partnership agreement, FIND is providing critical support to speed the research and development of the test including material, access to clinical samples, assistance with clinical trials and fast tracking registration.

Proteome Systems is making good progress and has identified a number of novel mycobacterial proteins in the sputum and blood of TB patients that are not detected in vitro from mycobacterial cultures. Thus, these antigens may be specifically expressed only in infection. A number of these proteins have been prioritised as targets for the development of point of care tests based on the level of concentration of the protein in sputum or plasma, the number of patient samples from which the protein was identified, and the ability to develop high-affinity monoclonal antibodies against them.

FIND launches a new program for diagnostics for human African trypanosomiasis



The tsetse fly feeds on the blood of animals and humans. Once inoculated by an infected fly, the trypanosomes proliferate and gradually invade all the organs of the host. Most of the parasites are effectively destroyed by the host's natural defenses, but some trypanosomes manage to evade the immune system by modifying their surface membrane, a process known as antigenic variation.

In late 2005, FIND received a grant from the Bill & Melinda Gates Foundation to begin work on the development and evaluation of new diagnostic tests for human African trypanosomiasis (HAT). The project is being carried out in collaboration with the World Health Organisation (WHO). Human African trypanosomiasis is a major public health problem in sub-Saharan Africa, with 100% fatality in untreated cases, as well as the potential to flare up into epidemics. The disease is endemic in 36 African countries, including some of the least developed countries in the world.

Control of HAT depends primarily on a combination of active case detection and curative treatment. It is believed, however, that fewer than 25% of infected people get detected through diagnosis, largely because the existing tools are not only difficult to implement in remote, impoverished settings but also because they are not sensitive enough. Diagnosis of HAT remains a major and neglected problem.

The parasite that causes sleeping sickness is called the trypanosome. It is transmitted to humans through the bite of a tsetse fly of the genus Glossina

There are two subspecies of the parasite causing infection *(T.b. gambiense* and *T.b. rhodesiense)* and two stages of infection. During the first stage, when treatment is safer and more effective, infection produces few symptoms and, given the current state of diagnostic services, is rarely detected. The second stage, which starts when the parasite invades the central nervous system (CNS), is difficult to treat, and results in considerable morbidity and mortality.

Because early-stage disease is so difficult to recognise clinically, and late-stage disease is so morbid, the WHO recommended disease control strategy relies on systematic screening of at-risk populations. Currently, the diagnosis of HAT is made by a serologic screening examination, followed by confirmatory test with microscopy, which is laborious, insensitive and costly, and many patients go undiagnosed. Individuals in whom infection is detected must go on to have cerebrospinal fluid (CSF)

© WHO/Guinea Bissao

examinations to determine whether specific treatment for central nervous system disease is required. The requirement for lumbar puncture and CSF examination is an additional complexity that seriously limits access to diagnosis.

Efforts of FIND and WHO will focus on developing point of care tests and better tools for disease staging, i.e., for determining whether the infection has reached the brain of the patient (late stage disease). It is critical to confirm that a patient has late stage disease prior to giving treatment since the drug commonly used for treating this stage, an arsenical compound, causes fatal arsenic encephalopathy in an unpredictable proportion of patients.

Better diagnostic tests – simple, accurate, robust, and capable of determining disease stage – would revolutionise HAT control, making mass screening a realistic goal. If such tests joined effective new drugs that were safe and simple enough for widespread implementation, sleeping sickness would reach a turning point in its long history, moving from current intense but unsustainable control efforts to the possibility of its elimination as a public health problem. This shift in control strategy, from focal application of complex and labor-intensive control efforts, to mass application of simple interventions, can only be achieved with the advent of better diagnosis and treatment.

FIND and WHO have currently started assessment studies of diagnostic approaches and look forward to identifying promising technologies for collaboration agreements.



FIND and its partners

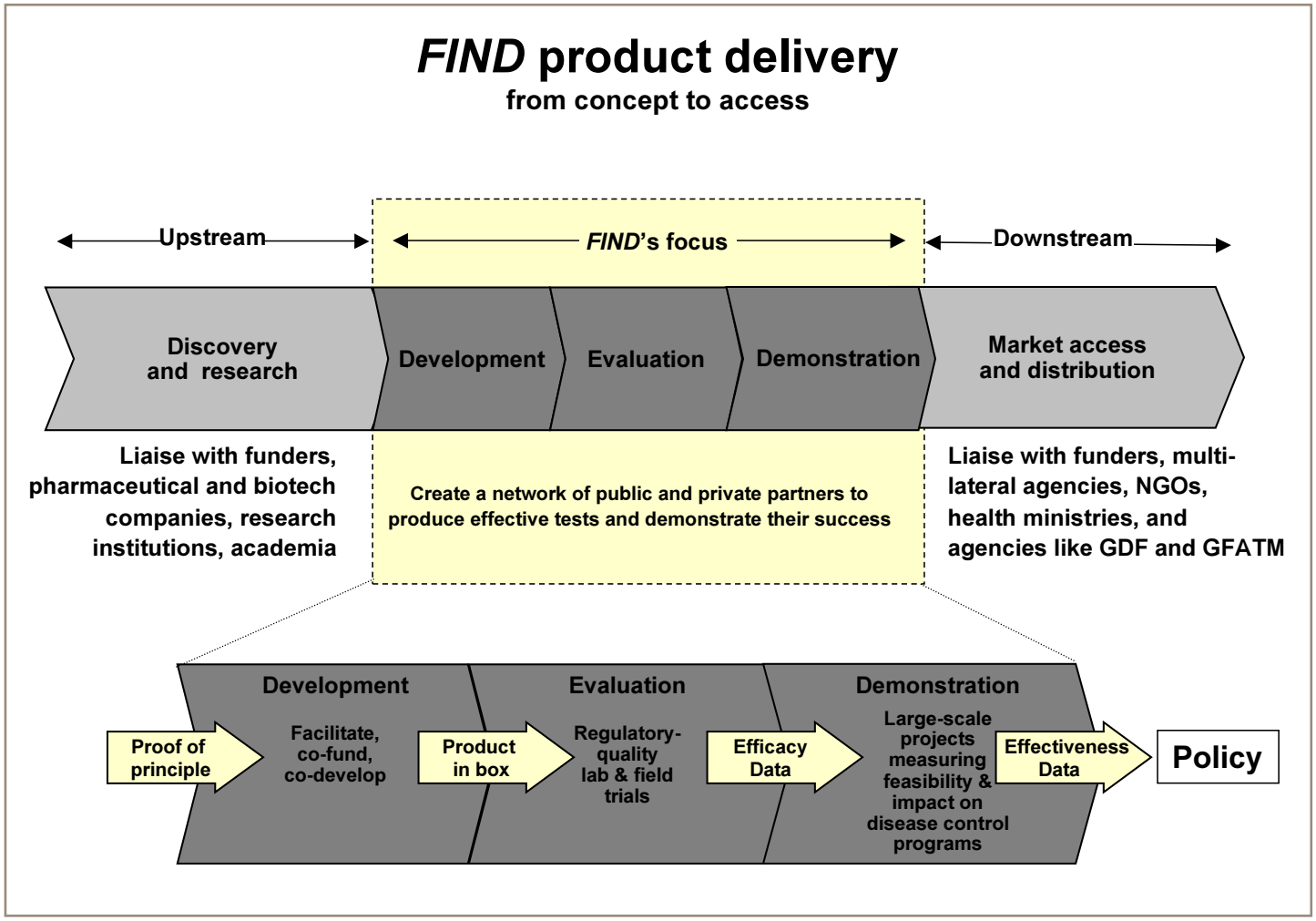
New team members – One new staff member and two new consultants joined FIND's scientific team this year, while another expanded his mandate.

Dr Catharina Boehme joined FIND as Medical Officer and project leader responsible for clinical trials. Prior to joining the FIND team, Catharina worked as a medical specialist for infectious and tropical diseases at the University of Munich and managed operational TB research projects in Tanzania.

Dr Ranald Sutherland, a trained clinical chemist with over 20 years of commercial experience in the in vitro diagnostics and the biotechnology industries, joined FIND in August 2005 as a consultant in Technology and Business Development. Prior to this he was Vice President of Program Management and Business Development at Boehringer Mannheim, and was Vice President of Business Development for GeneProt Inc., a proteomic research services company focused on drug discovery processes.

Dr Gerd Michel joined FIND in October 2005 as consultant for product development after spending several years heading research in cellular pharmacology at the department of internal medicine of Heidelberg University. Later, he joined Abbott Laboratories and among various management positions, he successfully directed the development and launch of a number of diagnostic assays for different laboratory systems primarily in the fields of infectious diseases, immunology and cardiology.

Dr Ralph Linke has been working with FIND since February 2004 to develop strategic plans for rapid diagnostic testing and quality assurance planning models. Since August 2005, FIND has benefited from Dr Linke's expertise in regulatory affairs quality assurance and project management.



FIND's product development process, from proof of principle to effectiveness

FIND project management restructured

FIND first began using a model for the public sector diagnostic development which proceeded along a standard industry-style path from development through evaluation, ending with demonstration of impact of well-performing technologies, with clear targets and timing defined at each stage of the R&D process.

FIND was originally structured around a single disease focusing on steps in product development, evaluation and demonstration. The addition of HAT this year shifted the focus toward portfolio management, which is now a centerpiece of the organization with scientific teams structured around project leaders in each of the technology areas.

Within these areas, development, evaluation and demonstration are still central to the product development process. A redefined diagnostic development strategy focuses on the development of point of care tests that have the best chance of being accessible to the greatest number of patients, allowing access to populations previously missed by referral health services.

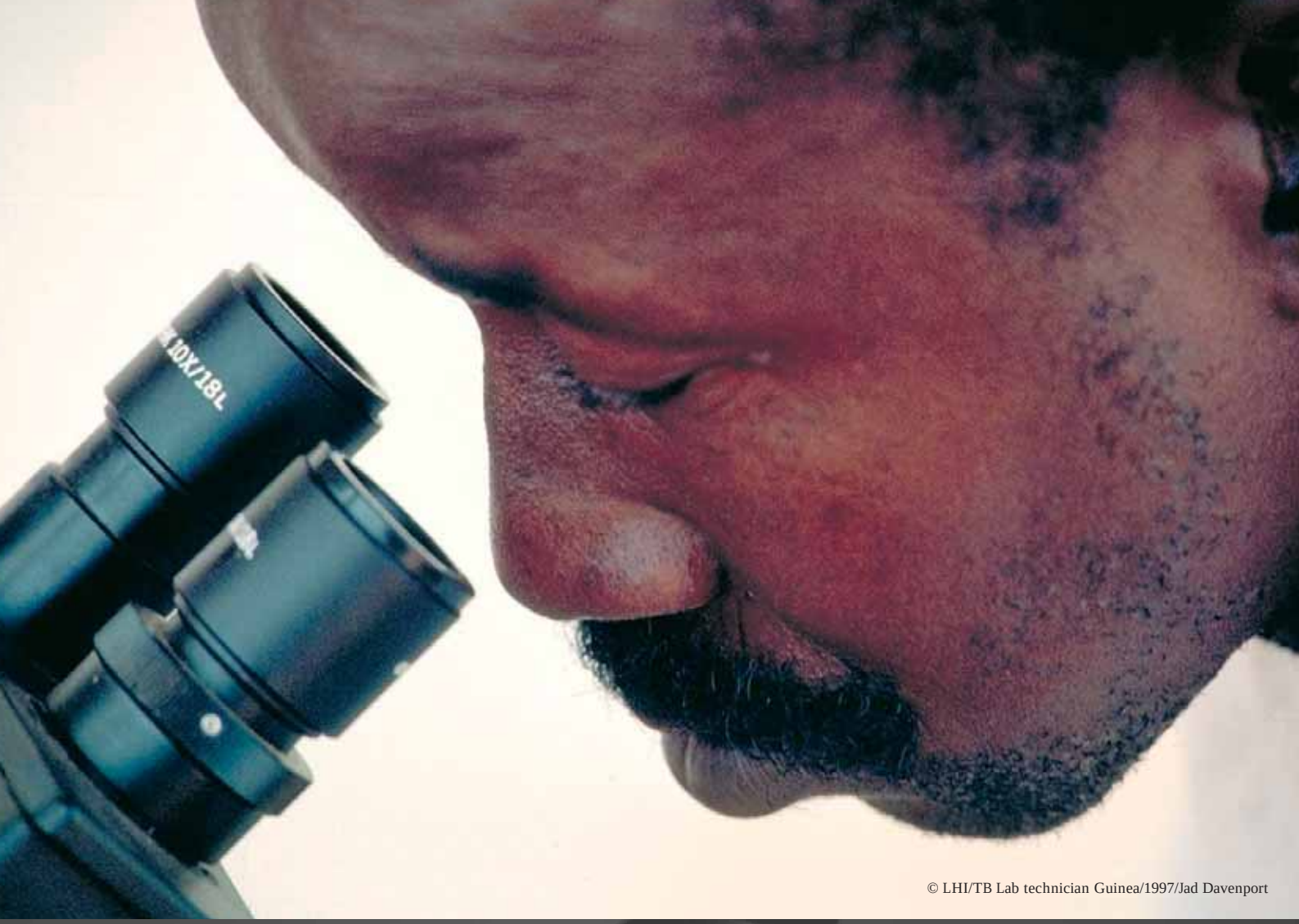
Intellectual property policy formalised

Legal agreements were signed with various commercial partners such as multinationals like Becton Dickinson and Company, and Eiken Chemical Co., as well as smaller biotechnology companies, such as Biotec, Salubris Inc., Chemogen and Proteome Systems.

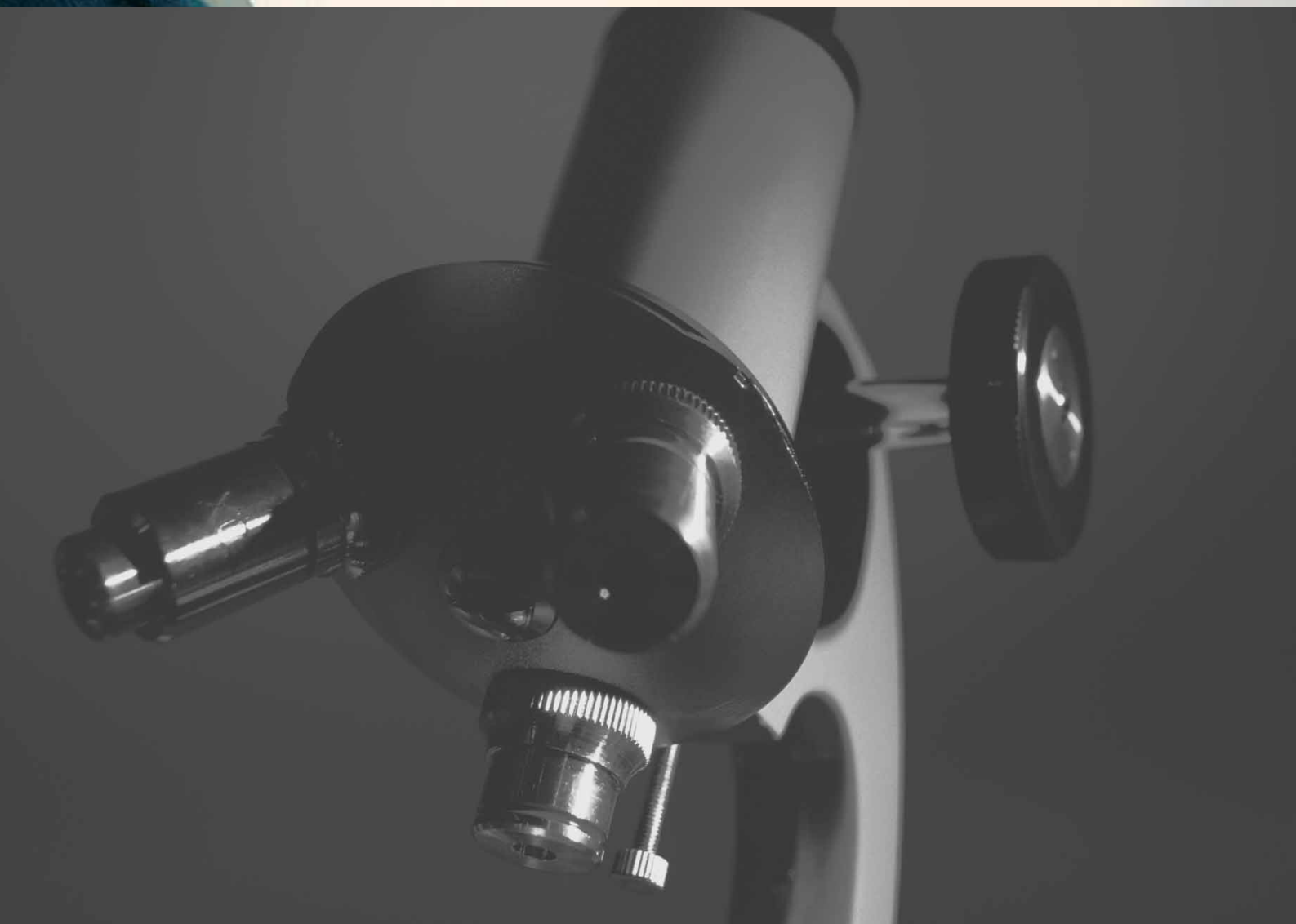
In all of FIND's contractual agreements with industry partners, methods are clearly defined to ensure that each dollar invested by FIND results in a return for the public and non-profit private health sectors in the form of affordability and access. This may be achieved in a variety of ways, depending on the nature of the project, the maturity of the technology, the size of the company, and the size of FIND's total investment. When there is significant intellectual property (IP), FIND typically seeks an irrevocable, royalty free license to the IP for the public sector in developing countries. If necessary in order to ensure access, FIND may purchase the IP outright. In other cases, when IP is either irrelevant or not negotiable, negotiated product pricing may be the primary mechanism to ensure that the tests are both affordable and accessible throughout the health system.

FIND Research and Development Partners – 2005

1. BD (Becton, Dickinson and Company)
2. Biotect Laboratories Ltd.
3. CDC (US Centers for Disease Control and Prevention)
4. Chemogen
5. Clinical TB and HIV group, Mycobacterium Reference Unit / Ministry of Health of Samara Oblast and Samara Oblast Tuberculosis Dispensary
6. CREATE (Consortium to Respond Effectively to the AIDS/TB Epidemic)
7. Cytoscience
8. Eiken Chemical Co. Ltd.
9. FHI (Family Health International)
10. GENETUP (German Nepal Tuberculosis Project) and NATA (Nepal Anti Tuberculosis Association) and Kuratorium Tuberkulose in der Welt, e.V.
11. HUG (Hopitaux Universitaires de Genève)
12. Institute of Tropical Medicine Alexander von Humboldt, Universidad Peruana Cayetano Heredia
13. Johns Hopkins University, in collaboration with the Municipal Health Secretariat in Rio de Janeiro
14. KNVC Tuberculosis Foundation
15. London School of Hygiene and Tropical Medicine (ZAMBART project)
16. LMU (Ludwig Maximilians University of Munich)
17. Moi University School of Medicine, the Moi Teaching and Referral Hospital and the AMPATH Care Program
18. PATH (Program for Appropriate Technology in Health)
19. Proteome Systems
20. Salubris Inc.
21. SBRI (Seattle Biomedical Research Institute)



© LHI/TB Lab technician Guinea/1997/Jad Davenport



Financial Information

Foundation for Innovative New Diagnostics (FIND)

Geneva

Financial Statements for the Year ended December 31, 2005 and Auditors' Report

Deloitte.

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AUDITORS' REPORT

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

As auditors, we have audited the accounting records and the financial statements of the Foundation for Innovative New Diagnostics (FIND) for the year ended December 31, 2005.

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 of 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 statements presentation. We believe that our audit provides a reasonable basis for our opinion.

In our opinion, the accounting records and the 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

Roland Loup

August 24, 2006

Attached : Financial statements (balance sheet, statement of income and expenditure, cash flow statement and notes)

A member firm of
Deloitte Touche Tohmatsu

BALANCE SHEET AS AT 31 DECEMBER 2005

(all amounts in US dollars)

	2005	2004
ASSETS		
Current assets		
Cash, current accounts & short-term deposits	2 403 083	3 455 705
Rental guarantee deposit	44 439	51 437
Accounts receivable	39 051	22 713
Prepayments	–	13 899
	2 486 573	3 543 754
Fixed assets		
Office furniture & fittings	26 276	34 531
Computers & printers	19 485	35 152
Electrical installations	23 103	30 077
Fax machine & telephones	7 617	4 070
	76 481	103 830
Patents	53 949	50 000
Total assets	$ 2 617 003	3 697 584
LIABILITIES AND CAPITAL		
Current liabilities		
Accounts payable	764 493	425 969
Accrued expenses	47 296	50 546
Contributions received in advance	544 221	2 763 003
	1 356 010	3 239 518
Capital and reserves		
Capital	40 430	40 430
General reserve	1 220 563	417 636
Total liabilities and capital	$ 2 617 003	3 697 584



STATEMENT OF INCOME AND EXPENDITURE FOR THE YEAR ENDED 31 DECEMBER 2005

(all amounts in US dollars)

	2005	2004
INCOME		
Contributions income	4 980 532	4 651 908
Sundry income	90 919	74 266
Exchange gains	37 858	26 513
Total income	5 109 309	4 752 687
Analytical & Project Work		
Project activities	2 193 605	1 934 722
Partnership building	391 858	341 687
Promotion & external relationships	274 795	202 458
Strategic planning & operations	239 839	424 142
Regulatory activities	24 196	–
Technical meetings	77 525	45 053
External consultants	49 413	49 927
	3 251 231	2 997 989
Information & Communication		
Publications production	14 572	16 451
Website	5 793	13 775
Representation	4 824	13 823
	25 189	44 049
Governing & Advisory Bodies		
Staff costs allocated	46 010	49 120
Business Advisory Committee	2 403	5 795
Foundation Board	17 408	25 853
	65 821	80 768
General Administration		
Staff costs allocated	345 007	331 837
Staff travel	4 776	4 745
IT expenses	97 568	13 965
Photocopies, stationery, printing & sundries	43 386	41 374
Rent of premises	212 448	136 793
Repairs & maintenance	17 585	23 548
Telecommunications	62 741	51 018
	783 511	603 280
Finance & Service Expenses		
Auditing & accounting	21 762	23 819
Bank charges	3 012	2 900
Legal fees	57 745	169 954
Insurance	64 180	42 003
	146 699	238 676
Depreciation	33 932	29 294
Total expenses	4 306 383	3 994 056
Excess of income over expenditure for year	802 926	758 631
Previous year surplus/(deficit) brought forward	417 637	(340 995)
Surplus carried forward in General Reserve	$ 1 220 563	417 636

CASH FLOW STATEMENT
FOR THE YEAR ENDED 31 DECEMBER 2005

(all amounts in US dollars)

		2005	2004
CASH FLOW			
Excess of income over expenditure for the year		802 926	758 631
Add back non-cash charge – depreciation		33 932	29 294
		836 858	787 925
Cash flows – operating activities			
Increase/(decrease) in contributions in advance		(2 218 782)	(382 908)
Increase/(decrease) in accounts payable		338 525	228 771
Increase/(decrease) in accrued expenses		(3 250)	25 738
(Increase)/decrease in accounts receivable		(16 338)	(20 428)
(Increase)/decrease in prepayments		13 899	(8 493)
		(1 885 946)	(157 320)
Cash flows – investing activities			
Additional office furniture & fittings		–	(19 470)
Additional computers & printers		(1 779)	(9 986)
New electrical installations		–	(34 869)
Additional telephones		(4 804)	–
Additional Patent Costs		(3 949)	(50 000)
(Increase)/decrease in rental guarantee account		6 998	(28 869)
		(3 534)	(143 194)
Net increase in cash and cash equivalents for year	$	(1 052 622)	487 411
Cash and cash equivalents, at start of year			
Cash on hand		2 619	1 617
Current accounts & short-term deposits		3 453 086	2 966 677
		3 455 705	2 968 294
Cash and cash equivalents, at end of year			
Cash on hand		426	2 619
Current accounts & short-term deposits		2 402 657	3 453 086
		2 403 083	3 455 705
Net increase in cash and cash equivalents for year	$	(1 052 622)	487 411

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



Notes to the Financial Statements for the year ended 31 December 2005

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 statutes 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 owned at 31 December 2005 were purchased as part of an agreement completed with a project partner on 8 March 2004. Under the agreement the project partner has a six-month option commencing on 8 March 2006 to buy the Patents at cost plus any maintenance costs incurred by FIND; if the option is not exercised the project partner is obliged to purchase on the same terms on 9 September 2006. As a result, the patents are not amortised.

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 2005, the rate of exchange used for the Swiss franc, the main foreign currency for 2005, was USD/CHF = 1.32 (2004 – 1.1371). 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 2005 provide for a total of USD 22.56 million to be paid to FIND between January 2006 and February 2010.

2.6 Accounts payable and accrued expenses

Accounts payable and accrued expenses represent expenditures chargeable in the 2005 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 Project expenditure

Project expenditure during 2005 under contracts signed up to 31 December 2005 totalled USD 1,077,535. Commitments at 31 December 2005 for future payments under those contracts total USD 494,165 (2004 – USD 924,050).

3. Fixed assets

Fixed assets as at 31 December 2005 were as follows:

		2005	2004
Cost price			
Office furniture & fittings		41,275	41,275
Computers & printers		53,672	51,893
Electrical installations		34,869	34,869
Fax machine & telephones		9,891	5,087
		139,707	133,124
Less			
Accumulated depreciation		63,226	29,294
Net book value	$	76,481	103,830

Fire insurance cover as at 31 December 2005 was USD 100,000 (2004 – USD 116,084).

4. Pension Fund liabilities

No amounts were due to the pension fund at 31 December 2005 (2004 – CHF 3,673).

5. Rent commitments

At 31 December 2005 FIND had annual future rent commitments amounting to USD 176,778 up to 31 May 2009 (2004 – USD 188,110 for 2005, thereafter USD 205,213 annually up to 31 May 2009).

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 2005

There were no events occurring subsequent to 31 December 2005 which could have a material bearing on the understanding of these financial statements.



FIND Board of Directors – Management and Staff

As at 31 December 2005

Board of Directors

Gerald Moeller
Chairman
CEO of HBM BioCapitalManagement, Heidelberg

Bernard Mach
Chairman and CSO, NovImmune, Geneva

Peter Small
Senior Program Officer, Tuberculosis, Bill & Melinda Gates Foundation

Management and Staff

Giorgio Roscigno
Chief Executive Officer

Catharina Boehme
Medical Officer

Herbert Clemens
Chief Financial Officer

Jacques Debayle
HR and Operations Manager

Richard O'Brien
Head of Product Evaluation

Mark Perkins
Chief Scientific Officer

Laurence Perret
Administrative Assistant to CEO

Julie Vercruysse
TB Scientific Team Administrator

Consultants

Heather Alexander
Health Scientist

Ralf Linke
Project Management, Quality Assurance and Regulatory Affairs

Gerd Michel
Product Development

Ranald Sutherland
Technology and Business Development

© LHI/MDR-TB patient Jaco (right), with friend, RSA/2003/Gary Hampton

© LHI/TB Cultures being stained, Peru/1997/Jad Davenport

FIND
FOUNDATION FOR INNOVATIVE NEW DIAGNOSTICS

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